

ETHIOPIAN NATIONAL DRUG FORMULARY

First Edition



**Drug Administration and Control
Authority of Ethiopia, 2008**

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INTRODUCTION

In places where health and communication infrastructures are at low level the opportunity of availing and accessing drug and health related information is uneasy. In such circumstances promotion of rational use of drugs is at stake,

which eventually shall harm the health of individuals and affect the overall health-care delivery service.

In Ethiopia, as the health service expands quite rapidly, in principle drug information resources need to be made available and accessible at equal pace. However, except the few promising efforts in availing some drug information materials, the gap between the demand and supply is still wide enough.

In relation to this the Drug Administration and Control Authority of Ethiopia recognizing the unmet need on drug information has been striving to develop and make accessible some information materials including, categorized drug formularies and standard treatment guidelines, leaflets in various issues and bulletin.

To widen the scope of the content and to provide maximum information from single source, a draft national drug formulary has been prepared by the Authority and after incorporation of the comments from workshop participants, the final draft is now ready for use.

The Formulary aims to provide standard information on drugs. And it targets all health professionals involved in patient care, training and research and others. Therefore the overall goal of the formulary is to help health professionals base their practice on solid information and knowledge to promote rational use of drugs.

While developing the formulary the “World Health Organization (WHO) Model Drug Formulary” has been used as a guiding tool and the pharmacotherapeutic classification is based on the list of drugs for Ethiopia (LIDE) and its supplement list. To accommodate as much information as possible on each drug, formularies of other countries (eg. South Africa) and standard text books of pharmacy, pharmacology and therapeutics has also been used. The District Hospital formulary has also been extensively referred.

The formulary contains detailed information on each pharmacotherapeutic class of drugs and specific information for each drug including indication, caution, drug interaction, contraindication, side effect, dose and administration and information on storage condition. The formulary also contains general notes on good prescribing and dispensing practices, and supplementary information as appendixes.

The formulary is designed as a digest for rapid reference and it may not always include all the information necessary for prescribing and dispensing. And by no means it does substitute standard treatment guidelines.

We hope, that this formulary will be of assistance in providing useful information to the health workers and in promoting the rational use of drugs and as result proviosn of quality health services. It is also hoped that the formulary will be of particular use to those health professionals working at the periphery who have no access to adequate and up to date information.

The Authority will continuously update the formulary and would like to invite readers to share their expertise in the field and provide comments to the following address:

Drug Administration and Control Authority of Ethiopia
Planning and Drug information establsihment and dissemination Department
P.o.Box 5681
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GENERAL ADVICE TO PRESCRIBERS AND DISPENSERS

RATIONAL APPROACH TO THERAPEUTICS

Drugs should only be prescribed when they are necessary, and in all cases the benefit of administering the medicine should be considered in relation to the risks involved. Bad prescribing habits lead to ineffective and unsafe treatment, exacerbation or prolongation of illness, distress and harm to the patient, and higher cost.

Therefore Good Prescribing Practice (GPP) is prescribing the right drug at the right time, in the right dosage of the right formulation and for the right length of time.

The following steps will help to remind prescribers of the rational approach to therapeutics.

1. Define the patient's problem

Whenever possible, making the right diagnosis is based on integrating many pieces of information: the complaint as described by the patient; a detailed history; physical examination; laboratory tests; X-rays and other investigations. This will help in rational prescribing, always bearing in mind that diseases are evolutionary processes.

2. Specify the therapeutic objective

Doctors must clearly state their therapeutic objectives based on the pathophysiology underlying the clinical situation. Very often physicians must select more than one therapeutic goal for each patient.

3. Select therapeutic strategies

The selected strategy should be agreed with the patient; this agreement on outcome, and how it may be achieved, is termed concordance.

The selected treatment can be non-pharmacological and/or pharmacological; it also needs to take into account the total cost of all therapeutic options.

a. Non-pharmacological treatment

It is very important to bear in mind that the patient does not always need a drug for treatment of the condition. Very often, health problems can be resolved by a change in life style or diet, use of physiotherapy or exercise, provision of adequate psychological support, and other non-pharmacological treatments; these have the same importance as a prescription drug, and instructions must be written, explained and monitored in the same way.

b. Pharmacological treatment

- *Selecting the correct group of drugs*

Knowledge about the pathophysiology involved in the clinical situation of each patient and the pharmacodynamics of the chosen group of drugs, are two of the fundamental principles for rational therapeutics.

- *Selecting the drug from the chosen group*

The selection process must consider benefit/risk/cost information. This step is based on evidence about maximal clinical benefits of the drug for a given indication (efficacy) with the minimum production of adverse effects (safety).

It must be remembered that each drug has adverse effects and it is estimated that up to 10% of hospital admissions in industrialized countries are due to adverse effects. Not all drug-induced injury can be prevented but much of it is caused by inappropriate selection of drugs.

In cost comparisons between drugs, the cost of the total treatment and not only the unit cost of the drug must be considered.

- *Verifying the suitability of the chosen pharmaceutical treatment for each patient*

The prescriber must check whether the active substance chosen, its dosage form, standard dosage schedule and standard duration of treatment are suitable for each patient. Drug treatment should be individualized to the needs of each patient.

- *Prescription writing*

The prescription is the link between the prescriber, the pharmacist (or dispenser) and the patient so it is important for the successful management of the presenting medical condition. This item is covered in more detail in the following section.

- *Giving information, instructions and warnings*

This step is important to ensure patient adherence and is covered in detail in the following section.

- *Monitoring treatment*

Evaluation of the follow up and the outcome of treatment allows the stopping of it (if the patient's problem is solved) or to reformulate it when necessary. This step gives rise to important information about the effects of drugs contributing to building up the body of knowledge of pharmacovigilance, needed to promote the rational use of drugs.

VARIATION IN DOSE RESPONSE

Success in drug treatment depends not only on the correct choice of drug but on the correct dose regimen. Unfortunately drug treatment frequently fails because

the dose is too small or produces adverse effects because it is too large. This is because most texts, teachers and other drug information sources continue to recommend standard doses.

The concept of a standard or 'average' adult dose for every medicine is firmly rooted in the mind of most prescribers. After the initial 'dose ranging' studies on new drugs, manufacturers recommend a dosage that appears to produce the desired response in the majority of subjects.

These studies are usually done on healthy, young male Caucasian volunteers, rather than on older men and women with illnesses and of different ethnic and environmental backgrounds. The use of standard doses in the marketing literature suggest that standard responses are the rule, but in reality there is considerable variation in drug response. As a result many prescribed doses are far too low or too high, leading to treatment failure or toxicity. There are many reasons for this variation which include adherence (see below), drug formulation, body weight and age, composition, variation in absorption, distribution, metabolism and excretion, variation in pharmacodynamics, disease variables, genetic and environmental variables.

Drug formulation

Poorly formulated drugs may fail to disintegrate or to dissolve. Enteric-coated drugs are particularly problematic, and have been known to pass through the gastrointestinal tract intact. Some drugs like digoxin or phenytoin have a track record of formulation problems, and dissolution profiles can vary not only from manufacturer to manufacturer but from batch to batch of the same company. The problem is worse if there is a narrow therapeutic to toxic ratio, as changes in absorption can produce sudden changes in drug concentration. For such drugs quality control surveillance should be carried out.

Body weight and age

Although the concept of varying the dose with the body weight or age of children has a long tradition, adult doses have been assumed to be the same irrespective of size or shape. Yet adult weights vary two to threefold, while a large fat mass can store large excesses of highly lipid soluble drugs compared to lean patients of the same weight.

Age changes can also be important. Adolescents may oxidize some drugs relatively more rapidly than adults, while the elderly may have reduced renal function and eliminate some drugs more slowly.

Physiological and pharmacokinetic variables

Drug absorption rates may vary widely between individuals and within the same individual at different times and in different physiological states. Drugs taken after a meal are delivered to the small intestine much more slowly than in the fasting state, leading to much lower drug concentrations. In the case of drugs

like paracetamol with a high rate of metabolism on 'first pass' through the liver, this may render a standard dose completely ineffective. In pregnancy gastric emptying is also delayed, while some drugs may increase or decrease gastric emptying and affect absorption of other drugs.

Drug distribution

Drug distribution varies widely: fat soluble drugs are stored in adipose tissue, water soluble drugs are distributed chiefly in the extracellular space, acidic drugs bind strongly to plasma albumin and basic drugs to muscle cells. Hence variation in plasma albumin levels, fat content or muscle mass may all contribute to dose variation. With very highly albumin bound drugs like warfarin, a small change of albumin concentration can produce a big change in free drug and a dramatic change in drug effect.

Drug metabolism and excretion

Drug metabolic rates are determined both by genetic and environmental factors. Drug acetylation shows genetic polymorphism, whereby individuals fall clearly into either fast or slow acetylator types. Drug oxidation, however, is polygenic, and although a small proportion of the population can be classified as very slow oxidizers of some drugs, for most drugs and most subjects there is a normal distribution of drug metabolizing capacity, and much of the variation is under environmental control. Many drugs are eliminated by the kidneys without being metabolized. Renal disease or toxicity of other drugs on the kidney can therefore slow excretion of some drugs.

Pharmacodynamic variables

There is significant variation in receptor response to some drugs, especially central nervous system responses, for example pain and sedation. Some of this is genetic, some due to tolerance, some due to interaction with other drugs and some due to addiction, for example, morphine and alcohol.

Disease variables

Both liver disease and kidney disease can have major effects on drug response, chiefly by the effect on metabolism and elimination respectively (increasing toxicity), but also by their effect on plasma albumin (increased free drug also increasing toxicity). Heart failure can also affect metabolism of drugs with rapid hepatic clearance (for example lidocaine, propranolol). Respiratory disease and hypothyroidism can both impair drug oxidation.

Environmental variables

Many drugs and environmental toxins can induce the hepatic microsomal enzyme oxidizing system (MEOS) or cytochrome P450 oxygenases, leading to more rapid metabolism and elimination and ineffective treatment.

Environmental pollutants, anaesthetic drugs and other compounds such as pesticides can also induce metabolism. Diet and nutritional status also impact on pharmacokinetics. For example in infantile malnutrition and in malnourished elderly populations drug oxidation rates are decreased, while high protein diets, charcoal cooked foods and certain other foods act as metabolizing enzyme inducers. Chronic alcohol use induces oxidation of other drugs, but in the presence of high circulating alcohol concentrations drug metabolism may be inhibited.

Rational Dispensing

Good dispensing practices ensure that the correct drug is delivered to the right patient, in the required dosage and quantities, with clear instructions, and in package that maintains an acceptable potency and quality of the drug. Dispensing includes all the activities that occur between the time the prescription or oral request of the patient or care provider is presented and the drug or other items are issued to them. This process may take place in health institutions and community drug retail outlets. It is often carried out by pharmacy professionals. No matter where dispensing takes place or who does it, any error or failure in the dispensing process can seriously affect the care of the patient mainly with medical and economical consequences.

Therefore, the dispenser plays a crucial role in the therapeutic process. The quality of dispensing may be determined by the training and supervision the dispenser has received and the drug information available to the dispenser. A shortage of dispensing materials and insufficient dispensing time due to heavy patients load may also have adverse impacts on dispensing.

One good way to reduce the dispensing time and potential errors is to prepackaging and labeling commonly used drugs. Another way to prevent staff from making errors when working under pressure is to organize the work so that more than one individual is involved in the dispensing process for each prescription.

Pharmacist or other health professionals involved in dispensing drugs have a need for drug information in order to keep themselves up to date with developments related to drugs and to provide such information to patients, other health professionals and to the general public. Because of an increasing number and complexity of drugs, the need for up-to-date information is greater than ever. The provision of drug information to physicians and other health care professionals is mainly directed at improving prescribing and drug administration. On the other hand, because counseling of patients on medications is an integral part of the dispensing of a prescription or their oral requests, drug dispensers should be adequately equipped with up-to-date drug information. Lack of knowledge and information by patients about the drugs

they take leads to incorrect use which in turn results in loss of efficacy or occurrence of adverse effects.

Communication skill is very important for dispensers dealing with patients or health care professionals to convey relevant drug information effectively and clearly, which can be done verbally and/or in written form. Drug dispensers must have the ability to explain information clearly by the language particularly the patient or care provider can understand and check whether the information is being understood by them.

Finally, an application of the professional code of ethics by pharmacy professionals is an important issue that needs due consideration

Particularly with respect to confidentiality of patient data, withholding therapeutic interventions and varying cost of drug

ADHERENCE (COMPLIANCE) WITH DRUG TREATMENT

It is often assumed that once the appropriate drug is chosen, the prescription correctly written and the medication correctly dispensed, that it will be taken correctly and treatment will be successful. Unfortunately this is very often not the case, and physicians overlook one of the most important reasons for treatment failure—poor adherence (compliance) with the treatment plan.

There are sometimes valid reasons for poor adherence—the drug may be poorly tolerated, may cause obvious adverse effects or may be prescribed in a toxic dose. Failure to adhere

with such a prescription has been described as ‘intelligent noncompliance’.

Bad prescribing or a dispensing error may also create a problem, which patients may have neither the insight nor the courage to question. Even with rational prescribing, failure to adhere to treatment is common. Factors may be related to the patient, the disease, the doctor, the prescription, the pharmacist or the health system and can often be avoided.

The Following points are recommended to increase patient compliance

- ✓ Review the prescription to be sure it is correct.
- ✓ Spend time explaining the problem and the reason for the drug.
- ✓ Establish a good relationship with the patient, rather than a hurried or brusque manner with little eye contact.
- ✓ Explore problems, for example reading the label, getting the prescription filled.
- ✓ Insist that patients bring their medication to the clinic ‘for checking’, so that tablet counts can be made unobtrusively.
- ✓ Insist that patients learn the names of their tablets, and review their regimen with them. Write notes for them.
- ✓ Keep treatment regimens simple.
- ✓ Communicate with the pharmacist, to develop teamwork and collaboration in helping and advising the patient.
- ✓ Involve the partner or another family member,
- ✓ Listen to the patient.

ADVERSE EFFECTS AND INTERACTIONS

Adverse drug reactions

An adverse drug reaction (ADR) may be defined as 'any response to a drug which is noxious, unintended and occurs at doses normally used for prophylaxis, diagnosis, or therapy. . . '.

ADRs are therefore unwanted or unintended effects of a medicine, including idiosyncratic effects, which occur during its proper use. They differ from accidental or deliberate excessive dosage or drug maladministration.

ADRs may be directly linked to the properties of the drug in use, the so-called 'A' type reactions. An example is hypoglycaemia induced by an antidiabetic drug. ADRs may also be unrelated to the known pharmacology of the drug, the 'B' type reactions including allergic effects, for example anaphylaxis with penicillins.

Any drug may produce unwanted or unexpected adverse reactions. Detection and recording of these is of vital importance. Health professionals are thus encouraged to record and report to:

Drug Administration and Control Authority of Ethiopia

ADR monitoring and promotion control division,

P.o.Box 5681

Fax. 251-115-521392

E-mail: daca@ethionet.et

Reporting format is annexed.

Major factors predisposing to adverse effects

It is well known that different patients often respond differently to a given treatment regimen. For example, in a sample of 2422 patients who had been taking combinations of drugs known to interact, only 7 (0.3%) showed any clinical evidence of interactions. In addition to the pharmaceutical properties of the drug therefore, there are characteristics of the patient which predispose to ADRs.

EXTREMES OF AGE. The very old and the very young are more susceptible to ADRs. Drugs which commonly cause problems in the elderly include hypnotics, diuretics, non-steroidal antiinflammatory drugs, antihypertensives, psychotropics and digoxin.

All children, and particularly neonates, differ from adults in the way they respond to drugs. Some drugs are likely to cause problems in neonates (for example **morphine**), but are generally tolerated in children. Other drugs (for example **valproic acid**) are associated with increased risk of ADRs in children of all ages. Other drugs associated with problems in children include

chloramphenicol (grey baby syndrome), **antiarrhythmics** (worsening of arrhythmias), **aspirin** (Reye syndrome).

INTERCURRENT ILLNESS. If besides the condition being treated the patient also suffers from another disease, such as kidney, liver or heart disease, special precautions are necessary to prevent ADRs. Remember also that, as well as the above factors, the genetic make-up of the individual patient may predispose to ADRs.

DRUG INTERACTIONS. Interactions may occur between drugs which compete for the same receptor or act on the same physiological system. They may also occur indirectly when a drug-induced disease or a change in fluid or electrolyte balance alters the response to another drug. Interactions may occur when one drug alters the absorption, distribution or elimination of another drug, such that the amount which reaches the site of action is increased or decreased. Drug-drug interactions are some of the commonest causes of adverse effects. When two drugs are administered to a patient, they may either act independently of each other, or interact with each other. Interaction may increase or decrease the effects of the drugs concerned and may cause unexpected toxicity. As newer and more potent drugs become available, the number of serious drug interactions is likely to increase. Remember that interactions which modify the effects of a drug may involve non-prescription drugs, non-medicinal chemical agents, and social drugs such as **alcohol, marijuana, and traditional remedies**, as well as certain types of food. The physiological changes in individual patients, caused by such factors as age and gender, also influence the predisposition to ADRs resulting from drug interactions.

Incompatibilities between drugs and IV fluids

Drugs should not be added to blood, amino acid solutions or fat emulsions. Certain drugs, when added to IV fluids, may be inactivated by pH changes, by precipitation or by chemical reaction. **Benzylpenicillin** and **ampicillin** lose potency after 6–8 hours if added to dextrose solutions, due to the acidity of these solutions. Some drugs bind to plastic containers and tubing, for example **diazepam** and **insulin**. **Aminoglycosides** are incompatible with **penicillins** and **heparin**. **Hydrocortisone** is incompatible with **heparin, tetracycline, and chloramphenicol**.

Adverse effects caused by traditional medicines

Patients who have been or are taking traditional herbal remedies may develop ADRs. It is not always easy to identify the responsible plant or plant constituent. Refer to the drug and toxicology information service if available and/or to suitable literature.

The effect of food on drug absorption

Food delays gastric emptying and reduces the rate of absorption of many drugs; the total amount of drug absorbed may or may not be reduced. However, some drugs are preferably taken with food, either to increase absorption or to decrease the irritant effect on the stomach.

PREScription WRITING

A prescription is an instruction from a prescriber to a dispenser. The prescriber is not always a doctor but can also be a paramedical worker, such as a medical assistant, a midwife or a nurse. The dispenser is not always a pharmacist, but can be a pharmacy technician, an assistant or a nurse.

The following guidelines will help to ensure that prescriptions are correctly interpreted and leave no doubt about the intention of the prescriber. The guidelines are relevant for primary care prescribing; they may, however, be adapted for use in hospitals or other specialist units.

Prescription form

The most important requirement is that the prescription be clear. It should be legible and indicate precisely what should be given. The local language is preferred.

The following details should be shown on the form:

- ✎ The prescriber's name, address and telephone number. This will allow either the patient or the dispenser to contact the prescriber for any clarification or potential problem with the prescription.
- ✎ Date of the prescription.
- ✎ Name, form and strength of the drug. The International Nonproprietary Name of the drug should always be used. If there is a specific reason to prescribe a special brand, the trade name can be added. The pharmaceutical form (for example 'tablet', 'oral solution', 'eye ointment') should also be stated.
- ✎ The strength of the drug should be stated in standard units using abbreviations that are consistent with the *Système Internationale* (SI). 'Microgram' and 'nanogram' should not, however, be abbreviated. Also, 'units' should not be abbreviated. Avoid decimals whenever possible. If unavoidable, a zero should be written in front of the decimal point.
- ✎ Specific areas for filling in details about the patient including name, address and age.

Directions

Directions specifying the route, dose and frequency should be clear and explicit; use of phrases such as 'take as directed' or 'take as before' should be **avoided**. For preparations which are to be taken on an 'as required' basis, the minimum dose interval should be stated together with, where relevant, the maximum daily dose. It is good practice to

qualify such prescriptions with the purpose of the medication (for example 'every 6 hours as required for pain', 'at night as required to sleep').

It is good practice to explain the directions to the patient; these directions will then be reinforced by the label on the medicinal product and possibly by appropriate counseling by the dispenser. It may be worthwhile giving a written note for complicated regimens although it must be borne in mind that the patient may lose the separate note.

Quantity to be dispensed

The quantity of the medicinal product to be supplied should be stated such that it is not confused with either the strength of the product or the dosage directions. Alternatively, the length of the treatment course may be stated (for example 'for 5 days').

Wherever possible, the quantity should be adjusted to match the pack sizes available.

For liquid preparations, the quantity should be stated in millilitres (abbreviated as 'ml') or litres (preferably not abbreviated since the letter 'l' could be confused with the figure '1').

Narcotics and controlled substances

The prescribing of a medicinal product that is liable to abuse requires special attention and may be subject to specific statutory requirements. Practitioners may need to be authorized to prescribe controlled substances; in such cases it might be necessary to indicate details of the authority on the prescription. In particular, the strength, directions and the quantity of the controlled substance to be dispensed should be stated clearly, with all quantities written in words as well as in figures to prevent alteration. Other details such as patient particulars and date should also be filled in carefully to avoid alteration.

1. DRUGS ACTING ON THE GASTROINTESTINAL SYSTEM

1.1. Antacids

Antacids are inorganic salts that dissolve in acid gastric secretions releasing anions that partially neutralized gastric hydrochloric acid.

Antacids (usually containing aluminium or magnesium compounds) can often relieve symptoms in ulcer dyspepsia and in non-erosive gastro-oesophageal reflux; they are also sometimes used in non-ulcer dyspepsia but the evidence of benefit is uncertain. Antacids also are used for the relief of, acid indigestion, heart burn and sour stomach; for the prevention of stress ulceration and gastrointestinal bleeding; and to reduce the risk associated with gastric aspiration and for the management of hyperphosphatemia.

Aluminium and/or Magnesium containing antacids are the most commonly used and are often administered concurrently or in commercially available combinations to control the frequency and consistency of bowel movements.

Aluminium salts tend to produce constipation and to delay gastric emptying because of its astringent property, while magnesium salts have the reverse effect; a combination of the two may reduce adverse gastro-intestinal effects. Another advantage of combined antacid formulations is that a slow-acting antacid such as aluminium hydroxide may be combined with a more rapidly acting agent such as magnesium hydroxide to improve the onset and duration of effect.

Some of the antacid combinations contain other ingredients that have no antacid properties. Simethicone, antiflatulent, has been added as an aid in those conditions in which the retention of gas may be a problem; however, in the treatment of peptic ulcer disease, the advantage of using antacid and simethicone combinations rather than antacids alone has not been clearly established.

The role of calcium carbonate in the management of peptic ulcer is controversial because this antacid may cause acid rebound, which is especially important when the drug is administered at bedtime. However, it is useful because it has a rapid onset of action, high acid effect and is relatively inexpensive.

Antacids should not be given to young children (up to 6 years of age) unless prescribed by a physician. Use of magnesium-containing antacids is contraindicated in very young children because there is a risk of hypermagnesemia, especially in dehydrated children or children with renal failure. Use of aluminum-containing antacids is contraindicated in very young children because there is a risk of aluminum toxicity, especially in dehydrated infants and children or infants and children with renal failure.

Antacids interfere with the gastro-intestinal absorption of a number of drugs taken orally by forming insoluble complexes, altering the gastric PH, or by effects on gastric emptying rates (fluoroquinolones, isoniazid, ketoconazole, tetracyclines, oral phosphates); changes in the urinary PH also affect tubular reabsorption (mecamylamine, methenamine; concurrent use is not recommended). Antacids may also damage enteric coatings designed to prevent dissolution in the stomach. The interaction between an antacid and another orally administered drug may be minimized by giving the drug 2 to 3 hours before or after antacid administration.

Osteomalacia, encephalopathy, dementia, and microcytic anaemia have been associated with aluminium accumulation in patients with chronic renal failure. Patients with renal failure taking aluminium compounds should avoid citrate - containing preparations.

Use of magnesium-containing antacids is contraindicated in patients with renal failure because of increased risk of hypermagnesemia.

Chronic administration of magnesium trisilicate infrequently produces silica renal stones.

Aluminium Hydroxide

Mixture or Gel, 320 mg/ml.

Suspension, 360mg/5ml.

Chewable tablet, 500mg

Indications: ulcer and non ulcer dyspepsia; gastro-oesophageal reflux, hyperphosphatemia.

Cautions: See notes above, uremia, congestive heart failure, renal failure, edema, cirrhosis, low sodium diets, gastrointestinal hemorrhage, and elderly.

Drug interactions: allupurinol, antibiotics (tetracycline, quinolones, some cephalosporins), biphosphonate derivatives, corticosteroids, cyclosporine, iron salts, imidazole antifungals, isoniazide, phenytoin, phenothiazines- absorption will be decreased; citric acid derivatives may decrease absorption of aluminum hydroxide. See also notes above

Contraindications: see notes above, hypophosphatemia, undiagnosed gastro intestinal or rectal bleeding; appendicitis; porphyria.

Side effects: see notes above, constipation, stomach cramps, fecal impaction, nausea, vomiting, and discoloration of feces, hypophosphatemia, and hypomagnesemia.

Dose and Administration: *Dyspepsia, gastro-oesophageal reflux: Oral:*

Adult: 5–10 ml suspension 4 times daily between meals and at bedtime

Child: 6–12 years 5 ml up to three times daily

Hyperphosphatemia: Oral: Adult: 2–10 g daily in divided doses with meals

Patient Advice. Do not take other medicines within 2–4 hours of aluminium hydroxide preparations.

Storage: at room temperature, avoid freezing.

Aluminium Hydroxide and Magnesium Hydroxide*

Suspension, 220mg+220mg/ 5 ml

Tablet (chewable), 400mg + 400mg

Indications, Cautions, Drug interactions, Contraindications, Side effects and Storage; see under individual preparations and notes above.

Note: a combination of Aluminium Hydroxide and Magnesium Hydroxide may reduce adverse gastro-intestinal effects. Another advantage of combined antacid formulations is that a slow-acting antacid aluminium hydroxide may be combined with a more rapidly acting agent such as magnesium hydroxide to improve the onset and duration of effect.

Dose and Administrations: *Oral:* shake the bottle well before use. 5-10 ml (2 teaspoonfuls) or 1-2 tablets every 6 hours usually between meals and at bedtime, or as required.

Storage: at room temperature.

Aluminium Hydroxide and Magnesium Trisilicate*

Tablet (chewable), 120 mg+250 mg

Suspension, 220 mg+ 620 mg/ 5 ml

Indications, Cautions, Drug interactions, Contraindications, Side effects and Storage; see under individual preparations and notes above.

Note: Magnesium trisilicate is often given in conjunction with other antacids in order to reduce adverse gastro-intestinal effects

Dose and Administrations: *Oral: Adult:* shake the bottle well before use. 5-10 ml (2 teaspoonfuls) every 6 hours usually between meals and at bedtime, or as required. Chew 1 - 2 tablets when required.

Storage: at room temperature.

* Any combination ratio proven to be therapeutically effective can be used.

Aluminium Hydroxide + Magnesium Hydroxide + Simethicone*Suspension, 225mg+200 mg+25 mg/ 5 ml***Indications:** temporary relief of hyperacidity associated with gas; may also be used for indications associated with other antacids.**Indications, Cautions, Drug interactions, Contraindications, Side effects and Storage;** see under individual preparations and notes above.

Note: Simethicone, antifatulent, has been added as an aid in those conditions in which the retention of gas may be a problem.

Dose and Administration: *Oral: Adult:* 10-20ml 4-6 times / day between meals and at bedtime; may be used every hour for severe symptoms.**Storage:** at room temperature.**Calcium Carbonate***Tablet, 350mg, 500mg, 700mg***Indications:** used as an antacid, and treatment or prevention of calcium deficiency or hyperphosphatemia.**Cautions:** renal impairment; renal calculi; hypercalcemia; hypophosphatemia.**Drug interactions:** thiazide diuretics, levothyroxine, digoxin, tetracycline, atenolol, iron, quinolones, sodium fluoride, and verapamil.**Side effects:** headache, hypophosphatemia, hypercalcaemia, constipation, laxative effect, acid rebound, nausea, vomiting, anorexia, abdominal pain, xerostomia, and flatulence.**Dose and Administration:** *Oral:***Adult:** *Antacid:* 1-2 tablets every 2 hours; maximum 7000 mg per 24 hours.**Magnesium Hydroxide***Tablet (chewable), 300 mg, 311 mg**Mixture, 375 mg/5ml, 7.75 %***Indications:** ulcer and non-ulcer dyspepsia; gastro-oesophageal reflux.**Cautions:** severe renal impairment, hypermagnesemia, see notes above.**Drug interactions:** as for Aluminum hydroxide, also see notes above.**Contraindications:** see notes above, hypersensitivity to any component of the formulation.**Side effects:** diarrhoea, abdominal cramps, muscle weakness, respiratory depression, hypermagnesemia and hypotension.**Dose and Administration:***Tablet, Adult:* Chew 2 - 4 tablets repeated according to patients needs with maximum daily dose of 16 tablets.**Child** (7-14 years) one tablet with maximum of 4 tablets per day.*Mixture, Adult:* 5 -15 ml repeated according to patient's needs with maximum daily dose of 60 ml. **Child:** 2.5-5ml as needed up to 4 times /day.**Storage:** at room temperature, avoid freezing.**Magnesium Trisilicate***Tablet (Chewable), 500 mg*

Indications, Cautions, Drug interactions, Contraindications, Storage - see notes under magnesium hydroxide above.

Side effects: see notes above, silica renal stones; diarrhoea

Dose and Administration: *Oral*, Chew 2 tablets as required.

Note: the antacid action is exerted slowly, so it does not give such rapid symptomatic relief as magnesium hydroxide.

1.2. Anti-ulcer Agents

Anti-ulcer agents, used in the treatment and prophylaxis of peptic ulcer disease, may be broadly divided into the antisecretory agents which suppress the production of gastric acid (e.g. cimetidine), and agents with cytoprotective or mucosal protectant properties (e.g. sucralfate). Antacids (see above) also play an adjuvant role in the symptomatic treatment of peptic ulcer and therapy to treat *Helicobacter pylori* is becoming more important.

H₂-receptor antagonists

The H₂-receptor antagonists, which include cimetidine, ranitidine, nizatidine and famotidine, reduce acid secretion by blocking the action of histamine at the H₂-receptors in the parietal cells of the stomach. Gastric acid secretion in response to other secretagogues (e.g. acetylcholine, gastrin) is also reduced. They are used in the management of peptic ulcer disease, reflux oesophagitis and hypersecretory states such as Zollinger-Ellison syndrome.

Cimetidine is used in conditions where inhibition of gastric acid secretion may be beneficial, such as duodenal and gastric ulcers.

Cimetidine binds to cytochrome P450 and inhibits the breakdown of drugs metabolized by this system; many interactions have been reported but only a few are of clinical significance.

Ranitidine differs structurally from cimetidine; it has been shown to be at least as effective as cimetidine as an ulcer-healing drug, and is less inclined to cross the blood-brain barrier.

Ranitidine and nizatidine do not appear to bind microsomal cytochrome P450 and thus the potential for drug interactions is lower. Unlike cimetidine, they have little or no antiandrogenic effect.

Famotidine has been shown to be 20-150 or 3-20 times as potent on a molar basis as cimetidine or ranitidine, respectively, in inhibiting stimulated gastric acid secretion.

Cimetidine

Tablet, 200mg, 400mg, 800mg

Tablet, (chewable), 200mg

Syrup, 200mg/5ml

Injection, 200mg/ml in 2ml ampoule

Indications: benign gastric and duodenal ulceration, stomach ulceration, gastro-oesophageal reflux, Zollinger-Ellison syndrome, and other conditions where gastric acid reduction is beneficial.

Cautions: hepatic impairment; renal impairment; pregnancy; breastfeeding; middle aged or older patients and in those whose symptom change may mask gastric cancer; preferably avoid intravenous injection (use intravenous infusion) particularly in high dosage and in cardiovascular impairment (risk of arrhythmias).

Drug interactions: tricyclic antidepressants, benzodiazepines, metoprolol, propranolol, carbamazepine, phenytoin, procainamide, quinidine, theophylline, valproic acid, and warfarin.

Contraindications: hypersensitivity to the drug.

Side effects: gastrointestinal disturbances, headache, dizziness, rash and tiredness; reversible confusional states, gynaecomastia and impotence, hypersensitivity reactions (rare).

Dose and Administration:

Adult:

Short-term treatment of active ulcers:

Oral: 300mg 4 times/day or 800mg at bedtime or 400mg twice daily for up to 8 weeks.

I.M., I.V.: 200mg 4-6 hourly (for IV, dilute in 20ml 0.9% sodium chloride solution and give slowly, over at least 2 minutes). In cardiovascular disease or if a higher dose is required, IV infusion is recommended: 400mg, diluted in 100ml 0.9% sodium chloride and given over 0.5-1 hour, may be repeated 4-6 hourly; or continuous infusion at a rate of 50-100mg/hour. Maximum 2.4g/24 hours.

Duodenal ulcer prophylaxis: oral: 400mg-800mg at bed time.

Gastric hypersecretory conditions: Oral, I.M., I.V.: 300mg –600mg every 6 hours; dosage not to exceed 2.4g/day.

Child \geq 12 years and Adult: *Oral: heart burn, acid indigestion, sour stomach:* 200mg up to twice daily; may take 30 minutes prior to eating foods or beverages expected to cause heart burn or indigestion.

Child: *Oral, I.M., I.V.:* 20-40mg/kg/day in divided doses every 6 hours.

Note:- Oral: Administer with meals so that the drug's peak effect occurs at the proper time (peak inhibition of gastric acid secretion occurs at 1 and 3 hours after dosing in fasting subjects and approximately 2 hours in non fasting subjects; this correlates well with the time food is no longer in the stomach offering a buffering effect).

Storage: store in airtight containers at a temperature of 15 to 30°C. Protect from light.

Famotidine

Tablet, 20 mg, 40 mg

Indications: therapy and treatment of duodenal ulcer, gastric ulcer, control gastric pH in critically-ill patients, symptomatic relief in gastritis,

gastroesophageal reflux, active benign ulcer, and pathological hypersecretory conditions.

Caution: see under cimetidine.

Drug interactions: ketoconazole, itraconazole and ethanol; the potential for drug interaction is much less than with cimetidine.

Contraindication: hypersensitivity to the drug.

Side effects: see under cimetidine; it has little if any anti-androgenic effect.

Dose and Administration: *Oral:*

Adult:

Duodenal ulcer: Acute therapy: 40mg/day at bed time for 4-8 weeks;

Maintenance therapy: 20mg/day at bedtime.

Gastric ulcer: Acute therapy: 40mg/day at bedtime.

Hypersecretory conditions: initial: 20mg every 6 hours; may increase in increments up to 160mg every 6 hours

Gastro-oesophageal reflux disease (GORD): 20mg twice daily for 6 weeks

Child:

Peptic ulcer: 1-16 years: 0.5mg/kg/day at bedtime or divided twice daily (maximum dose: 40mg/day)

GERD: <3 months: 0.5mg/kg once daily

3-12 months: 0.5mg/kg twice daily

1-16 years: 1mg/kg/day divided twice daily (maximum dose: 40mg twice daily).

Adult and Child \geq 12 years: *Heart burn, indigestion, sour stomach:* 10-20mg every 12 hours; dose may be taken 15-60 minutes before eating foods known to cause heartburn.

Storage: store at room temperature; protect from moisture.

Nizatidine

Capsule, 150mg, 300mg

Injection, 25mg/ml

Indications: see under dose.

Cautions, Drug interactions, see under cimetidine above.

Side effects: sweating, rarely vasculitis, hyperuricaemia, exfoliative dermatitis

Dose and Administration: **Adult:** *Oral: Benign gastric, duodenal or NSAID associated ulceration, treatment,* 300mg in the evening or 150 mg twice daily for 4-8 weeks; maintenance, 150mg at night;

Gastro-oesophageal reflux disease: 150-300mg twice daily for up to 12 weeks

IV infusion: for short term use in peptic ulcer hospital inpatients as alternative to oral route, by intermittent IV infusion over 15 minutes, 100mg 3 times daily, or by continuous IV infusion, 10mg/hour; max 480mg daily; **Child** not recommended.

Ranitidine

Tablet, 150 mg

Injection, 10 mg/ml in 5ml ampoule; 25mg/ml in 10ml ampoule

Indications: benign gastric and duodenal ulceration, gastro-oesophageal reflux, Zollinger–Ellison syndrome, other conditions where gastric acid reduction is beneficial

Cautions, Side effects, see under cimetidine above.

Drug interactions: ranitidine does not appear to bind to microsomal cytochrome P450 thus the potential for interactions is less than with cimetidine; sacralfate reduce absorption of ranitidine.

Dose and Administration:

*Benign gastric and duodenal ulceration: oral: **Adult:** 150 mg twice daily or 300 mg at night for 4–8 weeks, up to 6 weeks in chronic episodic dyspepsia, and up to 8 weeks in NSAID-associated ulceration (in duodenal ulcer 300 mg can be given twice daily for 4 weeks to achieve a higher healing rate); maintenance, 150 mg at night; **Child:** (peptic ulcer) 2–4 mg/kg twice daily, maximum 300 mg daily*

*Benign gastric and duodenal ulceration, reflux oesophagitis, Zollinger–Ellison syndrome: IM: **Adult:** 50 mg every 6–8 hours or by slow intravenous injection, 50 mg diluted to 20 ml and given over at least 2 minutes, may be repeated every 6–8 hours or by intravenous infusion, 25 mg/hour for 2 hours, may be repeated every 6–8 hours*

*Prophylaxis of NSAID-induced duodenal ulcer: oral: **Adult:** 150 mg twice daily*

*Reflux oesophagitis: oral: **Adult:** 150 mg twice daily or 300 mg at night for up to 8 weeks, or if necessary 12 weeks (moderate to severe, 150 mg 4 times daily for up to 12 weeks); long-term treatment of healed oesophagitis, 150 mg twice daily*

*Zollinger–Ellison syndrome: oral: **Adult:** 150 mg 3 times daily; up to 6 g daily in divided doses has been used*

*Gastric acid reduction (prophylaxis of acid aspiration) in obstetrics: oral: **Adult:** 150 mg at onset of labour, then every 6 hours; surgical procedures, IM or slow IV injection: **Adult:** 50 mg 45–60 minutes before induction of anaesthesia (intravenous injection diluted to 20 ml and given over at least 2 minutes), or orally, 150 mg 2 hours before induction of anaesthesia, and also, when possible on the preceding evening*

*Prophylaxis of stress ulceration: **Adult:** initial slow IV injection of 50 mg diluted to 20 ml and given over at least 2 minutes then by continuous IV infusion, 125–250 micrograms/kg per hour (may be followed by 150 mg twice daily by mouth when oral feeding commences)*

Storage: store injections between 4–30°C; and tablet between 15–30°C.

Prostaglandin

Misoprostol is a synthetic prostaglandin E₁ analogue used to inhibit gastric acid secretion by a direct action on the parietal cells and also have mucosal protectant property.

Misoprostol

Tablet, 100 mcg, 200 mcg, 400mcg, 800mcg

Indications: protection against NSAID associated gastric and duodenal ulceration, medical termination of pregnancy of ≤ 49 days in conjunction with mifepristone.

Cautions: renal impairment and elderly, inflammatory bowel disease (may exacerbate intestinal inflammation and produce severe diarrhea); patients prone to dehydration or in whom its consequence would be dangerous. Patients should understand Misoprostol's abortifacient properties and attendant risks, and that the drug is intended only for their use for the specific condition for which it was prescribed.

Drug interactions: oxytocin, diclofenac, phenylbutazone

Contraindications: pregnancy and allergy to prostaglandins.

Side effects: diarrhoea is the most common side effects; abdominal pain, dyspepsia, flatulence, and nausea and vomiting, increased utrine contractility, menorrhagia, vaginal bleeding, and intermenstrual bleeding, skin rashes, headache, dizziness, and constipation..

Dose and Administration:

Adult: *Oral:*

Prevention against NSAID associated duodenal ulcer: 800 mcg/day in four divided doses, with meals and at bedtime. Where appropriate, NSAIDs should be taken simultaneously.

Prevention against NSAID associated gastric ulcer: 200mcg twice daily with food and the prescribed NSAID; increased to 200mcg three times daily (maximum 200 mcg 4 times daily) to correspond with the NSAID administration schedule or if clinically indicated.

Note:-Taking with food or milk will lessen adverse effects such as loose stools, diarrhea, and abdominal cramping.

Misoprostol therapy should be started at the onset of treatment with NSAIDs, and continue for the duration of NSAIDs therapy. If required, antacids may be administered before or after misoprostol for the relief of pain. However, magnesium-containing antacids are not recommended since they may aggravate misoprostol-induced diarrhea.

Storage: store at or below 25°C.

Proton pump inhibitors

The proton pump inhibitors, which include omeprazole, esomeprazole and lansoprazole are the most potent suppressors of gastric acid secretion. They act by irreversibly binding to and inhibiting the H^+/K^+ ATPase enzyme of the gastric parietal cell.

They are indicated for short-term management of peptic ulcer disease and gastro-oesophageal reflux, long-term prevention of relapse of gastro-oesophageal reflux disease (GORD), and as part of *H. pylori* eradication regimens. In addition, omeprazole is registered for the treatment of Zollinger-Ellison syndrome, and the treatment and prevention of NSAID-associated erosions

Esomeprazole

Tablet (f/c), 20mg, 40mg

Capsule, 20mg

Indications: see under dose and Administration.

Cautions, Drug interactions, Contraindications, Side effects and Storage see under omeprazole.

Dose and Administration: Adult: Oral:

Erosive reflux oesophagitis: 40mg once daily for 4-8 weeks. Maintenance to prevent relapse, 20mg once daily.

GORD (without oesophagitis): 20mg once daily for 4 weeks.

Eradication of H. pylori: esomeprazole 20mg plus amoxicillin 1g and clarithromycin 500mg, all twice daily for 7 days.

Lansoprazole

Capsule, 15mg, 30mg

Tablet, 15mg, 30mg

Oral suspension (granule), 30mg/sachet

Indications: see under dose and administration.

Cautions, Drug interactions, Contraindications, Side effects and Storage see under omeprazole. Contraindicated in liver impairment.

Dose and Administration: Adult: Oral:

30mg daily for 2-8 weeks depending on the condition

Prevention of GORD: 15mg daily for upto 1 year. No efficacy or safety data available for therapy longer than 1 year.

Functional dyspepsia: 15mg daily for 2-4 weeks

Eradication of H. pylori: see under omeprazole

Heartburn and hyperacidity: 15mg daily for up to 14 days

Omeprazole

Capsule (enclosing e/c granules), 20 mg

Indications: management of gastric and duodenal ulcers, reflux oesophagitis and Zollinger Ellison syndrome; also eradication of *H. Pylori* in combination with appropriate antibiotics.

Cautions: pregnancy, lactating women, liver disease; porphyria.

Drug interactions: diazepam, warfarin, phenytoin, fluoxetine, propranolol, indinavir, ketoconazole, and carbamazepine.

Contraindications: known hypersensitivity to the drug, exclude malignancy.

Side effects: diarrhoea, headache, skin rashes, nausea, vomiting, constipation, flatulence and abdominal pain, pruritus, urticaria, dizziness,

Dose and Administration: Oral:

Adult:

Active duodenal ulcer: 20mg/day for 4-8 weeks.

Gastric ulcers: 40mg/day for 4-8 weeks.

NSAID-associated erosions: 20mg daily for 4-8 weeks. Prevention, 20mg daily.

Eradication of H.pylori: 20mg twice daily or 40 mg once daily for 7-14 days in combination with appropriate antibiotics (*clarithromycin 500 mg twice daily, amoxicillin 1 g twice daily, or as an alternative amoxicillin 1 g twice daily, metronidazole 500 mg (or tinidazole 500mg) twice daily*).

Zollinger-Ellison syndrome: initially 60mg once daily; dosage range 20-120mg/day, with doses over 80mg given in 2 divided doses.

Child: *Severe ulcerative reflux oesophagitis*: 10-20kg, 10mg once daily, increased to 20mg daily if necessary; over 20kg, 20mg once daily, increased to 40mg daily if necessary.

Note:-Taking the medication at least 1 hour before a meal will have maximum benefit.

Storage: store at room temperature.

Bismuth compounds

Bismuth compounds have been used for their antacid action and for their mildly astringent action in various gastro-intestinal disorders, including diarrhoea and dyspepsia.

Tripotassium dicitratobismuthate and the subsalicylate formulations are active against *H. Pylori* and commonly used as part of a multi drug regimen for *H. Pylori* eradication to reduce the risk of duodenal ulcer recurrence.

Excessive or prolonged use may lead to bismuth accumulation and toxicity, including renal failure, liver damage, and encephalopathy.

Bismuth subsalicylate*Liquid, 262 mg/15ml**Tablet, 300 mg***Indications:** as part of a multidrug regimen for *H. pylori* eradication to reduce the risk of duodenal ulcer recurrence.**Cautions:** patients taking aspirin, children < 3 years of age and those with viral illness.**Drug interactions:** warfarin, aspirin, hypoglycemics, tetracyclines and uricosurics.**Contraindications:** hypersensitivity to the drug, severe GI bleeding, history of coagulopathy, pregnancy (3rd trimester), renal impairment.**Side effects:** anxiety, confusion, headache, discoloration of the tongue, grayish black stools, hearing loss, tinnitus, nausea and vomiting.**Dose and Administration: Adult:** *Oral:* 524mg four times/day with meals and at bedtime; requires combination therapy.**Storage:** store in airtight containers and protect from light.**Tripotassium Dicitratobismuthate***Liquid, 120 mg/5ml**Tablet, 120 mg***Indications:** used as a mucosal protectant for the treatment of peptic ulcer disease; active against *Helicobacter pylori* and has been used as triple therapy (with metronidazole and either tetracycline or amoxicillin) to eradicate this organism and thereby prevent relapse of duodenal ulcer.**Cautions, Drug interactions, Contraindications, Side effects and Storage** see under bismuth subsalicylate.**Dose and Administration: Adult:** *Oral:**Gastric and Duodenal ulceration:* 240mg twice daily or 120mg four times daily before meals for 4 weeks, extended to 8 weeks if necessary.

When used as part of triple therapy 120mg 4 times daily for 2 weeks.

Storage: store in airtight containers and protect from light.**Sucralfate**

Sucralfate, a sucrose hydrogen sulphate aluminium complex, is a mucosal protective agent. It has a local protective action on the ulcer base, without the side-effects that may occur with other systemic agents. In the stomach a paste-like gel is formed from a reaction with HCl, which adheres to the base of ulcer craters (both in the stomach and duodenum), protecting ulcer epithelium from ulcerogenic substances such as gastric acid, pepsin and bile. It also directly adsorbs bile and pepsin. Sucralfate requires a strict, frequent administration dosage regimen which may produce problems with compliance, but if used correctly, its efficacy compares favourably with that of other ulcer-healing agents.

Sucralfate

Tablet, 1 g

Indications: for treatment of gastric and duodenal ulcers, chronic gastritis and reflux oesophagitis.

Caution: renal impairment.

Drug interactions: other antacids, tetracyclines, phenytoin, oral anticoagulants, digoxin, cimetidine.

Contraindications: hypersensitivity of the drug.

Side effects: constipation, diarrhoea, nausea, abdominal discomfort and indigestion.

Dose and Administration: **Adult:** *Oral:* 1g 4 times daily, 1 hour before meals and at bedtime. In *duodenal ulcer*, 2g twice daily has also been shown to be effective. Maintenance 1g twice daily, half an hour before morning and evening meals.

Storage: store at room temperature.

1.3. Antispasmodics/spasmolytic Analgesics

The Smooth muscle relaxant properties of antimuscarinic (formerly termed 'anticholinergics') and other antispasmodic drugs (e.g. Camylofin Hydrochloride) may be useful in some forms of dyspepsia, in irritable bowel syndrome and in diverticular disease. Other indications of antimuscarinic drugs include arrhythmias, asthma and airways disease, motion sickness, parkinsonism, urinary incontinence, mydriasis and cycloplegia, premedication and as an antidote to organophosphorous poisoning.

Antimuscarinics that are used for gastro-intestinal smooth muscle spasm include the tertiary amines **Atropine sulphate** and **Hyoscine (Scopolamine) Hydrobromide** and the quaternary ammonium compounds **Hyoscine (Scopolamine) Butylbromide** and **Propantheline Bromide**.

Antimuscarinics are commercially available in combination with Phenothiazines, or benzodiazepines or other anxiolytics (e.g. **chlordiazepoxide + clidinium Bromide**) for the benefit of its supportive role in patients with irritable bowel syndrome who respond to sedatives or in some patients with peptic ulcer disease.

The side effects frequently associated with the use of antimuscarinics include xerostoma (dry mouth), blurred vision, cycloplegia, mydriasis, photophobia, anhidrosis, urinary hesitancy and retention, tachycardia, palpitation, and constipation. Side effects that occur occasionally include confusion (particularly in elderly), nausea, vomiting and giddiness.

Antimuscarinics should be used with caution in geriatric-patients, and children, and also in patients with hyperthyroidism, hepatic or renal disease, or hypertension, tachyarrhythmias, congestive heart failure, or coronary artery disease; autonomic neuropathy, gastro-esophageal reflux, known or suspected GI infections, diarrhea and mild to moderate ulcerative colitis, and in patients

who may be exposed to elevated environmental temperatures or in patients who are febrile.

The drugs are contraindicated in patients with severe ulcerative colitis, obstructive disease of the GI tract, paralytic ileus, or intestinal atony, prostatic enlargement, known hypersensitivity to the drugs, angle-closure glaucoma, obstructive uropathy (caution for patients with partial obstructive uropathy) and myasthenia gravis (unless the antimuscarinic is used to reduce adverse muscarinic effects of an anticholinesterase agent).

The effect of antimuscarinic agents may be enhanced by the concomitant administration of other drugs with antimuscarinic properties, such as amantadine, some antimuscarinic, butyrophenones and phenothiazine, and tricyclic antidepressants. The reduction in gastric motility caused by antimuscarinic agents may affect the absorption of other drugs.

Atropine Sulphate

Injection, 1 mg/ml in 1ml ampoule

Indications: dyspepsia, irritable bowel syndrome, diverticular disease; premedication; mydriasis and cycloplegia; poisoning (section 17); see also notes above.

Cautions, Drug interactions, Contraindications, Side effects; See notes above

Dose and Administration:

Adult: *IM, S.C., I.V:* 0.4 - 0.6 mg every four to six hours.

Child: *SC:* 0.01 mg/kg of body weight, not to exceed 0.4 mg, every four to six hours.

Storage: at room temperature, protect from freezing.

Chlordiazepoxide + Clidinium Bromide

Tablet, 5 mg + 2.5 mg

Indications: used in the treatment of functional disturbances of GI motility such as irritable bowel syndrome, see also notes above.

Cautions, Drug interactions, Contraindications, Side effects - see notes above
The precautions and contraindications associated with chlordiazepoxide must be considered (see section 4.2).

Dose and Administrations: **Adult:** *Oral:* one or two tablets 3 or 4 times daily (i.e. 2.5 or 5 mg of Clidinium bromide 3 or 4 times a day)

Storage: store at room temperature in a tight, light resistant container.

Drotaverine

Tablet, 40 mg

Indications: smooth muscle spasm in connection with biliary tract diseases: cholecystolithiasis, cholangiolithiasis, cholecystitis, pericholecystitis, cholangitis, and papillitis.

Smooth muscle spasm in connection with urinary tract diseases: nephrolithiasis, ureterolithiasis, pyelitis, cystitis, and cramp of urinary bladder.

Cautions: hypotension, people with lactase insufficiency, galactosaemia.

Drug interactions: phosphodiesterase inhibitors like papverine decrease the antiparkinsonian effect of levodopa.

Contraindications: hypersensitivity reactions; severe hepatic, renal and cardiac insufficiency; children < 1 year of age.

Side effects: gastrointestinal disorders (nausea, constipation); nervous system disorders (headache, dizziness, insomnia); cardiovascular disorders (palpitation, hypotension).

Dose and Administration:

Adult: the usual average daily dose is 120-240 mg/day (in 2-3 divided doses).

Child > 1 year old: 40-120 mg/day divided in 2 to 3 doses between 1 and 6 years. 80-200 mg/day divided in 2 to 5 doses over 6 years.

Storage: store at a temperature not exceeding 25 °C.

Hyoscine (scopolamine) Hydrobromide

Tablet, 0.6 mg

Injection, 0.4 mg/ml, 0.6 mg/ml in 1ml ampoule

Indications: prevention and control of motion sickness, and also used as an adjunct to anesthesia to inhibit salivation and excessive respiratory secretions and to produce sedative and amnesia; see also notes above. Not indicated for peptic ulcer.

Note: - Hyoscine Butylbromide is preferable to Hyoscine hydrobromide in the relief of visceral spasms of the gastro-intestinal tract and pain associated with other smooth muscle spasm. (See below)

Cautions, Contraindications, Side effects; see notes above

Drug interactions: CNS depression - producing medications; see notes above.

Dose and Administration:

Adult: *Oral:* 0.3 mg 30 minutes before a journey to prevent motion sickness then 0.3 mg every 6 hours if required up to a maximum of 3 doses in 24 hours; *IM, IV, or SC,* 0.3 to 0.6 mg; if necessary, the dose may be repeated 3 or 4 times daily.

Child: *Oral:* aged 4 to 10 years, 75 to 150 microgram and those over 10 years, 150 to 300 microgram; *IM, IV, or SC,* 0.006 mg/Kg

Storage: store in a light - resistant container at room temperature. Protect from freezing.

Hyoscine (Scopolamine) Butylbromide

Tablet, 10mg

Drops, 5mg/5ml

Injection, 20mg/ml

Indications: symptomatic relief of visceral spasms of the gastro-intestinal tract, painful spasm of the biliary and genito-urinary system.

Cautions, Contraindications, Side effect, Storage; see notes above

Drug interactions: CNS depressants see also notes above.

Dose and Administrations:

Adult: *Oral:* 20mg four times daily; *IM or IV,* 20 mg repeated after 30 minutes if necessary.

Child: *Oral:* 6-12 years, 10mg 3 times daily; parenteral use not recommended.

Storage: at room temperature, in a well-closed container.

Propantheline Bromide

Tablet, 15 mg, 30 mg

Indications: adjunctive treatment of peptic ulcer, irritable bowel syndrome, pancreatitis, ureteral and urinary bladder spasm; reduce duodenal motility during diagnostic radiologic procedure.

Cautions, Drug interactions, Contraindications, Side effects, and Storage; see notes above.

Dose and Administration: *Oral:*

Antisecretory:

Adult: 15 mg 3 times/day before meals or food and 30mg at bedtime

Child: 1-2 mg/kg/day in 3-4 divided doses

Elderly: 7.5 mg 3 times/day before meals and at bedtime

Antispasmodic:

Adult: 15mg 3 times/day before meals or food and 30mg at bedtime

Child: 2-3mg/kg/day in divided doses every 4-6 hours and at bedtime

Storage: at room temperature in a well closed container.

1.4. Antiemetics

Antiemetics are a diverse group of drugs used to treat or prevent nausea and vomiting, including that associated with cancer therapy, anaesthesia and surgery, and motion sickness.

Antiemetics described here include: the dopamine antagonists metoclopramide and chlorpromazine hydrochloride; antihistamines such as Dimenhydrinate, Meclizine Hydrochloride and Promethazine Hydrochloride; and the Phenothiazine thiethylperazine maleate.

The choice of drug depends partly on the cause of nausea and vomiting. For example, hyoscine (see section 1.3.) or antihistamines are used in motion sickness where as dopamine antagonists, which act selectively on the chemoreceptor trigger zone, are ineffective for the treatment of motion sickness. Conversely, nausea and vomiting associated with cancer chemotherapy is often hard to control and special regimens have been devised including the use of metoclopramide in high doses and more recently 5 HT₃ antagonist ondansetron.

The antihistamines may be slightly less effective than hyoscine against motion sickness but are often tolerated.

There is no evidence that any one antihistamine is superior to another but their duration of action and incidence of adverse effects (drowsiness, and antimuscarinic effects) differ. For example Dimenhydrinate causes drowsiness more frequently; Meclizine has a longer duration of action than scopolamine and most other antihistamines. If a sedative effect is desired promethazine is useful.

A popular choice of antiemetic is metoclopramide which is effective against nausea and vomiting following surgery and chemotherapy. It is also effective against radiation - induced nausea and vomiting. Combining metoclopramide with corticosteroids (such as Dexamethasone) can improve its antiemetic effect in chemotherapy-induced nausea and vomiting. Metoclopramide may cause acute dystonic reactions with facial and skeletal muscle spasms and oculogyric crises. These reactions are most common in the young (especially girls and young women) and the elderly; they occur shortly after the start of treatment and subside within 24 hours of drug withdrawal.

Antiemetics are unnecessarily and some times harmful when the cause can be treated, e.g. as in diabetic ketoacidosis, or in excessive digoxin or antiepileptic dosage.

Pregnancy induced nausea and vomiting or “morning sickness” is common in the first trimester, but generally does not require drug therapy. Dietary modification such as taking of small frequent carbohydrate meals often helps. A few pregnant women may require a short-term promethazine treatment.

Chlorpromazine Hydrochloride

Tablet, 25 mg, 100 mg

Syrup, 25 mg/5 ml

Drop, 25 mg/ml

Injection, 25 mg/ml in 1 and 2 ml ampoules

Indications: For the prevention and control of severe nausea and vomiting, other indications (see section 4.2)

Note: It should not be used for motion sickness

Cautions, Drug interactions, Contraindications, and Side effects; see section 4.2 under chlorpromazine

Dose and Administration:

Adult: *Oral:* 12.5 – 25mg every 4 – 6 hours, as necessary.

Slow, deep I.M.: 25 mg as a single dose, the dosage being increased to 25 – 50mg every 3 – 4 hours until vomiting stops; it is then given orally if necessary.

Child (6 month and over): *Oral or slow, deep I.M.:* 0.55mg/kg every 6 – 8 hour as necessary.

Note: Patients should remain lying down for at least 30 minutes after injection.

Storage: at room temperature. Protect from light and freezing. Do not use if solution is markedly discolored or if a precipitate is present.

Dimenhydrinate

Tablet, 50 mg

Indications: prevention and treatment of nausea, vomiting and/or vertigo associated with motion sickness; see also notes above.

Cautions: as for meclizine Hydrochloride; also pregnant and nursing mothers.

Drug interactions: as for meclizine Hydrochloride; ototoxic drugs such as aminoglycoside antibiotics (dimenhydrinate may mask the early symptoms of ototoxicity)

Side effects: as for meclizine Hydrochloride; also, tinnitus.

Dose and Administration:

Adult: *Oral*, 50 to 100 mg every four to six hours.

Child: *Oral*, 6-12 Years of age, 25 to 50 mg every six to eight hours as needed, not to exceed 150 mg per day; 2-6 years of age, 12.5 to 25 mg every six to eight hours as needed, not to exceed 75 mg per day.

Note: Oral dosage forms used for motion sickness should be taken 30 minutes before motion

Storage: at room temperature, in a well-closed container.

Meclizine Hydrochloride

Tablet, 12.5 mg, 25 mg

Indications: prevention and treatment of nausea, vomiting and/or vertigo associated with motion sickness; see also notes above.

Cautions: warn the patients not to perform hazardous activities requiring mental alertness or physical condition; patients with angle closure glaucoma or prostatic hypertrophy bladder neck obstruction, coma, Jaundice; use with caution in hot weather, and during exercise. Elderly may be at risk for anticholinergic side effects

Drug interactions: alcohol, CNS depressants including barbiturates, tranquilizers, drugs with anti cholinergic effects including tricyclic antidepressants.

Contraindications: hypersensitive to the drug, pregnant women, children younger than 12 years of age.

Side effects: drowsiness, fatigue and rarely blurred vision, dryness of mouth, nose and throat, palpitations, thickening of bronchial secretions, increase appetite, weight gain, arthralgia, and pharyngitis.

Dose and Administration:

Adult and Child (>12 years of age):

Motion sickness (prophylaxis and treatment): Oral: 25 to 50 mg one hour before travel. Dose may be repeated every twenty-four hours as needed.

Vertigo (prophylaxis and treatment): Oral: 25 to 100 mg a day as needed; in divided doses.

Storage: at room temperature, in a well - closed container.

Metoclopramide Hydrochloride

Tablet, 10 mg

Syrup, 5mg/5ml

Drop, 0.2 mg/drop

Injection, 5 mg/ml in 2 ml ampoule

Indications: nausea and vomiting in gastrointestinal disorders and treatment with cytotoxics or radiotherapy; gastro-oesophageal reflux; gastroparesis; premedication and postoperatively; aid to gastrointestinal intubation; nausea and vomiting in migraine .

Cautions: elderly, children and young patients are at increased risk of extrapyramidal reactions; hepatic and renal impairment; may mask underlying disorders such as cerebral irritation, avoid for 3 - 4 days after gastrointestinal surgery; pregnancy; breast feeding; parkinson disease; depression; porphyria; patients should be warned that the drug may impair their ability to perform activities requiring mental alertness or physical coordination.

Drug interactions: alcohol, barbiturates, CNS depressants; phenothiazines and butyrophenones, lithium, antidepressants, antiepileptics, and sympathomimetics; antimuscarinic agents and opioid analgesics; digoxin, aspirin or paracetamol, suxamethonium, bromocriptine.

Contraindications: epilepsy; gastrointestinal hemorrhage, mechanical obstruction or perforation; pheochromocytoma; hypersensitivity to the drug.

Side effects: extrapyramidal symptoms (especially in children and young adults), tardive dyskinesia on prolonged use; hyperprolactinaemia; drowsiness, restlessness, dizziness, headache, diarrhoea, depression, hypotension and hypertension; rarely, neuroleptic malignant syndrome; cardiac conduction abnormalities following IV administration.

Dose and Administration:

Nausea and vomiting, gastro-oesophageal reflux, gastroparesis:

Adult: *Oral or IM, or slow IV injection:* 10 mg 3 times daily; **young Adult:** 15 - 19 years (under 60 Kg) 5 mg 3 times daily;

Child: *Oral, or IM, or slow IV injection:* up to 1 year (up to 10 Kg) 1 mg twice daily, 1 - 3 years (10-14 Kg) 1 mg 2 - 3 times daily, 3 - 5 years (15 - 19 Kg) 2 mg 2 - 3 times daily, 5 - 9 years (20-28 Kg.) 2.5 mg 3 times daily, 9 - 14 years (30 Kg and over) 5 mg 3 times daily. (Usual maximum 500 micrograms/Kg daily, particularly for children and young adults)

Pre-medication: **Adult,** *by slow I.V.,* 10 mg as a single dose.

Aid to gastrointestinal intubation, Orally, or IM or by Slow intravenous injection:

Adult: 10 - 20 mg as a single dose 5 - 10 minutes before examination; **Young Adult** (15 - 19 years) 10mg; **Child** under 3 years 1 mg, 3 - 5 years 2 mg, 5 - 9 years 2.5 mg, 9 - 14 years 5 mg.

Storage: at room temperature, protect from light.

Promethazine Hydrochloride

Tablets, 10 mg, 25 mg

Suppository, 25 mg, 50 mg

Elixir, 5 mg/5 ml.

Injection, 25 mg/ml in 1 ml and 2 ml ampoules

Indications: control of nausea, vomiting, and vertigo of various cause, as a sedative and hypnotic, and as a common ingredient of cough and cold preparations; also see notes above.

Cautions: see under Meclizine Hydrochloride, intravenous injection of promethazine hydrochloride must be given slowly and extreme care must be taken; should not be given by subcutaneous injection, avoid in porphyria.

Drug interactions: see under Meclizine hydrochloride; epinephrine, extrapyramidal reaction causing medications, levodopa, metrizamide and monoamine oxidase (MAO) inhibitors including furazolidone, procarbazine, and selegiline.

Contraindications: patients who have exhibited hypersensitivity to the drug; also in those who have received large doses of CNS depressants and/or in those who are comatose, in epileptic seizures.

Side effects: see under Meclizine Hydrochloride, and blood dyscrasias, sedative effect is more pronounced.

Dose and Administration:

Antiemetic: Oral:

Adult: 25 mg initially, then 10 to 25 mg every 4 - 6 hours as needed.

Note: For motion sickness, the initial 25 mg dose should be taken one half to one hour before travel, and the dose repeated 8 - 12 hours later, if necessary.

Child (>2 years of age): 0.25 to 0.5 mg per Kg of body weight every 4 to 6 hours or 10 to 25 mg every four to six hours as needed.

IM or IV:

Adult: 12.5 to 25 mg every 4 hours as needed.

Child (> 2 years of age): 0.25 to 0.5 mg per Kg of body weight every 4 to 6 hours as needed.

Rectal:

Adult: 25mg initially, then 12.5 to 25mg every 4 to 6 hours as needed.

Child (> 2 years of age): 0.25 to 0.5mg per kg of body weight, or 12.5 to 25mg every 4 to 6 hours as needed.

Antivertigo agent: Oral:

Adult: 25mg 2 times a day as needed.

Child (> 2 years of age): 0.5mg to 1mg per kg of body weight or 10 to 25mg 2 times a day as needed.

Rectal:

Adult: 25mg 2 times a day as needed.

Child (> 2 years of age): 0.5mg per kg of body weight, or 12.5 to 25mg 2 times a day as needed.

Storage: Suppositories: store between 2 and 8°C, in a tight, light-resistant container. Tablet & Injection - at room temperature protect from light and from freezing.

Thiethylperazine Maleate*Tablet, 6.5 mg**Suppository, 6.5 mg**Injection, 6.5 mg 1 ml in 1 ml ampoule*

Indications: for the control of nausea and vomiting associated with surgical procedures and cancer therapy.

Cautions, Drug interactions, Contraindications, and Side effects; as for Meclizine Hydrochloride

Dose and Administration:

Adult: *Oral, Rectal, IM*, 10mg 1-3 times a day.

Child: Safety and efficacy has not been established

Storage: protect from light. It should be stored in tight, light-resistant container at room temperature.

1.5. Cathartics and Laxative

Laxatives (purgatives or cathartics) promote defaecation and are used in the treatment of constipation and for bowel evacuation before investigational procedures, such as endoscopy or radiological examination, or before surgery.

Laxatives are usually subdivided into several categories including the bulk forming laxatives such as cellulose derivatives, psyllium preparations; stimulant laxatives (contact laxatives) that include anthraquinone-containing agents such as **senna** and **cascara**, diphenylmethane derivatives such as **bisacodyl** and also other miscellaneous agent such as **castor oil**, osmotic laxatives such as **glycerin**, lactulose and the saline laxative such as magnesium sulphate are also included in this group; faecal softeners (emollient laxatives) include sodium salt of docusate and the lubricant laxative liquid paraffin.

Bulk forming laxatives relieve constipation by causing retention of fluid and an increase in faecal mass resulting in stimulation of peristalsis; the full effect may take some days to develop and patients should be told this. They are of particular value in those with small hard stools, but should not be required unless fiber cannot be increased in the diet. They are useful in the management of patients with colostomy, ileostomy, haemorrhoids and fissure, chronic diarrhoea associated with diverticular disease, irritable bowel syndrome and as adjuncts in ulcerative colitis. Owing to their hydrophilic nature, bulk laxatives may also be used to control acute diarrhoea and to regulate the consistency of effluent in colostomy patients. Adequate fluid intake must be maintained to avoid intestinal obstruction. Unprocessed wheat bran taken with food or fruit juice, is a most effective bulk forming preparation. Methylcellulose is useful in patients who cannot tolerate bran. Methylcellulose also acts as a faecal softener.

Stimulant laxatives which increase intestinal motility and often cause abdominal cramp; they should be avoided in intestinal obstruction. Prolonged use of stimulant laxatives can precipitate the onset of an atonic non-functioning colon and hypokalaemia; however, prolonged use may be justifiable in some circumstances. Glycerin suppositories act as a rectal stimulant by virtue of the mildly irritant action of glycerin. Powerful stimulants such as cascara and castor oil are obsolete. Docusate sodium probably acts both as a stimulant and as a softening agent. This group of laxatives is most commonly associated with abuse. In general, use of stimulant laxatives should be avoided in children younger than 6-10 years of age unless prescribed by physician.

Faecal softeners such as liquid paraffin, which is the classical lubricant, lubricate and soften impacted faeces. Bulk laxatives and non-ionic surfactant 'wetting' agents e.g. docusate sodium also have softening properties. Such drugs are useful for oral administration in the management of haemorrhoids and anal fissures.

Osmotic laxatives act by retaining fluid in the bowel by osmosis or by changing the pattern of water distribution in the faeces. Saline purgatives such as magnesium salts are useful where rapid bowel evacuation is required. Lactulose is a semi-synthetic disaccharide, which is not absorbed from the gastrointestinal tract. It produces osmotic diarrhoea of low faecal PH, and discourages the proliferation of ammonia producing organisms. It is therefore useful in the treatment of hepatic encephalopathy.

Bulk-forming laxatives, stool softeners, or mineral oil are preferred to other laxatives in patients with conditions in which straining at defecation should be avoided (e.g. myocardial infarction, vascular diseases, diseases of the anus or rectum, hernias, recent rectal surgery). Oral stool softeners or mineral oil are preferred to bulk-forming laxatives to ease evacuation of feces in patients with constipation associated with hard, dry stools. Many clinicians consider the stool softeners to be the treatment of choice in childhood constipation associated with hard, dry stools and to be safer and more efficacious than mineral oil for conditions in which straining at defecation is to be avoided.

Bulk-forming and stimulant laxatives have been used to treat constipation that occurs following prolonged bed rest or hospitalization.

Saline laxatives have been used to eliminate parasites and toxic anthelmintics prior to and/or after therapy with some anthelmintics. However, most clinicians agree that with the newer anthelmintics use of laxatives to eliminate parasites or the anthelmintic is not necessary, may complicate identification of the parasite, and may be harmful to the patient.

Bisacodyl

Tablet, 5 mg

Suppository 5 mg, 10 mg

Indications: constipation and for bowel evacuation.

Cautions: inflammatory bowel disease, the suppositories should be used with caution in patients with rectal fissures or ulcerated haemorrhoids; it should be preferably avoided in children. See also notes above.

Contraindications: appendicitis, rectal bleeding, congestive heart failure, hypertension, diabetes mellitus, Intestinal obstruction or undiagnosed abdominal symptoms. See also notes above.

Side effects: abdominal discomfort (such as colic or cramp); gripping (tablets); local irritation (suppositories). Diarrhoea with excessive loss of water and electrolytes may occur on prolonged use. See also notes above.

Dose and Administration:

Oral: Adult and Child (>12 years): 1-3 tablets daily as a single dose. **Child (> 3 years):** 1-2 tablets or 0.3 mg/kg daily as a single dose.

Rectal: Adult and Child (>12 years): 10mg daily as a single dose.

Child 2-11 years: 5-10mg daily given as a single dose.

Child (< 2 years of age): 5mg daily as a single dose.

Note: - It is usually effective within 6 to 12 hours following oral administration and within 15 to 60 minutes following rectal administration. Oral bisacodyl should be administered the evening before a morning bowel-movement is desired. Swallow the enteric-coated bisacodyl whole and not crushed to avoid gastric irritation. Take each dose with a full glass of water or other liquid. Rectal bisacodyl suppositories and enemas may be administered at the time a bowel movement is desired.

Storage: at room temperature in a well-closed container.

Cascara Sagrada

Tablet, 125 mg

Indications : constipation

Cautions: care should be taken in patients with inflammatory bowel disease prolonged use should be avoided, it should be preferably avoided in children; avoid habitual use; See also notes above.

Contraindications: see notes under bisacodyl

Side effects: mild abdominal discomfort, diarrhoea (prolonged use), reversible melanosis coli, the urine may be coloured yellowish brown or red and also see notes above.

Dose and Administrations:

Adult and Child (10 years and over): 0.3 - 1g, usually at bedtime.

A laxative effect usually occur 6 to 8 hours after administration. As discussed above such laxatives have a limited role in the management of constipation.

Storage: at room temperature, in airtight container. Protect from light.

Castor oil

Liquid, 30ml

Indications: to facilitate defecation in geriatric patients with diminished colonic motor response; constipation occurring secondary to idiopathic slowing of transit time, to constipating drugs or to irritable bowel or spastic colon syndrome; neurologic constipation and to empty the bowel prior to surgery or radiologic proctoscopic or sigmoidoscopic procedure.

Cautions: avoid prolonged use, and use in children up to six years of age; elderly patient.

Drug interactions: avoid concomitant use of castor oil with potassium sparing diuretics, potassium supplements.

Contraindications: pregnancy, acute abdominal pain, nausea, vomiting or other symptoms of appendicitis or undiagnosed abdominal pain, intestinal obstruction.

Side effects: abdominal discomfort, nausea, mild cramp, gripping or faintness, excessive irritation of the colon, violent purgation.

Dose and Administration:

Oral: Constipation: **Adult:** 15 ml daily; **Child** (< 2 years) - 1-5 ml daily, (> 2 years) - 5 - 15 ml daily.

For total colonic evacuation prior to surgery or radiologic sigmoidoscopic or proctoscopic procedure administered as a single dose about 16 hours before the procedures.

Adult and Child (≥ 12 years): 15 - 60 ml; **Child**, 2 - 11 years: 5 -15 ml; (< 2 years): 1 - 5 ml.

Note: Drink increased fluid. Take each dose with a full glass of water or other liquid.

Storage: at room temperature in a tight container and in dry place. Protect from freezing.

Diocetyl sodium Sulphosuccinate (Docusate Sodium)

Tablet, 50 mg, 100 mg

Syrup, 4 mg/ml

Indications: constipation and as an adjunct in abdominal radiological procedure; prophylactically in patients who should not strain during defecation, such as those with an episiotomy wounds, painful thrombosed hemorrhoids fissures or perianal abscesses, body wall and diaphragmatic hernias, anorectal stenosis, or postmyocardial infarction.

Cautions: do not give with liquid paraffin.

Drug interactions: potassium sparing diuretics, potassium supplement, danthrol, mineral oil, phenolphthalein, aspirin.

Contraindications: symptoms of appendicitis, undiagnosed rectal bleeding, congestive heart failure, hypertension, intestinal obstruction, sensitivity to docusate.

Side effects: undetermined allergies (skin rash), stomach and/or intestinal cramping.

Dose and Administration: *Oral:* **Adult:** up to 500 mg daily in divided doses; **Child** over 6 months: 12.5 mg 3 times, daily; 2 – 12 years: 12.5 – 25 mg 3 times daily (use pediatric oral solution only).

Note: Take each dose with a full glass of water or other liquid.

Storage: at room temperature, in a dry place and in a tight container.

Glycerin (Glycerol)

Suppository, 1 g, 1.346 g, 2 g, 2.76 g

Indications: constipation, especially in children; see also notes above.

Cautions: avoid habitual use.

Contraindications: as for bisacodyl

Side effects: rectal discomfort such as irritation, burning and pain may occur rarely.

Dose and Administration: *Rectal:* **Adult:** 2 – 4g suppository; **Child:** 2g suppository; **Infant:** 1g suppository.

The suppositories should be moistened with water before insertion.

Storage: In a cool place, in airtight containers.

Lactulose

Enema

Syrup

Indications: constipation (may take up to 48 hours to act); hepatic encephalopathy (portal systemic encephalopathy).

Cautions: lactose intolerance, diabetic patients (presence of some free galactose and lactose)

Contraindications: as for bisacodyl; galactosaemia, intestinal obstruction, hypersensitivity to lactulose.

Side effects: flatulence, cramps, and abdominal discomfort, nausea & vomiting.

Dose and Administration: **Adult:** *Constipation:* *Oral:* Initially 10-20g (15-30ml) daily in a single or 2 divided doses; increased up to 40g (60ml) daily if necessary. Maintenance 7-10g (10-15ml) daily.

Hepatic encephalopathy: *Oral:* initially 60-100g (90-150ml) daily in 3-4 divided doses; doses should be adjusted after 1-2 days to produce 2-3 soft stools daily, or to keep the PH of the stool at about 5.

Child: *Constipation:* *Oral:* under 1 year, 2.5ml; 1-5 year, 5ml; 6-12 years, 10ml twice daily, gradually reduced.

Storage: in airtight container preferably at a temperature between 2⁰c and 30⁰c.

Liquid paraffin, Heavy

Indication: constipation associated with stricture of colon.

Cautions: avoid prolonged use and caution should be taken in children, pregnant women, elderly patients; caution is also recommended with bedridden patients who may develop lipid pneumonia from aspiration of mineral oil.

Drug interactions: avoid concomitant administration of the oil with fat

soluble vitamins (A,D,E,K), carotene, oral contraceptive, coumarine and indandione derivative anticoagulants.

Contraindications: as for bisacodyl; also colostomy, ileostomy.

Side effects: seepage of mineral oil that may cause soiling of the skin and clothing, anal irritation, pruritis, impair normal rectal reflex mechanism, granulomatous reaction caused by absorption of small quantities of liquid paraffin, lipoid pneumonia.

Dose and Administration: *Oral:* 5-20ml, when required.

Storage: at room temperature and protect from freezing.

Magnesium sulphate

Crystal

Indications: rapid bowel evacuation in preparations for rectal and bowel examination, and selective colon surgery; to hasten excretion of poisonous substances, except acids or alkalis, from the G.I.T.

Cautions: care should be taken in patients with renal impairment, hepatic impairment, in elderly and debilitated patients.

Drug interactions: coumarin or indandione derivative anticoagulants, digitalis glycoside, chlorpromazine, sodium polystyrene sulfonate, and tetracycline.

Contraindications: as for bisacodyl; acute GI conditions, colostomy, ileostomy, (increased risk of electrolyte or fluid imbalance); dehydration, renal impairment.

Side effects: colic, cramping, diarrhea, gas formation, increased thirst, electrolyte imbalance (confusion, irregular heart beat, muscle cramp, unusual tiredness or weakness).

Dose and Administration: *Oral: Adult:* 5 – 10 gm in a tumblerful of water preferably before breakfast (for rapid bowel evacuation).

Child: older than 6 years of age 5 – 10 gms dissolved in 120 ml of water.

Note: take each dose with a full glass of water. Dissolve or mix in water or other liquid before taking.

Storage: at room temperature in a well-closed container.

Methyl Cellulose

Tablet, 500 mg

Indications: see note above, adjunct in obesity.

Cautions: see notes above: adequate fluid intake should be maintained to avoid intestinal obstruction- it may be necessary to supervise elderly or debilitated patients or those with intestinal narrowing or decreased motility.

Contraindications: dysphagia, difficulty in swallowing, intestinal obstruction, colonic atony, faecal impaction, and infective bowel disease; see also under bisacodyl.

Side effects: flatulence, abdominal distensions, gastro-intestinal obstruction or impaction, hypersensitivity reactions reported.

Dose and Administration:

Adult and Child 12 and older: up to 6 g daily given in divided doses of 0.43 - 3 g per dose.

Child 6 - 11 years of age - up to 3g daily given in divided dose of 0.45 - 1.5 g per dose.

Storage: at room temperature in a well-closed container.

Psyllium

Powder

Indications: Constipation, especially in diverticular disease and irritable bowel syndrome, and when excessive straining at stool must be avoided.

Cautions: avoid prolonged use; adequate fluid should be taken to avoid intestinal obstruction. Caution on dispensing the powder to avoid sensitization to air born particles of psyllium

Drug interactions: tetracyclines.

Contraindications: see under bisacodyl; pre-existing faecal impaction, intestinal obstruction or colonic atony.

Side effects: hypersensitivity reactions; esophageal blockage or intestinal impaction.

Dose and Administration: *Oral:* **Adult and Child** (12 years and older): 30gm given daily in divided doses of 2.5 - 7.5gm per dose; Children 6-11 years old - 15gm daily given in divided doses of 2.5-3.75gm per dose.

Storage: at room temperature in a tight container and in a dry place.

Senna

Tablet (total sennosides), 7.5 mg

Indication: constipation and bowel evacuation.

Cautions, Contraindications: see under Cascara Sagrada

Side effects: see notes above.

Dose and Administrations: *Oral:*

Adult: 15 - 30 mg, as a single dose at bedtime.

Child (over 6 years of age), one half of the adult dose, and those aged 2 to 6 years are quarter the adult dose.

Note: - It is usually effective within 6 to 12 hours.

Storage: at room temperature in a dry place. Protect from freezing

1.6. Agents used in Diarrhoea

Antidiarrhoeal agents are used as adjuncts in the symptomatic treatment of diarrhea, although the main aim in the management of acute diarrhoea is the correction of fluid and electrolyte depletion with rehydration therapy; this is especially important in infants and young children and antidiarrhoeal agents are not generally recommended for this age group. Their use is also limited in chronic diarrhea for treatment aimed at the underlying disorder will often alleviate the diarrhoea.

The main groups of antidiarrhoeal agents are the drugs which reduce intestinal motility such as Diphenoxylate, and Loperamide. Bulk laxatives (see section 1.5) may also be used in the symptomatic treatment of diarrhoea.

Antiperistaltic agents (e.g. diphenoxylate, loperamide) are also used for symptomatic treatment of mild or uncomplicated travelers' diarrhoea, including that occurring in adult travelers with HIV infection. The most important measure in the management of travelers' diarrhoea is replacement of lost fluids and electrolytes.

Antidiarrhoeal agents, especially the adsorbents may interfere with the absorption of other drugs from the gastro-intestinal tract if administered concomitantly.

Diphenoxylate with Atropine

Tablet, diphenoxylate hydrochloride 2.5 mg and atropine sulphate 0.025 mg

Indications: acute diarrhoea (adjunctive therapy)

Cautions: inflammatory bowel disease; severe colitis.

Drug interactions: CNS depressants (alcohol, phenobarbitone, opioid analgesics), phenothiazines, tricyclic antidepressants, antimuscaranics.

Contraindications: severe hepatic disease, pseudomembranous colitis and diarrhoea from infective aetiology; elderly and patients with glaucoma or prostate hypertrophy; children under 4 years.

Side effects: nausea, dizziness, drowsiness, fatigue, sensitivity reactions include angioedema and giant urticaria, headache, euphoria, respiratory and mental depression. Anticholinergic symptoms such as dry mouth, fever, blurred vision; tachycardia and urinary retention may be produced by the atropine in the formulation, especially in children.

Dose and Administration: *Oral:*

Adult: initially 10 mg followed by 5 mg 6 - 8 hourly until diarrhoea is controlled.

Child: some authorities recommend that it should be avoided in children under 12 years. However, in certain circumstances the following doses have been used: 4 - 8 years, 2.5 mg upto 3 times daily, 9 - 12 years, 2.5 mg upto 4 times daily, 13 - 16 years, 5 mg upto 3 times daily.

Storage: store at room temperature and protect from light.

Loperamide

Capsule, 2 mg

Indications: acute and chronic diarrhoea.

Cautions: dehydration, impaired hepatic function; children and the elderly.

Drug interactions: opioid analgesics, CNS depressants (e.g. alcohol).

Contraindications: pseudomembranous colitis, diarrhoea of infective origin, or severe colitis from inflammatory bowel disease, history of allergic reaction to loperamide

Side effects: abdominal pain, nausea, constipation, dry mouth and blurred vision, CNS reactions such as dizziness, headache and fatigue, hypersensitivity reactions.

Dose and Administration: *Oral:*

Adult:

Acute diarrhoea: initially 4 mg, followed by 2 mg after each loose stool until diarrhoea is controlled; maximum 16 mg/24 hours.

Chronic diarrhoea: usually 4 - 8 mg daily in divided doses.

Child over 2 years: initially 1 mg/12.5 kg body mass, followed by 0.5 mg /12.5 kg after each loose stool. Alternatively, 0.08 - 0.24 mg/kg/day in 2 - 3 divided doses.

Note: If no improvement has been observed after treatment with 16mg daily for at least 10 days, further administration is unlikely to be of benefit.

Storage: store at room temperature.

Oral Rehydration salt

Powder -each sachet for 1 liter contains

Sodium chloride 3.5gm

Trisodium citrate Dihydrate 2.9gm

Potassium chloride 1.5gm

Glucose20.0gm

Indications: replacement of fluid and electrolyte loss in diarrhoea.

Cautions: ORS are not appropriate for patients with gastrointestinal obstruction, inability to drink, oliguric or anuric renal failure, or when parenteral rehydration therapy is indicated as in severe dehydration or intractable vomiting.

Side effects: Vomiting can occur after administration of ORS, the risk of hyponatremia or overhydration after administration of ORS is low in patients with normal renal function. Overdosage in patients with renal impairment may lead to hyponatremia and hyperkalemia.

Dose and Administration: reconstitute one sachet by adding sufficient water to make 1 liter Oral Rehydration Solution. Dose - according to fluid loss, usually 200-400ml solution after every loose motion, child - 200ml after every loose motion, infant 1 - 1½ times usual feed volume.

Storage: at room temperature.

1.7. Antiflatulants

Activated Charcoal

Tablet, 125 mg, 250mg

Indications: flatulence, indigestion and intestinal distention.

Cautions: advise patients not to take other medications orally within two hours of the activated charcoal, except when inactivation of the medication is desired.

Drug interactions: avoid simultaneous use of any other drugs with activated charcoal.

Side effects: vomiting, constipation, and pulmonary aspiration, intestinal obstruction (with multiple dose administration); it colours the stool black.

Dose and Administration: *Orally* with plenty of water chew a tablet every 8 hours daily after meals.

Note: FDA has classified activated charcoal as lacking substantial evidence of efficacy as an antifatulent or digestive aid.

Storage: at room temperature, in airtight containers.

1.8. Digestants

Pancreatic enzymes (as pancreatin or pancrelipase) hydrolyse fats to glycerol and fatty acids, break down protein into peptides, proteoses and derived substances, and convert starch into dextrins and sugars. They are given by mouth in conditions of pancreatic exocrine deficiency such as pancreatitis and cystic fibrosis.

Pancreatin

Tablet, 325 mg

Indications: replacement therapy in symptomatic treatment of malabsorption syndrome due to cystic fibrosis and other conditions associated with exocrine pancreatic insufficiency

Cautions: fibrotic strictures in the colon with high doses, especially in children, nursing women, pregnancy.

Drug interactions: iron, absorption may be decreased.

Contraindications: hypersensitivity to hog protein.

Side effects: diarrhea or other transient intestinal upset, hyperuricosuria and hyperuricemia, hypersensitivity reactions (e.g. sneezing, lacrimation, rash). Retention of pancreatin preparations in the mouth before swallowing may cause irritation of the mucosa and has resulted in ulceration and stomatitis.

Dose and Administration: **Adult:** *Oral:* 1-3 tablets before, during or one hour after meals, with an extra dose taken with any food eaten between meals.

Storage: store at a temperature not exceeding 15°C and in airtight containers.

1.9. Antihaemorrhoidal Agents

Haemorrhoids are enlarged or varicose veins of the tissues at the anus or rectal outlet. They are the most frequent cause of rectal bleeding. Anal and perianal pruritus, soreness and excoriation occur commonly in patient suffering from haemorrhoids, fistulas and proctitis. Careful local toilet with attention to any

minor, faecal soiling, adjustment of the diet to avoid hard stools, the use of bulk forming materials such as bran and a high residue diet are helpful.

Soothing preparations containing mild astringents such as bismuth subgallate, zinc oxide, peru balsam and hamamelis with lubricants, vasoconstrictors or mild antiseptics, in the form of topical ointments, creams and suppositories, are used to provide symptomatic relief. Local anesthetics may be included to relieve pain, and corticosteroids may be used when infection is not present; preparations containing either group of drugs are intended only for short term use after exclusion of infections, such as herpes simplex; prolonged use can cause atrophy of the anal skin.

Haemorrhoids in children are rare. Treatment is usually symptomatic and the use of locally applied cream is appropriate for short periods; however, local anaesthetics can cause stinging initially and this may aggravate the child's fear of defecation.

Bismuth Subgallate Compound (*Bismuth Subgallate + Bismuth Oxide + Peru Balsam + Zinc Oxide*)⁴

Ointment, 2.25% + 0.87% + 1.875% + 10.75%

Suppository, 5mg + 24mg + 49mg + 296mg

Indications: to relieve anal and perianal pain, itching and soreness associated with hemorrhoids, anal fissures.

Cautions: advise patients to regulate their diet to produce soft stools that pass through the anus with a minimum irritation. Patients should be instructed to take hygienic measures after defecation. See also notes above.

Dose and Administration: *Rectally*, wash and dry the anal area before application.

Unless otherwise indicated; Ointment – Apply *rectally* night and morning and after defecation. Suppositories – Insert in to the *rectum* night and morning and after defecation.

Storage: in a cool place.

Bismuth Subgallate Compound With Hydrocortisone (*Bismuth Subgallate + Bismuth Oxide + Peru Balsam + Zinc Oxide + Hydrocortisone acetate + Benzyl Benzoate*)⁴

⁴ Any antihaemorrhoidal preparation proven to be therapeutically effective can be used.

Ointment, 2.25% + 0.875% + 1.875% + 10.75% + 0.25% + 1.25%

Suppository, 59mg + 24mg + 49mg + 296mg + 10mg + 33mg

Indications: same as Bismuth Subgallate Compound, and anal inflammation in the absence of infection, see notes above.

Cautions: Same as Bismuth Subgallate Compound. Avoid this preparation in the presence of an infection in the rectal area.

Contraindications: known hypersensitivity to the preparation, untreated infection.

Side effects: worsening of untreated infection, and thinning of the skin structure on prolonged use.

Dose and Administration: *Rectally.* Wash and dry the rectal area before application.

Unless otherwise indicated, Ointments – Apply rectally night and morning and after defecation. Suppositories – Insert into the rectum night and morning and after defecation.

Storage: in a cool place.

Lidocaine + Aluminium Acetate + Zinc Oxide + Hydrocortisone Acetate⁴

Ointment, 50 mg + 35 mg + 180 mg + 2.5 mg

Suppository, 60 mg + 50 mg + 500 mg + 5 mg.

Indications: for treatment of hemorrhoids. They are suitable for occasional short-term use after exclusion of infection, such as herpes simplex.

Dose and Administration: Ointment – Apply several times daily, short – term use; Suppositories – insert 1 suppository at night and after a bowel movement; short-term use only.

Prednisolone Caproate + Dibucaine Hydrochloride + Hexachlorophene + Clemizole undecenoate⁴

Ointment, 0.19 % + 0.5 % + 0.5 % + 0.5 % + 1 %

Suppository, 1.3 mg + 1 mg + 2.5 mg + 5 mg.

⁴ Any antihemorrhoidal preparation proven to be therapeutically effective can be used.

Indications : short term symptomatic treatment of hemorrhoids.

Tribenoside + Lignocaine

Suppository, 400mg + 40mg

2. CARDIOVASCULAR DRUGS

2.1. Drugs used for Congestive Cardiac failure

Heart failure is a progressively disabling condition associated with considerable morbidity and mortality. Management is aimed therefore not only at providing symptomatic relief, but also at improving prognosis.

Drug therapy of heart failure is based on the use of Angiotensin Converting Enzyme (ACE) inhibitors, diuretics, cardiac glycosides, beta blockers, and vasodilators. Other drugs that may have a role include angiotensin II receptor antagonists and spironolactone.

In addition, any underlying cause of heart failure should be corrected and certain non-pharmacological interventions such as weight reduction and moderate salt restriction may be undertaken.

ACE inhibitors such as captopril, enalapril, fosinopril and lisinopril produce clinical benefit in all stages of chronic heart failure additional to that obtained from diuretics. They relieve symptoms such as dyspnoea and improve exercise tolerance. ACE inhibitors improve survival and reduce the progression of mild or moderate heart failure to more severe stages. ACE inhibitors may also be beneficial in asymptomatic left ventricular dysfunction. ACE inhibitors are recommended in all patients with symptomatic heart failure due to left ventricular systolic dysfunction, including those whose symptoms are controlled with diuretic therapy.

ACE inhibitors all appear to have a similar spectrum of adverse effects although at one time some, such as taste disturbance and skin reactions, were attributed to the presence of a sulphhydryl group (as in captopril) but have now also been reported with ACE inhibitors; however, they may be more common with captopril the most common adverse effects are due to the vascular effects of ACE inhibitors and include hypotension, dizziness, fatigue, headache, and nausea and other gastrointestinal disturbances. Other side effects include persistent cough and other upper respiratory tract symptoms, and angioedema. All ACE inhibitors are contraindicated in pregnancy; in patients with hypersensitivity to ACE inhibitors; in known or suspected renovascular disease; aortic stenosis or outflow tract obstruction.

Diuretics have been the mainstay in the treatment of heart failure. They provide very effective symptomatic control in patients with peripheral or pulmonary oedema and rapidly relieve dyspnoea. If symptoms of fluid retention are only mild, a thiazide diuretic such as hydrochlorthiazide may be adequate. However,

diuretics are not a sufficient treatment on their own as clinical stability tends to deteriorate over time.

Cardiac glycosides the benefit of cardiac glycosides such as digoxin in heart failure accompanied by atrial fibrillation is not disputed although their role in patients with sinus rhythm has been debated. There is evidence that withdrawal of digoxin from patients receiving diuretics or ACE inhibitors carries a considerable risk of clinical deterioration if they are stable on such combination therapy. Digoxin, given in addition to diuretics and ACE inhibitors, improved symptoms but had no effect on mortality. Digoxin may therefore have a role in patients who remain symptomatic despite ACE inhibitors, diuretic, and beta-blocker therapy, and in those unable to tolerate ACE inhibitors.

Beta-blockers have negative inotropic properties and have generally been contraindicated in patients with heart failure. However, persistent activation of the sympathetic nervous system is associated with disease progression and the benefit of beta-blockers such as carvedilol, bisoprolol, and metoprolol in the long-term management of heart failure is now established.

Phosphodiesterase inhibitors have a dual action being both positive inotropes and vasodilators. Although short-term haemodynamic variables are improved, long-term oral use has been associated either with an unacceptable incidence of adverse effects (amrinone) or with an increased mortality rate (milrinone). Thus, these phosphodiesterase inhibitors have been reserved for heart failure unresponsive to other treatment.

Amrinone Lactate

Injection, 5mg/ml in 20ml ampoule.

Indications: infrequently used as a last resort, short-term therapy in patients with intractable heart failure.

Cautions: severe aortic or pulmonic valvular disease.

Drug interactions: diuretics, digitalis.

Contraindications: gastrointestinal disturbances that may necessitate withdrawal of treatment, hypersensitivity reaction to the drug.

Side effects: arrhythmias, hypotension, thrombocytopenia, chest pain, fever, hepatotoxicity, and hypersensitivity.

Dose and Administration: Adult and Child: 0.75 mg/kg *IV bolus* over 2-3 minutes followed by maintenance infusion of 5-10 mcg/kg/minute; *IV bolus* may need to be repeated in 30 minutes.

Storage: store at room temperature and protect from light.

Captopril*Tablet, 12.5 mg, 25 mg, 50 mg, 100 mg***Indications:** treatment of congestive heart failure, management of hypertension, left ventricular dysfunction after myocardial infarction; diabetic nephropathy.**Cautions:** impaired renal function, patient with solitary kidney, collagen-vascular disease, patients receiving immunosuppressants or other drugs that cause leukopenia or agranulocytosis, coronary or cerebrovascular disease, severe salt/volume depletion.**Drug interactions:** potassium-sparing diuretics or potassium supplements (ACE inhibitors are 'potassium-sparing' agents); aspirin, indomethacin and probably other NSAIDs, antacids, digoxin and lithium, probenecid, food decreases absorption-take 30-60 minutes before meals.**Contraindications:** hypersensitivity to ACE inhibitors, drug related, idiopathic or hereditary angioedema; known or suspected venovascular disease; aortic or bilateral renal artery stenosis, outflow tract obstruction; pregnancy.**Side effects:** see notes above; slight increase in heart rate, first dose hypotension, dizziness, fainting; rash (maculopapular or urticarial), pruritus; hyperkalemia, neutropenia, proteinuria, increased serum creatinine, cough, hypersensitivity reactions; altered taste sensation.

Note:-In the treatment of heart failure severe first-dose hypotension on introduction of an ACE inhibitor is common in patients on loop diuretics.

Dose and Administration**Heart failure: Oral: Adult:** initially 6.25 - 12.5 mg 3 times/day in conjunction with cardiac glycoside and diuretic therapy; initial dose depends upon patient's fluid/electrolyte status. The usual maintenance dose is 25mg two or three times daily, and doses should not normally exceed 50 mg three times daily.**Prophylaxis after myocardial infarction (in clinically stable patients): Oral: Adult:** initially 6.25 mg, gradually increased over several weeks to 150 mg daily in divided doses.**Storage:** at room temperature in a tight container.**Captopril + Hydrochlorothiazide***Tablet, 50mg + 25mg***Indications:** treatment of congestive heart failure and management of hypertension.**Cautions, Drug interactions, Contraindications;** see captopril above and hydrochlorothiazide.**Side effects:** peripheral edema, hypotension, skin rash (with or without itching, fever, or joint pain), anaphylactic reactions, angioedema, chest pain, cholecystitis or pancreatitis, hepatic function impairment, hyperuricemia or gout, neutropenia or agranulocytosis, thrombocytopenia, and electrolyte imbalance.**Dose and Administration: Oral: Adult:** one tablet two or three times a day. Daily dose of captopril should not exceed 150mg; daily dose of hydrochlorothiazide should not exceed 50mg.

Digoxin*Tablet, 0.25 mg**Elixir, 0.05 mg/ml**Injection, 0.1 mg/ml in 1 ml ampoule; 0.25 mg/ml in 2 ml ampoule*

Indications: treatment of all degrees of congestive heart failure and supraventricular arrhythmias (particularly atrial fibrillation).

Cautions: patients with recent myocardial infarction, sick sinus syndrome, hypothyroidism, severe pulmonary disease; elderly patients and in patients with renal function impairment where dosage adjustment is necessary; pregnancy and breast-feeding; electrolyte disturbances; Avoid rapid intravenous administration (nausea and risk of arrhythmias)

Drug interactions: amiodarone, beta-adrenergic blocking agents, (including atenolol, carvedilol, metoprolol and propranolol), calcium channel blocking agents, especially verapamil, potassium-depleting diuretics (such as bumetanide, ethacrynic acid, furosemide, indapamide, mannitol, or thiazide), propafenone, quinidine or quinine, sympathomimetics.

Contraindications: hypersensitivity to digoxin or digitoxin, ventricular fibrillations, intermittent complete heart block, second degree AV block, supraventricular arrhythmias caused by wolf – Parkinson white syndrome, hypertrophic obstructive cardiomyopathy toxic effects present from prior administration of any digitalis preparation, ventricular fibrillation.

Side effects: anorexia, nausea, vomiting, lower stomach pain, diarrhea, weakness, blurred or yellow vision, drowsiness, confusion, mental depression, headache and hallucinations, arrhythmias, hypotension, AV block.

Dose and Administration:

Atrial fibrillation: Oral: Adult: 1–1.5 mg in divided doses over 24 hours for rapid digitalization or 0.25mg 1–2 times daily if digitalization less urgent; maintenance 0.0625–0.5 mg daily (higher dose may be divided), according to renal function and heart rate response; usual range 0.125–0.25 mg daily (lower dose more appropriate in elderly)

Emergency control of atrial fibrillation, IV infusion over at least 2 hours: Adult: 0.75–1 mg

Note. Infusion dose may need to be reduced if digoxin or other cardiac glycoside given in previous 2 weeks

Storage: at room temperature in a tight container, protect from freezing.

Enalaprilat*Injection, 1.25 mg/ml***Indications:** see under Enalapril Maleate

Note: Enalaprilat is an active metabolite of Enalapril and which is recommended when oral therapy is impractical. Enalaprilat is not absorbed by mouth but is given by intravenous injection; its haemodynamic effect develop with in 15 minutes of injection and reach a peak in 1 to 4 hours.

Cautions, Drug interactions, Contraindications, Side effects: see under captopril and notes above.

Dose and Administration:

Note: for the management of heart failure, Enalapril is usually given orally as Enalapril maleate.

Avoid I.V administration in patients with unstable heart failure or those suffering acute myocardial infarction

Storage: at room temperature.

Enalapril Maleate*Tablet, 2.5 mg, 5 mg, 10 mg, 20 mg, 40 mg.*

Indications: congestive heart failure, essential and renovascular hypertension; prevention of symptomatic heart failure and prevention of coronary ischemic events in patients with left ventricular dysfunction.

Cautions, Drug interactions, Contraindications and Side effects see under captopril and notes above

Dose and Administration: Adult: Oral:

Congestive heart failure: initially 2.5mg once or twice a day, usual maintenance dose 5 - 20 mg per day, as a single dose or in two divided doses (maximum 40 mg/day).

Left ventricular dysfunction, asymptomatic: 2.5 mg two times a day titrated as tolerated up to a target dose of 20 mg a day in divided doses.

Note: -The haemodynamic effects are seen with in 1 hour of a single oral dose and the maximum effect occurs after about 4-6 hours.

Storage: at room temperature in a well-closed container.

Enalapril Maleate + Hydrochlorothiazide*Tablet, 10 mg + 25 mg***Indications:** see under Enalapril maleate

Cautions, Drug interactions, Contraindications; see captopril above and hydrochlorothiazide.

Side effects: see notes above; chest pain, cholecystitis or pancreatitis, hepatic function impairment, hyperuricemia or gout, neutropenia or agranulocytosis, thrombocytopenia, and electrolyte imbalance.

Dose and Administration: Oral:

Congestive heart failure or Antihypertensive:

Adult: 1 tablet once or twice per day, as determined by individual titration with the component agents, for a maximum of 20 mg of Enalapril and 50 mg of Hydrochlorothiazide.

Child: as determined by individual titration with the component agents.

Enalapril: *Oral*, initially 0.1 mg per kg of body weight per day, the dosage being adjusted as needed and tolerated, up to a maximum of 0.5 mg per Kg of body weight per day.

Hydrochlorothiazide: *Oral*, 1 to 2 mg per kg of body weight or 30 to 60 mg per square meter of body surface per day, as a single dose or in two divided doses, the dosage being adjusted according to response.

Fosinopril

Tablet, 10mg, 20mg

Indications: treatment of congestive heart failure, left ventricular dysfunction after myocardial infarction.

Cautions, Drug interactions, Contraindications, Side effects; see notes above and under Captopril.

Dose and Administration: *Oral: Adult:*

Heart failure: initial: 10mg/day (5mg if renal dysfunction present) and increase, as needed, to a maximum of 40mg once daily over several weeks; usual dose: 20-40mg/day.

Storage: store at room temperature in a well-closed container.

Lisinopril

Tablet 2.5 mg, 5 mg, 10 mg, 20 mg

Indications: congestive heart failure, essential and renovascular hypertension; following myocardial infarction in haemodynamically stable patients, treatment of left ventricular dysfunction after myocardial infarction.

Cautions, Drug interactions, Contraindications, Side effects; see notes above and under Captopril.

Dose and Administrations:

Congestive heart failure: Adult: Oral: initially 5 mg per day under close medical supervision, usual maintenance dose of 5 - 20 mg daily.

Note: - An initial dose of 2.5 mg per day should be used in patients with hyponatremia or who have moderate to severe renal impairment.

Prophylaxis after myocardial infarction, systolic blood pressure over 120 mmHg, 5 mg with in 24 hours, followed by further 5 mg 24 hours later, then 10 mg after a further 24 hours, and continuing with 10 mg once daily for 6 weeks (or continued if heart failure); systolic blood pressure 100 - 120 mmHg, initially 2.5 mg, increasing to maintenance dose of 5 mg once daily.

Storage: at room temperature in a well-closed container.

2.2. Antiarrhythmics

Agents used in the management of cardiac arrhythmias form of a diverse group of drugs. Many of them, such as beta blockers, digoxin, lignocaine, magnesium and phenytoin have important actions in addition to their antiarrhythmic properties and thus, as well as being employed in the treatment of cardiac arrhythmias, have a wide range of other clinical applications.

Management of arrhythmias

In general, drug therapy of serious arrhythmias is unsatisfactory and dangerous. Antiarrhythmics may suppress arrhythmias successfully but paradoxically increase mortality. Cardiac arrhythmias can range from little more than asymptomatic ECG abnormalities through to severe or life-threatening events. In general, pharmacological therapy, particularly chronic therapy, should be instituted only for haemodynamically important, sustained arrhythmias after a search for and correction of any simple precipitating factors and consideration of alternative treatment (e.g. catheter ablation, implantable cardioverter defibrillator). The inappropriate use of an antiarrhythmic for a specific arrhythmia can not only be ineffective but, in view of the proarrhythmic potential of most of them, may even be deleterious.

Antiarrhythmics classes

Class I includes drugs, which directly interfere with depolarization of the cell membrane (membrane-stabilising drugs) by blocking the fast inward current of sodium into cardiac cells; they also have local anaesthetic properties.

Class Ia agents, which prolong action potential duration (APD) and include procainamide, disopyramide and quinidine.

Class Ib agents, shorten APD, includes lidocaine (lignocaine), mexiletine.

Class Ic agents do not affect APD, which include propafenone and flecainide. This class of drugs are not readily available in Ethiopia.

Although they are effective antiarrhythmics, the use of many of the class I agents is associated with an increased mortality (compared with placebo).

Class II agents are characterized by beta-blocking activity, leading to a reduction in heart rate, myocardial contractility, and the rate of conduction of impulses through the conducting system, and include propranolol, bretylium and others.

Class III includes those agents which prolong the duration of cardiac action potential, e.g. amiodarone and sotalol.

Class IV agents block the slow inward calcium channel of the SA and AV nodes, e.g. Adenosine, verapamil and diltiazem.

Adenosine

Injection 3mg/ml

Indications: conversion to sinus rhythm of paroxysmal supraventricular tachycardia.

Cautions: asthmatics.

Drug interactions: carbamazepine, dipyridamole, theophylline and caffeine.

Contraindications: sick sinus syndrome and AV block (in the absence of a pacemaker); known hypersensitivity to adenosine.

Side effects: bradycardia, prolonged hypotension, chest, joint and arm pain, dyspnoea, facial flushing, headache, cough and dizziness.

Dose and Administration: Adult: *IV* bolus always be followed by rapid saline flush. *IV*, 6mg over 1-2 seconds. If ineffective after 1-2 minutes give 12 mg

rapidly IV. If still no response after a further 2 minutes give another 12mg rapidly IV. Additional or higher doses are not recommended.

Child: IV: 0.05 mg/kg. Dose may be increased by 0.05mg/kg every 2 minutes up to a maximum dose of 0.25mg/kg.

Storage: store at controlled room temperature.

Amiodarone

Tablet, 100mg, 200 mg, 400mg

Injection, 50mg/ml

Indications: prophylaxis and treatment of supraventricular and ventricular arrhythmias.

Cautions: heart failure and impaired liver function, avoid exposure to sunlight.

Drug interactions: amiodarone may interact with other drugs for months after treatment is discontinued. It concentrates in the liver and may interfere with the hepatic metabolism of many drugs. Oral anticoagulants, other antiarrhythmics, digoxin, phenytoin; beta blockers, cimetidine and ritonavir.

Contraindications: unstable atrioventricular block, sinus bradycardia and sinoatrial block (unless functioning pacemaker is in position); hyperthyroidism, sensitivity to iodine; and added risk of torsades de pointes, e.g. associated hypokalaemia or pre-existing therapy with class Ia agents or sotalol; severe hypotension or severe respiratory failure.

Side effects: frequent - hyper- or hypothyroidism, neurotoxicity (including peripheral neuropathies), photosensitivity, headache, nausea, vomiting, anorexia, constipation, fatigue and dizziness. Less frequent - pulmonary fibrosis, interstitial or hypersensitivity pneumonitis (include cough, dyspnoea and slight fever), skin discoloration, ocular toxicity, arrhythmias, bradycardia, congestive cardiac failure.

Dose and Administration: Adult: *Oral:* 200 mg 3 times daily for the first week; the dose is gradually reduced at weekly intervals to the minimum required to control arrhythmias usually 200 mg daily (200mg on alternate day may be sufficient).

If rapid control of life-threatening ventricular arrhythmias is needed, loading with 1600 mg daily (400 mg 4 times daily) at the same time as IV infusion, can be used.

IV, slow infusion via a central line, 5mg/kg over 20-120 minutes. Maximum 1.2g in 24 hours.

In acute resuscitation, slow IV boluses of 150mg may be given.

Storage: store at room temperature; protect from light.

Bretylium Tosylate

Injection, 50 mg/ml in 2 ml ampoule

Indications: short term prophylaxis and treatment of ventricular fibrillation and other ventricular arrhythmias.

Cautions: impaired renal function, patients with fixed cardiac output, e.g. severe aortic stenosis or pulmonary hypertension, sinus bradycardia, digitalis induced arrhythmias.

Drug interactions: catecholamines, digoxine, erythromycin, class Ia and class III antiarrhythmics, specific quinolones.

Contraindications: hypersensitivity to bretylium.

Side effects: hypotension, a transient initial increase in blood pressure and heart rate, a worsening of cardiac arrhythmias, nausea and vomiting, increased frequency of pulmonary ventricular contractions, respiratory depression, exacerbation of digitalis-induced arrhythmias.

Dose and Administration: **Adult:** *IM or slow IV injection:* 5 to 10 mg per kg body weight; the intravenous dose may be repeated in 1 to 2 hours if the arrhythmia persists, and subsequently given every 6 to 8 hours; the intramuscular dose may also be given every 6 to 8 hours.

Storage: store at room temperature

Isoproterenol

Injection, 0.02mg/ml, 0.2mg/ml

Indications: ventricular arrhythmias due to AV nodal block; hemodynamically compromised bradyarrhythmias or atropine- and dopamine-resistant bradyarrhythmias (when transcutaneous/venous pacing is not available); temporary use in third-degree AV block until pacemaker insertion.

Cautions: elderly, diabetics, renal or cardiovascular disease, seizure disorder or hyperthyroidism.

Drug interactions: sympathomimetic agents, general anesthetics.

Contraindications: hypersensitivity, angina, pre-existing cardiac arrhythmias, tachycardia.

Side effects: bradycardia, tachycardia, headache, nervousness, nausea, vomiting, dyspnea.

Dose and Administration: *I.V: Cardiac arrhythmias:*

Adult: Initial: 2mcg/minute; titrate to patient response (2-10mcg/minute)

Child: Initial: 0.1mcg/kg/minute (usual effective dose 0.2-2mcg/kg/minute)

Storage: store at room temperature.

Lidocaine hydrochloride

Injection, 5 mg/ml, 10 mg/ml, 20 mg/ml in 20 ml

Indications: ventricular arrhythmias occurring during acute myocardial infarction, cardiac catheterization and those caused by digitalis intoxication; local anaesthesia (see section 5.4).

Cautions: lower dosage in congestive heart failure, bradycardia, renal & hepatic impairment, marked hypoxia, severe respiratory depression, following cardiac surgery and in elderly.

Drug interactions: other antiarrhythmics, anticonvulsants, cimetidine, beta-blockers.

Contraindications: sino-atrial disorder, any grade of atrioventricular block or any other type of conduction disturbances, severe myocardial depression, acute porphyria or hypovolaemia, history of hypersensitivity to amide type local anesthetics; pregnancy & children-safe use is not established.

Side effects: dizziness, paraesthesia, drowsiness, confusion, apnoea, respiratory depression, coma, seizures, and convulsions, hypotension, arrhythmias, heart block, cardiovascular collapse and brady cardia (may lead to cardiac arrest), nystagmus often an early sign of lidocaine overdosage.

Dose and Administration: *Antiarrhythmic:*

Adult: *slow IV*, initially 50-100mg (1mg/kg) repeated at 5-minute intervals, if required, to a total of 200-300mg; thereafter 1-3 mg/minute by IV infusion for 24-30 hours.

Child: usual loading dose 0.5-1mg/kg. continuous IV infusion (usually after loading dose) 0.02-0.05mg (20-50mcg)/kg/minute.

Storage: store at room temperature.

Metoprolol

Injection, 1 mg/ml

Tablet, 50 mg, 100 mg, 200 mg (s/r.)

Indications: hypertension, angina pectoris, cardiac arrhythmias, and myocardial infarction.

Cautions, Drug interactions, Contraindications, Side effects and Storage; see under propranolol.

Dose and Administration:

Adult: *Cardiac arrhythmias*

Oral: 50mg two or three times daily, increase if necessary up to 300mg daily in divided doses.

IV infusion: initial dose; 5mg at a rate of 1 to 2 mg/minute; repeat if necessary at intervals of 5 minutes to a total dose of 10 to 15mg. Maintenance dose; 50mg three times daily by *mouth* 4 to 6 hours after intravenous therapy.

Note: Do not crush or chew extended release tablets.

Storage: at room temperature

Mexiletin Hydrochloride

Capsules, 50 mg, 200 mg

Injection, 25 mg/ml, in 10 ml ampoule

Indications: ventricular arrhythmias, prevention of recurrent cardiac arrests, suppression of paroxysmal ventricular contractions.

Cautions: patients with sinus node dysfunction, conduction defect, bradycardia, hypotension, cardiogenic shock, or cardiac or hepatic failure.

Drug interactions: opioid analgesics, atropine, phenytoin, rifampicin, cimetidine, lignocaine, phenobarbital.

Contraindications: hypersensitivity to mexiletin.

Side effects: nausea, vomiting, heart burn, tremor, confusion, dizziness, and visual disturbances, hypotension, sinus bradycardia, conduction defects and exacerbation of arrhythmias.

Dose and Administration: Adult:

Oral: initially, 400 mg (loading dose) followed after 2 hours by 200 mg 3 - 4 times daily.

IV injection: 100 to 250 mg at a rate of 25 mg per minute, followed by an infusion at a rate of 250 mg over 1 hour, 250 mg over the next 2 hours, and then at about 0.5 mg per minute for maintenance, according to patient response.

Storage: store in airtight containers.

Phenytoin

Powder for injection, 250mg in vial

Phenytoin is primarily used for its antiepileptic activity. It has limited indications in the treatment of arrhythmias such as those induced by digoxin toxicity, ventricular arrhythmias which may occur after congenital heart- defect surgery, and it may be effective in the congenital prolonged QT syndrome, when beta blockade alone has failed. (See section 4.4).

Procainamide hydrochloride

Tablet, 250 mg,

Injection, 100 mg/ml, 10-ml ampoule

Indications: severe ventricular arrhythmias, especially those resistant to lidocaine or those appearing after myocardial infarction; atrial tachycardia, atrial fibrillation; maintenance of sinus rhythm after cardioversion of atrial fibrillation.

Cautions: elderly, renal and hepatic impairment, asthma, pregnancy; breastfeeding.

Drug interactions: other antiarrhythmics, anticholinergics, cimetidine, trimethoprim.

Contraindications: asymptomatic ventricular premature contractions, torsades de pointes, systemic lupus erythematosus, heart block, hypotension, myasthenia gravis, heart failure, digoxin toxicity.

Side effects: nausea, vomiting, diarrhoea, anorexia, severe hypotension, ventricular fibrillation, pericarditis, rashes, pruritus, urticaria, flushing, fever, and angioedema, depression, dizziness, and psychosis; blood disorders include leukopenia, haemolytic anemia and agranulocytosis after prolonged treatment; lupus erythematosus-like syndrome.

Dose and Administration: *Adult: Ventricular arrhythmias:*

Oral: up to 50 mg/kg daily in divided doses every 3 - 6 hours. Atrial arrhythmias higher doses may be required

IV injection: 25-50 mg over one-minute period then repeated every 5 minutes until the arrhythmia is controlled, hypotension results, or the QRS complex is prolonged more than 50%.

Child: *Oral:* 40-60 mg/kg/day divided every 4-6 hours. *I.V:* 3-6 mg/kg every 10-30 minutes (maximum 100mg/dose, then 0.02-0.08 mg/kg/minutes)

Storage: store in airtight containers and at room temperature. Protect from light.

Propranolol

Injection, 1 mg/ml in 1 ml ampoule

Tablet, 10 mg, 40 mg

Indications: cardiac arrhythmia, myocardial infarction, angina pectoris, hypertension, adjunct in the management of thyrotoxicosis, migraine prophylaxis.

Cautions: peripheral arterial insufficiency, first degree atrioventricular block, major surgery, renal & hepatic impairment, diabetes, myasthenia gravis, pregnancy. Avoid abrupt withdrawal.

Drug interactions: chlorpromazine, phenothiazines, thioxanthenes, lidocaine, cimetidine, hepatic enzyme inducers, (barbiturates, phenytoin, rifampicin), non-steroidal anti-inflammatory agents, digoxin, verapamil, neuromuscular blocking agents, anaesthetic agents, insulin or oral antidiabetic agents.

Contraindications: -asthma or bronchospasm, or those with a history of obstructive airways disease, cardiogenic shock, sinus bradycardia, 2nd or 3rd degree heart block, uncontrolled heart failure, patients with phaeochromocytoma should not receive beta blockers without concomitant alpha-adrenoceptor blocking therapy.

Side effects: heart failure, heart block, hypotension, bronchospasm, fatigue and coldness of the extremities, headache depression, dizziness, confusion and sleep disturbances, dry mouth, nausea, vomiting, diarrhea, impotence or decreased libido.

Dose and Administration: *Tachyarrhythmias:*

Oral: Adult: 10-30mg/dose every 6-8 hours.

Child: Initial: 0.5-1mg/kg/day in divided doses every 6-8 hours; titrate dosage upward every 3-7 days; usual dose: 2-6mg/kg/day; higher doses may be needed; do not exceed 16mg/kg/day or 60mg/day.

IV: Adult: 1mg/dose *slow IV injection*; repeat every 5 minutes up to a total of 5mg.

Child: 0.01-0.1mg/kg/dose *slow IV injection* over 10 minutes; maximum dose: 1mg for infants; 3mg for children.

Storage: store at room temperature.

Quinidine sulphate

Tablet, 200 mg

Indications: suppression of supraventricular arrhythmias and ventricular arrhythmias; maintenance of sinus rhythm after cardioversion of atrial fibrillation, atrial or ventricular premature contraction.

Cautions: partial heart block or uncompensated heart failure, myasthenia gravis; acute infections or fever (symptoms may mask hypersensitivity reaction to quinidine); breastfeeding, elderly, liver or renal disease.

Drug interactions: digoxin, amiodarone, rifampicin, Phenobarbital & phenytoin, nelfinavir & ritonavir, sodium bicarbonate, carbonic anhydrase inhibitors, other antiarrhythmics, phenothiazines, anticholinergics, reserpine, and anticonvulsants.

Contraindications: complete heart block, digitalis overdose.

Side effects: the elderly are particularly susceptible to adverse nervous system effects and diarrhea, abdominal cramps, bitter taste, nausea and vomiting. Hypersensitivity reactions may occur - monitor patient after first dose. Acute

hypotension, cinchonism and, in severe toxicity, photophobia, confusion, systemic lupus erythematosus and psychosis may occur.

Dose and Administration:

Adult: *Oral:*

Initial test dose of 200 mg to detect hypersensitivity to quinidine

Arrhythmias: 200 - 400 mg 3 - 4 times daily, increased if necessary in supraventricular tachycardia to 600 mg every 2 - 4 hours (Maximum 3 - 4 g daily); frequent ECG monitoring required.

Storage: store at room temperature and protect from light.

Sotalol

Tablet, 80mg, 120mg, 160mg, 240mg

Indications: treatment of ventricular arrhythmias.

Contraindications: bronchial asthma; sinus bradycardia; second and third degree AV block, cardiogenic shock, uncontrolled congestive heart failure.

Dose and Administration: **Adult:** *Oral:* Initial: 80mg twice daily. Dose may be increased gradually to 240-320 mg/day;

Verapamil Hydrochloride

Tablets, 40 mg, 80 mg, 120 mg

Injection, 2.5 mg/ml in 2 ml ampoule

Indications: Angina, paroxysmal supraventricular arrhythmias, atrial fibrillation and hypertension.

Cautions: first-degree atrioventricular block; acute phase of myocardial infarction; renal and hepatic impairment; children, pregnancy, breast-feeding, muscular dystrophy, aortic stenosis

Drug interactions: beta blocking-agents; antiarrhythmics, other highly protein-bound agents, carbamazepine, grape fruit juice, digoxin, lithium & cyclosporine and calcium salts.

Contraindications: hypotension, bradycardia, second and third degree atrioventricular block, sinoatrial block, sick sinus syndrome; cardiogenic shock, history of heart failure or significantly impaired left ventricular function, atrial flutter or fibrillation complicating Wolf- parkinson- white syndrome.

Side effects: frequent constipation, arising from IV administration-serious cardiovascular reactions, including severe hypotension, bradycardia, AV block, asystole, congestive heart failure and pulmonary oedema. Other less frequent effects include elevation of liver enzymes, nausea, headache, dizziness and fatigue. Facial flushing, gynaecomastia, and gastrointestinal bleeding occur rarely

Dose and Administration:

Adult: *arrhythmias:*

Oral: 80 - 120 mg 3 times daily (upto a total daily dose of 480mg); doses should be individualized. During chronic therapy, twice daily dosage should be adequate.

IV: initially 5mg, followed by 5-10mg after 10minutes if needed; *IV infusion,* initial rates 0.0001-0.005 mg/kg/minute, increase as required.

Child: *IV:* < 1year, 0.1-0.2 mg/kg; 1-15 years, 0.1-0.3 mg/kg (maximum 5mg). May be repeated once after 30 minutes if the response is inadequate.

Storage: store at room temperature; protect from light.

2.3. Antilipemic agents

Antilipemic agents are used to modify blood lipid concentrations in the management of hyperlipidaemias and for the reduction of cardiovascular risk. The principal groups of lipid regulating drugs are the statins, fibrates, bile-acid binding resins, nicotinate, and omega-3-triglycerides.

The **statins** are inhibitors of 3-hydroxy-3-methyl glutaryl co enzyme A (HMG-CoA) reductase, the rate determining enzyme for cholesterol synthesis. These agents include simvastatin, pravastatin, atorvastatin, fluvastatin and lovastatin. They are potent reducers of plasma LDL cholesterol and triglyceride. They are indicated in severe hypercholesterolaemia, and may also be effective in some cases of mixed hyperlipidaemia and even in mild hypertriglyceridaemia. They are regarded as the drugs of choice for the management of most dyslipidaemias. The commonest side effects of therapy with statins are gastrointestinal disturbances. Myalgia, muscle enzyme release, or both has been reported, especially in patients taking statins concurrently with ciclosporin, fibric acid derivatives, or nicotinic acid.

Fibrates inhibit the synthesis of cholesterol and bile acids, and enhance the secretion of cholesterol in bile. These agents include gemfibrozil, clofibrate, bezafibrate and fenofibrate. The main effect is to reduce triglycerides by reducing the concentration of VLDL; they also increase HDL-cholesterol and have variable effects on LDL-cholesterol. They are used mainly in patients with hypertriglyceridaemia. The most common side effects of fibrate therapy are gastrointestinal disturbances including anorexia, nausea, and gastric discomfort. Fibrate therapy may be associated with myositis, myopathy, rarely rhabdomyolysis and gallstones.

Bile-acid binding agents such as **cholestyramine** are basic anion-exchange resins that bind bile acids in the gut, preventing their enterohepatic recycling and causing the hepatocyte to upregulate LDL receptors to obtain cholesterol for compensatory increases in bile acid synthesis. It is not absorbed and is effectively and safely combined with other agents in the treatment of hypercholesterolaemia.

As cholestyramine reduces absorption, other medication should be taken at least an hour before, or delayed for at least four hours after administration of the resin.

Atorvastatin

Tablet, 10 mg

Indications: an adjunct to dietary therapy for reduction of raised cholesterol, LDL cholesterol and triglyceride levels.

Cautions, Drug interactions, Contraindications, Side effects and Storage; see under simvastatin.

Dose and Administration: **Adult:** *Oral:* initially 10 mg daily, adjusted according to response at intervals of at least 4 weeks. Maximum 40 mg/day. 80 mg may be used in homozygous familial hypercholesterolaemia.

Cholestyramine

Powder, anhydrous cholestyramine, 4 g/sachet.

Indications: hypercholesterolaemia, also used in pruritus associated with bile acid retention, and bile salt diarrhoea.

Cautions: patients with constipation and phenylketoneuria, risk of vitamin deficiencies in prolonged use.

Drug interactions: fat-soluble vitamins, warfarin, digoxin, thiazides, barbiturates, aspirin, tetracyclines and thyroxine.

Contraindications: complete biliary and bowel obstruction, active peptic ulcer disease; sensitivity to tartrazine.

Side effects: frequently unpalatable or associated with bloated feeling, nausea, vomiting, constipation occurs frequently, headache and dizziness (< 1%). May aggravate hypertriglyceridaemia; see also notes above.

Note: constipation, most common side effect of cholestyramine, may be countered by increased fiber and water intake

Dose and Administration: *Oral:*

Adult: Initially 4g once or twice daily in water or other beverage, increased gradually over 3- 4 weeks to 12-24 g (of active ingredient) daily in up to 4 divided doses with liquid. Maximum 24 g/day.

Child: over 6 years, 240 mg/kg/day in divided doses has been suggested.

Storage: store in airtight containers and at room temperature.

Ezetimibe

Tablet, 10mg

Indications: primary hypercholesterolaemia, alone or with an HMG-CoA reductase inhibitor, as an adjunct to diet; homozygous familial hypercholesterolaemia, combined with an HMG-CoA reductase inhibitor.

Drug interactions: cholestyramine, ciclosporine

Contraindications: moderate to severe hepatic impairment; children under 10 years of age.

Side effects: Common - headache, abdominal pain and diarrhoea, rash & angioedema. Also, when combined with a statin, constipation, flatulence, nausea, increased ALT/AST, myalgia and rhabdomyolysis.

Dose and Administration: **Adult:** *Oral:* 10 mg daily. Children: ≥ 10 years, 10 mg daily.

Fluvastatin*Capsule, 20mg, 40mg**Tablet, 80mg*

Indications: to be used as a component of multiple risk factor intervention in patients at risk for atherosclerosis vascular disease due to hypercholesterolemia.

Cautions: previous, liver disease or heavy ethanol use. Treatment in patients < 18 years of age is not recommended.

Drug interactions: cimetidine, omeprazole, ranitidine and ritonavir, erythromycin, gemfibrozil, digoxin, amiodarone, fluoxetine, phenytoin, warfarin and others.

Contraindications: hypersensitivity reaction, active liver disease, unexplained persistent elevations of serum transaminases, pregnancy, breast-feeding.

Side effects: headache, fatigue, insomnia, dyspepsia, diarrhea, abdominal pain, nausea, urinary tract infection, myalgia, sinusitis, bronchitis.

Dose and Administration: Adult: Oral:

Patients requiring $\geq 25\%$ decrease in LDL-C: 40mg capsule or 80mg extended release tablet once daily in the evening; may also use 40mg capsule twice daily
Patients requiring < 25% decrease in LDL-C: 20mg capsule once daily in the evening.

Note: Dosing range: 20-80 mg/day; adjust dose based on response to therapy; maximum response occurs within 4-6 weeks.

Storage: store at 25°C. Protect from light.

Gemfibrozil*Capsule, 300 mg*

Indications: treatment of hypertriglyceridemia in WHO types IV and V hyperlipidemia for patients who are at great risk for pancreatitis and who have not responded to dietary interventions.

Cautions: hyperthyroidism, gall bladder disorders, peptic ulcer, hyperalbuminaemic states and cardiovascular disease.

Drug interactions: warfarin, HMG CoA reductase inhibitors, phenytoin, sulphonylureas, and cholestyramine.

Contraindications: hypersensitivity to fibrates; renal or hepatic failure; primary biliary cirrhosis; gallstones.

Side effects: gastrointestinal disturbances, myalgia/myositis like syndrome, eczema, rash headache, dizziness, blurred vision; transient leucopenia may occur; see also notes above.

Dose and Administration: Adult: Oral: Initially 300 mg twice daily, increased to 600 mg twice daily, 30 minutes before the morning and evening meals. Dosage range, 0.9-1.5 g daily in 2 divided doses.

Storage: store in airtight containers and at room temperature.

Lovastatin*Tablet, 20 mg*

Indications: treatment of hypercholesterolaemia particularly in type IIa and IIb hyperlipoproteinaemias.

Cautions, Drug interactions, Contraindications, Side effects and Storage; see under simvastatin.

Dose and Administration: Adult: *Oral:* an initial dose of 10 to 20 mg daily in the evening with food, increased, if necessary, at intervals of 4 weeks or more to 80 mg daily in single or divided doses. In patients taking immunosuppressant drugs an initial dose of 10 mg daily is recommended; the daily dose should not exceed 20 mg.

Simvastatin

Tablets, 5mg, 10 mg, 20 mg, 40 mg

Indications: lowering LDL and total cholesterol in dyslipidaemias where this is the major problems; type IIa and IIb hyperlipidaemia of any cause, especially heterozygous familial hypercholesterolemia; coronary heart disease (reduction of risk of cardiovascular events).

Cautions: hepatic disease or elevated serum transaminases.

Drug interactions: alcohol, warfarin, cholestyramine, digoxin, drug which inhibit cytochrome P450 isoenzyme 3A4 (cyclosporin, macrolides, azoles, protease inhibitor; they increase risk of myopathy), fibrates, nicotinic acid, propranolol.

Contraindications: known hypersensitivity to the drug; active liver disease or unexplained persistently raised serum-aminotransferase concentrations, pregnancy.

Side effects: abdominal pain, constipation, diarrhea, flatulence, nausea, dyspepsia; myalgia associated with muscle stiffness or weakness, or elevations of creatine kinase; plasma transaminase elevation; headache, insomnia, skin rash, peripheral neuropathy and a hypersensitivity syndrome with angioedema. Rhabdomyolysis with renal failure has occurred. Incidence and severity of myopathy are increased by drug interactions-see above.

Dose and Administration: Adult: *Oral:* initially 10mg at night, adjusted, if required, at intervals of 4 weeks or more. Maximum 80 mg/day. Severe renal impairment (creatinine clearance <30 ml/min): 10 mg/day. If higher doses are necessary, implement with caution.

Storage: store in well-closed, light -resistant containers at 5 – 30°C.

2.4. Drugs used for angina /ischemic heart disease

Angina pectoris is a syndrome that arises from reduced myocardial oxygen supply. The prominent symptom is transient precordial distress ranging from discomfort to severe pain. The three main types of angina are: stable angina; unstable angina, and Prinzmetal's angina. These should not be regarded as discrete groups as more than one type is usually present in the patient with angina.

Treatment depends on the type of angina and includes drug therapy (nitrates, beta blockers and calcium channel blockers), percutaneous coronary interventions, and coronary artery bypass surgery. Antithrombotics are used in unstable angina and include anticoagulants and antiplatelets.

Glyceryl trinitrate and other organic nitrates have a vasodilator effect with venodilatation predominating over dilatation of the arterioles and they have a useful role in angina.

Sublingual Glyceryl trinitrate is one of the most effective drugs for providing rapid symptomatic relief of angina, but its effect lasts only for 20 to 30 minutes. Duration of action may be prolonged by modified - release and transdermal preparations (but tolerance may develop)

A sublingual tablet of isosorbide dinitrate is more stable in storage than glyceryl trinitrate and is useful in patients who require nitrates infrequently; it has a slower onset of action, but effects persist for several hours.

Beta-blockers, such as atenolol, block beta-adrenergic receptors in the heart, and thereby decrease heart rate and myocardial contractility and oxygen consumption, particularly during exercise. Beta-blockers are first-line therapy for patients with effort-induced chronic stable angina; they improve exercise tolerance, relieve symptoms, reduce the severity and frequency of angina attacks, and increase the anginal threshold.

Beta-blockers should be withdrawn gradually to avoid precipitating an anginal attack; they should not be used in patients with underlying coronary vasospasm (prinzmetal angina). The different beta-blockers appear to be equally effective in stable angina, although it has been suggested that those with intrinsic sympathomimetic activity should be avoided.

A calcium-channel blocker, such as verapamil, is used as an alternative, particularly in patients unable to tolerate beta-blockers. Calcium-channel blockers interfere with the inward movement of calcium ions through the slow channels in heart and vascular smooth muscle cell membranes, leading to relaxation of vascular smooth muscle. Calcium-channel blockers are used to improve exercise tolerance in patients with chronic stable angina due to coronary atherosclerosis or with abnormally small coronary arteries and limited vasodilator reserve. They can also be used in patients with unstable angina with a vasospastic origin, such as Prinzmetal angina, and in patients in whom alterations in cardiac tone may influence the angina threshold. Care is required in selecting an appropriate drug since the properties of dihydropyridine calcium-channel blockers (such as nifedipine) and rate-limiting calcium channel blockers (diltiazem and verapamil) are not the same. Studies comparing long-acting calcium-channel blockers (verapamil or modified-release nifedipine) with beta-blockers have shown similar outcomes in terms of symptom control and cardiovascular events. However, dihydropyridines may cause tachycardia and are less suitable than rate limiting calcium-channel blockers for monotherapy; they should not be used with out beta-blockers in unstable angina. Short-acting preparations of nifedipine have been associated with increased mortality and are not recommended.

Atenolol

Tablets, 50 mg, 100 mg

Indications: hypertension, angina, and arrhythmias.

Cautions, Drug interactions, Contraindications, Side effects; see section 2.2 under propranolol.

Dose and Administration: *Oral: Angina:*

Adult: 50 mg once daily, increased if necessary to 50 mg twice daily or 100 mg once daily.

Child: 0.8-1.5 mg/kg/day (maximum 2 mg/kg/day)

Storage: store at room temperature and protect from light.

Diltiazem Hydrochloride

Tablets, 60 mg, 90 mg, 120 mg, 90 mg (s/r), 120 mg (s/r)

Indications: angina (including Prinzmetal's angina), hypertension, supraventricular arrhythmias.

Cautions, Drug interactions, Containdications and Side effects; see section 2.2 under verapamil

Dose and Administration: *Oral: Adult:*

Angina: Immediate release: usual starting dose: 30mg 4 times/day; usual range: 180-360 mg/day in divided doses

Extended release: 180mg once daily; may increase at 7-14 day intervals (maximum recommended dose: 360mg/day).

Note: Do not crush long acting dosage forms.

Storage: store at room temperature.

Glyceryl trinitrate (Nitroglycerine)

Tablet (sublingual), 0.3mg, 0.5 mg, 0.4mg, 0.6mg

Tablet (Sustained released), 2.5 mg

Capsule (extended release), 2.5 mg, 6.5mg, 9mg

IV infusion, 0.1mg/ml, 0.2mg/ml, 0.4mg/ml

Injection, 5mg/ml

Spray, 0.4mg/dose

Patch, 0.1mg/hr, 0.2mg/hr, 0.4mg/hr

Ointment, 2%

Indications: prophylaxis and treatment of angina.

Cautions: severe hepatic or renal impairment; hypothyroidism, malnutrition, or hypothermia, recent history of myocardial infarction; conditions that cause dry mouth.

Drug interactions: alcohol, antihypertensive, vasodilators and sildenafil.

Contraindications: hypersensitivity to nitrates; hypertensive conditions and hypovolaemia; hypertrophic obstructive cardiomyopathy, aortic stenosis, cardiac tamponade, constrictive pericarditis, mitral stenosis; marked anaemia, head trauma, cerebral haemorrhage, closed - angle glaucoma.

Side effects: Flushing of the face, dizziness, tachycardia, and throbbing headache. Large doses cause vomiting, restlessness, blurred vision, hypotension (which can be severe), syncope and rarely cyanosis, and methaemoglobinaemia; impairment of respiration and bradycardia may ensue. Contact dermatitis (topical glyceryl trinitrate preparations), localized burning sensation (sublingual tablets). Tolerance may develop from uninterrupted, repeated use.

Note: tolerance may be managed by nitrate withdrawal (12-36 hours) and reinstitution with the same agent. Doses may need to be reviewed as tolerance develops.

Dose and Administrations: Adult:

Sublingual: 0.3 - 0.6 mg repeated at five-minute intervals for the maximum of 3 doses in 15 minutes, may also use prophylactically 5-10 minutes prior to activities which may provoke an attack

Oral: 2.5-9mg 2-4 times/day (up to 26 mg 4 times/day)

Ointment: topical to the skin, 15 to 30 mg of nitroglycerin (contained in 2.5 to 5cm [1 to 2 inches] of ointment as squeezed from the tube) every eight hours during the day and at bedtime. If angina occurs between doses, frequency of application may be increased to every six hours.

Buccal: Initial: 1mg every 3-5 hours while awake (3times/day); titrate dosage upward if angina occurs with tablet in place

IV: 5mcg/minute, increase by 5mcg/minute every 3-5 minutes to 20mcg/minute; if no response at 20mcg/minute increase by 10mcg/minute every 3-5 minutes, up to 200mcg/minute.

Patch, transdermal: initial: 0.2-0.4 mg/hour, titrate to doses of 0.4-0.8mg/hour.

Spray: 1-2 sprays into mouth under tongue every 3-5 minutes for maximum of three doses in 15 minutes

Dosage has not been established for pediatric use.

Note:

Sublingual tablet

- Instruct patient to sit or lie down upon first indication of incoming angina pain and to place tablet under tongue or in buccal pouch (hypotensive effect of drug is intensified in the upright position).
- Instruct patient to allow tablet to dissolve naturally and not to swallow until drug is entirely dissolved. Advise patient with dry mouth to take a sip of water or place 1ml saline under the tongue before taking the nitroglycerin tablet.

Sustained-release tablet or capsule

- Take on an empty stomach (1 hour before or 2 hours after meals), with a full glass of water, and swallowes whole.
- Sustained release form helps to prevent anginal attack, it is not intended for immediate relief of angina.
- Do not crush or chew

Transdermal ointment

Ointment is applied in a thin, even layer covering an area of the same size (measuring at least 2 by 3 inches) at each use, but it is not to be rubbed or massaged into the skin. The site of ointment application may be the non-hairy skin of the chest, stomach, front of the thighs, or any other accessible areas of clean, dry skin. Application to the chest is commonly preferred since the patient also benefits psychologically from applying medication to the area where the pain is experienced. Keep ointment container tightly closed and store in cool place

Storage: nitroglycerin tablets for sublingual use may easily lose half their potency in 24 hours if stored incorrectly.

- Tablets should be kept in the original container, which should be kept tightly closed and closed immediately after use.
- Patients should keep the container in a cool place, e.g. handbag or outer clothing pocket.
- Discard 60 days after opening.
- No more than 100 tablets should be dispensed at one time

Isosorbide dinitrate

Sublingual tablets, 5 mg, 10 mg

Indications: relief of acute anginal attacks and for management of long-term angina pectoris; congestive cardiac failure.

Cautions, Drug interactions, Contraindications and Side effects; see under glyceryl trinitrate.

Note: as with other long acting nitrates, tolerance develops rapidly.

Dose and Administration: Adult: *Sublingually:*

Angina (acute attack): 2.5 - 10 mg, if relief is not attained after a single dose, additional doses may be given at 5-10 minute intervals; no more than 3 doses should be given in a 15-30 minute period.

Angina prophylaxis: 2.5 - 10 mg 4-6 hourly.

Congestive cardiac failure: 40mg 4 times daily. However, as 6 hourly administrations may promote tolerance, 12 hourly dosage is preferable, alternatively dosing with a nitrate-free night restores tolerance.

Storage: store at room temperature.

Isosorbide mononitrate

Tablet, 10mg, 20mg, 25mg(m/r), 40mg(m/r), 60mg(f/c,m/r)

Capsule, 40mg(m/r), 50mg(m/r)

Dose and Administration: Adult: *Oral:* 20mg 8-12 hourly. 20-120mg/day in divided doses has been used.

Metoprolol

Injection, 1mg/ml

Tablets, 50mg, 100 mg, 200mg(s/r)

Indications, Cautions, Drug interactions, Contraindications, Side effects and Storage; see section 2.2, under metoprolol.

Dose and Administration: *Oral: Angina:* 50-100mg 2-3 times daily.

Nifedipine

Capsule, 5 mg, 10 mg 20 mg

Capsule (m/r), 30 mg

Tablet, 10 mg

Tablet (m/r), 10mg, 20 mg, 30 mg, 40 mg, 60 mg, 90 mg.

Indications: angina pectoris, hypertension (sustained release only).

Cautions, Drug interactions, Contraindications and Side effects; see section 2.5. under Nifedipine.

Dose and Administration: *Oral: Adult:*

Slow release preparation: 10 to 40mg twice daily or 30-90mg once daily, depending on the preparation.

Note: it should be swallowed whole with liquid. Once daily formulations should be taken at the same time each day, i.e. approximately 24 hourly; twice daily formulations approximately 12 hourly and dosage interval not less than 4 hours.

Short-acting preparations (not recommended)

Storage: store at room temperature.

Pentaerythritol Tetranitrate

Capsule, 80 mg

Tablet, 10 mg, 20 mg

Indications: angina pectoris.

Dose and Administration: *Oral: Adult:* up to 240mg daily, in divided doses, before a meal.

Propranolol

Tablet, 10 mg, 40 mg

Indications, Cautions, Drug interactions, Contraindications, Side effects and

Storage; see section 2.2 under propranolol.

Dose and Administration: Adult: Oral:

Angina: initially 20 - 40 mg twice daily, increasing gradually to 120 - 360 mg/day in 2 divided doses. A twice - daily dose of 80 mg (or 160 mg once daily of a long-acting preparation) may be adequate.

2.5. Antihypertensives

Management of hypertension

Since treatment for hypertension is often life-long, it is important to integrate the treatment of hypertension into an overall program of management of associated risk factors and conditions, particularly in elderly patients who often have multiple associated disorders.

Mild hypertension is defined as 140 - 159 mmHg systolic blood pressure and 90-99 mmHg diastolic blood pressure. Moderate hypertension 160 - 180 mmHg systolic and 100 - 109 mmHg diastolic and severe hypertension more than 180 mmHg systolic and more than 110 mmHg diastolic.

Lifestyle changes should introduce for all patients; they include weight reduction, reduction in alcohol intake, reduction of dietary sodium, stopping tobacco smoking, and reduction in saturated fat intake. The patient should eat a healthy nutritious diet including adequate fruit and vegetables and should exercise regularly. These measures alone may be sufficient in mild hypertension with no target organ damage, but patients with moderate to severe hypertension will also require specific antihypertensive therapy.

Drug treatment of hypertension

The goal of treatment is to obtain the maximum tolerated reduction in blood pressure.

Five classes of drug are used for first - line treatment of hypertension: Diuretics, Beta - adrenoceptor antagonists (beta blockers), Angiotensin - converting enzyme (ACE) inhibitors, calcium- channel blockers and alpha -adrenoceptor blocking drugs (alpha blockers). All five classes are effective in reducing blood pressure; thiazide diuretics and beta-blockers have been shown to reduce mortality due to cardiovascular complications of hypertension other classes of drugs may be used in certain situations.

Thiazide diuretics, such as Hydrochlorothiazide have been used as first-line antihypertensive therapy and are particularly indicated in the elderly. They have few adverse effects in low doses, but in large doses they may cause a variety of unwanted metabolic effects (principally potassium depletion), reduced glucose tolerance, ventricular ectopic beats and impotence; they should be avoided in gout. These effects can be reduced by keeping the dose as low as possible; higher doses do not produce an increased reduction in blood pressure. Thiazides are inexpensive and when used in combination, can enhance the effectiveness of many other classes of antihypertensive drug.

Beta adrenoceptor antagonist (beta-blockers) such as propranolol are effective in all grades of hypertension, and are particularly useful in angina and following myocardial infarction; they should be avoided in asthma, chronic obstructive pulmonary disease, and heart block.

Angiotensin - converting enzyme inhibitors (ACE inhibitors) such as captopril are effective and well tolerated by most patients (see also section 2.1). They can be used in heart failure, left ventricular dysfunction and diabetic nephropathy, but should be avoided in renovascular disease and in pregnancy. The most common adverse effect is a dry persistent cough.

Calcium Channel blockers such as Nifedipine are effective antihypertensives. Particularly for isolated systolic hypertension and in the elderly when thiazides

cannot be used. Short acting formulations of nifedipine should be avoided as they may evoke reflex tachycardia and cause large variations in blood pressure.

Alpha-adrenoceptor blocking drugs (alpha-blockers) such as prazosin are effective in lowering blood pressure but remain too expensive to be considered as first line therapy in many countries. They are particularly useful in prostatism, but should be avoided in urinary incontinence. They are usually used in combination with other antihypertensives, the first dose being given at bedtime, as profound hypotension may occur.

Drugs acting on the Central nervous system are also effective antihypertensive drugs. In particular, methyldopa is effective in the treatment of hypertension in pregnancy, and may also be used in asthma and heart failure. Reserpine is also used because of its effectiveness and low cost. It should be used in combination with diuretics and prescribed in much lower doses than were formerly used.

Combining antihypertensive drugs often produces a beneficial additive effect.

Hypertension in pregnancy

Drug therapy for chronic hypertension during pregnancy remains controversial. If diastolic blood pressure is greater than 95 mmHg. Methyldopa is the safer drug. Beta-blockers should be used with caution in early pregnancy. Since they may retard fetal growth they are effective and safe in the third trimester. ACE inhibitors are contraindicated in pregnancy since they may damage fetal and neonatal blood pressure control and renal function. Women who are taking these drugs and become pregnant should have their antihypertensive therapy changed immediately.

Pre-eclampsia and eclampsia. If pre-eclampsia or severe hypertension occurs beyond the 36th week of pregnancy, delivery is the treatment of choice. For acute severe hypertension in pre-eclampsia or eclampsia, intravenous hydralazine can be used.

Amiloride and Hydrochlorthiazide

Tablet, 2.5mg + 25 mg, 5mg + 50mg

Oral solution, 5mg+50mg/5ml

Indications: hypertension, especially when a potassium-sparing diuretic effect is desired.

Cautions: possibility of hypokalemia or hyperkalemia.

Drug interactions: chlorpropamide, carbenoxolone, see also hydrochlorthiazide.

Side effects: hyponatraemia, constipation, allergic reactions, cholecystitis or pancreatitis, gout or hyperuricemia, hepatic function impairment, thrombocytopenia.

Dose and Administration: *Oral: Adult:* start with 5mg+50mg per day, then may be increased to 10mg+100mg per day if needed; usually given in a single dose.

Storage: at room temperature.

Amlodipine Besilate

Tablet 2.5 mg, 5 mg, 10 mg

Indications: hypertension and angina pectoris.

Cautions, Drug interactions, Contraindications, Side effects; see under Nifedipine below.

Dose and Administration:

Hypertension: Oral: Adult: Initial dose 2.5 mg twice daily (1.25 mg twice daily in elderly, hepatic or renal impairment): increased if necessary after 3 - 4 weeks to 5 mg twice daily (exceptionally up to 10 mg twice daily); maintenance 2.5 or 5 mg once daily may be sufficient

Storage: at room temperature in a tight, light resistant container.

Candesartan

Tablet, 4mg, 8mg, 16mg

Indications: alone or in combination with other antihypertensive agents in treating essential hypertension.

Cautions: pre-existing renal insufficiency.

Drug interactions: concurrent use with potassium sparing diuretics (amiloride, spironolactone, triamterene), trimethoprim, avoid garlic.

Contraindications: hypersensitivity to candesartan; bilateral renal artery stenosis; pregnancy (2nd and 3rd trimesters)

Side effects: worsening of renal function in patients dependent on rennin-angiotensin-aldosterone system. tachycardia, dizziness, lightheadedness, drowsiness, headache, anxiety, depression, somnolence, fever, rash, hyperglycemia, hyperuricemia, dyspepsia, gastroenteritis, hematuria, dyspnea, pharyngitis, and epistaxis.

Dose and Administration: *Hypertension: Oral: Adult:*

usual dose is 14-32 mg once daily; dosage must be individualized. Blood pressure response is dose-related over the range of 2-32mg. The usual recommended starting dose of 16mg once daily when it is used as monotherapy in patients who are not volume depleted. It can be administered once or twice daily with total daily doses ranging from 8-32 mg. Larger doses do not appear to have a greater effect and there is relatively little experience with such doses.

Candesartan and Hydrochlorothiazide

Tablet, 16mg+ 12.5mg

Indications: treatment of hypertension; combination product should not be used for initial therapy.

Dose and Administration: *Oral: Adult: replacement therapy:* Combination product can be substituted for individual agents; maximum therapeutic effect would be expected within 4 weeks

Usual dosage range:

Candesartan: 8-32 mg/day, given once daily or twice daily in divided doses

Hydrochlorothiazide: 12.5-50mg once daily.

Captopril

Tablet 12.5 mg, 25 mg, 50 mg, 100 mg

Indications, Cautions, Drug interactions, Contraindications, Side effect; see section 2.1 and notes above

Dose and Administrations:

Hypertension: Oral: Adult: initially 12.5 mg twice daily, increased gradually at intervals of 2 to 4 weeks according to the response; usual maintenance dose 25 mg twice daily; maximum 50 mg twice daily (rarely 3 times daily in severe hypertension)

Captopril + Hydrochlorthiazide

Tablet, 50 + 25 mg

See section 2.1.under Captopril + Hydrochlorthiazide

Carvedilol

Tablet, 3.125 mg, 6.25 mg, 12.5 mg, 25 mg

Indications: hypertension; mild to moderate congestive heart failure as an adjunct to standard therapy.

Cautions: sinus bradycardia and partial heart block.

Drug interactions: as for other beta-blockers.

Contraindications: as for other beta-blockers, hepatic impairment.

Side effects: as for other beta-blockers; see atenolol, liver function abnormalities.

Dose and Administration: *Hypertension: Oral:*

Adult: Initially 12.5 mg once daily, increased after 2 days to 25 mg once daily; may be increased at intervals of at least 2 weeks up to a maximum of 50mg/day in single or divided doses.

Elderly: 12.5mg once daily, titrated at intervals of at least 2 weeks upto 25mg/day.

Storage: store at room temperature.

Clonidine Hydrochloride

Injection, 0.15 mg/ml in 1 ml ampoule

Tablet, 0.025 mg, 0.15 mg

Indications: management of mild to moderate hypertension either used alone or in combination with other antihypertensives.

Cautions: cardiovascular disease, ischaemic heart disease including myocardial infarction, renal impairment, occlusive peripheral vascular disorders such as raynaud's disease, or those with a history of depression; gradual withdrawal is needed.

Note:- it causes drowsiness and patients should not drive or operate machinery where loss of attention could be dangerous. IV injection of clonidine should be given slowly. Patients should be warned of the risk of missing a dose or stopping the drug as sudden discontinuation may cause rebound hypertension.

Drug interactions: Alcohol and other CNS depressants, tricyclic antidepressants, opiate analgesics, beta-blockers.

Contraindications: hypersensitivity to clonidine or any component of the formulation.

Side effects: drowsiness, dry mouth, dizziness, and headache, constipation, depression, anxiety, fatigue, nausea, anorexia, parotid pain, sleep disturbances, vivid dreams, impotence, loss of libido, urinary retention or incontinence, slight orthostatic hypotension, and itching, or burning sensation in the eye, fluid retention, and sudden withdrawal of clonidine may produce rebound hypertension.

Dose and Administration:

Hypertension: Oral

Adult: initial dose: 0.1 mg twice daily (maximum recommended dose: 2.4mg/day); usual dose range: 0.1-0.8mg/day in 2 divided doses.

Child: initial dose: 5-10 mcg/kg/day in divided doses every 8-12 hours, increase gradually at 5 to 7 day interval to 25 mcg/kg/day in divided doses every 6 hours, maximum: 0.9mg/day.

Acute Hypertension Urgency: Oral

Adult: initial dose 0.1-0.2 mg; may be followed by additional doses of 0.1mg every hour, if necessary, to a maximum total dose of 0.6mg.

Storage: at room temperature in tightly closed container.

Diazoxide

Injection, 15 mg/ml in 20 ml ampoule

Indications: hypertensive crisis, commonly used with a diuretic such as furosemide.

Caution: impaired cardiac or cerebral circulation and in patients with aortic coarctation, arteriovenous shunt, heart failure; impaired renal function, diabetes mellitus; during labour, history of gout, uremia.

Drug interactions: hyperglycaemic, hyperuricaemic, other antihypertensive or vasodilators; phenytoin.

Contraindications: hypersensitivity to diazoxide or to other thiazides, cerebral bleeding, eclampsia.

Side effects: hypotension, hyperglycaemia, heart failure, nausea, anorexia, and other gastrointestinal disturbances, mild hyperuricaemia, extrapyramidal symptoms, eosinophilia, dizziness, tinnitus and blurred vision; hypersensitivity reaction such as rashes, leucopenia, & fever.

Dose and Administration: *IV: Adult and Child:*

1-3 mg/kg up to a maximum of 150mg in a single injection; repeat dose in 5-15 minutes until blood pressure adequately reduced; repeat administration at intervals of 4-24 hours; monitor the blood pressure closely; do not use longer than 10 days.

Enalaprilat

Injection, 1.25 mg/ml

Indications, Cautions, Drug interactions, Contraindications, Side effects and Storage; see section 2.1 under Enalaprilat and notes above.

Dose and Administration: *Hypertension: I.V: Adult:* (over at least five minutes), 1.25 mg every six hours.

Enalapril Maleate

Tablet, 2.5mg, 5mg, 10mg, 20mg, 40mg

Indications, Cautions, Drug interactions, Contraindications, Side effects and Storage; see section 2.1 under Enalapril maleate and notes above.

Dose and Administrations: *Hypertension: Oral: Adult:*

Used alone, initially 5 mg once daily. If used in addition to diuretic in elderly patients, or in renal impairment, initially 2.5 mg daily, usual maintenance dose 10 mg - 20 mg once daily, in severe hypertension may be increased to maximum 40 mg once daily.

Enalapril Maleate and Hydrochlorothiazide

Tablet, 10 mg + 25 mg

See section 2.1 under Enalapril Maleate and Hydrochlorothiazide and notes above.

Felodipine

Tablet, 5 mg, 10 mg

Indications: hypertension, prophylaxis of angina.

Cautions, Drug interactions, Contraindications, Side effects; see under Nifedipine

Dose and Administrations:

Hypertension: Oral: Adult: initially 5 mg (elderly 2.5 mg) daily in the morning; usual maintenance dose 2.5 - 10 mg once daily; doses above 20 mg daily rarely needed

Storage: store below 30°C in a tight container - protect from light.

Fosinopril

Tablet, 10mg, 20mg

Indications: treatment of hypertension, either alone or in combination with other antihypertensive agents.

Cautions, Drug interactions, Contraindications, Side effects; see under captopril.

Dose and Administration: *Oral:*

Adult: initial: 10mg/day; usual maintenance 20- 40mg/day.

Child > 50kg: initial: 5-10mg once daily.

Hydralazine

Tablet, 25 mg, 50 mg

Injection, 20 mg /ml in 1 ml ampoule

Indications: moderate to severe hypertension (low doses used in combination therapy, especially with beta blockers).

Cautions: pregnancy, breast-feeding, in elderly patients, in patients with hepatic or renal impairment, with coronary artery disease.

Drug interactions: other antihypertensive drugs, nitrates, diazoxide.

Contraindications: coronary artery disease, rheumatic heart disease (mitral valvular), cerebrovascular disease or accident, idiopathic systemic lupus erythematosus, severe tachycardia, high output heart failure, myocardial insufficiency due to mechanical obstruction.

Side effects: tachycardia, palpitations, nausea, vomiting, diarrhoea, anorexia, fluid retention, headache, systemic lupus erythematosus like syndrome, fever, changes in blood count, peripheral neuritis.

Dose and Administration:

Hypertension: Oral: 25mg twice daily, increased to a maximum of 50mg twice daily.

Hypertensive crisis: slow IV injection: 5-10mg over 20 minutes; may be repeated after 20-30 minutes. *IV infusion:* initially 200-300 microgram/minute; Maintenance usually 50-150 mcg/minute.

Storage: at room temperature. Protect from freezing.

Irbesartan

Tablet, 75mg, 150mg

Indications: treatment of hypertension alone or in combination with other antihypertensives.

Cautions: safety and efficacy have not been established for pediatric patients < 6 years of age.

Drug interactions: potassium salts, co-trimoxazole, ACE inhibitors, potassium sparing diuretics, amiodarone, fluoxetine, glipizide, phenytoin, rosiglitazone, warfarin, sertraline.

Contraindications: bilateral renal stenosis, pregnancy (2nd and 3rd trimesters)

Dose and Administration: *Oral: Adult and Child* ≥ 13 years: 150 mg once daily; patients may be titrated to 300 mg once daily.

Child ≥ 6-12 years: 75mg once daily.

Storage: store at room temperature.

Isradipine

Tablet, 2.5 mg

Indications: treatment of hypertension.

Cautions, Drug interactions, Contraindication, Side effects; see under Nifedipine.

Dose and Administration: *Mild to moderate hypertension: Oral:*

Adult: 2.5 mg twice daily; may be increased after 4 weeks up to 5 mg twice daily. Hepatic or renal function impairment, and the elderly; initially 1.25 mg twice daily.

Labetalol

Tablets, 50 mg, 100 mg, 200 mg, 400 mg

Indications: treatment of mild to severe hypertension.

Cautions: as for other beta-blockers, and also, hepatic disease or treated heart failure.

Drug interactions: alcohol and anaesthetics; agents inhibiting or inducing liver enzymes, other antihypertensives.

Contraindications: second or third degree atrioventricular block, symptomatic heart failure, sinus bradycardia, or cardiogenic shock; asthma, severe bronchospasm, history of allergy.

Side effects: as for beta blockers; and it has also alpha blocking activity which contributes to its adverse effects such as orthostatic hypotension, impaired male sexual function to a greater extent than with beta blockade alone; muscle weakness, tremor, urinary retention, hepatitis and jaundice.

Dose and Administration: Adult: Oral: initially 100 - 200 mg twice daily, increased gradually if necessary to 300-600 mg/day; up to maximum of 2400 mg/day in severe hypertension in two to four divided doses.

Elderly: initial dose of 50mg twice daily.

Storage: store at room temperature.

Lisinopril

Tablet 2.5 mg, 5 mg, 10 mg, 20 mg

Indications, Cautions, Drug interactions, Contraindications, Side effects and

Storage; see section 2.1 and notes above

Dose and Administration:

Hypertension, initially 2.5 mg daily including patients with renal impairment, the elderly or those who receiving a diuretic; if possible, the diuretic should be withdrawn 2 or 3 days before Lisinopril is started and resumed later if required and usual maintenance dose 10 - 20 mg daily, maximum 40 mg daily.

Lisinopril and Hydrochlorothiazide

Tablet, 10mg + 12.5mg

Indications: treatment of hypertension

Dose and Administration: **Adult:** *Oral:* Dosage is individualized; doses > 80mg/day lisinopril or > 50mg/day hydrochlorothiazide are not recommended.

Losartan

Tablet, 25mg, 50mg, 100mg

Indications: treatment of hypertension.

Drug interactions: potassium sparing diuretics or potassium supplements.

Contraindications: bilateral renal stenosis, pregnancy (2nd and 3rd trimesters)

Side effects: dizziness, headache, skin rash, urticaria, cough, myalgia, GI effect, angio edema, hyperkalaemia.

Dose and Administration: *Oral:*

Adult: usual starting dose: 50 mg once daily; can be administered once or twice daily with total daily doses ranging from 25-100mg.

Child 6-16 years: 0.7mg/kg once daily (maximum: 50mg/day)

Methyldopa

Tablet, 250 mg, 500mg

Indications: hypertension in pregnancy, moderate to severe hypertension.

Cautions: renal or hepatic impairment, or with a history of haemolytic anaemia, liver disease, or depression; Parkinsonism.

Drug interactions: alcohol, CNS depression producing medications, monoamine oxidase inhibitors including furazolidine, paralyline, procarbazine; cocaine, norepinephrine, phenylephrine, anaesthetics, and lithium, diuretics, other antihypertensives, antipsychotics.

Contraindications: depression, active liver disease, pheochromocytoma, haemolytic anemia.

Side effects: dry mouth, sedation, depression, drowsiness, diarrhoea, fluid retention, failure of ejaculation, liver damage, haemolytic anaemia, lupus erythematosus like syndrome, parkinsonism, rashes, nasal stuffiness edema (swelling of feet or lower legs), gynaecomastia.

Dose and Administration: *Oral:*

Adult: 250mg 2-3 times daily gradually increased at intervals of two or more days to maximum daily dose 3gm.

Elderly: 120mg twice daily initially, gradually increased, maximum daily dose 2gm.

Storage: at room temperature.

Metoprolol

Injection, 1mg/ml

Tablets, 50mg, 100 mg, 200mg(s/r)

Indications, Cautions, Drug interactions, Contraindications, Side effects and Storage; see section 2.2 under metoprolol.

Dose and Administration: *Oral:*

Adult: initial dose 100mg daily, increased weekly according to response to 400mg daily. Maintenance dose 100-200mg daily.

Elderly: 25mg daily, usual range 25-300mg/day

Nifedipine*Tablet, 10 mg, 20 mg**Capsule, 5 mg, 10 mg, 20 mg*

Indications: used alone or in combination with other agents for treatment of hypertension and angina pectoris, Raynaud's phenomenon.

Cautions: aortic stenosis or hypertrophic obstructive cardiomyopathy (may worsen cardiac failure or increase outflow track obstruction); angina (may worsen symptoms); nursing mother, renal & hepatic impairment.

Drug interactions: other antihypertensives, beta blockers (use with special caution), digoxin, drugs that inhibit cytochrome P450 3A4 (cimetidine, erythromycin, fluoxetine, protease inhibitors, ketoconazole, itraconazole, fluconazole), drugs that induce cytochrome P450 3A4 (carbamazepine, phenobarbital e.t.c.), rifampicin, tacrolimus, valproic acid.

Contraindications: hypotension, unstable angina or acute myocardial infarction (increased infarct rate and mortality) in the absence of current beta blockade; cardiogenic shock. Avoid sudden withdrawal.

Side effects: peripheral edema (swelling at ankles, feet, or lower legs), dizziness or light – headedness, flushing or feeling of warmth, headache, nausea, congestive heart failure or pulmonary edema (breathing difficulty, coughing, or wheezing), tachycardia, constipation, unusual tiredness or weakness, palpitation, increased frequency of micturation, eye pain, gum hyperplasia, depression.

Dose and Administration: *Oral:*

Adult: 10-20mg three times a day up to 180mg/day or 30-90mg sustained release once per day.

Note:-Short acting preparation is not recommended for the management of hypertension.

Child: dosage has not been established

Storage: store between 15 and 25°C in a tight, light-resistant container.

Phenoxybenzamine Hydrochloride

Capsule, 10 mg

Indications: symptomatic management of pheochromocytoma, treatment of hypertensive crisis caused by sympathomimetic amines.

Cautions: renal impairment, cerebral or coronary arteriosclerosis, elderly, heart failure and ischaemic heart disease, it aggravates the symptoms of respiratory infections.

Drug interactions: beta-blockers, sildenafil, tadalafil, and adrenaline

Contraindications: instances when fall in blood pressure would be dangerous; compensated congestive failure.

Side effects: postural hypotension, tachycardia, shock, headache, confusion, fatigue, dry mouth, dizziness, miosis, nasal congestion, inhibition of ejaculation.

Dose and Administration: *Oral:*

Pheochromocytoma:

Adult: initial: 10mg twice daily, increase by 10mg every other day until optimum dose is achieved; usual range: 20-40mg 2-3 times/day.

Child: initial: 0.2mg/kg (maximum: 10mg) once daily, increase by 0.2mg/kg increments; usual maintenance dose: 0.4-1.2mg/kg/day every 6-8 hours, higher doses may be necessary.

Storage: store at room temperature.

Phentolamine mesylate

Injection, 10 mg/ml in 1ml

Indications: diagnosis of pheochromocytoma and treatment of hypertension associated with pheochromocytoma.

Cautions: gastritis or peptic ulcer.

Drug interactions: adrenaline, ethanol, sildenafil, and tadalafil.

Contraindications: as phenoxybenzamine & also angina pectoris or other evidence of ischemic heart disease.

Side effects: tachycardia, angina pain, arrhythmia, flushing, sweating, feeling of apprehension, orthostatic hypotension, dizziness, nausea, vomiting, diarrhea, nasal congestion, pulmonary hypertension, myocardial infarction & cerebrovascular spasm or occlusion.

Dose and Administration: *Surgery for pheochromocytoma hypertension: IM, IV:*

Adult: 5mg given 1-2 hours before procedure and repeated as needed every 2-4 hours.

Child: 0.05-0.1mg/kg/dose given 1-2 hours before procedure; repeat as needed every 2-4 hours until hypertension is controlled; maximum single dose: 5mg.

Storage: store powder for injection at room temperature. Reconstituted solution is stable for 48 hours at room temperature and 1 week when refrigerated.

Prazosin Hydrochloride

Tablet, 1 mg, 2 mg, 5 mg

Indications: hypertension, hypertension associated with pheochromocytoma.

Cautions: elderly patients, during pregnancy and breastfeeding, angina pectoris, narcolepsy, and in those sensitive to the drug. First dose may cause collapse due

to hypotension (should be taken on retiring to bed); hepatic or renal function impairment; advice patients not to do activities requiring alertness.

Drug interactions: nifedipine, other antihypertensive agents or nitrates, alcohol, beta blockers and calcium channel blockers.

Contraindications: heart failure caused by mechanical obstruction, for example aortic or mitral valve stenosis, pulmonary embolism, and restrictive pericardial disease.

Side effects: dizziness, orthostatic hypotension, edema, palpitations, dry mouth, urinary incontinence, angina, dyspnea, and priapism, drowsiness, headache, lack of energy, and nausea.

Dose and Administration: *Oral:*

Adult: 0.5 mg 2–3 times daily, the initial dose on retiring to bed or night (to avoid collapse) increased to 1 mg 2 – 3 times daily after 3 – 7 doses further increased if necessary to maximum 20 mg daily.

Child (under 7 years of age), initially 0.25 mg 2 – 3 times a day adjusted according to response. 7 to 12 years of age, initially 0.5 mg two or three times a day adjusted according to response.

Storage: at room temperature in a well-closed, light – resistant container.

Propranolol

Tablet, 10mg, 40mg

Injection, 1mg/ml in 1ml ampoule

Indications, Cautions, Drug interactions, Contraindications, Side effects and Storage; see section 2.2 under propranolol.

Dose and Administration: *Hypertension:*

Oral: 80mg twice daily increased at weekly intervals as required, maintenance 160-320mg daily.

IV injection: 1.3mg administered at a rate not to exceed 1mg/minute, repeated after two minutes and again after four hours if necessary (for Antiarrhythmic)

Ramipril

Capsule, 1.25mg, 2.5mg, 5mg, 10mg

Indications: treatment of hypertension, either alone or in combination with other antihypertensive agents.

Contraindications: bilateral renal stenosis, pregnancy (2nd and 3rd trimesters)

Dose and Administration: *Oral: Adult:* 2.5-5mg once daily, maximum: 20mg/day

Reserpine

Tablet, 0.1mg, 0.25mg

Injection, 1mg/ml in 1ml ampoule

Indications: mild to moderate hypertension.

Cautions: debilitated or elderly patients, during breastfeeding, in those patients with cardiac arrhythmias, myocardial infarction, severe cardiac damage, renal insufficiency, gallstones, epilepsy, or allergic conditions such as bronchial asthma.

Note: -Advice patients not to operate machineries or drive vehicles

Drug interactions: diuretic and hypotensive agents, cardiac glycosides or quinidine, monoamine oxidase inhibitors, CNS depressants.

Contraindications: mental depression, active peptic ulcer, with ulcerative colities and in patients receiving electroconvulsive therapy.

Side effects: nasal congestion, CNS symptoms including depression, drowsiness, lethargy, nightmares, diarrhoea, abdominal cramp; nausea, vomiting and anorexia, respiratory distress, cyanosis, breast enlargement and galactorrhoea, gynaecomastia, decreased libido, impotence, sodium retention, oedema, weight gain, miosis, dry mouth, sialorrhoea, dysuria, rashes, thrombocytopenia purpura..

Dose and Administration: *Oral:* **Adult:** initially 0.05 - 0.125mg once daily; this may be increased gradually to an accepted maximum of 0.25mg daily. The lowest effective dose should be used.

Child: 0.005 to 0.02mg per kg of body weight a day in one or two divided daily doses.

Note: - Take with meals or milks.

Storage: at room temperature, in tight, light-resistant containers.

Sodium Nitroprusside

Powder for injection, 50 mg in ampoule.

Indications: hypertensive crisis (when treatment by mouth not possible).

Cautions: impaired pulmonary function; hypothyroidism; renal impairment; ischaemic heart disease; impaired cerebral circulation; hyponatraemia; raised intracranial pressure; elderly; hypothermia; monitor blood pressure and blood-cyanide concentration, also blood –thiocyanate concentration if given for more than 3 days; avoid sudden withdrawal (reduce infusion over 15 - 30 minutes to avoid rebound effects); pregnancy; breast feeding.

Drug interactions: other antihypertensives; acetazolamide, alcohol.

Contraindications: severe hepatic impairment; compensatory hypertension; severe vitamin B12 deficiency; hereditary optic atrophy or increased intracranial pressure

Side effects: nausea and vomiting, headache, apprehension, restlessness, palpitations, dizziness and abdominal pain, convulsions, confusion and hyperreflexia.

Dose and Administration: *Hypertensive crisis: IV infusion:* **Adult:**

Initially 0.3 mcg/kg/minute; usual maintenance dose 0.5 - 6 mcg/kg/minute; maximum dose 8mcg/kg/minutes; stop infusion if no response after 10 minutes at maximum dose. Lower doses in patients already being treated with antihypertensives.

Storage: store at room temperature.

Tolazoline

Injection, 25mg/ml in 10ml ampoule

Indications: persistent pulmonary vasoconstriction and hypertension of the newborn (persistent fetal circulation), peripheral vasospastic disorders.

Caution: mitral stenosis

Note: - pretreatment of infants with antacid may prevent gastrointestinal bleeding

Drug interactions: ischaemic heart disease, hypotension or after a cerebrovascular accident; peptic ulcer disease.

Side effects: piloerection, headache, flushing, tachycardia, cardiac arrhythmias, tingling, chilliness, shivering, sweating, nausea, vomiting, diarrhoea, and epigastric pain, orthostatic hypotension or marked hypertension with large doses; peptic ulcer disease, oliguria, haematuria, myocardial infarction, gastrointestinal haemorrhage, thrombocytopenia and other blood dyscrasias.

Dose and administration:

Adult: *peripheral vasospastic disorder:* IM, IV, SC: 10-50mg 4 times/day.

Neonates: Initial: IV: 1-2mg/kg over 10-15minutes via scalp vein or upper extremity; Maintenance: 1-2mg/kg/hour; use lower maintenance doses in patients with decreased renal function.

Valsartan

Tablet, 40mg, 80mg, 160mg, 320mg

Indications: treatment of hypertension alone or in combination with other antihypertensives. Treatment of heart failure.

Contraindications: bilateral renal stenosis, pregnancy (2nd and 3rd trimesters)

Dose and Administration: *Oral:* **Adult:** Initial: 80 mg once daily; maximum recommended dose: 320mg/day

Heart failure: initial: 40mg twice daily; titrate dose to 80-160 mg twice daily, maximum daily dose 320mg. Note: Do not use with ACE inhibitors and beta blockers.

Verapamil

Tablets, 40 mg, 80 mg, 120 mg

Injection, 2.5 mg/ml

See section 2.2. under Verapamil

2.6. Diuretics

Diuretics promote the excretion of water and electrolytes by the kidneys. They are used in the treatment of heart failure or in hepatic, renal, or pulmonary disease when salt and water retention has resulted in oedema or ascites. Diuretics are also used, either alone, or in association with other agents, in the treatment of hypertension.

Low dose diuretics are recommended first-line therapy in uncomplicated cases of hypertension, especially in black patients and elderly patients with isolated systolic hypertension. High doses are not recommended because of biochemical repercussions, including an adverse lipid profile, hyperuricaemia and impaired glucose control.

The principal groups of diuretics are Low-ceiling diuretics, 'Loop' or 'high-ceiling' diuretics, potassium sparing diuretics, osmotic diuretics, mercurial diuretics and carbonic anhydrase inhibitors.

Low-ceiling diuretics: The thiazides, e.g. hydrochlorothiazide, are used as initial therapy for mild congestive heart failure and mild to moderate hypertension. Low doses are well tested in mild hypertension and in systolic hypertension, and should not exceed 25mg.

The low-ceiling diuretics do not induce a diuresis at low creatinine clearances.

In hypertension, diuretics may be used alone or in combination with potassium-sparing diuretics or other antihypertensive agents.

They are also used for the management of oedema associated with nephritic syndrome, liver cirrhosis (usually preceded by spironolactone) and heart failure, idiopathic hypercalciuria, nephrogenic diabetes insipidus (where they have an antidiuretic effect) and to help prevent osteoporosis.

High-ceiling diuretics: loop diuretics, e.g. furosemide, are used in the initial therapy of severe heart failure. Furosemide is effective in high doses even if there is severe impairment of renal function. Furosemide is similar chemically to the thiazide diuretics. It has prompt onset of diuretic action and acts primarily by inhibiting chloride and sodium reabsorption over the entire length of the thick ascending limb of the loop of henle.

The intravenous route is very fast-acting in emergency situations such as pulmonary oedema. In such circumstances it has an acute haemodynamic effect, i.e. venodilation with reduced venous return.

The oral form may be used for hypertension, either alone or in combination with other antihypertensive agents, but the thiazide-type diuretics are preferred unless there is renal impairment or cardiac failure.

Potassium-sparing diuretics: these include the aldosterone antagonists, e.g. spironolactone, which should only be used where specifically indicated.

Others are amiloride and triamterene. Amiloride inhibits sodium reabsorption in the distal tubule and is a weak diuretic when administered alone. It also has some antihypertensive activity. Its potassium and magnesium-sparing properties are useful if combined with a potassium-depleting diuretic, e.g. hydrochlorothiazide. It is the drug of choice in Liddle's syndrome and is an alternative to spironolactone in patients with primary aldosteronism, who experience adverse effects.

The adverse effect of diuretic therapy are mainly due to the fluid and electrolyte imbalance induced by the drugs. Hyponatraemia is an adverse effect of all diuretics. The risk of hypokalaemia, which may occur with both thiazide and loop diuretics, depends more on the duration of action than on potency and is thus greater with thiazides than with loop diuretics (when given in equipotent doses). Potassium-sparing diuretics can cause hyperkalaemia. Other electrolyte disturbances include hypercalcaemia (thiazides), hypocalcaemia (loop diuretics) and hypomagnesaemia (thiazide and loop diuretics).

Symptoms of fluid and electrolyte imbalance include dry mouth, thirst, gastrointestinal disturbances (including nausea, vomiting), weakness, lethargy, drowsiness, restlessness seizures, confusion, headache, muscle pains or cramps, hypotension (including postural hypotension), oliguria, arrhythmias.

The elderly are more susceptible to electrolyte imbalance than younger patients; treatment should begin with a lower initial dose of the diuretic (commonly about 50 % of the adult dose) and then adjusted carefully according to renal function, plasma electrolytes and diuretic response.

Acetazolamide

Tablet, 250 mg

Capsule (s/r), 500mg

Powder for injection, (sodium), 250mg, 500mg in vial

Indications: *reduction of intra-ocular pressure in open-angle glaucoma, secondary glaucoma, and peri-operatively in angle-closure glaucoma (see section 15.1); diuresis; epilepsy.*

Cautions: elderly; pregnancy; breastfeeding; diabetes; pulmonary obstruction; monitor blood count and electrolytes if used for long periods.

Drug interactions: quinidine, procainamide, mexiletine and TCAs, lithium, diuretics and potassium-depleting agents.

Contraindications: hypersensitivity to sulfonamides; chronic angle-closure glaucoma, hypokalaemia, hyponatraemia, hyperchloraemic acidosis; renal and hepatic impairment.

Side effects: nausea, vomiting, diarrhea, taste disturbance; loss of appetite, paraesthesia, flushing, headache, dizziness, fatigue, irritability, depression; thirst, polyuria; reduced libido; metabolic acidosis and electrolyte disturbances on long-term therapy; occasionally drowsiness, confusion, hearing disturbances, urticaria, melaena, glycosuria, haematuria, abnormal liver function, renal calculi, blood disorders including agranulocytosis and thrombocytopenia, rashes including Stevens-Johnson syndrom and toxic epidermal necrolysis; transient myopia reported.

Dose and Administration:

Edema: Oral, IV: Adult: 250-375mg once daily.

Child: 5mg/kg or 150mg/m² once every day

Epilepsy: Oral: Adult: 8-30mg/kg/day in 1-4 divided doses;

Child: 8-30mg/kg/day in 1-4 divided doses, not to exceed 1 g/day.

Note: sustained release capsule is not recommended for treatment of epilepsy

Storage: store at room temperature.

Amiloride

Tablet, 5mg

Indications: counteracts potassium loss induced by other diuretics in the treatment of hypertension or oedematous conditions including CHF, hepatic cirrhosis, and hypoaldosteronism.

Cautions: diabetes mellitus, elderly, pregnancy and breast-feeding.

Drug interactions: ACE inhibitors, potassium supplements and salt substitutes, NSAIDs.

Contraindications: hyperkalaemia, renal failure, and hypersensitivity; see also Hydrochlorothiazide

Side effects: except for hyperkalaemia serious adverse effects are uncommon; nausea, anorexia, abdominal pain and flatulence, headache, weakness and dizziness. Rarely - visual disturbances, blood dyscrasias, skin rashes, pruritus, bladder spasm, muscle cramps and jaundice.

Dose and Administration: *Edema: Oral:*

Adult: 5-10mg/day (up to 20mg)

Elderly: initial: 5mg once daily or every other day.

Storage: store at room temperature

Amiloride and Hydrochlorthiazide*Oral solution, 5mg + 50mg/5ml**Tablet, 2.5mg + 25mg; 5mg + 50mg*

See section 2.5. under Amiloride and hydrochlorthiazide

Furosemide*Tablet, 40 mg, 80mg**Elixir, 10 mg/ml**Injection, 10 mg/ml in 2 ml ampoule***Indications:** edema of cardiac, hepatic or renal origin, oliguria due to renal failure; mild to moderate hypertension, usually in combinations with other antihypertensive agents and as adjunct in the treatment of hypertensive crisis and for the treatment of hypercalcemia.**Cautions:** children, elderly patients, pregnancy (not used to treat hypertension in pregnancy) and breast feeding; hypotension; correct hypovolaemia before using in oliguria. It may cause hypokalaemia and hyponatraemia, aggravates diabetes mellitus and gout, liver failure, renal impairment, prostatic enlargement, porphyria.**Drug interactions:** antigout, potassium-depleting agents, cephalosporins, NSAIDs, thiazide diuretics.**Contraindications:** patients with precomatose states associated with liver cirrhosis, renal failure with anuria.**Side effects:** hyponatraemia, hypokalaemia, hypomagnesaemia, hypochloreaemic alkalosis, increased calcium excretion, hypotension, less commonly nausea, gastro-intestinal disturbances, hyperuricemia and gout, hyperglycemia, temporary increase in plasma cholesterol and triglyceride concentrations, photosensitivity and bone marrow depression, pancreatitis, tinnitus and deafness, orthostatic hypotension as a result of massive diuresis (dizziness or light-headedness when getting up from sitting position).**Dose and Administration:***Edema: Oral:***Adult:** initially 40 mg daily on rising, maintenance, 20 mg daily or 40 mg on alternate days, may be increased to 80 mg daily in resistant oedema;**Child:** 1 - 3 mg/Kg body weight daily (maximum 40 mg daily).*Acute Pulmonary edema: Slow IV injection:***Adult:** 20-50 mg, if necessary increase by 20 mg steps every 2 hours, if effective single dose is more than 50 mg, consider using slow intravenous infusion at a rate not exceeding 4 mg/minute.**Child:** 0.5-1.5 mg/kg body weight daily (maximum 20 mg daily).*oliguria (glomerular filtration rate less than 20 ml/minute): Slow IV infusion of a rate not exceeding 4mg/minute:***Adult:** initially 250 mg over 1 hour; if urine output not satisfactory during hour after first dose, infuse 500 mg over 2 hours then, if no satisfactory response during hour after second dose, infuse 1 g over 4 hours; if no response after third dose, dialysis probably necessary.*Hypertension:*

Oral: initially 40mg two times a day; the dosage being adjusted according to patient's need.

IV: hypertensive crisis in patients with normal renal function, *IV* 40 to 80mg. *Hypertensive crisis accompanied by pulmonary edema or acute renal failure IV* 100-200 mg.

Antihypercalcemic:

Oral: 120mg a day a single dose or divided into two or three doses;

IM or IV: **Adult**: 80-100mg in severe cases, the dosage being repeated if necessary every one to two hours until the desired response is obtained. In less severe cases smaller doses may be given every two or four hours.

Child: *IM or IV*: 25 to 50mg, the dosage being repeated if necessary every four hours until the desired response is obtained.

Storage: Store at room temperature in a well closed container, protect from freezing and light.

Hydrochlorothiazide

Tablet, 25 mg

Indications: oedema, hypertension and cardiac failure.

Cautions: paediatrics, elderly patients, during pregnancy and breast-feeding, heart failure, aggravates diabetes and gout, and may exacerbate systemic lupus erythematosus, dyslipidaemia.

Drug interactions: lithium, antidiabetic agents, hypotensive agents, NSAIDs, drugs causing potassium depletion, digoxin, cholestyramine.

Contraindications: refractory hypokalaemia, hyponatraemia, hypercalcemia, severe renal and hepatic impairment, and symptomatic hyperuricemia, Addison's disease, anuria.

Side effects: postural hypotension and mild gastrointestinal effects, impotence (reversible), hypokalaemia, hypomagnesaemia, hyponatraemia, hypercalcemia, hypochloreaemic alkalosis, hyperuricemia, gout, hyperglycemia, and increased in plasma cholesterol concentrations, less commonly rashes, photosensitivity, blood disorders (including neutropenia and thrombocytopenia), pancreatitis, intrahepatic cholestasis, hypersensitivity reaction.

Dose and Administration:

Hypertension: *Oral*: **Adult**: 12.5, 25 mg daily; elderly initially 12.5 mg daily.

Edema: *Oral*: **Adult**: initially 25 mg daily on rising increasing to 50 mg daily if necessary, elderly initially 12.5 mg daily.

Severe Oedema in patients unable to tolerate loop diuretics: *Oral*: **Adult**: up to 100 mg either daily or on alternate days (maximum 100 mg daily).

Nephrogenic diabetes insipidus: *Oral*: **Adult**: initially up to 100 mg daily.

Mannitol

Injection, 25 % in 50 ml, 20 % in 250 ml, 10 % in 500 ml

Indications: oliguria due to acute renal failure; reduction of intracranial pressure - cerebral oedema; reduction of intraocular pressure - for angle closure glaucoma.

Cautions: extravasation causes inflammation and thrombophlebitis.

Drug interactions: digitalis glycosides, lithium.

Contraindications: cardiac failure, pulmonary oedema, well established anuria caused by severe renal disease or impaired renal function who do not respond to a test dose, severe dehydration, metabolic edema, intracranial bleeding.

Side effects: chest pain or fast heartbeat, chills or fever, head ache, convulsions, difficulty in urination, electrolyte imbalance (confusion, irregular heartbeat, muscle cramps or pain, numbness, tingling, pain or weakness in hands or feet), pulmonary congestion, thrombophlebitis (redness or swelling or pain at injection site).

Dose and Administrations:

Test dose (to assess adequate renal function), by *intravenous infusion*, as a 20 % solution, 200 mg/kg body weight infused over 3-5 minutes, repeat test dose if urine output less than 30 - 50 ml/hour; if response inadequate after second test dose, re-evaluate patient.

Raised intracranial or intraocular pressure: I.V infusion: as a 20 % solution infused over 30 - 60 minutes, 0.25 - 2g/kg body weight.

Cerebral Oedema: I.V infusion: as a 20 % solution infused rapidly, 1g/kg body weight.

Storage: at room temperature protect from freezing.

Metolazone

Tablet, 2.5 mg, 5 mg, 10 mg

Indications: management of mild to moderate hypertension; treatment of edema in congestive heart failure and nephritic syndrome, impaired renal function.

Cautions: as for Hydrochlorothiazide.

Drug interactions: furosemide, see also under hydrochlorothiazide.

Contraindications: as for hydrochlorothiazide.

Side effects: as for hydrochlorothiazide, and also palpitation, chest pain, and chills.

Dose and Administration: Oral: Adult:

Edema: 5-20mg/dose every 24 hours.

Hypertension: 2.5-5mg/dose every 24 hours.

Storage: store at room temperature.

Spironolactone*Tablet, 25 mg, 100 mg***Indications:** oedema and ascites in cirrhosis of the liver, malignant ascites, nephritic syndrome, congestive heart failure; primary hyperaldosteronism.**Cautions:** renal and hepatic function impairment, diabetes mellitus, pregnancy, breast feeding, elderly, monitor electrolytes (discontinue if hyperkalaemia)**Drug interactions:** Angiotensin - converting enzyme (ACE) inhibitors, cyclosporin, diuretics, potassium containing medications, potassium supplements or substances containing high levels of potassium, lithium, digoxin, NSAIDs, warfarin.**Contraindications:** hyperkalaemia, hyponatraemia, pregnancy and breast-feeding, Addison's disease.**Side effects:** gastro-intestinal disturbances; impotence, gynaecomastia, menstrual irregularities; lethargy, headache, confusion; rashes, hyperkalaemia (discontinue), hyponatraemia, hepatotoxicity, osteomalacia, and blood disorders reported.**Dose and Administration:** *Oral:***Oedema: Adult:** 100 - 200 mg daily, increased if necessary to 400 mg daily in resistant oedema, usual maintenance dose 75 - 200 mg daily,**Child:** initially 3 mg/kg body weight daily in divided doses.**Primarily hyperaldosteronism: Adult:** diagnosis, 400 mg daily for 3 - 4 weeks; preoperative management, 100 - 400 mg daily; if not suitable for surgery, lowest effective dose for long term maintenance.**Adjunct in severe heart failure: Adult:** usually 25 mg daily.

Note: - Take with meals or milk.

Storage: at room temperature in a tight, light - resistant container**2.7. Sclerosing Agents**

Sclerosants are used in the management of varicosities including varicose veins and oesophageal varices when their capacity to damage veins is apparently put to good use. The mechanisms by which injection sclerotherapy works are not completely understood but are thought to involve damage to the intima, intraluminal thrombosis, and intravascular fibrous organisation. Sclerosants used include: ethanolamine oleate, sodium tetradecyl sulphate and sodium morrhuate.

Ethanolamine Oleate*Injection, 5 % in 2 ml ampoule***Indications:** treatment of varicose veins and oesophageal varices.**Cautions:** fatal anaphylactic shock has been reported following administration; use with caution and decrease dose in patients with significant liver dysfunction, with concomitant cardiorespiratory disease, or in the elderly or critically ill.**Contraindications:** varicose veins of the legs in patients with thrombosis or a tendency to thrombosis; acute phlebitis, marked arterial, cardiac, or renal

disease; local or systemic infections; or uncontrolled metabolic disorders such as diabetes mellitus. Known hypersensitivity to the agent or oleic acid.

Side effects: irritant to skin and mucus membranes; local injection may cause sloughing, ulceration, and in severe cases, necrosis and pain may occur at the site of injection. Patients receiving treatment for oesophageal varices may develop pleural effusion or infiltration. Hypersensitivity reactions have been reported.

Dose and Administration: IV: Adult:

Varicose veins: 2 to 5 ml of a 5 % solution of ethanolamine oleate is injected into empty isolated sections of veins, divided between 3 or 4 sites. Injection into full veins is also possible.

Oesophageal varices: 1.5 to 5 ml of a 5 % solution per varix to a maximum total dose of 20 ml per treatment session.

Storage: protect from light.

Morrhuate Sodium

Injection, 5% in 5ml ampoule

Indications: treatment of small, uncomplicated varicose veins of the lower extremities.

Cautions: should only be administered when adequate facilities, drugs (e.g. epinephrine, antihistamines, corticosteroids), and personnel are available for the treatment of anaphylactic reactions.

Contraindications: hypersensitivity reactions to the drug or to the fatty acids of cod liver oil. thrombophlebitis; arterial disease, varicosities caused by abdominal and pelvic tumors, uncontrolled diabetes mellitus, thyrotoxicosis, tuberculosis, neoplasms, asthma, sepsis, blood dyscrasias, acute respiratory or skin diseases; and in bedridden patients.

Side effects: thrombosis, valvular incompetency, vascular collapse, drowsiness, headache, dizziness, urticaria, nausea, vomiting, burning at the site of injection, severe extravasation effects, asthma, anaphylaxis, weakness.

Dose and Administration:

IV: Adult: Small veins: 50-100mg (1-2ml or 5% injection)

Large veins: 150-200 mg (3-5ml or 5% injection)

Storage: store at room temperature and protect from light.

Sodium Tetradecyl Sulphate

Injection, 1 % in 2 ml ampoule, 3 % in 2 ml ampoule and 5 ml vial.

Indications: varicose veins, management of bleeding oesophageal varices.

Cautions, Contraindications and Side effects; as for ethanolamine oleate.

Dose and Administration: IV: Test dose: 0.5ml given several hours prior to administration of larger dose; 0.5-2ml (preferred maximum: 1ml) in each vein, maximum: 10ml per treatment session; 3% solution reserved for large varices.

Storage: store at a temperature not exceeding 25°C. Protect from light.

2.8. Drugs used in vascular shock

Shock is a complex clinical syndrome of multiple aetiologies but the common factor in all types of shock is a failure of the circulatory system to maintain cellular perfusion and function.

Cardiac shock usually results from acute failure of the heart, leading to an inadequate stroke volume and reduced cardiac output. It has a number of causes, but is most commonly associated with acute myocardial infarction.

Successful correction of hypovolaemia may alleviate hypotension in some cases, but cardiac output may remain depressed and signs of impaired organ perfusion may persist, necessitating additional therapy.

In cardiogenic shock cardiac output is usually low but peripheral resistance is high and drugs that have predominantly inotropic effects are most suitable.

Dopamine or dobutamine are often chosen. Dopamine has been widely used in all forms of shock, often in combination with other inotropes. At low doses it causes peripheral vasodilation, which was thought to protect renal perfusion; however, any clinical benefit is unclear and at higher doses it causes vasoconstriction and is useful where hypotension is not significant. Noradrenaline causes peripheral vasoconstriction and should be reserved for severe hypotension. It is particularly useful in septic shock where the cardiac output is usually high but peripheral resistance is low. Adrenaline has also been used alone but renal artery vasoconstriction may limit its use, and it has also been reported to cause lactic acidosis.

In cardiogenic shock associated with myocardial infarction, specific therapy to restore myocardial perfusion is also indicated.

Adrenaline (Epinephrine)

Injection, 0.1 % in 1 ml ampoule

Indications: Anaphylactic shock, cardiac arrest; bronchospasms; open angle (chronic simple) glaucoma; added to local anaesthetics.

Cautions: hyperthyroidism, hypertension, diabetes mellitus, ischaemic heart disease, arrhythmias, cerebrovascular disease, and elderly, cerebral arteriosclerosis, parkinson's , rapid IV infusion may cause death from cerebrovascular hemorrhage or cardiac arrhythmias.

Drug interactions: other sympathomimetic agents (additive effects), alpha-adrenergic blocking agents, anaesthetics (volatile), beta blockers, digoxin, theophylline, tricyclic antidepressants, monoamine oxidase inhibitors.

Contraindications: asymmetric septal hypertrophy, pheochromocytoma, tachyarrhythmias.

Side effects: tachycardia and arrhythmia, hypertension, hypotension, tremor, anxiety, sweating, nausea, vomiting, weakness, dizziness, pulmonary oedema, headache, peripheral vasoconstriction.

Dose and Administration:

The 1:1000 (1mg/ml) concentration of epinephrine injection must be diluted before administering intravenously.

Adult: vasopressor-intravenous infusion, 1mcg per minute. The dose may be titrated up to 2 to 10microgram per minutes for desired hemodynamic response.

Storage: at room temperature. Protect from light and freezing.

Dobutamine

Powder for injection, 250 mg in vial

Indications: inotropic support in cardiogenic shock, acute myocardial infarction, post-cardiac surgery and septic shock after adequate volume replacement; management of refractory cardiac failure.

Cautions: pregnancy, severe hypotension, hypovolaemia should be corrected before treatment.

Drug interactions: beta-blocking agents; anaesthetic agents (eg, halothane); MAO inhibitors.

Contraindications: idiopathic hypertrophic cardiomyopathy with outflow obstruction.

Side effects: palpitations, ectopic heartbeats and, rarely, ventricular tachycardia, angina, increase in systolic blood pressure (10 - 20 mmHg, in most patient, but may be more dramatic, particularly in the presence of preexisting hypertension), nausea, vomiting, headache, paraesthesia and dyspnoea may occur.

Dose and Administration: Adult:

IV infusion: initially, 2.5 - 10 mcg /kg/minute, increasing gradually in increments of 2.5 mcg/kg/minute up to 15 mcg/kg /minute. Usually not > 20 mcg/kg/ minute is needed. May be infused for up to 72 hours, provide the patient is carefully monitored; thereafter intermittently.

Storage: store at room temperature.

Dopamine Hydrochloride

Injection, 40 mg /ml in 5 ml ampoule

Indications: cardiogenic shock in infarction or cardiac surgery, renal failure or septicaemia after adequate volume replacement; short-term management of refractory cardiac failure and treatment of acute hypotension.

Cautions: hypovolaemia; low dose in shock due to acute myocardial infarction, hypoxia, hypercapnia, and metabolic acidosis before or at some time as starting treatment, history of peripheral vascular disease, elderly.

Note:- hypovolaemia should be corrected before dopamine is used in shocked patients.

Drug interactions: halogenated anaesthetics (such as cyclopropane, halothane); monoamine oxidase inhibitors, betablockers, digoxin, ergotamine/ergotamine, tricyclic antidepressants.

Contraindications: tachyarrhythmias, ventricular fibrillation, ischaemic heart disease, Pheochromocytoma; hyperthyroidism.

Side effects: nausea and vomiting, peripheral vasoconstriction, hypotension with dizziness, fainting, flushing, tachycardia, ectopic beats, palpitations, anginal pain; headache dyspnoea, hypertension.

Dose and Administration:

Cardiogenic shock: I.V infusion into large vein: **Adult:** initially 2 - 5 micrograms/Kg/minutes; gradually increased by 5 - 10 micrograms/Kg/minutes according to blood pressure, cardiac output and urine output; seriously ill patients up to 20 - 50 micrograms/Kg minutes.

Child: IV same as for adults.

Storage: at room temperature protect from freezing.

Isoprenaline hydrochloride

Injection, 0.2 mg/ml in 1ml ampoule

Indications: severe bradycardia, unresponsive to atropine; short-term emergency treatment of heart block; ventricular arrhythmias secondary to atrioventricular nodal block.

Cautions, Drug interactions, Contraindications and Side effects; as for adrenaline above.

Dose and Administration:

Adult: Emergency treatment:

Slow IV bolus: 0.01 - 0.06 mg (10 - 60 mcg), with subsequent doses ranging from 0.01 - 0.2 mg.

IV infusion: initially 1 mcg/minute, adjusted according to response.

Child: IM or SC: 0.2 mg as a single dose. **IV:** 0.02 mg as a single dose. *IV infusion:* 0.2 mg (1ml) in 200 ml 5 % dextrose water; rate depends on size of patient and situation.

Storage: store in tight, light-resistant containers.

Levarterenol (Noradrenaline) Tartarate

Injection 8mg/ml in 1ml ampoule

Indications: treatment of shock which persists after adequate fluid volume replacement.

Cautions: never use leg veins for infusion sites, monitor blood pressure closely and adjust infusion rate, hypoxia or hypercapnia.

Drug interactions: tricyclic antidepressants, MAO inhibitors, antihistamines, beta-blockers (nonselective), ergot alkaloids, reserpine, and methyl dopa, alpha-blockers.

Contraindications: hypersensitivity to the drug, pregnancy, during anesthesia with cyclopropane or halothane anesthesia (risk of ventricular arrhythmias)

Side effects: bradycardia, arrhythmia, peripheral ischemia, headache, anxiety, and dyspnea, skin necrosis, respiratory difficulty.

Dose and Administration:

Vasopressor:

Adult: initial, *I.V infusion*, 0.5 to 1mcg (base) per minute; the dosage being adjusted gradually to achieve desired blood pressure. Maintenance: Intravenous infusion, 2 to 12 mcg (base) per minute.

Child: IV, 0.1mcg (base) per kg of body weight per minute; the dosage being adjusted gradually to achieve desired blood pressure, up to 1mcg per kg of body weight per minute.

Note:- Noradrenaline is administered only by intravenous infusion. Subcutaneous or intramuscular administration is not recommended because of the potent vasoconstrictor effect of norepinephrine.

Storage: store at room temperature.

Phenylephrine Hydrochloride

Injection, 10 mg/ml in 1 ml ampoule

Indications: treatment of vascular failure, unresponsive to adequate fluid volume replacement, in shock, shock like states, drug induced hypotension, or hypersensitivity.

Cautions: late pregnancy and during labour, diabetes mellitus, cerebral arteriosclerosis, bradycardia, elderly patients.

Drug interactions: alpha adrenergic blocking agents such as labetalol; phenoxy benzamine; phentolamine; prazosin, anaesthetics, tricyclic antidepressant, ergotamine, B-blockers, MAO inhibitors

Contraindications: hypertension, hyperthyroidism or myocardial disease or tachycardia.

Side effects: chest discomfort, pain, dizziness, nervousness, restlessness, trembling, troubled breathing, unusual paleness, and unusual weakness.

Dose and Administration:

Adult: *IM, SC:* 2-5 mg/dose every 1-2 hours as needed (initial dose should not exceed 5 mg),

IV. bolus: 0.1-0.5 mg/dose every 10 -15 minutes as needed (initial dose should not exceed 0.5 mg)

Child: *IM, SC:* 0.1mg/kg/dose every 1-2 hours as needed (maximum: 5 mg) *IV. bolus:* 5-20 mcg/kg/dose every 10-15 minutes as needed

IV. infusion: 0.1-0.5 mcg/kg/minute

Storage: at room temperature and protect from light and freezing.

2.9. Thrombolytic agent

Antithrombic enzymes convert plasminogen to plasmin, which in turn degrades fibrin thrombi and fibrinogen.

The most generally accepted indication for the use of antithrombic enzymes is in the treatment of selected cases of acute myocardial infarction. Other indications include acute severe pulmonary thromboembolism; acute arterial thrombosis and thromboembolism; severe deep-vein thrombosis; and clearance of arteriovenous catheters and cannulae. Thrombolytic agents should not be used to treat superficial thrombophlebitis.

Alteplase

Powder for injection, 50mg, 100mg / vial

Indications: management of acute myocardial infarction for the lysis of thrombi in coronary arteries; management of acute massive pulmonary embolism (PE) in adults.

Cautions: refractory hypertension, traumatic resuscitation, non-compressible vascular punctures, transient ischaemic attack (TIA) in preceding 6 months, warfarin therapy, recent retinal laser treatment.

Drug interactions: aminocaproic acid, oral anticoagulants, heparin, non steroidal ant inflammatory drugs, nitroglycerin.

Contraindications: cerebrovascular accident, or history of recent major trauma, surgery or head injury (within the preceding month); gastrointestinal bleeding within the last month; dissecting aneurysm, intracranial aneurysm, active bleeding or known bleeding disorder.

Side effects: hypotension, fever, bruising, GI hemorrhage, nausea, vomiting, GU hemorrhage, bleeding.

Dose and Administration: *Acute myocardial infarction: IV: Adult:* 15mg bolus, then 0.75mg/kg over 30 minutes, followed by 0.5mg/kg over 60 minutes. Total dose should not exceed 100mg.

Storage: store at room temperature or under refrigeration; once reconstituted it must be used within 8 hours.

Reteplase

Powder for injection, 10.4u

Indications: management of acute myocardial infarction (AMI); improvement of ventricular function; reduction of the incidence of CHF and the reduction of mortality following AMI.

Caution, Drug interactions and Contraindications; see under alteplase.

Side effects: bleeding, anemia.

Dose and Administration: Adult: 10 units IV over 2 minutes, followed by a second dose 30 minutes later of 10 units IV over 2 minutes.

Storage: store at 2-25°C.

Tenecteplase

Powder for injection, 50mg /vial

Indications: management of acute myocardial infarction (AMI)

Caution and Contraindications see under alteplase.

Side effects: hematoma, bleeding, stroke, GI hemorrhage, epistaxis, GU bleeding.

Dose and Administration: Adult: Acute myocardial infarction: *IV* bolus over 10 seconds, 30-50 mg according to body weight; maximum 50mg.

Storage: store at room temperature or under refrigeration 2-8°C. If reconstituted and not used immediately, store in refrigerator and use within 8 hours.

3. RESPIRATORY DRUGS

3.1. Antitussives/Expectorants

Cough is an important physiological protective mechanism, but may also occur as a symptom of an underlying disorder such as asthma, gastro-oesophageal reflux disease, and postnasal drip. Treatment of the disorder often alleviates the cough, but there are times when symptomatic treatment is appropriate. The treatment chosen depends on whether the cough is productive or non-productive.

A non-productive cough such as that often seen with the common cold serves no useful purpose for the patient, and cough suppressants may provide some relief, particularly if given at night. Of the commonly used cough suppressants, pholcodine and dextromethorphan are considered to have fewer adverse effects than codeine. However, there is little evidence that these drugs are effective in severe cough. Codeine or similar opioids are not generally recommended as cough suppressants in children, and should be avoided altogether in those under 1 year of age.

A productive cough is characterized by the presence of sputum and may be associated with conditions such as chronic bronchitis, bronchiectasis, or cystic fibrosis. Cough suppressants are inappropriate, since the cough serves the purpose of clearing the airways; expectorants such as guaifenesin have been used on the grounds that increasing the volume of secretions in the respiratory tract facilitates removal by ciliary action and coughing. Mucolytics such as carbocisteine have been shown to affect sputum viscosity and structure and patients with productive cough have reported alleviation of their symptoms, but no consistent improvement has been demonstrated in lung function.

Carbocisteine

Syrup, 2%, 5%

Indications: for its mucolytic activity in respiratory disorders associated with productive cough.

Cautions: history of peptic ulcer disease.

Contraindications: active peptic ulceration.

Side effects: headache, GIT disturbances such as nausea, diarrhea and gastrointestinal bleeding, and skin rashes.

Dose and Administration: *Oral:*

Adult: initially 750 mg 3 times daily, reduced to 1.5 g/day in divided doses, as soon as a response is obtained.

Child: 6-12 years, 250 mg 3 times daily; 2-5 years, 62.5-125 mg 4 times daily.

Storage: at room temperature.

Codeine Phosphate*Tablet, 30 mg**Linctus, 15 mg/5ml***Indications:** Antitussive in lower doses; treatment of mild to moderate pain.**Cautions:** patients with asthma, hepatic and renal impairment, history of drug abuse and also in children, hypersensitivity reactions to other phenanthrene derivative opioid agonists.**Drug interactions:** alcohol, CNS depressants, buprenorphine, monoamine oxidase (MAO) inhibitors, naltrexone, antidiarrhoeal agents.**Contraindications:** children under 1 year old, productive cough, elderly, respiratory depression, head injury, acute alcoholism, acute asthma, heart failure secondary to chronic lung disease.**Side effects:** constipation particularly troublesome in long term use; dizziness, nausea, vomiting; difficulty with micturation; ureteric or biliary spasm; dry mouth, headaches, sweating, facial flushing; dependence, euphoria, sedation, respiratory depression, circulatory collapse, anaphylactoid reaction.**Dose and Administration:****Tablet, Adult:** 10-20mg every 4 -6 hours. Maximum, 120mg in twenty-four hours.**Child:** (6-12 years of age), Oral, 5 to 10mg every four to six hours, not to exceed 60mg per day**Linctus, Adult:** 5-10ml 3 - 4 times daily,**Child** (but not generally recommended) 5-12 years, 2.5 - 5ml 3-4 times daily.**Storage:** at room temperature in a well-closed container.**Dextromethorphan Hydrobromide***Tablet, 15mg**Syrups, 5mg/5ml, 7.5mg/5ml, 15mg/5ml**Drops, 15mg/ml***Indications:** symptomatic relief of non-productive cough due to minor throat and bronchial irritation occurring with colds or inhaled irritants.**Cautions:** as for pholcodine**Drug interactions:** CNS depressants, monoamine oxidase inhibitors including furazolidine and procabazine, amiodarone, fluoxetine, haloperidol, quinidine, thioridazine.**Contraindications:** respiratory failure, acute asthma, in children up to two years of age.**Side effects:** mild dizziness, mild drowsiness, nausea or vomiting, stomach pain.**Dose and Administration:** *Oral:***Adult:** 10 to 20 mg every 4 hours, or 30 mg every 6 to 8 hours, to a usual maximum of 120 mg in 24 hours;**Child** (6-12 years), 5 to 10 mg every 4 hours or 15 mg every 6 to 8 hours to a maximum of 60mg in 24 hours, and children (2 to 6 years) 2.5 to 5 mg every 4 hours, or 7.5 every 6 to 8 hours, to a maximum of 30 mg in 24 hours.**Storage:** at room temperature in a well-closed container.

Guaifenesin*Tablet, 100mg, 200mg**Capsules, 200mg**Syrup, 100mg/5ml*

Indications: symptomatic relief of productive cough due to colds and minor upper respiratory infections.

Cautions: persistent or chronic cough such as that occurring with smoking, asthma, chronic bronchitis, or emphysema, or for cough accompanied by excessive phlegm.

Drug interaction: heparin

Contraindications: sensitive to Guaifenesin.

Side effects: diarrhoea, drowsiness, nausea or vomiting, stomach pain.

Dose and Administration: *Oral:*

Adult: 200-400mg every 4 hours.

Child (6 to 12 years), 100 to 200mg every 4 hours, and children (2 to 6 years), 50 to 100mg every 4 hours.

Storage: at room temperature in a tight container

Pholcodine*Syrup, 0.06%, 0.12%*

Indications: pholcodine is a semi-synthetic derivative of morphine used for its antitussive action. It has little if any analgesic or euphoriant effects and is non-constipating.

Cautions: hepatic disorders, decreased respiratory reserve, severe asthma.

Drug interactions: phenothiazines, benzodiazepines and TCAs.

Side effects: nausea and vomiting, constipation, biliary colic and epigastric pain. High doses may cause sedation, paradoxical excitement, ataxia and respiratory depression.

Dose and Administration: *Oral:*

Adult: 5-10mg 3-4 times daily.

Child: over 5 years, 2.5-5mg 3-4 times daily; 1-5 years, 2-2.5 mg 3 times daily.

3.2. Bronchodilators / Antiasthmatics**Management of Asthma**

Asthma is a chronic inflammatory disease in which the patient suffers episodes of reversible airways obstruction due to bronchial hyperresponsiveness; in a few patients, inflammation may lead to irreversible obstruction.

Common precipitating factors include exposures to cold weather, upper respiratory tract infections, bad smells, exercise, ingestion of drugs like aspirin and beta blockers e.t.c.

The course of acute asthmatic attack is often unpredictable and is potentially life threatening. Concerning the chronic form of the disease, one should always try to classify the disease based on severity before initiating treatment. Accordingly,

it is classified as intermittent or persistent asthma. The later is again divided into mild, moderate and severe persistent asthma.

Management of asthma involves prophylactic measures to reduce inflammation and airways resistance and to maintain airflow, as well as specific regimens for the treatment of acute attacks.

The standard drugs used for the management of asthma are the beta2 agonists and corticosteroids. Therapy is preferably given by inhalation to deliver the drug to the desired site of action. This permits smaller dosages than would be required with oral administration with a consequent reduction in side effects.

Pregnancy

Poorly controlled asthma in pregnant women can have an adverse effect on the fetus, resulting in perinatal mortality, increased prematurity and low birth weight. For this reason using medications to obtain optimal control of asthma is justified. Administration of drugs by inhalation during pregnancy has the advantage that plasma drug concentrations are not likely to be high enough to have an effect on the fetus. Acute exacerbations should be treated aggressively in order to avoid fetal hypoxia.

Management of Chronic obstructive pulmonary disease (COPD)

COPD is a common disorder frequently associated with cigarette smoking, infections, environmental pollution, and occupational dust exposure may also have an aetiological role.

The most important therapeutic intervention is encouraging those patients who smoke to stop; psychological support and adjunctive drug therapy may be required. Drug treatment is primarily symptomatic and palliative using bronchodilators, corticosteroids, and oxygen therapy.

First-line drug therapy for the treatment of COPD consists of bronchodilators to alleviate bronchospasm and any reversible component of the airways obstruction. For mild disease, bronchodilators such as beta2 agonists, ipratropium bromide or combination of both may be useful. Regular oral theophylline may be added, bearing in mind the risk of adverse events.

For moderate to severe cases a trial of oral corticosteroid therapy should be considered.

The use of mucolytics or expectorants is controversial.

Selective Beta2 agonist, inhaled and systemic

Beta2 agonists relax the bronchial smooth muscle to produce bronchodilation by selectively stimulating beta2-adrenergic receptors. Short-acting beta2 agonists such as salbutamol or terbutaline are the initial drugs of choice for acute bronchospasm; if inhaled, they can have an almost immediate bronchodilating effect. Simultaneous administration of more than one drug within this group is hazardous.

Short-acting beta2 agonists should not be used on a regular basis, but only "as required". Patients requiring beta2 agonists more than twice a week should be commenced on inhaled steroids.

Salmeterol and formoterol are selective beta₂ agonists with a prolonged duration of action. These agents are indicated for maintenance therapy in chronic persistent asthma, and COPD. Salmeterol has a delayed onset of action and is not suitable for treatment of an acute exacerbation.

Various formulations and routes of administration are available.

Inhalation:

Aerosol inhalers (metered dose) are highly effective and preferred to oral medication for mild to moderate attacks of bronchospasm. Bronchodilator response is rapid and is sustained for 4 hours or longer, depending on the severity of the asthma and the dose administered. Compared with oral preparations, the dose delivered is small and side effects few.

- Use of the inhaler should be demonstrated carefully to the patient and technique checked at subsequent visits. The importance of breathing out first, then inhaling slowly and holding the breath for 10 seconds after inhalation should be stressed. Some patients, especially the elderly, arthritic, and young children, may be unable to use metered-dose inhalers with out spacers.
- Use of one of the various spacer devices, preferably large volume ($\geq 500\text{ml}$), will often improve delivery of aerosol, eliminating the need for precise co-ordination of activation and inhalation.
- The maximum dose per 24-hour period and the number of inhalations permissible at one time should be explained carefully to the patient, and that if relief is not obtained with the prescribed dose, medical advice should be sought.
- When a patient requires a beta₂ agonist more than twice a week, add inhaled corticosteroids. Inhaled corticosteroids increase response to beta₂ agonist.

Dry powder inhalers are useful when patients cannot use pressured aerosols correctly, as they are activated by the patient's inspiration.

Oral:

Oral beta₂ agonists should rarely be prescribed. Onset of action is slower than inhaled therapy and incidence of side-effects significantly higher, but the action is slightly more prolonged than with aerosol inhalers. The slow-release preparations may be of value in patients with nocturnal asthma.

Intravenous:

Intravenous beta₂ agonists, used in severe asthma, possess bronchodilator potency comparable to that of aminophylline and are probably safer to use if blood level measurement of the latter is not possible.

Glucocorticoids, inhaled

Inhaled corticosteroids reduce airways inflammation and are very effective in the prophylactic management of chronic persistent asthma. They must be used regularly for maximum benefit.

Beclometasone, budesonide and fluticasone are equally effective if used in equivalent doses. There appears to be a relatively flat dose response within the high-dose range. Suppression of the adrenohypophyseal axis has been reported with high doses, especially with fluticasone.

Chlorofluorocarbon (CFC) propellants in aerosol metered-dose inhalers are being replaced by hydrofluoroalkane (HFA) propellants, and doses may differ.

Anticholinergics, inhaled

An antimuscarinic may be the bronchodilator of choice in the management of chronic obstructive pulmonary disease. In patients with asthma they are usually reserved for use in life-threatening acute asthma exacerbations.

Ipratropium bromide an atropine derivative anticholinergic agent, is a potent inhibitor of vagus mediated bronchoconstriction and has significant bronchodilator capacity, exerted by blocking vagal influences on bronchomotor tone

Xanthines

These agents have a narrow therapeutic index with significant toxicity.

Theophylline, a methylxanthine derivatives, is used primarily for the relief of bronchospasm. Recent evidence indicates that theophyllines have some anti-inflammatory effect. Once a day administration in lower doses, previously considered to be sub-therapeutic, may be of some benefit.

Other effects include CNS stimulation, increased gastric secretion, vasodilation and mild diuresis; increased rate and depth of respiration, an increase in diaphragmatic contractility, and positive inotropic and chronotropic effects on the heart.

Aminophylline is a combination of theophylline with ethylenediamine which dissociates in the stomach to be absorbed as theophylline. (Aminophylline 1.27g is equivalent to about 1g theophylline). Aminophylline is more water soluble than theophylline and may be given parenterally.

- IV infusion has not been shown to be beneficial in acute asthma or exacerbations of COPD when added to corticosteroids and nebulized bronchodilators.

Compound bronchodilator preparations

Most compound bronchodilator preparations have no place in the management of patients with airways obstruction.

In general, patients are best treated with single-ingredient preparation, such as a selective beta₂ adrenoceptor stimulant or ipratropium bromide, so that the dose of each drug can be adjusted. This flexibility is lost with combinations, although those in which both components are effective may occasionally have a role when compliance is a problem.

Adrenaline (Epinephrine)

Injection, 0.1 % in 1 ml ampoule

Indications: for acute bronchial asthma, and acute anaphylactic reactions; see section 2.8. under Adrenaline.

Cautions, Drug interactions, Contraindications, Side effects; see section 2.8. under Adrenaline.

Dose and Administration: *Acute bronchial asthma: S.C or I.M:*

Adult: *S.C.* initially, 0.2 – 0.5mg (0.2—0.5ml), repeated every 20 minutes as necessary up to 3 doses or IV (slow & cautions), 0.1 to 0.25mg;

Child: *S.C.* 0.01mg (0.01ml)/ kg of body weight, up to a maximum of 0.3mg (0.3ml)/dose. The dose may be repeated every 15 minutes for 3 or 4 doses as necessary.

Note: only a 1: 10, 000 epinephrine solution should be used for intravenous administration.

Storage: at room temperature, in a light – resistant container.

Aminophylline (Theophylline and Ethylenediamine)

Tablet, 100mg, 200mg

Tablet (m/r), 100mg, 225mg, 350mg

Injection, 250mg/10ml, 10ml, in 10 and 20ml

Indications: reversible airways obstruction, acute severe asthma.

Cautions: as for theophylline, and also, IV injection must be administered very slowly to prevent dangerous CNS and cardiovascular side effects.

Drug interactions, Contraindications; see under theophylline

Side effects: as for theophylline; also allergy to Ethylenediamine can cause urticaria, erythema, and exfoliative dermatitis.

Dose and Administration:

Tablet, Oral: **Adult,** 100-300mg, 3-4 times daily, after food.

Tablet (m/r, 225mg), 1 tablet twice daily initially, increased after 1 week to 2 tablets twice daily. *Tablet (m/r, 350mg)* is for smokers and other patients with decreased theophylline half-life. *Tablet (m/r, 100mg),* children over 3 years, 6mg/kg twice daily initially, increased after 1 week to 12mg/kg twice daily; some children with chronic asthma may require 13-20mg/kg every 12 hours.

Slow I.V. injection or preferably by slow I.V. infusion. Avoid rapid intravenous injection.

It should be given cautiously, particularly in patients who have previously been taking theophylline and/or ephedrine.

Adult: *Slow, I.V.,* 250—500mg (5mg/kg) over 20 minutes, or diluted with 10ml of water for injection.

Maintenance—If required, 0.5mg/kg of body weight per hour *by slow I.V. infusion* for a period of 24 hours only.

Child: *Slow I.V.* 5mg/kg of body weight

Maintenance—If required, 6 months-9 years-1mg/kg of body weight per hour by slow intravenous infusion.

10 -16 years—0.8mg/kg of body weight per hour by slow intravenous infusion.

Storage: at room temperature protect from light.

Beclomethasone Dipropionate

Oral inhalation (aerosol), 50 mcg/dose, 100 mcg/dose

Indications: chronic persistent asthma.

Cautions: active or quiescent pulmonary tuberculosis; pregnancy, particular care is required when patients are transferred from systemic corticosteroid to

inhaled products; diabetes, hypertension, osteoporosis, peptic ulcer, glaucoma, cataracts, hepatic impairment, withdrawal should be slowly.

Drug interactions: salmeterol

Contraindications: bronchiectasis (moderate to severe), sensitivity to the drug or any ingredient (e.g. fluorocarbons, oleic acid) in the formulation; not to be used in status asthmaticus or for the relief of acute bronchospasm; children less than 6 years of age.

Side effects: oral candidiasis (creamy white, curd like patches inside mouth); cough without symptoms of infection; rarely skin rash and difficulty in swallowing; hoarseness.

Dose and Administration:

Adult: 200 micrograms twice daily or 100 micrograms three or four times daily. Severe cases 600 – 800 micrograms daily;

Child: 50 – 100 micrograms two to four times daily.

Note: Gargling and rinsing the mouth with water after each dose is recommended to help prevent hoarseness, throat irritation, and oral candidiasis. The use of a spacing device may also greatly decrease the incidence of these local adverse effects.

Storage: at room temperature

Budesonide + Formoterol Fumarate

Aerosol, 80mcg + 4.5mcg, 160mcg + 4.5mcg

Cautions, Drug interactions, Contraindications and Side effects; see under Salmeterol and Fluticasone.

Dose and Administration:

Adult: 1-2 inhalations twice daily; may be temporarily increased to a maximum of 4 inhalations twice daily. When control has been achieved, titrate to lowest dose at which effective control is maintained.

Child: over 12 years, as for Adults.

Ephedrine + Theophylline

Tablet, 11mg + 120mg

Elixir, 6mg + 30mg in each 5ml

Syrup, 2.24% + 0.30%

Formoterol

Inhalational powder, 12mcg/dose

Indications: maintenance treatment of asthma and prevention of bronchospasm in patients ≥ 5 years of age with reversible obstructive airway disease, including patients with symptoms of nocturnal asthma, who require regular treatment with inhaled, short-acting beta₂ agonists; maintenance treatment of bronchoconstriction in patients with COPD; prevention of exercise-induced bronchospasm in patients ≥ 5 years of age.

Cautions: do not use as a component of chronic therapy without an anti-inflammatory agent; do not exceed recommended dose; cardiovascular disease, convulsive disorders, diabetes, glaucoma, hyperthyroidism or hyperkalemia. Safety and efficacy have not been established in children < 5 years of age.

Drug interactions: adrenergic agonists, antidepressants (tricyclic), beta-blockers, corticosteroids, diuretics, MAO inhibitors, theophylline derivatives.

Contraindications: hypersensitivity reactions.

Side effects: children are more likely to have infection, inflammation, abdominal pain, nausea and dyspepsia. Serum glucose increased, serum potassium decreased, chest pain, tremor, dizziness, insomnia, dysphonia, rash, bronchitis, infection, dyspnea, tonsillitis.

Dose and Administration:

Relief of bronchoconstriction: **Child ≥ 12 years and Adult:** 6mcg or 12mcg as a single dose (maximum dose: 72 mcg in any 24-hour period). The prolonged use of high dosage (48 mcg/day for ≥ 3 consecutive days) may be a sign of suboptimal control, and should prompt the re-evaluation of therapy.

Storage: prior to dispensing, store in refrigerator at 2 to 8°C; after dispensing store at room temperature.

Ipratropium Bromide

Aerosol Solution, 20mcg/metered

Inhalation; 400mcg/metered inhalation

Indications: relief of bronchospasm in reversible air ways obstruction, especially COPD and in elderly patients, it has also been used in cystic fibrosis.

Cautions: prostatic hypertrophy; pregnancy; acute angle closure glaucoma.

Drug interactions: anticholinergics.

Side effects: dry mouth occasionally reported, rarely urinary retention, constipation, tachycardia, palpitations and arrhythmias, hypersensitivity reactions, including urticaria, angioedema, anaphylaxis.

Dose and Administration:

Chronic asthma or chronic obstructive pulmonary disease:

Aerosol inhalation:

Adult: 20-40 micrograms, in early treatment up to 80 micrograms at a time, 3-4 times daily;

Child: up to 6 years, 20 micrograms 3 times daily; 6-12 years, 20-40 micrograms 3 times daily.

Inhalers: **Adult:** 40 micrograms 3 times daily; if necessary, a second dose may be inhaled 5 minutes after the first.

Storage: at room temperature protect from freezing. Protect from light.

Isoprenaline Sulphate

Tablet (Sublingual), 5mg, 10mg

Indications: symptomatic treatment of bronchial asthma and reversible bronchospasm which may occur association with chronic bronchitis, pulmonary emphysema, bronchiectasis and other chronic obstructive pulmonary diseases.

Cautions, Cotraindications, Side effects - see under Adrenaline, sec. 2.8

Drug interactions: see under Adrenaline and also beta1 agonists such as Adrenaline: -dryness or irritation of mouth or throat, nervousness, or restlessness, pinkish to red coloration of saliva, insomnia, anxiety, tension, fear, or excitement, chest discomfort or pain, dizziness or light headedness, continuing fast heartbeat, continuing or severe headache.

Dose and Administration: *Sublingual,*

Adult: 10-20mg, not to exceed 60mg;

Child: 5-10mg, not to exceed 30mg

Storage: at room temperature in a well closed, light resistant container.

Theophylline

Tablet (anhydrous theophylline), 100mg, 200mg, 200mg (s/r)

Elixir, 33mg in each 15 ml (anhydrous theophylline)

Indications: treatment of acute, severe and chronic persistent asthma and other conditions associated with reversible bronchospasm; COPD.

Cautions: peptic ulcer, hyperthyroidism, hypertension, cardiac arrhythmias or other cardiovascular disease, or epilepsy; heart failure, hepatic dysfunction or chronic alcoholism, acute febrile illness, and to neonates and the elderly (since in all of these circumstances theophylline clearance may be decreased)

Drug interactions: other xanthine medications, allopurinol, antiarrhythmics, cimetidine, disulfiram, fluvoxamine, interferon-alfa, macrolide antibacterials and quinolones, oral contraceptives, phenytoin, alcohol, ritonavir, rifampicin,

sulfinpyrazone, smoking, sympathomimetic agents, corticosteroids, diuretics, halothane or ketamine, lithium, beta blockers.

Contraindications: hypersensitivity to theophylline or xanthine derivatives; coronary artery disease (when, in the physician's judgment, myocardial stimulation might prove harmful).

Side effects: tachycardia, palpitations, nausea, gastro-intestinal disturbances, headache, insomnia, arrhythmias.

Dose and Administration:

Adult: as anhydrous theophylline, *Oral:* general range 6-18mg/kg/day.

Chronic bronchospasm: sustained-release formulations; initially the usual daily dose is 12mg/kg or 400mg (whichever is less) divided into 2-3 doses 8-12 hourly; dose may be increased by 2-3mg/kg/day at 3-day intervals.

- Addition as a once-daily slow-release formulation at night may ameliorate night dipping.
- The general therapeutic range is 10-20mcg/ml (55-110mcmol/l), although benefit may be seen at sub-therapeutic doses.

Child: *Oral:* 1-9 years, 20mg/kg/day; 9-12 years, 16mg/kg/day.

- The total daily dose is divided into 2-3 doses for 8-12 hourly administration of sustained release preparations, or into 4 doses for 6 hourly administrations of short-acting preparations.
- Because of a general higher metabolic rate of theophylline in children, the sustained-release agents often have to be given 8 hourly.
- Both the final maintenance dose and the dose interval should be guided by serum levels obtained after steady state has been achieved.

Note: patients should not be transferred from one modified release theophylline or aminophylline preparation to another without clinical assessment and the measurement of serum-theophylline concentrations because of bioavailability.

Storage: store in a well-closed container at room temperature.

Theophylline and Guaifenesin

Tablet 150mg + 90mg

Capsule, 150mg + 90mg; 300mg + 180mg

Elixir, 150mg + 90mg/15ml

Indications: for relief and/or prevention of symptoms of bronchial asthma and reversible bronchospasm associated with chronic bronchitis and pulmonary emphysema.

Cautions, Drug interactions and Contraindications; see notes under theophylline and guaifenesin

Side effects: gastroesophageal reflux: see notes under theophylline & guaifenesin

Dose and Administration:

Adult: *Oral:* 16mg/kg/day or 400mg theophylline/day, in divided doses, every 6-8 hours.

Note:- complete prescribing information for this medication should be consulted for additional detail.

Storage: Guaifenesin preparations should be stored in tight containers at room temperature.

Salbutamol (Albuterol)

Tablet, 2mg, 4mg, 4mg (s/r)

Syrup, 2mg/5ml

Oral inhalation (aerosol), 0.1mg per dose

Indications: asthma and other conditions associated with reversible airways obstruction.

Cautions: hyperthyroidism, myocardial insufficiency, arrhythmias, susceptibility to QT-interval prolongation, hypertension, elderly.

Note: it is important that asthma be well controlled throughout pregnancy. Inhaled administration is particularly advantageous as therapeutic action can be achieved at lower plasma levels with very little risk to the fetus.

Drug interactions: corticosteroids, cardiacglycosides, diuretics, xanthines and antidepressants.

Contraindications: eclampsia and severe pre-eclampsia, intra-uterine infection, intra-uterine fetal death, antepartum haemorrhage (which requires immediate delivery), placenta praevia, and cord compression; threatened miscarriage.

Side effects: fine tremor, nervousness, headache, dizziness, cardiac stimulation with tachycardia & palpitations (infrequent with aerosol inhalation) are usually dose-related. High doses may cause nausea & vomiting, and prolonged use has led to reversible hypertrichosis. Hypersensitivity reactions are rare.

Dose and Administration:

Tablets – Oral: Adult: 2 to 6mg (base) - three or four times a day initially, the dosage being increased and tolerated up to a maximum of 8mg four times a day.

Child (6-12 years): 2mg (base) - three or four times a day initially, the dosage being increased and tolerated up to a maximum of 24mg per day in divided doses.

Syrup – Oral: Adult: 2 to 6mg (base) three or four times a day initially, the dosage being increased as needed and tolerated up to a maximum of 8mg four times a day.

Child (2-6years): 0.1mg (base) per kg of body weight three times a day initially, the dosage being increased as needed and tolerated up to 0.2mg per kg of body weight, not to exceed 4mg three times a day.

Child (6-14 years): 2mg (base) three or four times a day initially, the dosage being increased as needed and tolerated up to a maximum of 24mg per day in divided doses.

Inhalation (aerosol) - Oral inhalation: Adult: 0.18 to 0.2mg (1-2 inhalations/puffs) every four to six hours as required

Note: - Shake well before use.

Storage: Aerosol - store at room temperature away from heat and direct sunlight.

Syrup, Tablet - store between 2 and 30°C, in a well-closed container, protect from light and from freezing.

Salmeterol + Fluticasone

Powder for oral inhalation, 50mcg + 100mcg, 50mcg + 250mcg, 50mcg + 500mcg

Indications: maintenance treatment of asthma in adults and children ≥ 4 years; not for use for relief of acute bronchospasm; maintenance treatment of COPD associated with chronic bronchitis.

Cautions: see under beclomethasone and salbutamole.

Drug interactions: diuretics (loop, thiazide); CYP3A4 inhibitors (e.g. azole antifungals, ciprofloxacin); MAO inhibitors, TCAs (wait at least 2 weeks after discontinuing these agents); beta-adrenergic blockers (e.g. propranolol), beta2 agonists.

Contraindications: hypersensitivity to salmeterol or fluticasone; status asthmaticus; acute episodes of asthma.

Side effects: headache, hyperglycaemia, hypokalaemia, pharyngitis, upper respiratory tract infection, diarrhea, GI pain/discomfort, oral candidiasis, nausea/vomiting, musculoskeletal pain, bronchitis, cough, dysphonia, sinusitis, upper respiratory tract inflammation, viral respiratory tract infection.

Dose and Administration: *Oral inhalation:* Note: Do not use to transfer patients from systemic corticosteroid therapy.

COPD: Adult: 50/250 mcg twice daily, 12 hours apart.

Asthma: Adult and Child ≥ 12 : One inhalation twice daily, morning and evening, 12 hours apart.

Child 4-11 years: 50/250 mcg twice daily, 12 hours apart.

Note: this drug is available in 3 strengths, initial dose prescribed should be based upon previous asthma therapy. Dose should be increased after 2 weeks if adequate response is not achieved. Patients should be titrated to lowest effective dose once stable. (Because each strength contains salmeterol 50mcg/inhalation, dose adjustments should be made by changing inhaler strength. No more than 1 inhalation of any strength should be taken more than twice a day). Maximum dose: 50/500 mcg, one inhalation twice daily.

Patients not currently on inhaled corticosteroids: 50/100 mcg

Patients currently using inhaled beclomethasone dipropionate: ≤ 420 mcg/day: 50/100 mcg. 462-840 mcg/day: 50/250 mcg

Storage: store at room temperature.

Sodium Cromoglycate

Capsules with inhaler, 20 mg

Indications: indicated as a prophylaxis in the management of bronchial asthma in patients who require continuing symptomatic relief.

It has no role in the treatment of an acute attack of asthma, especially status asthmaticus, because it has no intrinsic bronchodilating activity.

It is also indicated to prevent bronchospasm induced by exercise or by exposure to allergens, cold dry air, environmental pollutants, or other known precipitating factors when exposure is either episodic or continuous

Cautions: nursing women, pediatric and geriatric patients. Caution should also be used when decreasing the dosage of cromolyn or discontinuing the drug in patients with asthma.

Contraindications: sensitivity to cromolyn, coronary artery disease or history of cardiac arrhythmias.

Side effects: wheezing, nasal congestion, cough, hoarseness, irritation of the throat and trachea, bronchospasm, nausea, headache, dizziness, unpleasant taste, joint pain and swelling.

Dose and Administration: Adult and Child 2 years and older:

Asthma, bronchial (prophylaxis): Oral inhalation: 20 mg (1 capsule) four times a day at regular intervals, the dosage being adjusted as needed and tolerated.

Bronchospasm (prophylaxis): Oral inhalation: 20 mg (1capsule) as a single dose just prior to exposure to the precipitating factor; or, if used chronically, 20 mg (1 capsule) four times a day at regular intervals, the dosage being adjusted as needed and tolerated.

Child up to 2 years of age: The capsule for inhalation should not be used.

Storage: at room temperature in tight, light-resistant containers.

4. CENTRAL NERVOUS SYSTEM DRUGS

4.1. Analgesics / Antipyretics

Pain is not only associated with physical suffering or hurting but has an emotional or mental component, hence it is defined as an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage.

Pain can be classified as acute or chronic. Acute pain is usually of short duration and the cause often identifiable (disease trauma). Chronic pain persists after healing is expected to be complete, or is caused by a chronic disease. Pain may be modified by psychological factors and attention to these is essential in pain management. Drug treatment aims to modify the peripheral and central mechanisms involved in the development of pain.

Non-opioid analgesics are particularly suitable for pain in musculoskeletal conditions where as the opioid analgesics are more suitable for moderate to severe visceral pain. Those non-opioid analgesics which also have anti-inflammatory actions include salicylates and NSAIDS (Non steroidal anti-inflammation drugs), they can reduce both pain and inflammation of chronic inflammatory disorders such as rheumatoid arthritis, but they do not alter or modify the disease process itself.

Fever (pyrexia) is defined as an increase in body temperature due to an elevated thermoregulatory set-point temperature. Common causes of fever include infections, inflammatory disorders, neoplastic disease, and some drug treatment. Methods for reducing body temperature in fever include the use of antipyretic drugs and/or physical means. Antipyretic agents used include paracetamol, salicylates and some other NSAIDs.

Migraine is characterized by recurrent attacks of headache which may take up to 72 hours to resolve. Treatment of migraine attacks may be successfully carried out with non-opioid analgesics such as aspirin, other NSAIDs, or paracetamol (preferably in a soluble or dispersible form) taken at the earliest signs of an attack concomitant anti-emetic treatment may be required. Attacks which do not respond to non-opioid analgesics may be treated with ergot preparations such as Ergotamine Tartrate. But the value of ergotamine for migraine is limited by difficulties in absorption and by its side effects, particularly nausea, vomiting, abdominal pain, and muscular cramps; it is best avoided. The recommended doses of ergotamine preparations should not be exceeded and treatment should not be repeated at intervals of less than 4 days.

To avoid habituation the frequency of administration of ergotamine should be limited to no more than twice a month. It should never be prescribed prophylactically but in the management of cluster headache a low dose is occasionally given for 1 to 2 weeks.

An alternative to ergot compounds for the acute treatment of migraine is the selective serotonin agonist sumatriptan succinate, this drug act by constricting

dilated cranial blood vessels and inhibiting release of sensory neuropeptides from the perivascular trigeminal afferents, thereby blocking the consequences of trigeminovascular activation. Sumatriptan is relatively safe and well tolerated but should be avoided in patients with known, or at risk of, cardiovascular disease.

Non - opioid analgesics

Paracetamol, aspirin, and other non steroidal anti-inflammatory drugs (NSAIDs) are the first choice for treating mild or moderate pain and are used in moderate or severe pain to potentate the effects of opioids. They are suitable for use in acute or chronic pain.

Acetylsalicylic acid

Aspirin is indicated for headache, transient musculoskeletal pain, dysmenorrhoea and pyrexia. In inflammatory conditions, most physicians prefer anti-inflammatory treatment with another NSAID which may be better tolerated and more convenient for patient. Acetylsalicylic acid is also used for its anti platelet properties.

Adverse effects with analgesic doses are generally mild but include a high incidence of gastro-intestinal irritation with slight blood loss (Minimized by taking the dose after food, or enteric coated preparations), bronchospasm and skin reactions in hypersensitive patients, and increased bleeding time. Anti-inflammatory doses are associated with a much higher incidence of adverse reactions, and they also cause mild chronic salicylism which is characterized by tinnitus and deafness. Its use is not advisable in the latter stage of pregnancy, or in children because of an association with Reye syndrome (encephalopathy and liver damage).

Paracetamol

Paracetamol is similar in analgesic and antipyretic efficacy to acetylsalicylic acid. Unlike acetyl salicylic acid and other NSAIDs, paracetamol has little anti-inflammatory activity which limits its usefulness for long-term treatment of pain associated with inflammation; however it is useful in the management of osteoarthritis, a condition with only a small inflammatory component.

Since paracetamol does not have aspirin's hypersensitivity hematological or gastro-intestinal adverse effects, it is particularly useful in patients in whom salicylates or other NSAIDs are contraindicated, such as asthmatics and those with a history of peptic ulcer, or for children under the age of 12 years in whom salicylates are contraindicated because of the risk of Reye syndrome. However large doses of paracetamol can produce severe or sometimes fatal hepatotoxicity; patients with cachexia or those with existing liver disease may be more susceptible.

Dipyrone, a sodium sulphonate of amidopyrine, is a nonsteroidal anti-inflammatory drug. Because of the risk of serious adverse effects its use is justified only in severe pain where no alternative is available or suitable. Administration of Dipyrone is associated with an increased risk of

agranulocytosis and with shock. In Ethiopia, only the parenteral form of Dipyrone is available, which is to be used in place of narcotic analgesics.

Acetylsalicylic acid (Aspirin)

Tablet, 75mg, 81mg, 100mg (soluble); 300mg, 324mg (microfined); 500 mg (enteric coated)

Indications: relief of mild to moderate pain, pyrexia; prophylaxis of platelet aggregation; treatment of rheumatic fever, and acute and chronic inflammatory disorders.

Cautions: caution in patients with gastritis, peptic ulcer, elderly, lactation (high dose)

Drug interactions: antidiabetic agents, including insulin; agents inhibiting platelet aggregation (e.g. penicillins, dipyridamole and valproic acid); thrombolytic agents and heparin; agents causing gastric irritation; methotrexate, probenecid; zidovudine.

Contraindications: history of severe sensitivity reaction to acetylsalicylic acid, bleeding ulcers or other hemorrhagic states, nasal polyps associated with asthma, febrile and dehydrated children (especially with viral infections).

Side effects: gastrointestinal irritation causing abdominal pain, nausea, vomiting and occult or overt mucosal bleeding. Chronic administration of high doses may cause gastric erosion and acute haemorrhage, potentiated by alcohol. Pseudo-allergic reactions such as bronchospasm, rhinitis, urticaria, angioedema and anaphylaxis like shock may occur, most frequently in asthmatics, or in patients with nasal polyps or severe atopy. True hypersensitivity reactions may also occur. Tinnitus and decreased hearing, impaired renal function, decreased prothrombin time and hepatotoxicity are more likely when serum levels are > 200mcg/ml, but may be caused by low doses, especially in the elderly.

Dose and Administration: *Oral:*

Adult:

Analgesic and antipyretic: 325-650mg every 4-6 hours up to 4g/day.

Anti-inflammatory: initial: 2.4-3.6g/day in divided doses; usual maintenance: 3.6-5.4 g/day

Child:

Analgesic and antipyretic: 10-15mg/kg/dose every 4-6 hours, up to a total of 4g/day.

Orally, preferably with or after food with a full glass of water. Child should not take more than 5 doses/day or for longer than 10 days at a time, and adult should not take for longer than 10 days at time.

Note: - Aspirin tablets or dispersible aspirin tablets are adequate for most purposes as they act rapidly. Enteric-coated tablets are beneficial in minimizing gastric irritation effect of aspirin, but have a slow onset of action and are therefore unsuitable for single-dose analgesic use (though their prolonged action may be useful for night pain).

Acetylsalicylic acid preparations should not be used if a strong vinegar-like odor is present.

Storage: at room temperature, in a tight container. Protect from heat.

Dipyrone

Injection, 500mg/ml in 1ml ampoule

Indications: severe pain where no alternative is available or suitable.

Side effects and Cautions:

The risk of agranulocytosis in patients taking Dipyrone is sufficiently great to render this drug unsuitable for use. Onset of agranulocytosis may be sudden and unpredictable.

Dose and Administration:

IM or IV: up to 7.5g daily in divided doses.

Paracetamol

Tablet, 100mg, 500mg

Suppository, 125mg, 250mg

Syrup, 120mg/5ml, 250mg/5ml

Drops, 100mg/ml

Injection, 1g in 100ml

Indications: mild to moderate pain or pyrexia.

Cautions: caution in alcoholics, and in patients with hepatic diseases, and severe renal function impairment, anaemia and other disorders of the haemopoietic system.

Drug interactions: avoid simultaneous use of single toxic doses or long-term high doses of paracetamol with alcohol, or phenobarbitone; oral anticoagulants.

Contraindications: severe hepatic or renal disease.

Side effects: rare in therapeutic doses. Allergic reactions such as skin rashes, neutropenia and thrombocytopenia may occur rarely.

Dose and Administration:

Mild to moderate pain, pyrexia,

Oral: Adult: 0.5 - 1g every 4-6 hours, maximum 4g daily;

Child: 3 months-1 year 60-125mg, 1-5 years 120 - 250mg, 6-12 years 250 - 500mg these doses may be repeated every 4 - 6 hours if necessary (maximum 4 doses in 24 hours).

Rectum: Adult: 0.5 - 1g, every 4-6 hours, maximum 4g daily.

Child: 1 - 5 years 125 - 250mg, 6 - 12 years 250 - 500mg; doses inserted every 4 - 6 hours if necessary, maximum 4 doses in 24 hours.

Post - immunization pyrexia: **Oral:** infant 2-3 months, 60mg followed by a second dose if necessary 4-6 hours later; warn parents to seek medical advice if pyrexia persists after second dose.

Injection:

Adult and Adolescents > 50 kg: 1g per administration (100ml vial), up to 4 times a day. Maximum daily dose not exceed 4g.

Child weighing more than 33 kg (approximately 11 years old), adolescents and adults weighing less than 50 kg: 15 mg/kg per administration, i.e. 1.5 ml solution per kg up to 4 times a day. The minimum interval between each

administration must be 4 hours. The maximum daily dose must not exceed 60 mg/kg (without exceeding 3 g).

Children weighing more than 10 kg (approximately 1 year old) and less than 33 kg: 15 mg/kg per administration, i.e. 1.5 ml solution per kg up to 4 times a day. The minimum interval between each administration must be 4 hours. The maximum daily dose must not exceed 60mg/kg (without exceeding 2 g).

Storage: at room temperature

Paracetamol+Acetylsalicylic acid+Caffeine

Tablet, 250mg+250mg+65mg

Indications: relief of mild to moderate pain; mild to moderate pain associated with migraine headache.

Dose and Administration: *Oral: Adult:*

Based on acetaminophen component:

Mild to moderate pain: 325-650mg every 4-6 hours as needed; do not exceed 4 g/day

Mild to moderate pain associated with migraine headache: 500mg/dose (in combination with 500mg aspirin and 130mg caffeine) every 6 hours while symptoms persist; do not use for longer than 48 hours

Based on aspirin component:

Mild to moderate pain: 325-650mg every 4-6 hours as needed; do not exceed 4 g/day

Mild to moderate pain associated with migraine headache: 500mg/dose (in combination with 500mg acetaminophen and 130mg caffeine) every 6 hours; do not use for longer than 48 hours.

Opioid analgesics

The opioid analgesics may be usefully classified as low-efficacy opioids (e.g. codeine) and high-efficacy opioids (e.g. morphine, methadone and pethidine).

Codeine may effectively relieve mild to moderate pain not responding to aspirin or paracetamol. It has useful antitussive activity at doses lower than those required for analgesia, and is also effective in controlling diarrhoea. Because of their different mechanisms of action, codeine has additive analgesic effects with paracetamol, aspirin or other non-steroidal anti-inflammatory agents, and such combinations can be used beneficially. Combination with other opioids should be used with caution. It is much less potent than morphine and much less liable, in normal doses, to produce adverse effects including dependency. It is effective for mild to moderate pain but is too constipating for long-term use.

Morphine and Pethidine are opioid analgesics which are effective in relieving moderate to severe pain, particularly of visceral origin; there is a large variation in patient response. Weaker opioids such as codeine are suitable for mild to moderate pain. Pethidine produces prompt but short-acting analgesia, it is less constipating than morphine, but even in high doses it is less effective.

Morphine remains one of the most valuable opioid analgesics. Its euphoriant action can be a useful property for providing a sense of well-being in patients with severe pain. It is used to relieve severe acute pain, or chronic pain, e.g. in terminally ill patients. It is also used for pre-operative sedation, as a supplement to anaesthesia and in acute pulmonary oedema secondary to left ventricular failure, and is the choice to relieve pain in acute ischaemic myocardial conditions.

A neurotoxic metabolite, norpethidine, accumulates during repeated administration and can cause central nervous system excitation, including myoclonus and seizures. These adverse effects together with the short duration of analgesic action make pethidine unsuitable for severe, continuing pain. It is used for analgesia in labor; however other opioid analgesics such as morphine are often preferred.

Pethidine is preferred to morphine in certain clinical situation, e.g. during labour, in biliary, bowel or ureteric colic. It is less bronchospasmogenic than morphine.

Methadone as an antitussive linctus, it may be used to control non-productive cough in special cases, e.g. lung cancer. It may be used in the management of opioid dependence and withdrawal; prolonged therapy may be required, with carefully adjusted, individualized doses.

Other agent such as tramadol is an atypical opioid structurally akin to tilidine, but apart from its morphine-receptor agonist action, it inhibits neuronal reuptake of serotonin and noradrenaline. It does not appear to release histamine.

Pentazocine has both agonist and antagonist properties and precipitates withdrawal symptoms, including pain in patients dependent on other opioids. By injection it is more potent than dihydrocodeine or codeine, but hallucinations and thought disturbances may occur. It is not recommended and, in particular,

should be avoided after myocardial infarction as it may increase pulmonary and aortic blood pressure as well as cardiac work.

- Opioid analgesics have neither antipyretic nor anti-inflammatory activity.
- The risk of dependency with the weaker opioids is lower than with the high-efficacy opioids, but a considerable potential may exist in patients with a history of drug abuse or patients who are “dependence-prone”.
- Tolerance to the analgesic efficacy of opioids may develop with repeated and prolonged administration, and dependence and abuse are further problems. However, in the management of chronic pain in terminal illness the dependence-producing potential is of less importance, and doses should be titrated up wards until adequate analgesia is provided. Their tendency to cause respiratory depression should also be noted.
- The low-efficacy opioids also have a tendency to suppress respiration, and in overdosage they are marked respiratory depressants. Toxicity is aggravated by alcohol or other CNS depressants.
- The opioids all have, in varying degrees, the potential to cause constipation, urinary retention, nausea, vomiting and cough suppression; combinations of opioids should be avoided.
- Opioids should be used with caution in hypotensive states, in impaired hepatic function, when decreased respiratory reserve is present, and in combination with certain drugs such as MAO inhibitors.
- Morphine should be used with caution in asthmatic patients.
- At higher doses, all opioids may cause muscle rigidity.
- Prolonged administration of opioids and addiction during pregnancy may cause dependence and withdrawal in the neonate.

Codeine Phosphate

Tablet, 30mg

Injection, 30mg/ml in 1ml ampoule

Indications: mild to moderate pain, also used in the symptomatic relief of non-productive cough (section 3.1)

Cautions: renal and hepatic impairment, dependence; and also see section 3.1

Drug interactions: see section 3.1, under codeine phosphate

Contraindications: respiratory depression, obstructive airways disease, acute asthma attack; where risk of paralytic illness.

Side effects: see section 3.1, under codeine phosphate

Dose and Administration:

Mild to moderate pain:

Oral: Adult: 30 - 60 mg every 4 hours when necessary to a maximum of 240mg, daily;

Children 1-12 years, 3mg/kg daily in divided doses.

I.M: 30-60mg every 4 hours when necessary.

Storage: at room temperature

Ergotamine Tartrate

Tablet, 1mg, 2mg (sublingual)

Injection 0.25 mg/ml in 1ml ampoule

Indications: as single agent or in combination with caffeine to prevent or abort migraine, cluster headache (histamine cephalgia), and other vascular headaches. Not recommended for migraine prophylaxis because of the possibility of adverse effects.

Cautions: risk of peripheral vasospasm (stop medication immediately if numbness or tingling in extremities or anginal pain develops, may aggravate MI, or aggravate intermittent claudication), elderly, daily rebound headaches indicative of ergotamine dependence; discontinuation after regular normal dosage may result in withdrawal headache; See also notes above.

Drug interactions: beta blockers, macrolide antibiotics, sumatriptan - containing preparation, sympathomimetic agents such as adrenaline; vasoconstrictor - containing local anesthetic, systemic vasoconstrictors, ciprofloxacin, diclofenac, doxycycline, quinidine, verapamil, MAO inhibitors.

Contraindications: hypersensitivity to ergotamine, pregnancy and breastfeeding, children, peripheral vascular disorders, coronary artery disease, obliterative vascular disease and Raynaud Syndrome, severe hypertension, sepsis, severe renal or hepatic dysfunction; hyperthyroidism, prolonged use of excessive dosage

Side effects: nausea, vomiting, vertigo, abdominal pain, diarrhea, muscle cramps, increased headache; pericardial pain, myocardial ischaemia; rarely myocardial infarction; repeated high dosage may cause ergotism with gangrene and confusion; pleural and peritoneal fibrosis may occur with excessive use.

Dose and Administration:

Treatment of acute migraine attack:

Sublingual: **Adult:** 2mg under tongue at the start of the attack, repeated at intervals of at least thirty minutes, if necessary, up to a total of 6mg per day.

Oral: **Adult:** 1- 2 mg at first sign of attack, maximum 4mg in 24 hours; do not repeat at intervals of less than 4 days maximum 8mg in any one week; not to be used more than twice in any 1 month.

****Ergotamine Tartrate** was formerly given by subcutaneous or IM injection but dihydroergotamine mesylate is generally used if parenteral administration is necessary.

Storage: at room temperature in a well closed, light resistant container.

Ergotamine Tartrate + Caffeine

Tablet, 1mg + 100mg

Suppository, 2mg + 100mg

Indications: as for ergotamine.

Cautions: as for ergotamine; and also, breast-feeding women.

Drug interactions: as for ergotamine, also CNS stimulant, MAO inhibitors.

Contraindications: as for ergotamine, also anxiety disorders, insomnia, peptic ulceration, and severe cardiac disease.

Side effects: as for ergotamine above, also insomnia.

Dose and Administration:

Oral: Adult: 1 - 2 tablets at onset; maximum 4 tablets in 24 hours; not to be repeated at intervals of less than 4 days; maximum 8 tablets in one week; child not recommended.

Rectal: 1 suppository at onset; maximum 2 in 24 hours; not to be repeated at intervals of less than 4 days; maximum 4 suppositories in one week.

Ergotamine Tartrate + Cyclizine Hydrochloride + Caffeine Hydrate

Tablet, 2 mg + 50mg + 100mg

Indication: as for ergotamine and caffeine above.

Cautions: as for ergotamine and caffeine, also pediatrics, geriatrics.

Drug interactions: as for ergotamine and caffeine, also drugs with anticholinergic effect.

Contraindications: as for ergotamine and caffeine, also patients which may adversely affected by anticholinergic effects.

Side effects: as for ergotamine and caffeine, also cyclizine has antihistaminic, anticholinergic, and CNS depressant effects.

Dose and Administration:

Oral: Adult: 1 tablet at onset, followed after 30 minutes by ½ - 1 tablet, repeated every 30 minutes if necessary; maximum 4 tablets per attack and 6 tablets in one week, child not recommended.

Methadone hydrochloride

Injection, 10 mg/ml in 1 ml ampoule

Tablet, 5 mg

Indications: for relief of severe pain, cough suppressant, opioid dependence.

Cautions: as for morphine. Methadone has a long half-life and accumulation may occur with repeated doses, especially in elderly or debilitated patients; caution in hepatic and renal impairment.

Drug interactions: as for morphine, and also fluconazole, zidovudine.

Contraindications: as for morphine, see also notes above.

Side effects: as for morphine. Methadone has a more prolonged effect than morphine and readily accumulates with repeated doses. It may have a relatively greater respiratory depressant effect than morphine and, although reported to be less sedating, repeated doses of methadone may result in marked sedation. It causes pain at injection sites; subcutaneous injection causes local tissue irritation and induration.

Dose and Administration: Adult:

Analgesia: Oral: 2.5-10mg every 3-4 hours as needed.

IV: initial: 2.5-10mg every 8-12 hours in opioid-naive patients, also be administered by *SC* or *IM* injection.

Storage: store at room temperature.

Morphine Sulphate

Tablets, 5mg, 10 mg, 15mg, 20mg, 30mg

Oral solution, 10 mg / 5ml, 100 mg/5ml

Suppository, 10mg, 15mg, 20mg, 30mg

Granules for oral suspension, 20mg, 60mg, 100mg, 200mg per sachet

Capsule (modified release), 20mg, 50mg, 100mg, 200mg

Injection (as hydrochloride), 10 mg/ml, 20mg/ml in 1ml ampoule

Indications: analgesic, antidiarrhoeal, anaesthesia adjunct and antitussive; see also notes above.

Cautions: renal and hepatic impairment; elderly and debilitated, dependence; hypothyroidism; convulsive disorders; decreased respiratory reserve and acute asthma; hypotension, prostatic hypertrophy; pregnancy and breastfeeding, adrenocortical insufficiency, obstructive bowel disorders, myasthenia gravis, withdraw gradually, not drive or operate machinery; see also notes above.

Drug interactions: CNS depressants; e.g alcohol, anaesthetic agents; antidiarrheals; anticholinergics, antihypertensives; cimetidine; metoclopramide; MAO inhibitors.

Contraindications: acute respiratory depression, acute alcoholism, where risk of paralytic ileus; raised intracranial pressure or head injury; avoid injection in pheochromocytoma; during labour, diarrhea caused by poisons, antibiotic-associated pseudomembranous enterocolitis, acute abdominal conditions and biliary colic; see also notes above.

Side effects: nausea, vomiting, constipation, drowsiness, also dry mouth, anorexia, spasm of urinary and biliary tract, bradycardia, tachycardia, palpitations, euphoria, decreased libido, rash, urticaria, pruritus, sweating, headache, facial flushing, vertigo, postural hypotension, hypothermia, hallucinations, confusion, tolerance & dependence, miosis, larger doses produce respiratory depression and hypotension.

Dose and Administration:

Adult: *IM or SC:* 5 -15mg (usually 10 mg initially, based on an adult weighing 70 Kg); repeated 3-4 hourly as required.

IV: 2.5 mg increments every 5 - 10 minutes, up to a maximum of 15 mg.

Oral: 5 - 20 mg 4 hourly. When changing to a controlled release formulation, give the current total 24 - hour requirement in 2 divided doses.

Controlled - release tablets: Initially 10 - 20 mg twice daily, increased according to individual requirements.

Child: *IM or SC:* over one month old, 0.1-0.2 mg/kg.

Neonates: *IM or SC:* 0.1mg/kg.

Facilities must be available to provide ventilatory support if necessary.

Storage: store at room temperature.

Pentazocine

Tablet, 50mg

Injection, 30mg/ml in 1ml ampoule

Indications: moderate to severe pain.

Cautions: as for morphine; pentazocine has weak opioid antagonist actions and may precipitate withdrawal symptoms if given to patients who are physically dependent on opioids.

Drug interactions: see under pethidine Hydrochloride.

Contraindications: see under Pethidine Hydrochloride and notes above; patients dependent on opioids; arterial or pulmonary hypertension, heart failure.

Side effects: as for morphine; also hallucinations, nightmares, thought disturbances, hypertension, tachycardia, agranulocytosis, toxic epidermal necrosis.

Dose and Administration:

Oral: **Adult:** Pentazocine hydrochloride 50mg every 3 - 4 hours preferably after food (range 25 - 100mg); maximum 600mg daily; **Child** 6 - 12 years 25 mg every 3-4 hours.

SC, IM, or IV injections: **Adult:** moderate pain, 30mg; severe pain 45 - 60 mg every 3 - 4 hours when necessary; **Child** over 1 year, *by S.C or IM injection*, up to 1mg/kg, *by IV injection* up to, 500 micrograms/kg.

Storage: at room temperature in a tight, light resistant container. Protect from freezing (Injection).

Pethidine Hydrochloride*Tablet, 50mg**Injection, 50mg/ml in 1 and 2ml ampoules*

Indications: analgesia in moderate to severe pain including labour, anaesthesia adjunct; see also introduction notes.

Cautions: as for morphine above, also atrial fibrillation or other cardiac diseases where tachycardia might pose a problem.

Drug interactions: as for morphine, also MAO inhibitors, and cimetidine

Contraindications: as for morphine above, also renal failure or severe hepatic disease.

Side effects: as for morphine above; the effect on smooth muscle may be relatively less intense than with morphine and constipation occurs less frequently. Local reactions often follow injection of pethidine; general hypersensitivity reactions occur rarely. Pethidine given intravenously may increase the heart rate.

Dose and Administration:

Adult: *Oral:* 50 - 150mg every 4 hours

IM (preferred), SC: 50 -150mg (usually 100mg) every three to four hour as needed;

Child: *Oral or IM:* 0.5-2.0mg/kg/dose, repeated 8 hourly if required. Maximum 6mg/kg/day.

Storage: store at room temperature protect from light and from freezing.

Phenazopyridine*Tablet, 100 mg*

Indications: symptomatic relief of urinary burning, itching in association with urinary tract infection.

Cautions: G6PD deficiency or discontinue if the skin or sclerae become discolored.

Contraindications: allergic reaction to phenazopyridine; hepatitis, impaired renal function.

Side effects: anemia, aseptic meningitis, dermatitis, allergic, hepatotoxicity, methemoglobinemia, renal function impairment or failure, dizziness, headache, indigestion, pruritus, stomach cramps or pain.

Dose and Administration: *Oral:*

Adult: 100-200 mg 3 times /day, after meals for up to 2 days when it is used concomitantly with an antibacterial agent.

Child: 12 mg/kg/day in 3 divided doses administered after meals for 2 days.

Storage: store at room temperature in a tight container.

Sumatriptan

Tablets, 50 mg, 100 mg

Injection, 12 mg/ml

Nasal spray, 20 mg/0.1ml

Indications: treatment of acute migraine attacks with or without aura, cluster headache.

Cautions: patients with a history of seizure disorder, impaired hepatic or renal function, nursing mothers, safety and effectiveness in children have not been established.

Drug interactions: ergotamine, MAO inhibitors, selective serotonin re-uptake inhibitors, lithium.

Contraindications: hypersensitivity to the drug, IV use, coronary artery disease (CAD); risk factor for CAD such as hypertension, hypercholesterolemia, obesity, diabetes, smoking, and strong family history.

Side effects: chest pain, heaviness or tightness, transient increase in blood pressure, bronchospasm, flushing, tingling, dizziness, dysphagia, muscle cramps and weakness; transient pain at injection site, nausea and vomiting; vertigo.

Dose and Administration: Adult:

Oral: initially 50 mg; depending on response, this may be increased to 100 mg. If symptoms recur after an initial beneficial response, the dose may be repeated after 2 - 4 hours; maximum 300 mg in 24 hours.

SC: 6 mg. If symptoms recur after an initial beneficial response, 6 mg may be repeated after at least 1 hour; maximum 12 mg/24 hours.

Intranasal: 20 mg. If symptoms recur, the dose may be repeated after a minimum of 2 hours; Maximum 40 mg/24 hours.

Storage: store at 2-30 °C; protect from light.

Tramadol

Tablet / Capsule, 50 mg, 75 mg, 100 mg, 150 mg, 200 mg, 300 mg

Drops, 100 mg/ml (40 drops)

Nasal spray, 20 mg/0.1ml

Injection, 50 mg/ml

Indications: moderate to severe pain.

Cautions: hepatic or renal impairment, and when risk of seizures exists.

Drug interactions: carbamazepine, CNS depressants, anaesthetics, alcohol, MAO inhibitors.

Contraindications: increased intracranial pressure or head injury, respiratory depression.

Side effects: as for morphine, but less potential for abuse, respiratory depression, or constipation.

Dose and Administration: Adult:

Oral: 50 - 100 mg 4 - 6 hourly, maximum 400 mg/day.

Sustained - release formulation, initially 100 mg twice daily, increased to 150 mg or 200 mg twice daily.

Drops: initially 50 mg (20 drops or 0.5 ml), repeated in 30-60 minutes if analgesia is not achieved; maximum 400 mg/day (160 drops).

IV: over 2 - 3 minutes or by infusions, IM or SC, 50-100 mg 4 - 6 hourly; maximum 400 mg/day.

Elderly >75 years: *Oral:* 50-100 mg every 4-6 hours (not exceed 300 mg/day)

Storage: store at room temperature.

4.2. Anxiolytics Sedatives, Hypnotics and Antipsychotics

The drugs in this section include:

- Anxiolytic sedatives, formerly called minor tranquilizers
- Drugs used to produce sleep (hypnotics)
- Drugs used in the treatment of psychoses (antipsychotics, formerly called major tranquillizers)

The difference in action between anxiolytics and hypnotics is mainly one of degree and the same drug or group of drugs can have both effects, larger doses being necessary to produce a state of sleep.

Anxiolytics

Benzodiazepine therapy

The benzodiazepines are primarily indicated for the treatment of anxiety states and as hypnotics.

Other indications include:-

- Peri-operative- as premedication
- Management of alcohol withdrawal (delirium treatments)- attenuating the acute withdrawal symptoms
- Treatment of seizure disorders
- Muscle relaxant

All benzodiazepines act by facilitating the action of gamma-aminobutyric acid (GABA) which is the major inhibitory neurotransmitter in the CNS. Benzodiazepine receptors have been identified in the brain, located in close proximity to GABA receptors. Activation of the benzodiazepine receptors promotes the activity of the GABA receptors.

The benzodiazepines may be divided into four groups on the basis of the elimination half-lives of the parent compound and the active metabolites (if any):

- Ultra short-acting (half life < 6 hours); Midazolam.
- Short-acting (half life 6-12 hours); oxazepam, temazepam
- Intermediate-acting (half life 12-24 hours); Alprazolam, bromazepam
- Long-acting (half life > 24 hours); chlordiazepoxide, diazepam, medazepam, flurazepam

It should be noted that the pharmacological duration of action of a drug is dependent on many factors other than elimination half-life. This system of classification may thus not always accurately predict the duration of clinical effect.

Alprazolam

Tablet, 0.25mg, 0.5mg, 1mg

Indication: anxiety (short-term use)

Cautions, Drug interactions, Contraindications, Side effects; see under diazepam and also notes above.

Dose and Administration: *Oral:*

Adult: 0.25 - 0.5mg 3 times daily (elderly or debilitated 0.25 mg 2-3 times daily), increased if necessary to a total of 3mg daily.

Storage: store at room temperature in a tight, light resistant container.

Bromazepam

Tablet, 1.5mg, 3mg, 6mg

Indications: anxiety (short - term use)

Cautions, Drug interactions, Contraindications, Side effects; see under diazepam, and also notes above.

Dose and Administration: *Oral:*

Adult: 3 - 18mg daily in divided doses; elderly (or debilitated) half adult dose; maximum (in exceptional circumstances in hospitalized patients) 60mg daily in divided doses.

Storage: store at room temperature in a well-closed container.

Chlordiazepoxide

Tablet, 5mg, 10mg, 25mg

Indications: anxiety (short - term use); adjunct in acute alcohol withdrawal.

Cautions, Drug interactions, Contraindications, Side effects; see under diazepam, and also notes above.

Dose and Administration: *Anxiety: Oral:*

Adult: 10mg 3 times daily increased if necessary to 60 - 100mg daily in divided doses; elderly (or debilitated) half adult dose.

Note: - the doses stated above refer equally to chlordiazepoxide and to its hydrochloride.

Storage: store at room temperature in a tight, light resistant container.

Diazepam

Tablet, 2mg, 5mg, 10mg

Suppository, 5mg, 10mg

Syrup, 2mg/5ml

Injection, 5mg/ml in 2ml ampoule

Indications: short-term treatment of anxiety or insomnia; adjunct in acute alcohol withdrawal; status epilepticus; febrile convulsions; muscle spasm; peri-operative use.

Cautions: elderly, in patients with impaired liver or kidney function, muscle weakness; elderly or debilitated patients; respiratory disease, history of alcohol abuse, marked personality disorder; pregnancy; breastfeeding; avoid prolonged use and abrupt withdrawal; porphyria.

Note:- drowsiness may affect performance of skilled tasks (e.g. driving); effects of alcohol enhanced.

Drug interactions: alcohol, antidepressants, antihistamines, antipsychotics, sedative, general anaesthetics, other hypnotics or sedatives, and opioid analgesics (sedation or respiratory and cardiovascular depression may be enhanced); fluvoxamine, ketoconazole, nefazodone (concurrent use may inhibit the hepatic metabolism of benzodiazepines that are metabolized by oxidation); plastic infusion tubing (diazepam may adhere to plastic infusion tubing), zidovudine, aminophylline.

Contraindications: preexisting CNS depression or coma, acute pulmonary insufficiency, or sleep apnoea, severe hepatic impairment; myasthenia gravis; respiratory depression; diazepam should not be used for the treatment of chronic psychosis or for phobic or obsessional states. Avoid injections containing benzyl alcohol in neonates.

Side effects: drowsiness and light headedness the next day; confusion and ataxia (especially in the elderly); amnesia; dependence; paradoxical increase in aggression; muscle weakness; occasionally headache, vertigo, salivation changes, gastrointestinal disturbances, visual disturbances, dysarthria, tremor, changes in libido, incontinence, urinary retention, blood disorders and jaundice, skin reactions raised liver enzymes, on IV injection, pain, thrombophlebitis and rarely apnea.

Dose and Administration: *Oral:*

Adult: *Anxiety:* 2mg 3 times daily increased if necessary to 15 - 30 mg daily in divided doses; elderly (or debilitated) half adult dose.

Insomnia associated with anxiety: 5- 15 mg at bedtime.

Child: *night terrors and somnambulism:* 1 - 5 mg at bedtime.

IM or slow IV injection (into a large vein, at a rate of not more than 5mg/minute): for severe acute anxiety, control of acute panic attacks, and acute alcohol withdrawal, 10mg, repeated if necessary after not less than 4 hours.

Note: - Only use intramuscular route when oral and intravenous routes not possible.

Rectum as suppositories: *anxiety* when oral route not appropriate, 10 - 30mg (higher dose divided), dosage form not appropriate for less than 10mg.

Storage: at room temperature in light resistant container protect from freezing.

Flurazepam

Capsule, 15 mg, 30 mg

Indications: short-term treatment of insomnia.

Cautions: elderly, pregnancy and children < 15 years of age.

Drug interactions:azole antifungals, ciprofloxacin, clarithromycin, diclofenac, doxycycline, erythromycin, isoniazide, protease inhibitor, quinidine, verapamil, cimetidine, clozapine, CNS depressants, digoxin, disulfiram, metoprolol.

Contraindications: narrow -angle glaucoma, pregnancy.

Side effects: chest pain, constipation, drowsiness, memory impairment, hangover effect, euphoria, hallucinations, rash, vomiting, diarrhea, nausea, blurred vision, tinnitus, and apnea.

Dose and Administration: *Oral:*

Adult: 15-30 mg at bedtime.

Elderly: 15mg at bedtime; avoid use if possible

Storage: store in light-resistant containers and at room temperature.

Medazepam

Capsule, 5mg, 10mg

Medazepam is a long acting benzodiazepine with properties similar to those of diazepam.

Indications: used for short-term treatment of anxiety disorders.

Cautions, Drug interactions, Contraindications, Side effects; see under diazepam, and also notes above.

Dose and Administration: *Oral:* **Adult:** 10-30mg daily in divided doses; in severe conditions up to 60mg daily has been given.

Storage: store at room temperature.

Midazolam Hydrochloride

Injection, 1mg/ml, 2 mg/ml in 5ml ampoule, 5 mg/ml in 2ml ampoule

Syrup, 2mg/ml

Indications: preoperative sedation and provides conscious sedation prior to diagnostic or radiographic procedures; intravenous anesthesia (induction and maintenance).

Cautions, Drug interactions, Contraindications and Side effects; see under diazepam.

Dose and Administration: Adult:

Preoperative sedation:

IM: 0.07-0.08 mg/kg 30-60 minutes prior to surgery/procedure; usual dose: 5mg.

IV: 0.02-0.04mg/kg; repeat every 5 minutes as needed to desired effect or up to 0.1-0.2mg/kg.

Conscious sedation:

IV: initial; 0.5-2mg slow IV over at least 2 minutes; slowly titrate to effect by repeating doses every 2-3 minutes if needed; usual total dose: 2.5-5mg; use decreased doses in elderly.

Anesthesia:

IV: Induction: Unpremedicated patients: 0.3-0.35mg/kg (up to 0.6mg/kg in resistant cases)

Premedicated patients: 0.15-0.3 mg/kg.

Maintenance: 0.05-0.3mg/kg as needed or continuous infusion 0.25

1.5mcg/kg/minute

Conscious sedation for procedures or preoperative sedation:

Oral: 0.25-0.5 mg/kg as a single dose procedure, up to a maximum of 20 mg; administer 30-45 minutes prior to procedure. **Child** < 6 years or less-

cooperative patients may require as much as 1 mg/kg as a single dose; 0.25 mg/kg may suffice for child 6-16 years of age.

Storage: store at room temperature.

Oxazepam

Tablet, 10 mg

Indications: short-term management and relief of anxiety.

Cautions, Drug interactions, Contraindications, Side effects; see under diazepam, and also notes above.

The elderly are more sensitive to CNS effects, use the smallest effective dose.

Dose and Administration: *Oral*

Adult: *Anxiety:* 10 - 15 mg 2 - 4 times daily.

Insomnia: 5 - 30 mg 1 - 2 hours before bedtime.

Psychotic patients and alcoholics: 30 mg 3 - 4 times daily may be required.

Note: if used as hypnotic, it should be administered at least 1-2 hours before bedtime as absorption is slower than with diazepam.

Storage: store at room temperature

Temazepam

Capsules, 10mg, 15mg, 20mg, 30mg

Indications: short-term treatment of insomnia.

Cautions: elderly or debilitated patients; respiratory disease, renal and hepatic impairment.

Drug interactions: narcotic analgesics, barbiturates, phenothiazins, MAO inhibitors, cimetidine, ciprofloxacin, clozapine, and oral contraceptive.

Contraindications: narrow-angle glaucoma, pregnancy.

Side effects: confusion, dizziness, drowsiness, anxiety, headache, hangover, euphoria, rash, decreased libido, diarrhea, blurred vision, diaphoresis.

Dose and Administration: **Adult:** 15-30mg at bedtime.

Elderly or debilitated patients: 15mg

Storage: store at room temperature.

Zolpidem

Tablet, 10mg

It is an imidazopyridine, chemically distinct from the benzodiazepines, but exhibiting selective high affinity for a benzodiazepine receptor subtype. Its sedative action predominates over its muscle relaxant and anticonvulsant activity (in contrast to the benzodiazepines), and its indication is for the treatment of insomnia.

Dose and Administration: *Oral:* **Adult:** 10mg at bedtime. Hepatic impairment and the elderly: 5 mg.

Hypnotics

These agents act by depressing the central nervous system. Although widely prescribed, both physical and psychological dependence, as well as tolerance, occur. They have no analgesic effects, and in the presence of pain, adequate analgesia is desirable. Anterograde amnesia has been described even with single doses of hypnotics.

Chloral Hydrate

Capsule, 500 mg

Suppository, 60 mg

Syrup, 250 mg/5ml, 500 mg/5ml, 1 g/ml

Indications: short term sedative and hypnotic (< 2 weeks), sedative / hypnotic for diagnostic procedures; sedative prior to EEG evaluations.

Cautions: respiratory disease, pregnancy and breast-feeding, neonates.

Drug interactions: CNS depressants, warfarin, IV furosemide, benzodiazepine.

Contraindications: hepatic or renal impairment; cardiac disease, gastritis or ulcers.

Side effects: gastric irritation with nausea and vomiting, ataxia, headache, malaise, nightmares and delirium; eosinophilia, reduction in white cell count; dependence with prolonged use.

Dose and Administration:

Adult: *Oral, Rectal:*

Sedation, anxiety: 250 mg 3 times / day

Hypnotic: 500 - 1000 mg at bed time or 30 minutes prior to procedure, not to exceed 2 g/24 hours.

Child:

Sedation or anxiety: *Oral, Rectal:* 5 - 15 mg/kg/dose every 8 hours (maximum: 500 mg/dose)

Prior to EEG: *Oral, Rectal:* 20 - 25 mg/kg/dose, 30-60 minutes prior to EEG; may repeat in 30 minutes to maximum of 100 mg/kg or 2 g total.

Hypnotic: *Oral, Rectal:* 20 - 40 mg/kg/dose up to a maximum of 50 mg/kg/24 hours or 1 g/dose or 2 g/24 hours

Conscious sedation: *Oral:* 50 - 75 mg/kg/dose 30 - 60 minutes prior to procedure; may repeat 30 minutes after initial dose if needed, to a total maximum dose of 120 mg/kg or 1 g total.

Storage: store in light resistant, airtight container and at room temperature.

Pentobarbitone (pentobarbital)

Capsule, 50mg

Suppository (Sodium), 30mg, 60mg

Injection (sodium), 50mg/ml in 50ml

Indications: sedative/hypnotic; preanesthetic; high-dose barbiturate coma for treatment of increased intracranial pressure or status epilepticus unresponsive to other therapy.

Cautions: elderly, debilitated, renally impaired, hepatic dysfunction, or paediatric patients. Patients with depression or suicidal tendencies.

Drug interactions: other CNS depressants, ethanol, narcotic analgesics, antidepressants, or benzodiazepines, chloramphenicol, MAO inhibitors, valproic acid, griseofulvin, clarithromycin, cyclosporine, erythromycin, nevirapine, protease inhibitors, rifampin, oral contraceptives, oral anticoagulants.

Contraindications: hypersensitivity to barbiturates; hepatic impairment; dyspnea or airway obstruction; porphyria; pregnancy.

Side effects: bradycardia, hypotension, drowsiness, CNS excitation or depression, lethargy, headache, insomnia, anxiety, dizziness, rash, nausea, vomiting, constipation, thrombocytopenia.

Dose and Administration:

Adult: *Hypnotic: IM:* 150-200mg

IV: initial: 100mg, may repeat every 1-3 minutes up to 200-500 mg total dose.

Preoperative sedation: IM: 150-200mg

Child: *Hypnotic: IM:* 2-6 mg/kg; maximum 100mg/dose

Preoperative sedation: ≥ 6 months: IM: 2-6mg/kg; maximum: 100mg/dose

IV: 1-3mg/kg to a maximum of 100mg until asleep.

Storage: at room temperature in air tight container.

Phenobarbitone (Phenobarbital)*Tablet 10mg, 15mg, 30mg, 60mg, and 100mg**Elixir, 20mg/ 5ml**Injection (Sodium), 25mg/ml in 1ml ampoule, 100mg/ml in 1ml ampoule, 4%***Indications:** sedative-hypnotic.**Cautions:** pediatric, elderly, and debilitated patients.**Drug interactions:** alcohol, CNS depressants, adrenocorticoids, glucocorticoids and mineralocorticoids; or chloramphenicol; corticotropin; coumarin or indandione - derivative anticoagulants, carbamazepine, estrogen-containing contraceptives; valproic sodium or valproic acid; vitamin D; xanthines such as aminophylline, caffeine, oxtriphylline, theophylline, rifampin; monoamine oxidase inhibitors including furazolidone, paralyline and procarbazine; doxycycline.**Contraindications:** pregnancy and breastfeeding, and in patients with acute intermittent or variegated or history of porphyria, insomnia caused by pain, drug abuse or dependence (history of), hepatic coma or hepatic function impairment, acute or chronic pain; respiratory disease involving dyspnea or obstruction, particularly status asthmaticus; sensitivity to barbiturates.**Side effects:** Common – drowsiness (especially with initiation of therapy).

Uncommon – ataxia and nystagmus (usually dose-related), dizziness and psychomotor impairment.

Rare – skin reactions, including Stevens-Johnson syndrome, photosensitivity; folic acid deficiency and megaloblastic anaemia. Prolonged use may lead to dependence, with a withdrawal syndrome on termination of treatment; also rickets and osteomalacia due to vitamin D deficiency, hypoprothrombinaemia and hepatitis.

Dose and Administration:**Hypnotic: Adult:** *Oral:* 100 to 320mg (base) at bedtime;*IM or IV:* 100 to 325mg.**Child:** dosage must be individualized by physician.**Sedative: Oral:****Adult:** daytime- 30-120mg (base) in two or three divided doses a day;**Child:** *daytime,* 2mg (base)/kg of body weight three times a day; Preoperative, 1 to 3mg (base) per kg of body weight.*IM or IV:***Adult:** *daytime,* 30 to 120mg a day in two or three divided doses, preoperative (*IM*), 130-200mg sixty to ninety minutes before surgery.**Child:** preoperative, 1 to 3mg per kg of body weight, sixty-ninety minutes prior to surgery.**Storage:** at room temperature in a tight container protect from freezing.**Promethazine***Tablet, 25mg***Indications:** night sedation and insomnia or it is indicated as sedative hypnotic.

Cautions: epilepsy, prostatic hypertrophy, urinary retention, glaucoma, hepatic disease, jaundice, also during pregnancy and breast-feeding, in children and elderly. It causes drowsiness. Patients should be advised to avoid car driving, machine operating or doing activities requiring alertness.

Drug interactions: alcohol, CNS depressants, anticholinergics, antithyroid, epinephrine, extrapyramidal reaction causing medication, levodopa, metrizamide, monoamine oxidase inhibitors including furazolidone and procarbazine.

Contraindication: hypersensitivity to promethazine; coma; treatment of lower respiratory tract symptoms, including asthma; children < 2 years of age.

Side effects: drowsiness, headache, psychomotor impairment, urinary retention, dry mouth, blurred vision, gastrointestinal disturbances, rashes, photosensitivity reactions, palpitation, and arrhythmias, hypersensitivity reaction (including bronchospasm, angioedema, and anaphylaxes), convulsions, sweating, myalgia, paraesthesia, blood disorders, tremor, liver dysfunction, sleep disturbance, depression, hypotension, and hair loss, extra pyramidal effects.

Dose and Administration:

Adult: *Oral:* 25mg at bed time, increased to 50mg if necessary.

Child (2-5 years): 15 to 20mg; 5-10 years: 20 to 25mg at bed time.

Storage: at room temperature in a tight, light-resistant container.

Antipsychotics

Antipsychotics may be used in a wide variety of psychotic disorders including schizophrenia, organic psychoses, the manic phase of bipolar affective disorder (manic depressive illness), psychotic depression, and other acute psychotic illnesses.

Chlorpromazine Hydrochloride

Tablet, 25 mg, 50mg, 100mg

Drop, 25mg/ml in 10ml bottle, 40mg/ml in 10ml and 30ml bottles

Syrup, 25mg/5ml

Injection, 25mg/ml in 1 and 2ml ampoules, 50mg/ml in 2ml ampoule

Indications: symptomatic management of psychotic disorders in non-hospitalized patients with relatively mild symptomatology and for the management of excessive anxiety, tension, and agitation.

Cautions: cardiovascular and cerebrovascular disease, respiratory disease, parkinsonism, epilepsy, acute infection, pregnancy, breast-feeding, renal and hepatic impairment, history of jaundice, leucopenia, hypothyroidism, myasthenia gravis, prostatic hypertrophy, closed-angle glaucoma. Caution also in elderly particularly in very hot or cold weather.

Note: Avoid abrupt withdrawal. Avoid direct contact with chlorpromazine for it causes contact sensitization. Advise patients not to drive cars or operate machineries or do activities requiring alertness.

Drug interactions: alcohol, CNS depressants, tricyclic antidepressants such as amitriptyline, antithyroid agents, epinephrine, extra pyramidal reaction causing

medication, hypotension producing medication, levodopa, lithium, metrizamide, amphetamines, anticonvulsants including barbiturates.

Contraindications: severe cardiovascular disease, severe CNS depression, and comatose states.

Side effects: akathisia (restlessness or need to keep moving), blurred vision associated with anticholinergic effects; deposition of opaque material in lens, cornea and retina (blurred vision), diatonic extrapyramidal effects (muscle spasms of the face, neck, and back; tic-like or twitching movements; twisting movements of the body; inability to move eyes; weakness of arms and legs); parkinsonian extrapyramidal effects (difficulty in speaking or swallowing; loss of balance control; mask like face; shuffling walk; stiffness of arms or legs; trembling and shaking of hands and fingers); hypotension (fainting), pigmentary retinopathy (blurred vision, detective colour vision, difficulty seeing at night); tardive dyskinesia (lip smacking or packering; putting of cheeks, rapid or work-like movements of tongue; uncontrolled chewing movements; uncontrolled movements of arms and legs); ammenorrhea and gallactorrhea (female), gynecomastia and impotence (in male), hypothermia (decrease body temperature below Normal); dry mouth; tachycardia, urinal retention; increased appetite and weight gain, cholestatic jaundice, corneal capacity.

Dose and Administration: *Oral and IM:*

Adult: Psychotic disorder:

Oral: 10 to 25mg (base) two or four times a day, the dosage being increased by 20 - 50mg a day over 3 or 4 days as needed or tolerated.

IM: (sever) - 25 to 50mg (base), the dosage being repeated in one hour if needed and every three to twelve hours thereafter as needed and tolerated. The dosage may be gradually increased over several days as needed and tolerated.

Child (6 and older):

Oral: 0.5mg per kg of body weight every four to six hours, the dosage being adjusted as needed and tolerated.

IM: 0.55 mg per kg of body weight one or two hours before surgery.

Storage: At room temperature. Protect from light and freezing

Clozapine

Tablet, 25 mg, 50 mg, 100 mg

Indications: schizophrenia.

Cautions: prostatic enlargement, narrow-angle glaucoma, history of seizures.

Drug interactions: benzodiazepines, risperidone, amiodarone, ciprofloxacin, ketoconazole, norfloxacin, lidocaine, dextrometorphan, lidocaine, amphetamines, codein, tramadol, and phenobarbital.

Contraindications: history of drug-induced agranulocytosis, bone marrow disorders, severe liver, renal or cardiac disease, toxic or alcoholic psychoses, uncontrolled epilepsy.

Side effects: drowsiness, sedation, fatigue, orthostatic hypotension, dizziness, headache, dry mouth, blurred vision, hypersalivation (common), weight gain, nausea, vomiting, constipation, urinary incontinence and retention, increase in

hepatic enzymes. Risk of agranulocytosis and neutropenia is far greater than with other neuroleptics. Fatal myocarditis and cardiomyopathy.

Dose and Administration: *Oral: Adult:*

Initially 12.5 - 25 mg daily gradually increased in 25 - 50 mg increments to achieve therapeutic doses in 2 - 3 weeks. Usual range 200 - 450 mg/day in divided doses; up to 600 mg/day may be required. Maximum 900 mg/day.

Storage: store in tight containers at a temperature not exceeding 30 °C.

Fluphenazine decanoate

Depot injection, 25 mg/ml in 1ml and 2ml ampoules and in 10ml vial.

Indications: psychotic disorders, particularly chronic schizophrenia.

Cautions: cardiovascular and cerebrovascular disorders, respiratory disease, epilepsy, acute infections, pregnancy, breastfeeding, renal and hepatic impairment, history of jaundice, leukopenia, hypertrophy, angle-closure glaucoma, elderly.

Drug interactions: anticholinergics, antiepileptics, antihypertensives, antiparkinsonian agents, CNS depressants, metabolic enzyme inducers, antacids.

Contraindications: children, confusional states, impaired consciousness due to CNS depression, parkinsonism, intolerance to antipsychotics, depression, bone-marrow depression, and pheochromocytoma.

Side effects: extrapyramidal side effects, especially in the elderly; anticholinergic effects, hypotension and sedation; photosensitivity, effects on the heart, jaundice and blood dyscrasias. Increased risk of extrapyramidal reactions with depot injections. Pain may occur at the injection site, and occasionally erythema, swelling and nodules.

Dose and Administration: *Fluphenazine decanoate depot: Adult:*

Deep IM: initially 12.5 mg; subsequent doses determined by individual response. Usual range 6.25 - 25 mg every 2 - 4 weeks. Higher doses (up to 50 mg) are rarely required.

Elderly: Doses at the lower end of the range should be used.

Storage: store at room temperature.

Fluphenazine Hydrochloride

Tablet, 1mg

Indications: schizophrenia, mania, severe anxiety, and other psychoses.

Cautions: pregnancy, breast-feeding, cardiovascular and cerebrovascular disease, parkinsonism, epilepsy, acute infections, history of jaundice, leucopenia, liver and kidney disease, hypothyroidism, myasthenia gravis, prostatic hypertrophy, closed angle glaucoma and elderly patients particularly in very hot or very cold weather

Drug interactions: alcohol, CNS depression – producing medications, tricyclic anti-depressants, anti-thyroid agents, epinephrine, extrapyramidal reaction causing medications, hypotension-producing medications, levodopa, lithium,

metrizamide, fluoxetine, fluvoxamine, paroxetine, maprotiline, astemizole, terfenadine, sotalol.

Contraindications: severe CNS depression, comatose states, active alcoholism, blood dyscrasias, hepatic function impairment, Reye's syndrome, bone marrow disorders, history of cardiac arrhythmias, congenital long QT syndrome, marked cerebral atherosclerosis.

Side effects: extrapyramidal symptoms, akathisia, tardive dyskinesia, blurred vision, hypothermia, drowsiness, apathy, pallor, night mares, insomnia, depression and more rarely agitation, EEG changes, convulsions; anti muscarnic and cardiovascular symptoms.

Dose and Administration:

Adult:

Initial: *Oral:* 2.5 to 10 mg a day in divided doses every six to eight hours, the dosage being gradually increased as needed and tolerated.

Maintenance: *Oral:* 1 to 5 mg a day as a single dose or in divided doses.

Note: Emaciated or debilitated patients usually require a lower initial dosage (1 to 2.5 mg daily), the dosage being gradually increased as needed and tolerated.

Usual adult prescribing limits: - up to 20 mg a day

Child: *Oral:* 250 to 750 mcg (0.25 to 0.75 mg) one to four times a day.

Elderly: *Oral:* 1 to 2.5 mg a day, the dosage being gradually increased as needed and tolerated.

Storage: in a tight, light-resistant container at room temperature.

Haloperidol*Tablet, 1mg, 2mg, 5mg**Oral liquid, 2ml/ml**Injection, 5mg/ml in 1ml ampoule***Indications:** schizophrenia and other psychotic disorders, mania, psychomotor agitation and violent behaviour; adjunct in severe anxiety.**Cautions:** cardiovascular and cerebrovascular disorders, respiratory disease, parkinsonism, epilepsy, acute infections, pregnancy, breastfeeding, renal and hepatic impairment (avoid if severe), history of jaundice, leucopenia (blood counts if unexplained fever or infection); hypothyroidism, myasthenia gravis, prostatic hypertrophy, angle-closure glaucoma; elderly (particularly in very hot or very cold weather); children and adolescents; avoid abrupt withdrawal; patients should remain supine and the blood pressure monitored for 30 minutes after intramuscular injection; see also interactions.**Drug interactions:** amitriptyline, carbamazepine, clomipramine, ether (anaesthetic), ethosuximide, halothane, ketamine, nitrous oxide, phenobarbital, phenytoin, procainamide, quinidine, rifampicin, ritonavir, thiopental, valproic acid.**Contraindications:** impaired consciousness due to CNS depression; bone-marrow depression; phaeochromocytoma; porphyria, basal ganglia disease.**Side effects:** see notes above and under chlorpromazine; but less sedating and fewer antimuscarinic or hypotensive symptoms; pigmentation and photosensitivity reactions rare; extrapyramidal symptoms, particularly dystonic reactions and akathisia especially in thyrotoxic patients; rarely weight loss, hypoglycaemia, inappropriate antidiuretic hormone secretion.**Dose and Administrations:***Schizophrenia and other psychoses, manic, psychomotor agitation, violent behaviour, and severe anxiety (adjunct):**Oral: Adult:* initially 1.5 - 3mg 2 - 3 times daily or 3 - 5mg 2 - 3 times daily in severely affected or resistant patients (up to 30mg daily in resistant schizophrenia);*Elderly* (or debilitated) initially half adult dose;*Child* initially 25 - 50 micrograms/kg daily in 2 divided dose (maximum 10mg daily).*Acute psychotic conditions: deep IM injection:**Adult:* 2 - 10mg, subsequent doses every 4 - 8 hours according to response (up to every hour if necessary) to total maximum of 18 mg; Child not recommended.**Storage:** at room temperature in light resistant container. Protect from freezing.**Haloperidol Decanoate***Injection (Depot Oily), 50mg/ml, 100mg/ml in ampoule of 1ml***Indications:** maintenance in schizophrenia and other psychoses.**Cautions, Contraindications, and Side effects** see under haloperidol.**Dose and Administration:**

Adult: *deep I.M injection:* initially 50mg every 4 weeks, if necessary increasing by 50 mg increments to 300 mg every 4 weeks; higher doses may be needed in some patients;

Elderly: initially 12.5 - 25 mg every 4 weeks.

Adult: *Psychosis: Oral:* 0.5-5mg 2-3 times/day; usual maximum: 30 mg/day

IM (as decanoate): initial; 10-20 times the daily oral dose administered at 4-week intervals.

Lithium

Lithium is regarded as a mood stabilizer, with antimanic and antidepressant effects. Primary use is as a prophylactic agent in bipolar affective disorders, where it has been shown to reduce chiefly the manic, but also the depressive relapses. It is also useful in treating the acute manic stage, but is rarely recommended for depressive illnesses of the unipolar type.

Lithium carbonate

Tablet, 300 mg, 400 mg

Indications: treatment and prophylaxis of mania, prophylaxis of bipolar disorder and recurrent depression.

Cautions: measure serum-lithium concentration about 4 days after starting treatment, then weekly until stabilized, then at least every 3 months, monitor thyroid function and renal function, maintain adequate fluid and sodium intake, reduction of dose or discontinuation may be necessary, in diarrhoea, vomiting and intercurrent infection, pregnancy, breastfeeding, elderly, diuretic treatment, myasthenia gravis, surgery, if possible, avoid abrupt withdrawal.

Drug interactions: combination of lithium with other drugs, including over-the-counter medicines, should be carefully monitored, ACE inhibitors, antithyroid agents of iodides, neuroleptics, non-steroidal anti-inflammatory agents, thiazide and loop diuretics, xanthines.

Contraindications: cardiac disease, renal impairment or urinary retention, CNS disorders, e.g. epilepsy.

Side effects: gastrointestinal disturbances, fine tremor, polyuria, polydipsia, weight gain and oedema; signs of intoxication include blurred vision, muscle weakness, increasing gastrointestinal disturbances, increased CNS disturbances and require withdrawal of treatment, with severe overdosage, hyperreflexia and hyperextension of the limbs, convulsions, toxic psychoses, syncope, oliguria, circulatory failure, coma, occasionally death, goitre, raised antidiuretic hormone concentration, hypothyroidism, hypokalaemia, ECG changes, exacerbation of psoriasis and kidney changes may occur.

Dose and Administration: *Oral:*

Adult: initially 20 mg/kg/day in divided doses, adjusting the dose, if necessary, to achieve a plasma concentration of 0.4 - 0.8 millimol/L. Sustained - release preparations are given once or twice daily.

Storage: store in a well-closed container at room temperature.

Olanzapine*Tablet, 5mg***Indications:** schizophrenia.**Cautions:** hepatic impairment, diabetes mellitus; porphyria.**Contraindications:** narrow-angle glaucoma.**Side effects:** somnolence, agitation, dizziness, asthenia, weight gain, constipation, dry mouth, rhinitis, headache, fever, myalgia and musculoskeletal pains, neck rigidity, orthostatic hypotension, tachycardia, peripheral oedema, raised hepatic enzymes, hypertriglyceridaemia.**Dose and Administration:** *Oral:* **Adult:** initially 5-10 mg once daily. Usual therapeutic dose, 10 mg.**Storage:** store at room temperature and protect from light and moisture.**Pimozide***Tablet, 2mg, 4mg, 10mg***Indications:** suppression of severe motor and phonic tics in patients with Tourette's disorder who have failed to respond satisfactorily to standard treatment.**Caution:** neuroleptic malignant syndrome; renal or hepatic impairment.**Drug interactions:** barbiturates, alcohol, analgesics.**Contraindications:** treatment of simple tics, patient with severe toxic CNS depression, hypersensitivity to the drug.**Side effects:** amenorrhea, dysmenorrhea, vomiting, anorexia, rash and urticaria.**Dose and Administration:** *Tourette's disorder:* *Oral:***Adult and Child >12 years:** initial: 1-2mg/day in divided doses, then increase dosage as needed every other day; range is usually 7-16 mg/day, maximum dose: 10mg/day or 0.2mg/kg/day are not generally recommended.**Child ≤ 12 years:** initial: 0.05mg/kg preferably once at bed time; may be increased every third day; usual range: 2-4 mg/day; do not exceed 10mg/day (0.2mg/kg/day).**Storage:** store at room temperature.**Risperidone***Tablets, 1 mg, 2 mg, 3 mg, 4 mg, 6 mg**Oral solution, 1 mg/ml***Indications:** for acute and chronic schizophrenic psychoses with positive and/or negative symptoms, or when affective symptoms are prominent. It is also used for the management of behavioural symptoms (aggression, wandering, agitation) and psychosis associated with dementia.**Cautions:** Parkinson's disease, cardiovascular disease, and hepatic or renal impairment.**Drug interactions:** chlorpromazine, fluoxetine, miconazole, quinidine, quinine, ritonavir, clozapine, metoclopramide, levodopa, carbamazepine.**Contraindications:** hypersensitivity to risperidone.

Side effects: are similar to those of chlorpromazine; it is claimed to have a lower tendency to induce extrapyramidal symptoms than the classic neuroleptics, although extrapyramidal phenomena, tardive dyskinesia and the neuroleptic malignant syndrome have all been reported. Orthostatic hypotension has been observed, particularly with high initial doses. It can induce a dose dependent increase in plasma prolactin concentration. Weight gain may be notable.

Dose and Administration: *Oral:*

Adult: 2 mg/day on the 1st day, 4 mg/day on the 2nd day, 6 mg/day on the 3rd day; then individualised if necessary. Usual range 4 - 8 mg/day. Doses > 10 mg/day do not appear to produce increased efficacy, and may cause increased side effects.

Elderly (or in renal or hepatic impairment): initially 1 mg/day, increased by 1 mg/day up to 2 - 4 mg/day.

Storage: protect from light.

Thioridazine Hydrochloride

Tablet, 10mg, 25mg, 100mg

Indications: under specialist supervision, second line treatment of schizophrenia in adults (see notes above).

Cautions: see under chlorpromazine; ECG screening and electrolyte measurement before treatment, after each dose increase and at 6 month intervals; also monitor for visual defects on prolonged use; avoid in porphyria.

Drug interactions: antiepileptics (except carbamazepine), barbiturates, antihypertensives and B-blockers, anticoagulants; anaesthetics, analgesics, anti-arrhythmics, antibacterials, antidepressants, antifungals, antihistamines, antimalarials, other antipsychotics, antivirals, diuretics, lithium, pentamidine isetionate, sibutramine

Contraindications: Thioridazine is contraindicated in patients with:

- Clinically significant cardiac disorders (e.g. cardiac failure, angina, cardiomyopathy or left ventricular dysfunction)
- QTC interval prolongation (see cautions & Drug interactions)
- A history of ventricular arrhythmias or Torsades de pointes
- Bradycardia or 2nd or 3rd degree heart block
- A family history of QTc interval prolongation
- Uncorrected hypokalaemia or hypomagnesaemia

Side effects: see under chlorpromazine; less sedating than chlorpromazine, and extrapyramidal symptoms and hypothermia rarely occur; more likely to induce hypotension and increased risk of cardiotoxicity and prolongation of QT interval, pigmentary retinopathy (with reduced visual acuity, brownish colouring of vision, and impaired night vision) occurs rarely with high doses; sexual dysfunction, particularly retrograde ejaculation may occur.

Dose and Administration: *Oral: Adult:*

50 – 300 mg daily (initially in divided doses): Max. 600 mg daily (in hospital patients only); child not recommended.

Storage: at room temperature in a tight, light resistant container.

Trifluoperazine hydrochloride*Tablets, 1 mg, 5 mg**Capsules, 2 mg, 10 mg**Syrup, 1 mg/5 ml**Injection, 1 mg/ml; 2 mg/ml***Indications:** treatment of schizophrenia and for management of psychotic disorders.**Cautions:** cardiovascular disease, seizures, hepatic dysfunction, narrow-angle glaucoma, or bone marrow suppression, myasthenia gravis or parkinson's disease.**Drug interactions:** aminoglutethimide, carbamazepine, nevirapine, phenobarbital, phenytoin, azole antifungals, ciprofloxacin, clarithromycin, diclofenac, doxycycline, isoniazid and protease inhibitors.**Contraindications:** severe CNS depression; bone marrow suppression; blood dyscrasias, coma.**Side effects:** hypotension, cardiac arrest, extrapyramidal symptoms, dizziness, headache, constipation, stomach pain, vomiting, hepatotoxicity, dizziness, and headache.**Dose and Administration:***Psychoses:***Adult:** *Oral:* initially 5 mg twice daily or 10 mg daily in modified - release form, increased by 5 mg after 1 week, then at intervals of 3 days, according to the response;*I.M.:* 1- 2 mg every 4-6 hours as needed up to 10 mg/24 hours maximum; for elderly 1 mg every 4 - 6 hours; increase at 1 mg increments; do not exceed 6 mg/day.**Child** up to 12 years: *Oral:* initially up to 5 mg daily in divided doses, adjusted according to response, age, and body weight.*I.M.:* 1 mg twice daily.*Short term adjunctive management of severe anxiety: Oral:***Adult:** 2 - 4 mg daily in divided doses or 2 - 4 mg daily in modified-release form, increased if necessary to 6 mg daily;**Child** 3 - 5 years, up to 1 mg daily, 6 - 12 years, up to 4 mg daily.**Storage:** store at room temperature.**4.3. Antidepressants**

The major classes of Antidepressants include the tricyclic and related antidepressants, the Selective Serotonin Re-uptake Inhibitors (SSRIs), and the Mono-Amine Oxides Inhibitors (MAOIs); and a range of other compounds not usually categorized in to groups.

This section covers Tricyclic Antidepressants (TCAs), Selective Serotonin Re-uptake Inhibitors (SSRIs) and Serotonin and noradrenaline re-uptake inhibitors (SNRIs). (TCAs) are most effective for treating moderate to severe endogenous

depression associated with psychomotor and physiological changes such as loss of appetite and sleep disturbances; improvement in sleep is usually the first benefit of therapy. Since there may be an interval of 2 weeks before the antidepressant action takes place electroconvulsive treatment may be required in severe depression when delay is hazardous or intolerable. Some tricyclic antidepressants are also effective in the management of panic disorder.

TCAs are also important in some forms of neuralgia; and in nocturnal enuresis in children. Tricyclic and related antidepressant drugs can be roughly divided into those with additional sedative properties and those, which are less so.

Amitriptyline: it is tertiary amine tricyclic antidepressants. Agitated and anxious patients tend to respond best to this drug because of its additional sedative property. Though amitriptyline can be sedating, it is not recommended for use purely as a sedative - hypnotic, as other agents have greater efficacy with fewer adverse effects.

Amitriptyline and imipramine are well established and relatively safe and effective, but nevertheless have more marked antimuscarinic and cardiac side effects than other TCAs.

(SSRIs), which include fluoxetine, fluvoxamine, sertraline, escitalopram and others have minimal anticholinergic effects and are less cardiotoxic than the TCAs. Recent evidence suggests that there is an increased risk of suicidality in depressed children and adolescents given antidepressant medications, and SSRIs in particular. This increased risk has not been identified with SSRI treatment for anxiety disorders.

Serotonin and noradrenaline re-uptake inhibitors (SNRIs), e.g. duloxetine, have tolerability profiles comparable to those of SSRIs. Duloxetine weakly inhibits dopamine re-uptake with no significant affinity for histaminergic, dopaminergic, cholinergic or adrenergic receptors.

Tricyclic Antidepressants (TCAs)

Amitriptyline

Tablet, 10mg, 25mg, 50mg

Indications: depressive illness, particularly where sedation is required; nocturnal enuresis in children.

Cautions: cardiac disease (Particularly with arrhythmias), history of epilepsy, pregnancy and breastfeeding, elderly, hepatic impairment (avoid if severe), thyroid disease, pheochromocytoma, history of mania, psychoses (may aggravate psychotic symptoms) angle closure glaucoma, history of urinary retention, concurrent electro-convulsive therapy; if possible avoid abrupt withdrawal; anaesthesia (increased risk of arrhythmias and hypotension); porphyria

Drug interactions: alcohol, other CNS depressants, antithyroid agents, phenothiazine, cimetidine, clonidine, guanadrel, guanethidine, extrapyramidal reaction causing medications, metrizamide, MAO inhibitors and sympathomimetics.

Contraindications: recent myocardial infarction, arrhythmias (particularly heart block), not indicated in manic phase, severe liver disease.

Side effects: dry mouth, sedation, blurred vision (disturbance of accommodation, increased intraocular pressure), constipation, nausea, difficulty with micturition; cardiovascular.

Side effects such as ECG changes, arrhythmias, postural hypotension, tachycardia, syncope, particularly with high doses; sweating, tremor, rashes and hypersensitivity reactions (including urticaria, photosensitivity), behavioural disturbances (particularly children), hypomania or mania, confusion (particularly elderly), interference with sexual function, blood sugar changes; increased appetite and weight gain (occasionally weight loss), endocrine side effects such as testicular enlargement, gynaecomastia, galactorrhoea; also convulsions, movement disorders and dyskinesias, fever, agranulocytosis, leucopenia, eosinophilia, purpura, thrombocytopenia, hyponatraemia (may be due to inappropriate antidiuretic hormone secretion), abnormal liver function tests (jaundice);

Dose and Administration: *Oral*

Adult: *Depression:* initially 50-75 mg (elderly and adolescents 30 - 75 mg) daily in divided doses or as a single dose at bedtime increased gradually as necessary to 150 - 200 mg;

Child under 16 years not recommended for depression; *Nocturnal enuresis:*

Child 7 - 10 years, 10 - 20 mg, 11 - 16 years 25 - 50mg at night; maximum period of treatment (including gradual withdrawal) 3 months full physical examination before further course.

Storage: at room temperature in a well closed container.

Amitriptyline + Chlordiazepoxide

Capsule, 12.5mg + 5mg; 25mg + 10mg

Indications: treatment of moderate to severe anxiety and/or agitation and depression.

Dose and Administration: *Oral:* 3-4 tablets in divided doses; this may be increased to 6 tablets/day as required; some patients respond to smaller doses and can be maintained on 2 tablets.

Clomipramine Hydrochloride

Capsules, 10mg, 25mg, 50mg

Indications: phobic and obsessional states, panic attacks.

Cautions: cardiac disease, history of epilepsy, pregnancy, breastfeeding, elderly, hepatic impairment, thyroid disease, pheochromocytoma, history of mania, psychoses, angle-closure glaucoma, history of urinary retention, concurrent electroconvulsive therapy, avoid abrupt withdrawal, anaesthesia.

Drug interactions: alcohol, artemether + Lumefantrine, carbamazepin, chlorpromazine, epinephrine, ethosuximide, fluphenazine, haloperidol, phenobarbital, phenytoin, procainamide, quinidine, ritonavir, valproic acid.

Contraindications: recent myocardial infarction, arrhythmias (especially heart block); manic phase in bipolar disorders, severe liver disease; children, porphyria.

Side effects: sedation, dry mouth, blurred vision, constipation, nausea, difficulty in micturition; cardiovascular adverse effects particularly with high dosage including ECG changes, arrhythmias, postural hypotension, tachycardia, syncope, sweating, tremor, rash and hypersensitivity reactions, behavioral disturbances, hypomania or mania, confusion, interference with sexual function, blood sugar changes, increased appetite and weight gain, endocrine adverse effects, convulsions, movement disorders and dyskinesias, fever, agranulocytosis, leukopenia, eosinophilia, purpura, thrombocytopenia, hyponatraemia, abnormal liver function test.

Dose and Administration: *Oral:*

Adult: initially 50 - 75mg/day, increased gradually to 150 mg/day if necessary. May be given as a single dose at night or in 2-3 divided doses.

Elderly: initially 10mg/day, increasing carefully to 30 - 50mg/day.

Obsessive-Compulsive disorder: Dosage may have to be increased beyond those generally used, e.g. to more than 200mg/ day; maximum 250mg/day.

Child: initially 10/mg/day, increased gradually to 20mg for 5-7 years old, and to 20 - 50 mg for 8 - 14 year olds. Alternatively, 18 - 23kg, 0.5 - 0.9 mg/kg/day; 25 - 48 kg, 0.8 - 1.1mg/kg/day.

Storage: store at room temperature.

Imipramine

Tablet, 10mg, 25mg.

Indications: management of depressive illness. Nocturnal enuresis (adjunctive therapy) in children over 6 years of age, after exclusion of organic pathology; adjuvant to pain relief in chronic pain syndromes, also drug management of panic disorders.

Cautions: hyperthyroidism (or on thyroxin therapy), arrhythmias, epilepsy, prostatic enlargement, closed-angle glaucoma or impaired liver function.

Drug interactions: antihistamines, antipsychotics and anti-cholinergic type antiparkinsonian agents, cimetidine, fluoxetine, paroxetine and steroids, hepatic enzyme-inducing agents, MAO inhibitors.

Contraindications: early post myocardial infarction period and heart block.

Side effects: dry mouth, blurred vision, constipation, and difficulty with micturition. Blood pressure changes, syncope, tachycardia, arrhythmias, precipitation of epileptic seizures, sedation, excessive sweating, muscle tremors, restlessness, weakness, interference with sexual function and confusional states, especially in the elderly, extrapyramidal symptoms, allergic skin reactions and, rarely, cholestatic jaundice and blood disorders, including agranulocytosis. Occasionally produce agitation and insomnia.

Dose and Administration: *Oral:*

Adult: *Depression:* initial: 25mg 3-4 times/day, increase dose gradually, total dose may be given at bedtime; maximum: 300mg/day.

Elderly: initially 10-25mg at bedtime; increasing up to 100mg/day as required and if tolerated.

Child: *Nocturnal enuresis:* 6 - 7 years, 10 - 25mg; 8 - 11 years, 25 - 50mg; > 11 years, 25 - 75mg; given as a single dose after the evening meal.

Storage: store at room temperature.

Selective Serotonin Re-uptake Inhibitors (SSRIs).

Escitalopram

Tablet, 5mg, 10mg, 20mg

Indications: treatment of major depressive disorder; generalized anxiety disorder (GAD).

Cautions: previous seizure disorder, monitor worsening of depression or suicidality.

Drug interactions: non selective MAO inhibitors (phenelizine), fluconazole, fluvoxamine, gemfibrozil, isoniazid, omeprazole, ciprofloxacin, clarithromycin, diclofenac, doxycycline, erythromycin, protease inhibitors, quinidine and verapamil. Combined use of sumatriptan; NSAIDs, aspirin. Carbamazepine, phenytoin, rifampin, nevirapine, phenobarbital, phenytoin and rifamycins.

Contraindications: hypersensitivity reaction, concomitant use or within 2 weeks of MAO inhibitors.

Side effects: headache, somnolence, insomnia, nausea, chest pain, hypertension, palpitation, dizziness, fatigue, dreaming abnormal, concentration impaired, fever, irritability, lethargy, lightheadedness, migraine, vertigo, yawning, rash, hot flashes, libido decreased, anorgasmia, menstrual cramps, menstrual disorder, diarrhea, xerostomia, appetite decreased, constipation, indigestion, abdominal pain, abdominal cramps, appetite increased, flatulence, heartburn, toothache, vomiting, weight gain/loss, impotence, urinary tract infection, blurred vision, sinusitis, cough.

Dose and Administration: *Depression, GAD: Oral:*

Adult: initial: 10mg/day; dose may be increased to 20mg/day after at least 1 week

Elderly: 10mg/day; bioavailability and half-life are increased by 50% in the elderly

Storage: store at room temperature.

Fluoxetine

Capsule, 20mg

Indications: depressive disorders, bulimia nervosa; obsessive-compulsive disorder (OCD).

Cautions: hepatic or renal impairment, epilepsy and diabetes.

Drug interactions: flecainide, metoprolol, nifedipine, diclofenac, omeprazole, clozapine, fluphenazine, haloperidol, risperidone, antidepressants, terfenadine, carbamazepine and phenytoin; CNS depressants, diazepam and alprazolam; highly protein-bound drugs; lithium, MAO inhibitors; moclobemide, serotonergic agents.

Side effects: headache and gastrointestinal disturbances, CNS effects; mania or hypomania may be precipitated in some patients. Seizure threshold may be lowered, predisposing to epilepsy. Skin rashes have been reported and may be a warning of a serious systemic reaction, possibly related to vasculitis. Decreased libido and sexual dysfunction, weight loss, asthenia, hypoglycemia,

hyponatraemia, and elevated transaminase levels. Altered platelet function and abnormal bleeding.

Dose and Administration: *Oral:*

Adult: *Depression:* 20mg/day. May be increased by 20mg/day, if required; maximum 60 mg/day. The elderly: use the lowest effective dose.

Bulimia nervosa: increase up to 60mg/day.

OCD: 20-60mg/day; maximum 80 mg/day

Child: *Depression:* 8-18 years: 10-20 mg/day; lower-weight children can be started at 10mg/day, may increase to 20 mg/day after 1 week if needed.

OCD: 7-18 years: initial: 10mg/day; in adolescents and higher-weight children, dose may be increased to 20mg/day after 2 weeks. Range: 10-60 mg/day.

Storage: store at controlled room temperature.

Fluvoxamine maleate

Tablets, 40 mg, 100 mg

Indications: Major depressive disorders, especially where sedation is undesirable; panic disorder; obsessive-compulsive disorder, social phobia.

Cautions: mania, epilepsy, cardiac disease, hepatic or renal impairment.

Drug interactions: MAO inhibitors, cimetidine, lithium, phenytoin, serotonergic agents, sumatriptan, TCAs, phenothiazine neuroleptics, antiarrhythmics class Ic (e.g. propafenone), warfarin.

Contraindications: hypersensitivity to fluvoxamine.

Side effects: nausea, somnolence, sweating, tremor, dry mouth, asthenia, insomnia, constipation, dizziness, sexual dysfunction, dyspepsia, vomiting, diarrhea, anxiety, decreased appetite and headache. Extrapyramidal effects have been reported, also skin rashes, bruising and elevations of hepatic enzymes, with isolated reports of serious liver function abnormalities. Hyponatraemia has been reported, especially in the elderly,

Dose and Administration: *Oral:*

Adult:

Depression: initially 100mg daily as a single dose in the evening, increased if necessary; usual range 100 - 200 mg/day; maximum 300mg/day. Doses above 150mg/day should be given in 2-3 divided doses.

OCD: initially 50mg daily for 3- 4 days, increased gradually; usual range 100-200mg/day; maximum 300mg/day. If no improvement within 10 weeks, treatment should be reconsidered.

Child:

OCD: 8-17 years: initial: 25mg at bedtime; adjust in 25 mg increments at 4-7 day intervals, as tolerated, to maximum therapeutic benefit: Range: 50-200mg/day.

Maximum: 8-12 years: 200mg/day, adolescents: 300mg/day; lower doses may be effective in female versus male patients.

Storage: store at room temperature.

Sertraline hydrochloride

Tablets, 50mg, 100mg

Indications, Cautions, Drug interactions and Side effects; see under fluvoxamine.

Dose and Administration: *Oral:*

Adult: *Depression:* initially 50mg daily, usual range 50 - 100 mg/day. May be increased, if necessary, by increments of 50mg over several weeks up to a maximum of 200 mg/day.

OCD: the minimum effective dose is 50mg/day. Increase, if necessary, in 50mg increments over several weeks up to a maximum of 200mg/day.

Panic disorder: initially 25mg daily, increased to 50mg/day after 1 week, and thereafter, if necessary, in 50mg increments up to a maximum of 200mg/day.

Child: *OCD:* 6-12 years: initial: 25mg once daily.

13-17 years: initial: 50mg once daily.

Storage: store at controlled room temperature.

Serotonin and noradrenaline re-uptake inhibitors (SNRIs)

Duloxetine

Tablet, 30mg, 40mg, 60mg

Indications: treatment of major depressive disorder.

Cautions: renal impairment or with concomitant CNS depressants.

Drug interactions: MAO inhibitors, TCAs, buspirone, SSRIs, tramadol, amiodarone, chlorpromazine, ciprofloxacin, delavirdine, fluvoxamine, fluoxetine, ketoconazole, miconazole, norfloxacin, ofloxacin, aminoglutethimide, carbamazepine, phenobarbital, and rifampicin.

Contraindications: hypersensitivity to the drug, concomitant use or within 2 weeks of MAO inhibitors; uncontrolled narrow angle glaucoma.

Side effects: insomnia, somnolence, dizziness, headache, nausea, xerostomia, constipation, appetite decreased.

Dose and Administration: *Oral:* **Adult:** initial: 40-60 mg/day; dose may be divided (i.e., 20 or 30 mg twice daily) or given as a single dose of 60mg; maximum dose: 60 mg/day.

Elderly: treatment of major depressive disorder; initial dose; 20mg 1-2 times/day; increase to 40-60mg/day as a single daily dose or in divided dose.

Storage: store at room temperature.

4.4. Anticonvulsants

Treatment should always be started with a single drug, but the choice of an anticonvulsant can only be made on an individual basis and will depend on the efficacy of the drug and the patient's tolerance of treatment. If a drug fails to control the seizures after it has been used in full therapeutic dosage for an adequate period, or if it is not tolerated, it should be gradually substituted with another with the first drug being withdrawn only when the new regimen is mainly established. If monotherapy is ineffective, two drugs should be given in

combination and several regimens may need to be tried before the most appropriate is found.

Carbamazepine is used as a first-line drug in the treatment of partial seizures with or without secondary generalization and tonic-clonic seizures; it is also effective in other forms of epilepsy. It may exacerbate absence and myoclonic seizures, and may cause deterioration of juvenile myoclonic epilepsy if used to treat tonic-clonic seizures occurring within the syndrome. Carbamazepine is often preferred in children because it lacks the dysmorphic adverse effects associated with phenytoin. However, carbamazepine does possess some unique pharmacokinetic characteristics, particularly in children and manipulation of dosage forms and schedules to accommodate individual needs may be necessary. Carbamazepine elimination is more rapid in children and accumulation of the active metabolite is often higher than in adults.

Phenytoin is used as a first-line drug in the treatment of partial and tonic-clonic seizures; it may also be used in other forms of epilepsy, with the exception of absence and myoclonic seizures. The non-linear pharmacokinetics of phenytoin make it difficult to use, particularly at higher doses, because small increases in doses may produce large rises in plasma concentrations. Phenytoin may be unsuitable in adolescents and women because of potential coarsening of the facial features, acne, or hirsutism. Gingival hyperplasia and tenderness can also be a problem. The potential effects of phenytoin on cognition may make it less suitable in young children.

Valproic acid or valproate is used as a first-line drug in the treatment of absence, tonic-clonic, and myoclonic seizures. It may also be used for partial seizures and is effective in some epileptic syndromes.

Phenobarbitone is used in all forms of epilepsy with the exception of absence seizures. It has been widely used in children and neonates in particular, perhaps because of convenient administration and linear pharmacokinetics, but there is concern about its effects on cognition.

The use of benzodiazepines for the long-term treatment of epilepsy is limited by problems of tolerance, sedation, and the development of dependence; withdrawal seizures are also a problem. *Diazepam* is not used in the prophylaxis of epileptic seizures but is of value in the treatment of febrile convulsions

Withdrawal

Treatment is normally continued for a minimum of two years after the last seizure. Withdrawal should be extended over a period of several months since abrupt withdrawal can lead to complications such as status epilepticus. Abrupt discontinuation is therefore never warranted. Many adult patients relapse once treatment is withdrawn and it may be justified to continue treatment indefinitely, particularly when the patient's livelihood or lifestyle can be endangered by recurrence of a seizure.

Pregnancy and Breastfeeding;

There is an increased risk of birth defects with the use of anticonvulsants, particularly carbamazepine, valproate and phenytoin. However, if there is good seizure control, there is probably no advantage in changing pregnant patients'

antiepileptic drugs. In view of the risks of neural tube and other defects, patients who may become pregnant should be informed of the risks and referred for advice, and pregnant patients should be offered counseling and antenatal screening. To counteract the risk of neural tube defects, adequate foliate supplements are advised for women before and during pregnancy. In view of the risk of neonatal bleeding associated with carbamazepine, phenobarbital and phenytoin, prophylactic phytomenadione (vitamin K1) is recommended for the neonatal and the mother before delivery. Antiepileptic drugs can be continued during breastfeeding.

Acetazolamide

Tablet, 125 mg, 250 mg

Indications: treatment of centrencephalic epilepsies.

Cautions, Drug interactions, Contraindications, Side effects and Storage; see section 2.6. under acetazolamide.

Dose and Administration: *Oral:*

Adult: 8-30mg/kg/day in 1-4 divided doses.

Child: 8-30 mg/kg/day in 1-4 divided doses, not to exceed 1g/day.

Carbamazepine

Tablet, 100mg, 200mg

Syrup, 100mg/5ml

Indications: partial and secondary generalized tonic-clonic seizures, some primary generalized seizures; trigeminal neuralgia, prophylaxis of bipolar disorder unresponsive to lithium.

Cautions: hepatic or renal impairment; cardiac disease (see also contraindications). Skin reactions, history of hematological reactions to other drugs; glaucoma; pregnancy (see notes above), breastfeeding (see notes above); avoid abrupt withdrawal (see notes above); see also interactions

Drug interactions: acetazolamide, amitriptyline, chloroquine, chlorpromazine, ciclosporin, cimetidine, clomipramine, clonazepam, oral contraceptives, dexamethasone, erythromycin, ethosuximide, fludrocortisone, fluphenazine, haloperidol, hydrocortisone, isoniazide, levonorgestrel, medroxyprogesterone, mefloquine, norethisterone, phenobarbital, phenytoin, prednisolone, valproic acid, verapamil, warfarin.

Contraindications: atrioventricular conduction abnormalities; history of bone marrow depression; porphyria.

Side effects: dizziness, drowsiness, headache, ataxia, blurred vision, diplopia (may be associated with high plasma levels); gastrointestinal intolerance including nausea and vomiting, anorexia, abdominal pain, dry mouth, diarrhea or constipation; commonly, mild transient generalized erythematous rash (withdraw if worsens or is accompanied by other symptoms); leukopenia and other blood disorders (including thrombocytopenia, agranulocytosis and aplastic anemia); cholestatic jaundice, hepatitis, acute renal failure, Stevens Johnson syndrome (erythema multiform), toxic epidermal necrolysis, alopecia,

thromboembolism, arthralgia, fever, proteinuria, lymphnode enlargement, arrhythmias, heart block and heart failure, dyskinesias, parasthesia, depression, impotence, male infertility, gynaecomastia, galactorrhoea, aggression, activation of psychosis, photosensitivity, pulmonary hypersensitivity, hyponatraemia, oedema, disturbances of bone metabolism with osteomalacia also reported; confusion and agitation in elderly.

Dose and Administration: Adult:

Oral: Epilepsy: initially, 100 - 200 mg twice daily, with increments of 100-200mg/day at weekly intervals according to seizure control and adverse symptoms.

Maintenance range (i.e. minimum effective dosage) is generally 600-1200 mg/day in divided doses, but up to 1.6g/day may occasionally be necessary.

Elderly: start with 100mg twice daily and increase as required.

Trigeminal neuralgia and pain syndromes: initially 100mg twice daily, increased by 100mg every 12 hours until pain is relieved (maximum 1.2g/day). Once pain is controlled, the dose may be decreased over a period of a few weeks to a maintenance dose, usually 400-800 mg/day.

Prophylaxis of bipolar disorder unresponsive to lithium: initially 400mg daily in divided doses increased until symptoms controlled; usual range 400 - 600mg daily; max. 1.6 g daily.

Mood stabilizer: Dosage as for epilepsy (usually 400-600mg/day). Response usually takes 7-10 days to become evident.

Child: Epilepsy: 12-15 years, as for adults but maximum 1g/day.

6-12 years, initially 100mg twice daily, increasing by 100mg/day at weekly intervals until optimal response and plasma levels are obtained. Usual maintenance, 400-800 mg/day (maximum 1g/day)

Under 6 years, initially 10-20mg/kg/day in 2-3 divided doses, increasing by up to 100mg/day at weekly intervals as needed. Usual maintenance 200-350 mg/day, maximum 400 mg/day; under 1 year, 100-200 mg/day.

Storage: at room temperature in a tight, light-resistant container. Protect from freezing (syrup).

Clonazepam

Injection, 1 mg/ml in 1ml ampoule

Tablet, 0.5 mg, 1mg, 2 mg.

Indications: management of myoclonic and atonic / akinetic seizures in children, and as an adjuvant agent in the management of other forms of epilepsy. It is used as an alternative to diazepam in the emergency treatment of status epilepticus.

Cautions: respiratory disease; hepatic impairment, renal impairment; elderly and debilitated; pregnancy; breastfeeding; avoid sudden withdrawal, porphyria.

Drug interactions: acetazolamide, alcohol, carbamazepine, phenobarbital, phenytoin, ritonavir.

Contraindication: hypersensitivity to clonazepam.

Side effects: frequently - fatigue, drowsiness, ataxia and clumsiness, especially early in treatment. Paradoxical hyperkinesia, excitability, aggressiveness and other behavioral problems may occur, particularly in children with pre-existing brain damage or in patients with a history of aggressiveness. Other effects include headache and muscle weakness.

Dose and Administration:

Adult: *Oral:* start with small doses and increase gradually to an optimum dose according to individual response. Initially 1mg at night for 4 nights, increased over 2 - 4 weeks to usual maintenance of 4 - 8 mg/day.

Status epilepticus: IV: 1mg injected slowly, over 30 seconds; may be repeated as required.

Child: *Oral:* initially 0.05mg/kg/day in 3 divided doses, increased slowly if needed to a maximum of 0.3 mg/kg/day. Usual maintenance: < 1 year, 0.5 - 1mg/day; 1 - 5 years, 1 - 3mg/day; 5 - 12 years, 3 - 6mg/day, in 3 divided doses.

Status epilepticus: IV: 0.5mg by slow injection.

Storage: store tablets at room temperature.

Diazepam

Suppository, 5mg, 10mg

Injection, 5mg/ml in 2ml ampoule

Indications: It is indicated as adjunct in static epilepticus and severe recurrent convulsive seizures.

Cautions, Drug interactions, Contraindications, and Side effects; see notes on diazepam under 4.2.

Dose and Administration:

Adult: *anticonvulsants: IV:* 5-10mg initially, the dosage being repeated, if necessary, at 10-15 minutes interval up to a maximum dose of 30mg.

Child: *Anticonvulsant: status epilepticus and severe recurrent convulsive seizures.*

Infants over 30 days of age and children up to 5 years of age:

IV (slow): 0.2 to 0.5 mg every 2-5 minutes up to a maximum of 5mg. If necessary, therapy should be continued.

Child 5 and older: *IV (slow):* 1mg every two to five minutes up to a maximum of 5mg. If necessary, therapy may be repeated in two or four hours

Elderly: *Anticonvulsant: IM or IV,* initially, 2 to 5 mg per dose, the dosage being increased gradually as needed and tolerated.

Storage: store at room temperature. Protect from light and freezing.

Diphenylhydantoin (Phenytoin)

Tablet, 50 mg, 100mg

Capsule, 50 mg, 100 mg

Suspension, 30 mg/ 5 ml

Powder for injection (sodium), 250 mg in vial

Indications: generalized tonic-clonic seizures; partial seizures; status epilepticus.

Cautions: renal and hepatic function impairment (reduce dose), porphyria, blood dyscrasias, and during pregnancy, breast feeding; avoid sudden withdrawal; blood counts should be determined prior to and during therapy with these drugs. Caution for sensitive to hydantoin anticonvulsants.

Drug interactions: alcohol, CNS depressant, chloramphenicol, antituberculosis agents, amiodarone, corticosteroids, cimetidine, calcium, diazoxide (oral), antacids (aluminium-magnesium – containing and calcium carbonate – containing), anticoagulants (coumarin – or indandione – derivative), disulfiram, contraceptives, fluconazole, intraconazole, ketoconazole, miconazole, estrogen, progestins, felbamate, fluoxetine, lidocaine, phenacemide, methadone, sucralfate, valproic acid, theophylline.

Contraindications: cardiac function impairment, such as Adams- Stokes syndrome, second and third degree AV block, sino-atrial block, and sinus bradycardia (parenteral Phenytoin administration may affect ventricular automaticity and result in ventricular arrhythmias).

Side effects: nausea, vomiting, mental confusion, dizziness, headache, tremor, transient nervousness, insomnia occur commonly; rarely dyskinesias, peripheral neuropathy; ataxia, slurred speech, nystagmus and blurred vision are signs of overdosage; rashes (discontinue, if mild re-introduce cautiously but discontinue immediately if recurrence), coarse facies, acne and hirsuties, fever and hepatitis, lupus erythematosus, erythema multiforme, toxic epidermal necrolysis, polyarteritis nodosa lymphadenopathy; gingival hypertrophy and tenderness; rarely haematological effects, including megaloblastic anaemia, leucopenia, thrombocytopenia, agranulocytosis and aplastic anaemia; plasma calcium may be lowered (rickets and osteomalacia).

Dose and Administration:

Generalized tonic-clonic seizures, partial seizures: Oral:

Adult: initially 3-4 mg/kg daily (as a single dose or in 2 divided doses), increased gradually at intervals of 2 weeks as necessary (with plasma-phenytoin concentration monitoring); usual dose 200 – 500 mg daily; **Child:** initially 5 mg/kg daily in 2 divided doses; usual dose range 4-8 mg/kg daily (maximum 300 mg)

Note. Plasma concentration for optimum response 10-20 mg/litre (40-80 micromol/litre)

Patient advise: Preferably taken with or after food

Status epilepticus: Slow IV injection or by IV infusion (with blood pressure and ECG monitoring),

Adult: 15 mg/kg at rate of not more than 50 mg/minute, as a loading dose; maintenance doses of about 100mg by mouth or by slow IV injection should be given thereafter at intervals of 6-8 hours, monitored by measurement of plasma concentrations; rates and dose reduced according to weight;

Child: 15 mg/kg as loading dose at rate of 1 mg/kg/minute (not exceeding 50 mg/minute);

Neonate: 15-20 mg/kg as a loading dose at rate of 1-3 mg/kg/minute.

Storage: store in a well-closed container at room temperature, protect from freezing.

Ethosuximide

Capsule, 250 mg,

Syrup, 250 mg/5ml

Indications: Management of absence (petitmal) epilepsy.

Cautions: hepatic or renal impairment; blood counts and hepatic and renal function tests recommended; pregnancy; breastfeeding; avoid sudden withdrawal; porphyria.

Note: patients or their carers should be told how to recognize signs of blood disorder, and advised to seek immediate medical attention if symptoms such as fever, sore throat, mouth ulcers, bruising or bleeding develop.

May impair ability to perform skilled tasks, for example operating machinery, driving.

Drug interactions: other antiepileptics, CNS depressants.

Contraindications: hypersensitivity to the drug.

Side effects: frequently- gastrointestinal disturbances, causing anorexia, diarrhoea, epigastric pain, nausea and vomiting.

Less frequently - adverse CNS effects including drowsiness, headache, dizziness, euphoria, ataxia and depression.

Rarely - haematopoietic disorders (leucopenia, agranulocytosis, pancytopenia, aplastic anaemia), psychotic states.

Skin reactions, including Stevens - Johnson syndrome, may occur.

Dose and Administration: *Oral:*

Adult: initially 500mg daily, increased according to need by 250mg every 4 - 7 days to a maximum of 1.5g/day, in divided doses.

Child: 3 - 6 years, initially 250mg daily; > 6 years, 500mg daily; adjust according to plasma levels and clinical response.

Doses exceeding 1.5g/day (in divided doses), should be used only under strict supervision.

Note: Daily doses of 1 g and above should be taken as 2 or more divided doses.

Plasma concentration for optimum response 40-100mg/litre (300-700 micromol/litre)

Storage: store at room temperature.

Magnesium Sulfate

Injection, 50% in 20 ml

Indications: prevention of recurrent seizures in eclampsia.

Cautions: hepatic impairment, renal failure.

Drug interactions: alcuronium, nifedipine, suxamethonium, vacuronium.

Contraindications: heart block, serious renal impairment, myocardial damage, hepatitis, Addison's disease.

Side effects: hypermagnesaemia, nausea, vomiting, thirst, flushing of skin, hypotension, arrhythmias, respiratory depression, drowsiness, confusion, loss of tendon reflexes, muscle weakness.

Dose and Administration: **Adult:** *IV injection*, initially 4g over 5 - 10 minutes followed by *IV infusion* at a rate of 1g every hour for at least 24 hours after the last seizure, recurrence of seizures may require additional *IV bolus* of 2g.

Storage: store at room temperature.

Paraldehyde

Injection, in 2ml, 5ml and 10ml ampoules

Indications: used to control status epilepticus resistant to conventional treatment.

Cautions: bronchopulmonary disease or hepatic impairment. Plastic syringes should be avoided.

Drug interactions: CNS depressants (alcohol, barbiturates, and other sedatives).

Contraindications: hypersensitivity to the drug.

Side effects: tissue necrosis, sterile abscesses, and nerve damage.

Dose and Administration: *IM:*

Adult: 5 -10ml up to a maximum of 20ml daily. Not more than 5ml being given at any one site.

Child: up to 3 months, 0.5ml; 3-6 months, 1ml; 6-12 months 1.5ml; 1-2 years, 2ml; 3-5 years, 3-4 ml; 6-12 years, 5-6 ml.

Storage: store in small well-filled airtight containers. Protect from light.

Phenobarbitone (Phenobarbital)

Tablets, 15mg, 30mg, 100mg.

Elixir, 20mg/5ml

Injection (sodium), 25mg/ml in 1ml ampoule, 100mg/ml in 2ml ampoule; 4%

Indications: for the control of seizures (epilepsy).

Long - acting barbiturate is indicated as long-term anticonvulsant therapy for the treatment of generalized tonic-clonic and simple partial (cortical focal) seizures.

Cautions: liver or renal diseases, acute or chronic pain, in weak patients, in children and the elderly, during pregnancy, labour, delivery, and breast-feeding. It has a sedative effect, and driving and operating machines should be avoided.

Also treatment should not be stopped abruptly as rebound seizures may occur.

Drug interactions: central nervous system (CNS) depressants (e.g. alcohol), paracetamol, isoniazid, chloramphenicol, and oral contraceptives containing estrogens.

Contraindications: respiratory depression.

Side effects: drowsiness or sedation, respiratory depression, and a hangover effect may occur more frequently. Unusual excitement may occur in children, the elderly, and in patients with severe pain. It should be discontinued if severe skin reactions with fever occur.

Continued use may result in psychic or physical dependence. With excessive doses in coordination of muscular motion and continuous rolling movement of eyeball may also occur.

Dose and Administration: *Oral:* Several weeks (2 - 3) of therapy may be required to achieve maximum antiepileptic effect.

Adult: *Oral:* 50 – 100 mg every 12 hours daily.

Child: *Oral:* 15 – 50 mg every 12 hours daily. Or 1 –2 mg/kg of body weight every 8 hours daily.

Anticonvulsant: **Adult:** *Oral:* 60-250 mg per day as a single dose - or in divided dose; *IV*-100-320 mg, repeated if necessary up to a total dose of 600 mg during a 24 hour period;

Child: *Oral:* 1 to 6 mg per kg of body weight per day as a single dose or in divided doses.

Status epilepticus: *IV (slow):* 10 to 20 mg per kg of body weight, repeated, if necessary.

Storage: at room temperature, in a well-closed container.

Primidone

Tablet, 250 mg

Indications: management of grandmal, psychomotor, and focal seizures.

Cautions: renal and hepatic impairment, pulmonary insufficiency.

Drug interactions: narcotic analgesics, antidepressants, chloramphenicol, MAO inhibitors, valproic acid, phenobarbitol.

Contraindications: pregnancy, porphyria.

Side effects: drowsiness, vertigo, ataxia, fatigue, hyperirritability, rash, nausea, vomiting, anorexia, impotence, agranulocytopenia, anemia, diplopia, nystagmus.

Dose and Administration: *Oral:*

Adult: initial: 125-250mg/day at bed time; increase by 125-250mg/day every 3-7 days; usual dose: 750-1500mg/day in divided doses 3-4 times/day with maximum dosage of 2g/day.

Child: initial: 50-125mg/day given at bed time; increase by 50-125mg/day increments every 3-7 days; usual dose: 10-25mg/kg/day in divided doses 3-4 times/day.

Storage: store at room temperature.

Sodium Valproate

Tablet, 200mg, 500mg

Syrup, 200mg/5ml

Indications: for all forms of epilepsy

Cautions: patients under 3 years of age, especially those with congenital metabolic disorders, organic brain disease, or mental retardation may be at particular risk of hepatotoxicity (liver function test should be carried out in those at risk). The drug should be discontinued if signs of liver dysfunction occur; bruising, or bleeding (withdraw or reduce the dose); systemic lupus

erythematous, care in withdrawing the therapy; renal impairment, breastfeeding, pregnancy, false - positive urine tests for ketenes, interactions restrictions on driving in patients with epilepsy

Drug interactions: amitriptyline, carbamazepine, chloroquine, chlorpromazine, cimetidine, clomipramine, ethosuximide, fluphenazine, haloperidol, mefloquine, phenobarbital, phenytoin.

Contraindications: pre-existing liver disease or a family history of severe hepatic dysfunction, pancreatitis; porphyria.

Side effects: gastrointestinal disturbances, particularly an initiation of therapy (use of entericoated formulations, administration with meals, and commencement of therapy with low dose may minimize symptoms); increased appetite and weight gain, tremor, drowsiness, ataxia, confusion, headache, reversible prolongation of bleeding time and thrombocytopenia; liver dysfunction (necessitates valproate withdrawal), elevation of liver enzyme values, hyperammonaemia, pancreatitis, leucopenia and bone marrow depression.

Dose and Administration:

Oral: Adult: initially, 600mg daily given in 2 divided doses, preferably after food, increasing by 200mg/day at 3 days intervals to a max. of 2.5g daily in divided doses, usual maintenance 1 - 2g daily (20 - 30 mg/kg daily);

Child up to 20kg, initially 20mg/kg daily in divided doses, may be increased provided plasma concentrations monitored (above 40mg/kg daily also monitor clinical chemistry and haematological parameters); over 20kg, initially 400mg daily in divided doses increased until control (usually in range of 20 - 30 mg/kg daily); max. 35mg/kg daily.

Storage: at room temperature in a tight container. Protect from freezing.

Topiramate

Tablet, 25mg, 50mg, 100mg

Indications: in adults and paediatric patients, adjunctive therapy for partial onset seizures and adjunctive therapy of primary generalized tonic-clonic seizures; treatment of seizures associated with Lennox-Gastaut syndrome; prophylaxis of migraine headache.

Cautions: hepatic, respiratory, or renal impairment.

Drug interactions: concomitant administration with other CNS depressants and anticholinergic drugs; phenytoin, carbamazepine, digoxin, ethinyl estradiol.

Contraindications: hypersensitivity reactions.

Side effects: dizziness, ataxia, somnolence, nervousness, speech problems, fatigue, nausea, tremor, abnormal vision, upper respiratory infection.

Dose and Administration: *adjunctive therapy for partial onset seizures and adjunctive therapy of primary generalized tonic-clonic seizures:*

Adult: Initial: 25-50mg/day; titrate in increments of 25-50mg per week until an effective daily dose is reached; the daily dose may be increased by 25mg at weekly intervals for the first 4 weeks; thereafter, the daily dose may be increased

by 25-50mg weekly to an effective daily dose (usually at least 400mg); usual maximum dose: 1600mg/day

Child 2-16 years: Initial dose titration should begin at 25mg (or less, based on a range of 1-3mg/kg/day) nightly for the first week; dosage may be increased in increments of 1-3mg/kg/day (administer in 2 divided doses) at 1 or 2 week intervals to a total daily dose of 5-9 mg/kg/day.

Adult: *Migraine prophylaxis:* Initial: 25mg/day, titrated at weekly intervals in 25mg increments, up to the recommended total daily dose of 100mg/day given in 2 divided doses.

Storage: store at room temperature.

4.5. Antiparkinson Agents

Antimuscarinic agents are used in Parkinson's disease (idiopathic or primary Parkinsonism) and drug - induced Parkinsonism. Those commonly used are the tertiary amine, benzhexol hydrochloride, benzotropine mesylate, orphenadrine hydrochloride, and procyclidine hydrochloride.

In Parkinson's disease, antimuscarinics are generally used in the early stages when the condition is mild and tremor is the predominant symptom as they provide little benefit in bradykinesia. They can also reduce the diarrhoea experienced by patients with this disease.

The most effective form of therapy is a combination of levodopa and peripheral dopa-decarboxylase inhibitor, such as carbidopa. The response to levodopa with carbidopa is a compromise between increased mobility and adverse effects. Dyskinesias may be dose limiting and increasingly frequent with increased duration of treatment. Many factors including tolerance and progression of the disease may result in complications after 2-5 years of treatment. 'End-of-dose' deterioration occurs when there is a reduced duration of benefit from a dose, resulting in disability and dystonias. The 'on-off' phenomenon is characterized by sudden swings from mobility to episodes of akinesia, tremor and rigidity lasting from a few minutes to several hours. Amelioration of these effects can sometimes be achieved by administering levodopa in a sustained-release preparation or in a greater number of fractionated dose throughout the day. Psychiatric symptoms inducing disruption of sleep, vivid dreams and hallucinations are characteristic adverse effects that may occur at any time, especially in the elderly, and may require dose reduction or withdrawal of levodopa.

Amantadine Hydrochloride

Capsule, 100mg

Indications: Parkinson's disease (not for drug - induced Parkinson like syndromes); influenza prophylaxis.

Cautions: epilepsy, confusional or hallucinational states, history of eczema, congestive heart failure and/or peripheral oedema, orthostatic hypotension; renal or liver impairment.

Drug interactions: agents with anticholinergic effects, alcohol, CNS stimulants, hydrochlorothiazide and triamterene.

Contraindication: hypersensitivity to amantadine.

Side effects: livedo reticularis (skin discolouration) mainly of the legs; oedema of the legs. CNS reactions (psychotic episodes, convulsions and nausea), especially when doses exceed 200 mg/day. Mild headache, constipation, insomnia, nervousness, urinary retention, dry mouth, blurred vision as well as neutropenia and skin rashes have occurred.

Dose and Administration: *Oral:*

Adult: initially 100mg daily, increased to 100mg twice daily after 7 days, maximum 400mg/day.

Elderly (> 65 years): Maximum 100mg daily

Storage: store at room temperature.

Benzhexol (Trihexyphenidyl Hydrochloride)

Tablet, 2mg, 5mg

Indications: Parkinsonism; drug induced extrapyramidal symptoms (but not tardive dyskinesia).

Cautions: as antimuscarinics in general (see section 1.3), and cardiovascular disease, hepatic or renal impairment; elderly, avoid abrupt discontinuation of treatment; liable to abuse (may produce euphoric effect)

Drug interactions: as antimuscarinics (section 1.3); antipsychotics, TCAs, antihistamins, amantadine, alcohol, CNS depressants, levodopa.

Contraindications: untreated urinary retention, angle-closure glaucoma, gastrointestinal obstruction, myasthenia gravis.

Side effects: as antimuscarinics (see section 1.3); Common - anticholinergic symptoms such as dry mouth, blurred vision, dizziness, mild nausea or nervousness, CNS stimulation (dose related and in the elderly), manifested by restlessness, confusion, hallucinations or euphoria, amnesia and impaired recall. Constipation and urinary retention or hesitancy may occur, particularly in the elderly. Other effects include tachycardia, drowsiness and raised intraocular pressure. Rare - psychiatric disturbances such as excitation, mania and delusions.

Dose and Administration: *Oral: Adult:* initially, 1-2mg daily with increments of 2 mg every 3-5 days, as required, to 6-10 mg/day in 3-4 divided doses (maximum 15mg/day).

Concomitant with levodopa: usually 1-2 mg 3 times daily is adequate.

Drug-induced Parkinsonism: Effective dosage range varies widely – from 1-15mg/day.

Storage: at room temperature in a tight container.

Benztropine Mesylate

Tablet, 2mg

Injection, 1mg/ml in 2ml ampoule

Indications, Caution, Drug interactions; see under Trihexyphenidyl hydrochloride.

Contraindications: see Trihexyphenidyl Hydrochloride; avoid in children less than 3 years.

Side effects: see trihexyphenidyl Hydrochloride, but causes sedation rather than stimulation.

Dose and Administration: Adult:

Oral: 0.5 – 1 mg daily usually at bedtime, generally increased, max. 6 mg daily; usual maintenance dose 1 – 4 mg daily in single or divided dose; elderly preferably lower end of range.

IM or IV: 1 – 2 mg repeated if symptoms reappear; Elderly preferably lower end of range.

Storage: at room temperature in a well-closed container. Protect from freezing.

Levodopa

Tablet, 250mg, 500mg

Indications: Parkinson's disease (not for drug-induced parkinson like syndromes).

Cautions: asthmatics, patients with chronic obstructive airway disease, renal, hepatic or endocrine diseases, a history of peptic ulceration, open - angle glaucoma, and diabetics

Drug interactions: MAO inhibitors, antipsychotic agents, metoclopramide, antihypertensive agents.

Contraindications: closed-angle glaucoma, a history of malignant melanoma, patients younger than 25 years, psychosis, history of myocardial infarction, particularly residual arrhythmias; convulsive disorders.

Side effects: gastric intolerance, nausea, vomiting, anorexia, peptic ulceration and gastrointestinal bleeding may occur; also psychiatric disturbances including nervousness, mild anxiety and depression to overt psychotic reactions. Complex involuntary movements. Postural hypotension and dizziness are common during the first few months of therapy. Cardiac arrhythmias, hypertension may occur.

Urinary frequency or retention, visual abnormalities, flushing, blood dyscrasias (thrombocytopenia), raised liver enzymes, increased urea and uric acid serum concentrations, and the development of a scleroderma-like illness.

Dose and Administration: *Oral: Adult:* 500mg to 1g daily administered in 2 or more equally divided doses. Daily dosage may be increased by 100-750mg every 3-7 days until a maximum response is achieved, the maximum recommended daily dosage is 8 g.

Storage: store at room temperature.

Preparations include:

Levodopa + benserazide

Tablets, 50mg+12.5mg, 100mg+25mg, 200mg+50mg

Capsules, 50mg+12.5mg, 100mg+25mg, 200mg+50mg

Dose and Administration: Adult: Initially 25/100mg 3 times daily, increased by 25/100mg weekly until desired response is obtained. Usual effective range 100/400 - 200/800 mg/ day.

Levodopa + Carbidopa

Tablets, carbidopa 10mg+ levodopa 100mg; carbidopa 25mg+ levodopa 250mg

Dose and Administration: Adult:

10/100 tablets: initially 50 -100 mg (with carbidopa 10) 3-4 times daily, increased by 50 - 100 mg daily or alternate days according to response, up to 800 mg (with carbidopa 80) daily in divided doses.

25/250 tablets: initially 12.5/125mg (half a tablet) once or twice daily, increased gradually by 12.5/125mg every day or alternate day. Maximum 200/2000 mg/day (8 tablets).

Orphenadrine hydrochloride

Tablet, 50mg

Indications: Parkinson's disease and drug induced extrapyramidal reactions (but not tardive dyskinesia).

Cautions, Drug interactions, Contraindication and Side effects; see under trihexyphenidyl.

Dose and Administration: Adult: *Oral:* initially 50mg 3 times daily, increased gradually according to the individual response. Usual range, 150 - 250 mg/day (maximum 400mg)

Storage: store at room temperature.

Procyclidine

Injection, 5 mg/ml; 2ml ampoule

Indications: relieves symptoms of parkinsonian syndrome and drug –induced extrapyramidal symptoms.

Cautions: tachycardia, cardiac arrhythmia, hypertension, hypotension, liver or kidney disorder, prostatic hyperplasia, elderly.

Drug interactions: amantadine, narcotic analgesics, phenothiazines, TCA, antiarrhythmics, quinidine, levodopa, digoxin.

Contraindications: angle-closure glaucoma, myasthenia gravis.

Side effects: tachycardia, palpitation, confusion, drowsiness, headache, loss of memory, fatigue, constipation, nausea, vomiting, difficult urination, increased intraocular pain, blurred vision, mydriasis, epigastric stress.

Dose and Administration: Adult: *IM:* 5-10mg may be given as a single injection, repeated if necessary after 20 minutes to a maximum of 20mg daily. Parenteral doses are usually effective within 5 to 10 minutes but may need 30 minutes to produce relief.

4.6. CNS Stimulant

Registered medicines in this group include methylphenidate and atomoxetine. They are indicated in attention deficit hyperactivity disorder. Owing to their dependence-producing liability, these drugs should not be used for the relief of fatigue or in the treatment of debility or depression. They should only be used for their specific indications and after careful diagnosis.

Atomoxetine

Capsule, 5mg, 10mg, 18mg, 25mg, 40mg, 60mg

Indications: attention deficit/hyperactivity disorder in children, adolescents and adults.

Cautions: liver dysfunction.

Drug interactions: β_2 agonists (e.g. salbutamol), pressor agents and drugs that affect noradrenaline; drugs that induce or inhibit CYP2D6; drugs metabolized by CYP3A4, e.g. midazolam; MAO inhibitors.

Contraindications: uncontrolled hypertension, hepatic impairment, narrow angle glaucoma.

Side effects: Children- abdominal discomfort, nausea and vomiting, decreased appetite, dizziness, somnolence, irritability, mood swings and pruritis.

Adult- dry mouth, sinus, headache, nausea, constipation, loss of appetite and weight, insomnia, palpitations, sweating, fatigue, hot flushes and urogenital dysfunction.

Dose and Administration:

Adult and (Child/Adolescent ≥ 70 kg): initiate at 40 mg/day for 7 days and titrate gradually up to a maximum of 80mg/day.

Child and (Adolescent < 70 kg): 0.5 mg/kg/day for 7 days followed by gradual titration up to a maximum of 1.2 mg/kg/day.

Storage: store at room temperature.

Methylphenidate

Tablets, 5 mg, 10 mg, 20 mg

Indications: attention deficit hyperactivity disorders in children; narcolepsy.

Cautions: hypertension, vocal or motor tics, epilepsy.

Drug interactions: barbiturates, primidone, phenytoin, phenyl butazone, tricyclic antidepressants, warfarin, and MAO inhibitors.

Contraindications: absolute-history of schizophrenia, drug dependence or personality disorders; patients with glaucoma, thyrotoxicosis, tachyarrhythmias, anxiety, tension or ischaemic heart disease.

Side effects: nervousness, insomnia; weight loss and growth retardation may occur (particularly in children receiving > 30 mg/day for prolonged periods); changes in blood pressure and pulse rate, nausea, drowsiness, dyskinesia, tremor, skin rash and dependence, especially if predisposed.

Dose and Administration: *Oral:*

Adult: usually 10 mg 2 - 3 times daily; maximum 60mg/day.

Child over 6 years: initially 5mg twice daily (at breakfast and lunch), increased at weekly intervals, if necessary, to 20-30mg/day; maximum 1mg/kg/day.

Storage: store in airtight container and at room temperature.

5. DRUGS USED IN ANESTHESIA

5.1. General Anesthetics

General Anesthetics depress the central nervous system and produce loss of consciousness. An ideal anesthetic agent would produce unconsciousness, analgesia, and muscle relaxation suitable for all surgical procedures and be metabolically inert and rapidly eliminated. No single agent in safe concentrations fulfills all these requirements and it is customary to employ a number of agents to produce the required conditions. A typical anesthetic sequence is: induction with a short-acting intravenous agents such as thiopentone, intubations after the use of a short-acting muscle relaxant such as suxamethonium chloride, maintenance of unconsciousness with nitrous oxide and oxygen: supplementary analgesics and muscle relaxants may be given by injection.

Intravenous anaesthetics

Intravenous anesthetics may be used either to induce anesthesia or for maintenance of anesthesia throughout surgery. They can produce apnea and hypotension and thus facilities for adequate resuscitation must be available. They are contraindicated if the anaesthetist is not confident of being able to maintain an airway. Before intubation is attempted, a muscle relaxant must be given. Individual requirements vary considerably; lesser dosage is indicated in the elderly, debilitated or hypovolaemic patients.

Thiopental sodium is a widely used intravenous anesthetic, but it has no analgesic properties. Induction is generally smooth and rapid, but owing to its narrow therapeutic margin, over dosage with cardiorespiratory depression may occur. The reconstituted solution is highly alkaline and therefore irritant on misplaced injection outside the vein; arterial injection is particularly dangerous. Thiopental is contraindicated in porphyria.

Awakening from a moderate dose of thiopental is rapid due to redistribution of the drug in the whole body tissue. Metabolism is, however, slow and some sedative effects may persist for 24 hours. Repeated doses have a cumulative effect.

Anaesthesia with ketamine persists for up to 15 minutes after a single intravenous injection and is characterized by profound analgesia. It may be used as the sole agent for diagnostic and minor surgical interventions. Subanaesthetic concentrations of ketamine may be used to provide analgesia for painful procedures of short duration such as the dressing of burns, radio therapeutic procedures, marrow sampling and minor orthopedic procedures. It is of particular value in children.

Propofol is suitable for both induction and maintenance of anaesthesia. Recovery from anaesthesia is rapid as cumulative effects are minimal. It does not cause histamine release; it reduces intraocular pressure, has a low incidence of excitatory effects, and extravasation is not associated with local necrosis.

Etomidate is used as induction agent. It has minimal respiratory and cardiovascular depressant properties, while causing little 'hangover' effect or histamine release. It has no analgesic properties.

Etomidate

Injection, 20 mg/ml in 10ml and 20ml ampoules

Indications: induction agent, or for general anaesthesia.

Cautions: porphyria.

Drug interactions: CNS depressants including alcohol; ketamine.

Contraindication: hypersensitivity to etomidate.

Side effects: pain on injection, a high incidence of involuntary muscle movements (may be reduced by premedication with diazepam or one of the opiates), post-operative nausea and vomiting and brief periods of apnoea. Rarely myospasm, skin rashes.

Dose and Administration: *Dose should be individualized.*

Adult: Induction: *IV*: 0.2 - 0.3mg/kg slowly over 30 - 60 seconds. Smaller doses may be used as supplements for other anaesthetic agents.

Storage: store at room temperature.

Ketamine Hydrochloride

Injection, 10 mg/ml in 20ml, 50 mg/ml in 20 ml

Indications: anesthesia for short diagnostic and surgical procedures that do not require skeletal muscle relaxation; to induce anaesthesia prior to administration of other general anaesthesia. It is also used to supplement low potency anaesthetic such as nitrous oxide.

Cautions: warn the patient not to drive or operate machinery for about 24 hours of postanesthesia or avoiding alcohol and other CNS depressants within 24 hours following anaesthesia; pregnancy.

Drug interactions: anaesthetics such as enflurane, isoflurane, methoxyflurane, antihypertensives; CNS depressants, thyroid hormones.

Contraindications: ketamine is contraindicated in any condition in which significant elevation of blood pressure would be hazardous such as severe cardiovascular disease, Heart-failure, severe-hypertension, myocardial infarction, stroke (history); cerebral trauma, Intracerebral mass or hemorrhage; eye injury, increased cerebrospinal fluid pressure and increased intraocular pressure; psychiatric disorders such as schizophrenia or acute psychosis, thyrotoxic states.

Side effects: increased blood pressure, tachycardia, tonic or clonic muscle movements, emergence reaction (alteration in mood or body image, delirium, dissociative or floating sensation), vivid dreams or illusions, visual hallucinations.

Dose and Administration:

Adult: Induction: *IV*: 1 to 2mg per kg of body weight administered as a single dose or by *IV* infusion at a rate of 0.5mg per kg of body weight per minute. *IM* - 5-10mg per kg of body weight.

Maintenance: *IV*: 0.01-0.05mg (base) per kg of body weight by continuous infusion at a rate of 1-2mg per minute.

Child and Elderly: Same as adult

Storage: at room temperature, protect from light and heat and from freezing.

Propofol

Injection (emulsion), 10mg/ml in 20ml ampoule

Indications: intravenous anaesthesia (both induction and maintenance).

Cautions: cardiac, respiratory, renal or hepatic function impairment, epilepsy, elderly and hypovolaemic or debilitated patients.

Drug interactions: benzodiazepines, opiates, ethanol, narcotics, phenothiazines, fluconazole, ketoconazole, NSAIDs.

Contraindications: hypersensitivity to propofol.

Side effects: hypotension and transient apnoea, bradycardia; headache during recovery; involuntary muscle movements in unpremedicated patients; seizures.

Dose and Administration:

Adult: Induction: *Slow IV injection or infusion*, titrated against the response obtained from 40mg every 10 seconds. Most adult patients under 55 years require 1.5- 2.5mg/kg.

Maintenance: continuous infusion, the rate varying from 4 - 12 mg/kg/hour. Alternatively a technique of repeat bolus injections may be used: increments of 25 - 50mg may be given at intervals determined by clinical signs of lightening anaesthesia (usually every 6 minutes).

*Patients over 55 years and high- risk patients may require less than the usual doses. For induction: 1- 1.5 mg/kg may be adequate.

Maintenance: 2 - 6 mg /kg hour.

Child: over 3 years: Induction: 2.5 mg/kg adjusted as necessary.

Maintenance: IV infusion, 9 - 15 mg/kg/hour.

Storage: store at room temperature.

Thiopental sodium

Powder for injection, 0.5 g, 1 g in ampoule

Indications: induction of general anesthesia; anaesthesia of short duration; control of convulsions (especially in status epilepticus).

Cautions: reduce induction dose in severe liver disease. Extreme care is required in surgery of the mouth, pharynx, or larynx and in patients with acute circulatory failure (shock) or fixed cardiac out put, dehydration, hypovolaemia, severe anaemia, hyperkalaemia, toxemia, myasthenia gravis, myoedema or in severe renal disease.

Caution should be taken during pregnancy, in geriatric and patients sensitive to any one of barbiturates.

Drug interactions: alcohol, CNS depressant, dopaminergics, antihypertensives, especially diazoxide or ganglionic blockers, & hypotension producing medication, aspirin, probenecid.

Contraindications: porphyria (thiopental sodium may aggravate symptoms by inducing enzymes responsible for porphyria in synthesis).

Side effects: apnea, hypotension, allergic reaction, cardiac arrhythmias, circulatory depression, emergence delirium, and thrombophlebitis.

Dose and Administration:

Dosage must be individualized by physician; however, as a general guideline the following can be used.

Adult:

Induction: IV: 50 to 100 mg (2 to 4 ml of a 2.5 % solution) as require; or 3 to 5mg per Kg of body weight as a single dose.

Maintenance: IV (Intermittent) 50 to 100 mg (2 to 4 ml of a 2.5 % solution) as required.

Status epilepticus refractory to other treatment: IV, 2-4mg/kg bolus over 20 seconds, then further 50mg boluses every 2-3 minutes until seizures are controlled; then infusion to maintain 1-5 mg/kg/hour using EEG control if possible.

Child:

Children up to 15 years of age

Induction: IV: 3 to 5 mg per Kg of body weight.

Maintenance: IV: (intermittent), about 1 mg per Kg of body weight as required.

Storage: prior to reconstitution, store at room temperature, unless otherwise specified by manufacturer.

Volatile inhalation agents

One of the volatile anesthetics, ether, halothane (with or without nitrous oxide), must be used for induction when intravenous agents are contraindicated and particularly when intubations is likely to be difficult.

Full muscle relaxation is achieved in deep anesthesia with ether. Excess bronchial and salivary secretion can be avoided by premedication with atropine. Laryngeal spasm may occur during induction and intubations. Localized capillary bleeding can be troublesome and postoperative nausea and vomiting are frequent; recovery time is slow particularly after prolonged administration.

If intubation is likely to be difficult, halothane is preferred. It does not augment salivary or bronchial secretions and the incidence of postoperative nausea and vomiting is low. Severe hepatitis, which may be fatal, sometimes occurs; it is more likely in patients who are repeatedly anaesthetized with halothane with in a short period of time.

Isoflurane is an isomer of enflurane. It is more irritant to the airway than halothane and thus unsuitable for inhalational induction. In comparison with the other two, induction of anaesthesia is more rapid, and it is less arrhythmogenic. It is a potent vasodilator with minimal cardiac depressant effect. It is used in neurosurgical anaesthesia because it causes less increase in intracranial blood flow and a smaller subsequent rise in intracranial pressure.

Enflurane

Inhalation, 250ml

Indications: Induction and maintainance of general anaesthesia.

Cautions: increased intracranial pressure, epilepsy, elderly, porphyria

Drug interactions: as for halothane; isoniazid, non-depolarizing muscle relaxants.

Contraindications: history of malignant hyperthermia, or jaundice/hepatic dysfunction (for which no other cause could be established) after exposure to a volatile agent; renal failure.

Side effects: hypotension and tachycardia may occur. Respiratory depression, an increase in salivation and bronchial secretions, and hepatic impairment have been reported. Malignant hyperthermia may be precipitated in susceptible patients.

Dose and Administration: Adult: Maintenance range 1-3%

Child: not used for inhalational induction. Maintenance range 1-3 %.

Ether, anesthetic

Inhalation, 100gm, 250gm

Indications: general anesthesia before surgery.

Cautions: ether is explosive. Mixture of its vapor with oxygen, nitrous oxide or air at certain concentration causes explosion and hence it should be avoided. It should not be used in the presence of open flame or any electrical appliances liable to produce a spark.

Premedication with atropine is necessary to inhibit bronchial and gastric secretion induced by ether.

Drug interactions: avoid concomitant use of ether with competitive muscle relaxants.

Contraindications: diabetes mellitus, impaired kidney function, severe liver disease.

Side effects: irritation on the mucous membrane of the respiratory tract, pharyngeal spasm, decreased blood pressure, capillary bleeding, malignant hyperpyrexia (in some individuals), convulsions in children and young adults.

Dose and Administration:

Inhalation: Induction: **Adult and Child:** up to 15 % in impaired gases. Maintenance of light anesthesia, 3 - 5 % in air (with or without muscle relaxants); up to 10 % for deep anesthesia.

Halothane

Inhalation, 250 ml

Indications: induction and maintenance of anesthesia in major surgery, often combined with nitrous oxide/oxygen mixtures.

Cautions: during pregnancy, breast-feeding, in children and elderly patients.

Drug interactions: sympathomimetics, especially catecholamines such as dopamine, epinephrine, norepinephrine; or cocaine, ephedrine, levodopa, metraminol, methenamine, nephrotoxic agents, xanthines; alcohol, aminoglycosides; capreomycin, citrate-anticoagulated blood, lincomycin (systemic), neuromuscular blocking agents (non depolarizing), polymyxins (systemic). Amiodarone, cumarine or indandione derivative anticoagulants; antihypertensives, especially diazoxide or ganglionic blockers such as guanethidine, guanethidine, mecamylamine or trimethaphan, neostigmine and pyridostigmine.

Contraindications: malignant hyperthermia, biliary tract disease or hepatic function impairment, jaundice or acute hepatic damage; cardiac arrhythmias, head injury or increased intracranial pressure, myasthenia gravis, pheochromocytoma, sensitivity to halothane.

Side effects: hepatotoxicity, impairment of psychomotor skills, emergence delirium (postanaesthesia), shivering or trembling, nausea or vomiting (mild).

Dose and Administration: *inhalation*

Adult: Induction: Increase gradually to 2-3% in oxygen or nitrous oxide/oxygen mixture. Maintenance range 0.5-1.5%

Child: Induction: 1.5-2%, though up to 3% may be required. Maintenance: 0.5-2%

Storage: at room temperature in a tight, light-resistant container.

Isoflurane

Inhalation, 100 ml

Indications: Inhalational anaesthesia.

Cautions: debilitated patients, elderly, ischaemic heart disease.

Drug interactions: sympathomimetics and xanthines, anticonvulsants, non-depolarizing muscle relaxants, blood pressure lowering agents.

Contraindications: history of malignant hyperthermia

Side effects: respiratory depression and airway irritation (may result in retardation of inhalational induction due to breathholding or coughing if the inspired concentration is increased too rapidly). Increase in heart rate and significant hypotension with increasing concentrations.

Malignant hyperthermia may be precipitated in susceptible patients.

Dose and Administration: Adult and Child: Maintenance range usually 0.75-1.5%.

Storage: store at room temperature.

Inhalational gases

Nitrous oxide is used for the maintenance of anesthesia. It is too weak to be used alone, but it allows the dosage of other anesthetic agents to be reduced. It has a strong analgesic action.

Nitrous oxide

Inhalation

Indications: maintenance of anaesthesia and, in sub-anaesthetic concentrations, for analgesia.

Cautions: caution is needed in the presence of air-enclosing cavities (such as pulmonary, renal or occluded middle ear air cysts or air embolism).

Drug interactions: alcohol; alfentanil, fentanyl, sufentanil; amiodarone, anticoagulants (coumarin- or indandione – derivative); antihypertensive agents, especially diazoxide or ganglionic blockers; chlorpromazine; diuretics; CNS depressant, methyl dopa, xanthines.

Contraindications: pneumothorax, head injury or increased intracranial pressure, pre-existing or intracranial lesions, space – occupying or tumors, history of sensitivity to the anaesthetic being considered for use.

Side effects: mild nausea or vomiting and rarely respiratory depression, neurologic injury, malignant hyperthermic crisis, megaloblastic anaemia.

Dose and Administration:

Adult: *Inhalation:*

Anaesthetic (general): Induction: 70 % with 30 % of oxygen.

Maintenance: 30 to 70 % with oxygen

For obstetrics or procedures not requiring loss of consciousness: 25 to 50 % with oxygen.

Child: Dosage must be individualized.

Storage: store at room temperature, unless otherwise specified by manufacturer.

Sevoflurane

Inhalation, 250ml

Indications: Inhalational anaesthesia

Cautions: porphyria, paediatrics, pregnancy.

Drug interactions: non-depolarizing muscle relaxants, nitrous oxide, opioids and benzodiazepines.

Contraindications: known sensitivity to halogenated agents; history of malignant hyperthermia; liver dysfunction, unexplained fever or leucocytosis occurring after a previous halogenated anaesthetic.

Side effects: may cause dose-dependent cardiorespiratory depression. Malignant hyperthermia may be precipitated in susceptible patients.

Dose and Administration: **Adult:** Induction: In adults inspired concentrations of up to 5% usually produce surgical anaesthesia in < 22 minutes. A short acting intravenous induction agent may be used prior to inhalation. Maintenance: Surgical levels of anaesthesia may be sustained with concentrations of 1-3% sevoflurane, with or without the concomitant use of nitrous oxide.

Child: Inspired concentrations of up to 6% usually produce surgical anaesthesia in < 2 minutes. Maintenance: 2-3%.

Trichloroethylene

Inhalation

Indications: used for maintenance of light anaesthesia.

Cautions: it should not be used in closed-circuit apparatus.

Drug interactions: sympathomimetics such as adrenaline; alcohol.

Side effects: acute exposure leads to dizziness, lightheadedness, lethargy, nausea and vomiting and hepatic and renal dysfunction. Chronic poisoning may result in visual disturbances, impairment of performance, hearing defects, neuralgia and mild liver function.

Dose and Administration: administered by inhalation.

5.2. Neuromuscular Blockers

These drugs affect transmission at the neuromuscular junction and are used as adjuncts to general anesthesia, particularly to enable adequate muscle relaxation to be achieved with light anesthesia. There are 2 main types of neuromuscular blocking agents: competitive or non-depolarizing agents and depolarizing agents.

Generally, the competitive neuromuscular blocking agents, having a longer duration of action, are used in major operations, while the depolarizing agents,

with a much shorter effects, are used for minor operations or manipulations and particularly for intubations. Following administration of a depolarizing agent, such as suxamethonium, to aid intubation, a longer acting competitive agent may be given to maintain muscle relaxation throughout an operation.

Suxamethonium is the only widely used depolarizing muscle relaxant. It produces rapid, complete paralysis, which is very short-lasting in most patients and is of particular value for laryngoscopy and intubation. Prolonged paralysis may occur in those with low or atypical plasma cholinesterase. Assisted ventilation should be continued until muscle function is restored. Suxamethonium normally produces a phase I (depolarizing) neuromuscular block. After high dose or prolonged use, the nature of the block changes to a phase II (non-depolarizing) block; this phase II block (also known as dual block) is associated with prolonged neuromuscular blockade and apnoea.

Non-depolarizing (competitive) muscle relaxants include atracurium besylate, pancuronium bromide, vecuronium bromide and gallamine. These agents compete with acetylcholine at the neuromuscular receptor sites. Their action is reversible by anticholinesterase agents, which allow the concentration of acetylcholine to increase at these receptor sites and displace the 'blocker'.

Gallamine has vagolytic and sympathomimetic properties and frequently increases pulse rate and blood pressure. It is rarely used since the other neuromuscular blocking drugs have a more predictable response and it should be avoided in patients with renal impairment.

Non-depolarizing muscle relaxants

Atracurium Besylate

Powder for Injection, 10mg/ml in 2.5, 5ml, 25ml ampoules

Indications: adjunct to general anesthesia to facilitate endotracheal intubation and to relax skeletal muscles during surgery.

Cautions: previous anaphylactic reaction.

Drug interactions: aminoglycosides, beta-blockers, clindamycin, calcium channel blocker, ketamine, lidocaine, loop diuretics, theophylline, and sympathomimetics.

Side effects: flushing, bronchial secretion, erythema, itching, wheezing.

Dose and Administration: Adult: IV: usual range initially 0.3 – 0.6 mg/kg, depending on the duration of block required, with supplementary doses of 0.08-0.2 mg/kg as needed.

Storage: store in refrigeration.

Pancuronium bromide

Injection, 2mg/ml in 2ml ampoule

Indications: management of mechanically ventilated patients and used for surgery.

Cautions: renal and hepatic disease.

Drug interactions: aminoglycosides, clindamycin, lincomycin, polymyxin antibiotics, tetracyclines, quinidine, lignocaine, verapamil, lithium, magnesium

salts, anaesthetic agents such as enflurane and ether, and potassium - depleting drugs such as amphotericin B and diuretics; digoxin, phenytoin and carbamazepine.

Contraindications: conditions in which tachycardia would be undesirable.

Side effects: tachycardia and a dose - related elevation in blood pressure (due to vagolytic and indirect sympathomimetic effects on the cardiovascular system).

Rarely - hypersensitivity reactions.

Dose and Administration: *IV*:

Adult: initially: 0.04 - 0.1mg/kg; further doses of 0.01 - 0.02 mg/kg may be given as required.

In intensive care: 0.06 mg/kg every 1 - 1.5 hours.

Following administration of suxamethonium, dose should be reduced; 0.02 - 0.06 mg/kg may be adequate for the initial dose.

Child: over 2 months: 0.04 - 0.1mg/kg; increments of 0.01 - 0.02 mg/kg if required.

Neonates: 0.03 - 0.04 mg/kg with increments of 0.01 - 0.02 mg/kg if needed. Should be used with extreme caution.

Storage: store in refrigerator. Stable at room temperature up to 6 months.

Vecuronium Bromide

Powder for Injection, 10mg in vial

Indications: muscle relaxant during surgery.

Cautions: renal impairment, hepatic impairment, electrolyte disturbances, asthma, pregnancy and breastfeeding.

Drug interactions: carbamazepine, clindamycin, gentamicin, lithium, neostigmine, nifedipine, phenytoin, procainamide, propranolol, pyridostigmine, quinidine, streptomycin, verapamil.

Contraindications: respiratory insufficiency or pulmonary disease; dehydrated or severely ill patients; myasthenia gravis or other neuromuscular disorder.

Side effects: hypersensitivity reactions including bronchospasm, hypotension, tachycardia, oedema, erythema, pruritus.

Dose and Administration: *IV: Intubation:*

Adult and Child over 5 months: 80-100mcg/kg; maintenance of relaxation 20-30mcg/kg.

Child under 4 months: initially 10-20mcg/kg, followed by increments according to response.

IV infusion: **Adult:** initial bolus 40-100mcg/kg then 0.8-1.4mcg/kg/minute.

Storage: store at room temperature.

Depolarizing muscle relaxant

Suxamethonium Chloride (succinylcholine)

Powder for injection, 100 mg, 500 mg in vial

Injection, 50mg/ml

Indications: rapid and complete depolarizing muscle relaxation of short duration; used mainly for endotracheal intubation.

Cautions: children, during pregnancy, and cardiovascular function impairment. Caution is also required:

In conditions that may be adversely affected by increased potassium concentrations (severe burns, digitalis toxicity, or recent digitalization, degenerative or dystrophic neuromuscular disease, paraplegia, pre-existing hyperkalemia, spinal cord injury, severe trauma).

Conditions that may lead to low plasma pseudocholine esterase activity (severe anemia, dehydration, exposure to neurotoxic insecticides or other cholinesterase inhibitors, severe hepatic disease or cirrhosis, malnutrition, recessive hereditary trait).

Conditions that may be adversely affected by increase in intraocular pressure (open eye injury, glaucoma, ocular surgery).

Fracture or muscle spasm and malignant hyperthermia.

Drug interactions: cholinesterase inhibitor specially echothiopate, demecarium, isofluorophate, cyclophosphamide. Avoid exposure to insecticides such as Malathion. Avoid also simultaneous use of digitalis glycosides, procainamide, physostigmine, calcium salts, and succinylcholine.

Contraindications: allergic to succinylcholine, pulmonary function impairment or respiratory depression, renal function impairment.

Side effects: increased intra ocular pressure, muscle pain and stiffness (postoperative), excessive salivation, cardiac arrhythmias, bradycardia.

Dose and Administration:

Adult: *IV injection:* initially 0.6-1mg/kg (range 20-100 mg). Subsequent doses must be individualized according to the patient's needs.

IV infusion, as a 0.1% solution, 2-5 mg/minute for up to 1 hour.

Child: *IV: 1-12 years,* 1mg/kg; under 1 year, 2mg/kg.

Storage: store between 2 and 8°C. Protect from freezing.

5.3. Anesthetic Adjuncts and Adjuvants

A balance combination of agents with different actions is often used to provide the various components of general anesthesia including hypnosis muscle relaxation. This technique has been reported to minimize intra-operative cardiovascular depression, to facilitate a rapid return of consciousness, and to have a low incidence of postoperative adverse effects such as nausea, and vomiting, and excitation.

Antimuscarinics, including atropine, hyoscine, and glycopyrronium, have been used as pre-operative medication to inhibit salivation and excessive secretions of the respiratory tract. This use is less important now that less irritating anesthetics are used. Atropine, hyoscine and glycopyrronium are also given as premedications to reduce intra-operative bradycardia and hypotension induced by agents such as suxamethonium, halothane, or following vagal stimulation.

At the end of surgery drugs are sometimes administered to accelerate recovery from the effects of the various agents used during anesthesia. Non-depolarizing muscle relaxants may be reversed with anticholinesterases such as neostigmine

but concomitant administration of atropine or glycopyrronium is required to prevent bradycardia and other muscarinic actions developing.

Oxygen should be added routinely during anesthesia with inhalational agents, even when air is used as the carrier gas, to protect against hypoxia.

Atropine is now rarely used for premedication but still has an emergency role in the treatment of vagotonic side effects.

Hyoscine effectively reduces secretion and also provides a degree of amnesia, sedation and anti-emesis. Unlike atropine it may produce bradycardia rather than tachycardia. In some patients, especially the elderly, hyoscine may cause the central anti-cholinergic syndrome (excitement, ataxia, hallucinations, behavioral abnormalities and drowsiness) glycopyrronium produces good drying of salivary secretions. When given intravenously it produces less tachycardia than atropine. It is widely used with neostigmine for reversal of non-depolarizing muscle relaxants.

Neostigmine is the specific drug for reversal of non-depolarizing (competitive) blockade. It acts within one minute of intravenous injection and lasts for 20 to 30 minutes; a second dose may then be necessary. Atropine or preferably glycopyrronium should be given before or with neostigmine in order to prevent bradycardia, excessive salivation; and other muscarinic actions of neostigmine.

Atropine Sulphate

Injection, 1 mg/ml in 1 ml ampoule

Indications: as antisialagogue pre-anaesthetic medication to prevent or reduce salivation and respiratory tract secretions.

Cautions: pregnancy, breastfeeding, in children and elderly patients. Caution is also needed in patients with hyperthyroidism, hepatic or renal disease, hypertension, tachyarrhythmias, congestive heart failure, coronary artery disease, gastric ulcer, esophageal reflex, and cardiac insufficiency. Extreme caution is required in patients with known or suspected GI-infection and with autonomic neuropathy. There should be caution also in debilitated patients with chronic pulmonary disease.

Advise patients not to drive vehicle or operate machinery

Drug interactions: atropine with antacids, antidiarrhoeals (adsorbent), other anticholinergic, cyclopropane anaesthesia, ketoconazole.

Contraindications: severe ulcerative colitis, obstructive disease of the GI tract e.g. pyloroduodenal stenosis, achalasia, cardiospasm, paralytic ileus or intestinal atony (especially in geriatric or debilitated patients), known hypersensitivity, angle-closure glaucoma, obstructive uropathy, myasthenia gravis.

Side effects: dryness of mouth, nose and throat, skin; constipation decreased sweating, redness or other signs of irritation at injection site, blurred vision, decreased salivary secretion (difficulty in swallowing), mydriatic effect (increased sensitivity of eyes to light), increased intraocular pressure, bradycardia followed by tachycardia, palpitation and arrhythmias.

Dose and Administration:

Adult: IV: 0.3-0.6mg immediately before induction of anaesthesia.

IM: 0.3-0.6mg, 30-60 minutes before induction

Child: *IM*: 20 micrograms per kg of body weight

Storage: store at room temperature protect from freezing.

Droperidol

Injection, 2.5 mg/ml in 2ml ampoule

Indications: antiemetic in surgical and diagnostic procedures; preoperative medication in patients when other treatments are ineffective or inappropriate.

Cautions: hypokalemia, hypomagnesemia, pheochromocytoma, alcoholism (acute), Parkinsonism

Drug interactions: anesthetics, bromocriptine, levodopa, CNS depression - producing medications, epinephrine, extrapyramidal reaction, hypotension-producing medications, propofol.

Contraindications: hypersensitivity to droperidol.

Side effects: akathisia, anxiety, hypertension, dystonia, hyperpyrexia, oculogyric crisis, hypotension, tachycardia, excessive sedation.

Dose and Administration: *Nausea and Vomiting: IM, IV:*

Adult: initial; 2.5mg; additional doses of 1.25mg may be administered to achieve desired effect; administer additional doses with caution.

Child 2-12 years: 0.05-0.06mg/kg (maximum initial dose: 0.1mg/kg).

Storage: store at room temperature.

Fentanyl

Injection, 0.05mg/ml in 2ml ampoule

Indications: general or local adjunct anesthesia, pain of labor and vaginal delivery.

Cautions: cardiac bradyarrhythmias, hepatic impairment, hypothyroidism, renal functions impairment, respiratory impairment, elderly.

Drug interactions: antihypertensives, diuretics, benzodiazepines, cimetidine, erythromycin, CNS depression- producing medications, MAO inhibitors, nalbuphine, pentazocine, naloxone, naltrexone, neuromuscular blocking agents, nitrous oxide, phenothiazines.

Contraindications: hypersensitivity reaction to fentanyl.

Side effects: drowsiness, nausea or vomiting, brady cardia, hypotension, respiratory depression, cardiac arrhythmia, biliary spasm, changes in vision, chills, constipation, ureteral spasm, urinary retention.

Dose and Administration: *IV:*

Adult: *Spontaneous respiration:* initially 50 - 200mcg, and 50mcg as supplements when needed.

Assisted respiration: Initially 300-3500mcg (up to 50mcg/kg), then 100-200mcg as required.

Child over 2 years:

Spontaneous respiration: 1-3mcg/kg in small increments, and supplements of 1mcg/kg as required.

Assisted respiration: initially 10 - 15 mcg/kg, followed by 1 - 3 mcg/kg as required.

Storage: store at room temperature and protect from light.

Glycopyrronium Bromide (Glycopyrrolate)*Injection, 0.2 mg/ml in 1 ml and 3 ml ampoules*

Indications: as antisialagogue in preanesthesia. Also, indicated as antiarrhythmic in pre-anesthesia, anesthesia, and surgery. In addition, indicated to prevent aspiration pneumonitis during anesthesia. May be used as antidiarrheal and for cholinesterase inhibitor toxicity

Cautions: close supervision is recommended for infants, children and geriatric patients. Cardiovascular disease, prostatic enlargement, ulcerative colitis, and pyloric stenosis; pregnancy and breast-feeding.

Drug interactions: anti-cholinergics, cyclopropane, ketoconazole (***) patients should be advised to take this medication at least two hours after ketoconazole), potassium chloride (especially wax –matrix preparations).

Contraindications: symptomatic reflux, paralytic ileus, glaucoma, cardiac disease, hemorrhage, myasthenia gravis, prostate hypertrophy.

Side effects: constipation; blurred vision; clumsiness or unsteadiness, confusion; difficulty in breathing; dryness of mouth, nose, or throat; drowsiness; muscle weakness; tiredness; tachycardia, hesitate micturation

Dose and Administration:**Adult:**

Anticholinergic – prophylaxis of excessive salivation and respiratory tract secretions, in anesthesia; and prophylaxis of gastric hypersecretory conditions, in anesthesia:

IM: 4.4 mcg (0.004mg) per kg of body weight one-half to one hour before induction of anesthesia or at the time the preanesthetic narcotic and/or sedative are administered.

Antiarrhythmic, in anesthesia; or Antiarrhythmic, in surgery: IV: 100 mcg (0.1mg), the dosage being repeated if necessary at two to three minute intervals.

Cholinergic adjunct (curariform block): IV: 200mcg (0.2 mg) for each 1 mg of neostigmine or 5 mg of pyridostigmine given simultaneously; may be mixed in the same syringe.

Note: Geriatric patients may be more sensitive to the effects of the usual adult dose.

Child:

Anticholinergic –Prophylaxis of excessive salivation and respiratory tract secretions, in anaesthesia; and Prophylaxis of gastric hypersecretory conditions, in anaesthesia; IM, 4.4 to 8.8 mcg (0.0044 to 0.0088 mg) per Kg of body weight one half to one hour before induction of anesthesia or at the time the preanesthetic narcotic and/or sedative are administered

Antiarrhythmics, in anesthesia; or Antiarrhythmics, in surgery: IV: 4.4 mcg (0.0044 mg) per Kg of body weight up to a maximum of 100 mcg (0.1 mg) the dosage being repeated, if necessary, at two-to three minute intervals.

Cholinergic adjunct (curariform block) IV – the same as usual adult and adolescent dose.

Storage: store at room temperature unless otherwise specified by manufacturer.

Hyoscine Hydrobromide

Injection, 0.4 mg/ml, 0.6 mg/ml in 1 ml ampoule

Indications: as antisialogogue pre anaesthetic medication to prevent or reduce salivation and respiratory tract secretion.

Parenteral administration of scopolamine in combination with morphine or mepridine is indicated in pre-anaesthesia to reduce excitement and produce amnesia.

Cautions: pregnancy and breast-feeding, in children and elderly patients. Advise patients to avoid alcohol, driving vehicle and operating machineries.

Drug interactions: antacids, antidiarrhoeals (adsorbents), other anticholinergics, cyclopropane anaesthesia, CNS depressants.

Contraindications: angle closure glaucoma, pyloric obstruction, urinary bladder neck obstruction, tachycardia, paralytic ileus, hypersensitivity to the drug, ulcerative colitis.

Side effects: constipation, decreased sweating, drowsiness, dryness of mouth, skin, throat and nose, loss of memory, redness or other signs of irritation at injection site.

Dose and Administration:

Adult: *Prophylaxis of excessive salivation and respiratory tract secretion in anaesthesia:* IM 0.2-0.6mg, 30 minutes to 1 hour before induction of anaesthesia.

Anaesthetic Adjunct - sedation - hypnosis: IM, IV or SC: 0.6mg three or four times a day.

Amnesia: IM, IV, SC: 0.32 to 0.05mg

Child: *Prophylaxis of excessive salivation and respiratory tract secretion in anaesthesia:*

IM: administered 45 minutes - 1 hour before induction of anaesthesia. Child (4-7 months) - 0.1mg. Child (7months - 3 years) - 0.15mg, Child (3-8 years) - 0.2mg, Child (8-12 years) - 0.3mg

Storage: store at room temperature in light-resistant container, protect from light.

Neostigmine

Injection (Methylsulphate), 0.5 mg/ml, 2.5 mg/ml in 1 ml ampoule

Indications: for reversal of the effects of Non-depolarizing Neuromuscular blocking agents (e.g. tubocurarine, metocurine, gallamine or pancuronium) after surgery; in the treatment of post-operative non-obstructive urinary retention; for prevention and treatment of post-operative gastro intestinal ileus and prevention of postoperative distention and urinary retention.

Cautions: caution should be taken during near term pregnancy, in elderly and in those patients with epilepsy, bronchial asthma, bradycardia, recent coronary occlusion, vagotonia, hyperthyroidism, cardiac arrhythmias, or peptic ulcer.

Drug interactions: anticholinergics especially atropine and related compounds, local and some general anaesthetics such as chloroform, cyclopropane, enflurane, halothane, lidocaine; systemic aminoglycosides, succinylcholine or decamethonium; other cholinesterase inhibitors including demecarium,

echothiopate isophlurophate, edrophonium; ganglionic blocking agents such as guanethidine, mecamlamine, trimethaphan; procainamide.

Contraindications: intestinal or urinary tract obstruction (mechanical), hypersensitivity to the drug or bromide, peritonitis, urinary tract infection.

Side effects: diarrhoea, increasing sweating, increasing of watering of mouth, nausea, vomiting, stomach cramp, frequent urge to urinate, increased bronchial secretion, miosis, bradycardia, bronchospasm, weakness, muscle cramp, fasciculation, hypotension.

Dose and Administration:

Adult: *Antidote (to non-depolarizing neuromuscular blocking agents)*

after surgery: IV: 0.5mg - 2mg administered slowly, repeated as required up to a total dose of 5mg.

Note: 0.6mg - 1.2mg of atropine is administered prior to or concurrently with neostigmine to counteract its muscarinic side effect.

Prevention of post-operative distention or retention: IM or SC - 0.25mg immediately following surgery, repeated every four to six hours for 2 or 3 days.

Prevention of post-operative distention: IM or SC - 0.5mg as needed.

Prevention of urinary retention: IM or SC - 0.5mg; dose repeated every 3 hours for at least five doses after patient has voided or the bladder has been emptied.

Note: - If urination doesn't occur within one hour following the initial - 0.5mg per dose, the patient should be catheterized.

Child: *Antidote (to non-depolarizing neuromuscular blocker) after surgery: IV*, -0.04mg per kg of body weight administered with 0.02mg of atropine per kg of body weight.

Storage: at room temperature. Protect from freezing and light.

Oxygen (white-colored cylinder)

Indications: oxygen is given by inhalation to correct hypoxia in conditions causing under ventilation of the lungs, such as exacerbations of chronic bronchitis, pneumonia, or pulmonary oedema, where bronchospasm causes hypoxia, as in asthma, in extensive fibrosing alveolitis after general anaesthesia and in conditions where the oxygen content of the air breathed is inadequate as at high altitudes.

Cautions: any fire or spark is highly dangerous in the presence of increased oxygen concentrations especially when oxygen is used under pressure.

Metal cylinders containing oxygen should be fitted with a reducing valve by which the rate of flow can be controlled.

Side effects: CNS, toxicity (nausea, mood change, vertigo, twitching, convulsions, loss of consciousness), pulmonary toxicity (decrease in vital capacity, cough, substernal distress, and later atelectasis), retinopathy of prematurity.

Dose and Administration: *by inhalation.* It is administered by means of nasal catheter, facemask, endotracheal tube, or oxygen tent. Concentration of oxygen in inspired anesthetic gases should never be less than 21 % sideline (carbondioxide absorbent).

Soda lime

Used to absorb carbon dioxide, for instance in closed-circuit anaesthetic apparatus.

5.4. Local Anesthetics

The local anesthetics are compounds which produce reversible loss of sensation by preventing or diminishing the conduction of sensory nerve impulses near to the site of their application or injection. Local anesthetics could also be described as local analgesics as they are most often used to produce loss of pain without loss of nervous control. Also because their mode of action is to decrease permeability of the nerve cell membrane to sodium ions they are considered to have a membrane stabilizing effect.

Local anesthetics are used very widely in dental practice, for brief and superficial interventions for obstetric procedures, and for specialized techniques of regional anesthesia calling for highly developed skills. Where patient cooperation is required the patient must be psychologically prepared to adopt the proposed procedure. Facilities and equipment for resuscitation should be readily available at all times. Care must always be taken to avoid inadvertent intravascular injection.

The drugs used vary widely in their potency, toxicity, duration of action, stability in water, and ability to penetrate mucous membranes. These variations determine their suitability for use by various routes, e.g. topical (surface), infiltration, plexus, epidural (extradural) or spinal block.

The cold sensation produced by ethyl chloride spray is used to test the onset of regional anaesthesia.

Local infiltration anesthesia. Many simple surgical procedures that neither involve the body cavities nor require muscle relaxation can be performed under local infiltration anesthesia. Lower segment caesarean section can also be performed under local infiltration anesthesia. The local anesthetic drug of choice is lidocaine 0.5 % with or without epinephrine. No more than 4 mg/Kg of plain lidocaine or 7 mg/kg of lidocaine with epinephrine should be administered on any one occasion. The addition of epinephrine (adrenaline) diminishes local blood flow, slows the rate of absorption of the local anesthetic, and prolongs its effect. Care is necessary when using epinephrine for this purpose since, in excesses, it may produce ischaemic necrosis.

Surface anesthesia. Topical preparations of lidocaine are available and topical eye drop solutions of tetracaine are used for local anaesthesia of the cornea and conjunctiva.

Regional Block. A regional nerve block can proceed safe and effective anesthesia but its execution requires considerable training and practice. Nevertheless, where the necessary skills are available, techniques such as axillary's or ankle block can be invaluable. Either lidocaine 1 % or bupivacaine 0.5 % is suitable. Bupivacaine has the advantage of a longer duration of action.

Spinal Anesthesia. This is one of the most useful of all anaesthetic techniques and can be used widely for surgery of the abdomen and the lower limbs. It is a

major procedure requiring considerable training and practice. Either lidocaine 5 % in glucose or bupivacaine 0.5 % in glucose can be used but the latter is often chosen because of its longer duration of action.

Bupivacaine

Injection, 0.25%, 0.5%

Indications: the 0.5% solution is chiefly indicated for peripheral nerve blocks, eye blocks, spinal and epidural (including caudal) anesthesia. Diluted solutions (0.25%) have been used for local infiltration. Bupivacaine is particularly useful for producing prolonged analgesia during labour, where the interval between doses is usually 2-3 hours.

Cautions: respiratory impairment; hepatic impairment; epilepsy; porphyria; myasthenia gravis; pregnancy and breastfeeding.

Drug interactions: hyaluronidase.

Contraindications: adjacent skin infection, inflamed skin, concomitant anticoagulant therapy, severe anaemia or heart disease; spinal or epidural anaesthesia in dehydrated or hypovolaemic patient.

Side effects: cardiac arrest, hypotension, bradycardia, seizures, restlessness, anxiety, dizziness, nausea, vomiting, blurred vision, tinnitus and apnea.

Dose and Administration:

Adult: *Dosage depends on site of injection, procedure used, and the status of the patient:* Not more than 2mg/kg (with or without adrenaline) should be administered in any 4 hour period, and in 24 hours the total amount should not exceed 400mg.

Child: *Local infiltration:* 2mg/kg. *Regional anaesthesia:* 2.5mg/kg

Storage: store at room temperature.

Ethyl Chloride

Spray, 50ml

Indications: as a local anaesthetic in minor operative procedures such as incision of boils and removal of localized growths.

Cautions: during application, the skin adjacent to the area being treated should be covered with vaseline to protect against tissue sloughing. Inhalation of ethyl chloride should be avoided.

Contraindications: broken skin or mucous membrane.

Side effects: freezing may injure cells, decrease resistance to infections, and delay healing. The frozen tissue may be painful, as it gets warm. And cutaneous sensitization may occur rarely.

Dose and Administration: the container should be held about 12 inches (30 cm) from the area being treated and the spray directed downward until light frosting appears. Because the local anaesthetic effect is very brief, incision should be made as soon as the tissue become white.

Storage: at room temperature, in tight containers, away from fire. Protect from light.

Lidocaine Hydrochloride

Ointment, 5 % in 10 g; Jelly, 2% in 30 ml; Cartridge, 2% in 1.8 ml ampoule; Spray, 4 %, 10 % in 80 g; Viscous, 2 % in 100 ml; Injection, 0.5 %, 1 %, 2 % in 2 and 20 ml vials; Injection Heavy, 5 % in 2 ml ampoule

Indications: surface anaesthesia of mucous membranes; infiltration anesthesia; peripheral and sympathetic nerve block; dental anaesthesia; spinal anaesthesia; intravenous regional anaesthesia; arrhythmias.

Cautions: caution in patients with inflammation and/or infections at site of injection, and in very young, the elderly, acutely ill, or weak patients.

Drug interactions: avoid simultaneous use of lidocaine with vasoconstrictors (e.g. adrenaline) on the extremities such as the finger, toes...etc.

Contraindications: known hypersensitivity.

Side effects: a transient burning sensation may occur at the site of injection.

Dose and Administration:

Note: Intradermally, subcutaneously, or submucosally (local infiltration). Inject indirectly in to the tissue to be incised or in the immediate area surgery. It should be injected slowly, with frequent aspirations before and during the injection, to reduce the risk of inadvertent intravascular administration.

The total dose should not exceed 300mg/dose (4.5mg/kg of body weight). Children should receive smaller amounts of lidocaine, generally in lower concentration than adults.

By injection, infiltration anesthesia, according to patient's weight and nature of procedure, max, 300 mg,

Ointment, Topical, Adult and Child 2 years of age and older as a 5 % ointment, to the affected area three or four times a day as needed.

Jelly, Topical, Adult, to the affected area three or four times a day as needed

Spray, Topical, Adult, sprayed and/or applied to affected area three or four times a day as needed.

Storage: at room temperature. Protect from freezing.

Lidocaine Hydrochloride and Adrenaline

Injection, 1 % + 1:200,000 in 30 ml Vial

Injection, 2 % + 1:200,000 in 20 ml vial

See under Lidocaine Hydrochloride

Dose and Administrations: *Dental Anaesthesia (for infiltration or nerve block)*

Adult: 20 to 100 mg (1 to 5 ml) of lidocaine hydrochloride as 2 % solution with epinephrine 1:200,000; **Child**, 4 to 5 mg of Lidocaine Hydrochloride per kg of body weight or 100 to 150 mg as a single dose.

Local infiltration or nerve block 7 mg of lidocaine hydrochloride per kg of body weight as a 0.25 to 1 % solution with epinephrine 1:200,000.

Storage: at room temperature protect from light and freezing.

Tetracaine hydrochloride

Injection, 0.5%, 2%, 4% in 2ml vial

Indications: spinal anesthesia.

Dose and Administration: Adult: *Subarachnoid injection:* 5-20mg

6. DRUGS USED IN MUSCLOSKELETAL AND JOINT DISEASE

6.1. Antirheumatics

Many different drugs have been used for rheumatoid arthritis. The choice of drugs for relief of pain depends up on the severity of symptoms. In mild cases an analgesic alone may be all that is required but most patients need the additional anti-inflammatory effect provided by a non steroidal anti-inflammatory drug (NSAID).

Non-steroidal anti-inflammatory drugs (NSAIDs)

Many of the effects of non-steroidal anti-inflammatory drugs (NSAIDs) appear to be due to their inhibitory action on cyclo-oxygenases which are involved in the biosynthesis of prostaglandins. Prostaglandins have an important role in the production of pain, inflammation, and fever and NSAIDs therefore find their main use as analgesics, anti-inflammatory agents, and antipyretics. Administered as a single doses or in short-term intermittent therapy they provide adequate analgesia to relieve mild to moderate pain. However, it may take several days to two weeks of use before their anti-inflammatory effects become evident.

The combined analgesic and anti-inflammatory effects of NSAIDs make them particularly useful for the symptomatic relief of painful and/or inflammatory conditions including musculoskeletal and joint disorders.

Differences in anti-inflammatory activity between different NSAIDs are small, but there is considerable variation in individual patient tolerance and response. The main differences between NSAIDs are in the incidence and type of side effects. Before treatment is started the prescriber should weigh efficacy against possible side effects.

Side effects:

The commonest side-effects occurring during therapy with NSAIDs are generally gastrointestinal disturbances; these are usually mild and reversible but in some patients peptic ulcer and severe gastro-intestinal bleeding have been reported; CNS related side effects include headache, dizziness, nervousness, tinnitus, depression, drowsiness, and insomnia; hypersensitivity reactions may occur occasionally and include fever, asthma, and rashes. Hematological adverse effects of NSAIDs include anaemias, thrombocytopenia, neutropenia, eosinophilia, and agranulocytosis. Fluid retention may occur (rarely precipitating congestive heart failure in elderly patients). Renal failure may be provoked by NSAIDs especially in patients with pre-existing renal impairment. Rarely, papillary necrosis or interstitial fibrosis associated with NSAIDs may lead to renal failure. Hepatic damage alveolitis, pulmonary eosinophilia, pancreatitis, eye changes, Stevens – Johnson syndrome and toxic epidermal necrolysis are other rare side effects. Induction of or exacerbation of colitis has been reported. Aseptic meningitis has been reported rarely with NSAIDs. Patients with connective tissue disorders such as systemic lupus erythematosus may be especially susceptible.

Cautions and contraindications:

NSAIDs should be used with caution in the elderly (risk of serious side effects and fatalities), in allergic disorders (they are contraindicated in patients with a history of hypersensitivity to aspirin or any other NSAID. Which include those in whom attacks of asthmas, angioedema, urticaria or rhinitis have been precipitated by aspirin or any other NSAID), during breast-feeding and pregnancy and in coagulation.

In patients with renal, cardiac, or hepatic impairment caution is required since the use of NSAIDs may result in deterioration of renal function; the dose should be kept as low as possible and renal function should be monitored.

NSAIDs should not be given to patients with active peptic ulceration. While it is preferable to avoid them in patients with current or previous gastro-intestinal ulceration or bleeding, and to withdraw them if gastro-intestinal lesions develop, nevertheless patients with serious rheumatic diseases (e.g. rheumatoid arthritis) are usually dependent on NSAIDs for effective relief of pain and stiffness.

Acetylsalicylic acid

Tablet, 75 mg, 100 mg (soluble), 300 mg, 324 mg (microfined), 500 mg (enteric coated)

See section 4.1 and notes above.

Diclofenac sodium

Tablet (e/c), 25 mg, 50 mg

Tablet (s/r), 75mg

Sachet, 50mg (as potassium)

Suppository, 12.5mg, 25mg, 50mg, 100 mg

Injection, 25 mg/ml, 3 ml ampoule

Indications: pain and inflammation in rheumatic disease (including juvenile arthritis) and other musculoskeletal disorders; acute gout; postoperative pain.

Cautions: see notes above.

Drug interactions: coumarin or indandione derivative anticoagulants, or heparin or thrombolytic agents, antihypertensives or diuretics, especially triamterene, aspirin and anti-inflammatory, blood dyscrasia causing medications and bone marrow depressants, radiation therapy, colchicine, lithium, methotrexate, probenecid.

Contraindications: see notes above, porphyria.

Side effects: see notes above; suppositories may cause rectal irritation, injection site reactions.

Dose and Administration:

Adult:

Oral: Rheumatoid arthritis: 150-200mg per day in three or four divided doses, initially. After a satisfactory response has been obtained, dosage should be reduced to the minimum dose that provides continuing control of symptoms, usually 75 – 100 mg a day in 3 divided doses.

Deep IM injection into the gluteal muscle: acute exacerbations and post-operative: 75 mg once daily (twice daily in severe cases) for maximum of 2 days.

Ureteric colic: 75 mg then a further 75 mg after 30 minutes if necessary.

IV infusion (in hospital setting), 75 mg repeated if necessary after 4 – 6 hours for maximum 2 days.

Prevention of postoperative pain, initially after surgery 25 – 50 mg over 15 – 60 minutes then 5 mg/hour for maximum 2 days.

Rectum in suppositories, 75 – 150 mg daily in divided doses.

Maximum total daily dose by any route 150 mg.

Child 1 – 12 years, *juvenile arthritis*, *Oral* or *rectum*: 1 – 3 mg/kg daily in divided doses (25 mg e/c tablets, 12.5 mg and 25 mg suppositories only).

Storage: at room temperature in a tight container, protect from moisture.

Diclofenac sodium + Misoprostol

Tablet, 50mg + 200mcg

Indications: the diclofenac component is indicated for the treatment of osteoarthritis and rheumatoid arthritis; the misoprostol component is indicated for the prophylaxis of NSAID-induced gastric and duodenal ulceration.

Dose and Administration: *Oral:*

Adult: *Osteoarthritis:* 1 tablet 2-3 times/day

Rheumatoid arthritis: 1 tablet 3-4 times/day

Ibuprofen

Tablet, 200 mg, 400 mg

Capsule, 300 mg

Syrup, 10 mg/5ml

Indications: pain and inflammation in rheumatic disease (including juvenile arthritis) and other musculoskeletal disorders; mild to moderate pain including dysmenorrhoea, postoperative analgesia; migraine; fever and pain in children.

Cautions: see notes above

Drug interactions: coumarin or indandione derivative anticoagulants, heparin, or thrombolytic agents, antihypertensives or diuretics, especially triamterene; aspirin and anti-inflammatory, blood dyscrasia causing medications and bone marrow depressants, radiation therapy, colchicine, lithium, methotrexate, probenecid.

Contraindications: see notes above

Side effects: see notes above

Dose and Administration:

Adult: *Antirheumatic:* *Oral:* 1.2 to 3.2gms a day in three or four divided doses.

After a satisfactory response has been obtained, the dosage should be reduced to the lowest maintenance dose that provides continuing control of symptoms.

Note - Higher doses are generally required in rheumatoid arthritis than in osteoarthritis.

Analgesia/pain/fever/dysmenorrhea: 200-400 mg/dose every 4-6 hours (maximum daily dose: 1.2g, unless directed by physician)

OTC labeling (analgesic, antipyretic): 200mg every 4-6 hours as needed (maximum: 1200 mg/24 hours)

Child: *Antirheumatics:* (1-12 years of age): *Oral:* initially 30 to 40mg per kg of body weight a day in three or four divided doses then reduced to the lowest dose needed to control disease activity.

Storage: store at room temperature in a well-closed, light resistant container. Protect from freezing.

Indomethacin

Capsule, 25 mg, 50mg, 75mg

Suppository, 100 mg

Syrup, 25mg/5ml

Indications: acute or chronic rheumatoid arthritis, for relief of acute or chronic osteoarthritis and for relief of acute or chronic ankylosing spondylitis; acute gout (section 6.2). It is also indicated for relief of acute or chronic juvenile arthritis and in the treatment of psoriatic arthritis.

Cautions: see notes above, also epilepsy, parkinsonism, psychiatric disturbances, during prolonged therapy ophthalmic and blood examinations particularly advisable; avoid rectal administrations in proctitis and haemorrhoids. Dizziness may affect performance of skilled tasks (e.g. driving)

Drug interactions: coumarin or indandione derivative anticoagulants, heparin or thrombolytic agents, antihypertensives or diuretics, especially triamterene; aspirin and anti-inflammatory, blood dyscrasias causing medications and bone marrow depressants, radiation therapy, colchicine, lithium, methotrexate, probenecid.

Contraindications: see notes above

Side effects: see notes above; frequently gastrointestinal disturbances (including diarrhea, headache, dizziness, and light - headedness; also gastro-intestinal ulceration and bleeding; rarely, drowsiness, confusion, insomnia, convulsions, psychiatric disturbances, depression, syncope, blood disorders (particularly thrombocytopenia), hypertension, hyperglycaemia, blurred vision, corneal deposits, peripheral neuropathy, and intestinal strictures; suppositories may cause rectal irritation and occasional bleeding.

Dose and Administration:

Adult: *Anti-rheumatic:*

Oral: initially 25 to 50mg two or four times a day, if well tolerated, the dosage per day may be increased by 25 or 50mg at weekly intervals until a satisfactory response is obtained or up to a maximum dose of 200mg per day.

Rectal: 50mg four times a day

Child: *Anti-rheumatic:*

Oral: 1.5 to 2.5mg per kg of body weight, per day, administered in three or four divided doses, up to a maximum of 4mg per kg of body weight per day or 150 to 200mg per day, whichever is less.

Rectal: same as oral (for children)

Storage: store at room temperature in a well-closed container.

Leflunomide

Tablet, 10mg, 20mg

Indications: treatment of active rheumatoid arthritis; indicated to reduce signs and symptoms, and to retard structural damage and improve physical function.

Cautions: hepatic disease, patients with severe immune deficiency, uncontrolled infection; hematologic abnormalities; renal impairment.

Drug interactions: NSAIDs, methotrexate, rifampin.

Contraindications: pregnancy, hypersensitivity reaction.

Side effects: diarrhea, respiratory tract infection, hypertension, chest pain, headache, dizziness, fever, sleep disorder, rash, alopecia, eczema, nausea, weight loss, anorexia, vomiting, bronchitis, cough.

Dose and Administration: *Oral:*

Adult: Initial: 100mg/day for 3 days, followed by 20mg/day; dosage may be decreased to 10 mg/day in patients who have difficulty tolerating the 20mg dose.

Storage: store at room temperature and protect from light.

Piroxicam

Tablet, 10 mg, 20 mg

Capsule, 10 mg, 20 mg

Suppository, 20 mg

Indications: pain and inflammation in rheumatic disease (including juvenile arthritis) and other musculoskeletal disorders; acute gout.

Cautions: CHF, hypertension, dehydration, history of GI disease.

Drug interactions: lithium, methotrexate, amiodarone, fluoxetine, glimepiride, glipizide, phenytoin, sertraline, warfarin, and other CYP2C8/9 substrates; diuretics; beta-blockers; aspirin; antacids, and cholestyramine.

Contraindications: hypersensitivity to piroxicam, aspirin, or other NSAIDs; active GI bleeding; pregnancy (3rd trimester or near term).

Side effects: dizziness, rash, abdominal cramps, heartburn, indigestion, nausea, headache, nervousness, itching, fluid retention, vomiting and tinnitus.

Dose and Administration: *Oral, Rectum:*

Adult: *Rheumatic disease:* initially 20 mg daily, maintenance 10 - 30 mg daily, in single or divided doses.

Child over 6 years: *Oral: juvenile arthritis,* less than 15 kg, 5 mg daily; 16 - 25 kg, 10 mg; 26 - 45 kg, 15 mg ; over 46 kg, 20 mg.

Acute musculoskeletal disorders: **Adult:** 40 mg daily in single or divided doses for 2 days, then 20 mg daily for 7 - 14 days.

Acute gout: **Adult:** 40 mg initially, then 40 mg daily in single or divided doses for 4 - 6 days.

Sulphasalazine

Tablet (e/c), 500mg

Indications: severe rheumatoid arthritis.

Cautions: renal or hepatic impairment, or urinary tract obstruction, pregnancy and breast-feeding, G6PD deficiency, intestinal obstruction, blood dyscrasias, porphyria.

Drug interactions: digoxin, diuretics, oral contraceptives, oral antidiabetic agents, phenytoin or phenobarbital, pyrimethamine, warfarin, zidovudine and lamivudine.

Contraindications: hypersensitivity to salicylates and sulphonamides; child under 2 years of age.

Side effects: nausea, vomiting, diarrhea and anorexia; reversible oligospermia and infertility are common in males; haematological disturbances, hypersensitivity reactions and hepatic function disturbances. Photosensitivity may occur.

Dose and Administration: Adult: *Oral:* initially 500mg daily, increased by 500mg at intervals of 1 week to a maximum of 2-3g daily in divided doses.

Storage: protect from light.

Tenoxicam

Tablet, 20mg

Suppository, 20mg

Indications: symptomatic management of osteoarthritis and rheumatoid arthritis and also in the short term management of soft-tissue injury.

Cautions and Side effects: as for non-steroidal anti-inflammatory drug in general.

Drug interactions: see under indomethacin

Dose and Administrations: *Oral:* as a single daily dose usually of 20mg. In acute skeletal disorders treatment for up to 7 days is usually sufficient but in severe cases it may be given for up to a maximum of 14 days. Dose similar to those given by mouth have been given *by rectal* suppository. Child not recommended.

Tolmetin sodium

Capsule, 200 mg, 400 mg

Tablet, 200 mg

Indications: treatment of rheumatoid arthritis and osteoarthritis, juvenile rheumatoid arthritis.

Cautions: as piroxicam.

Drug interactions: digoxin, methotrexate, cyclosporine,

Contraindications: hypersensitivity to tolmetin, aspirin, or other NSAIDs, pregnancy (3rd trimester or near term).

Side effects: chest pain, hypertension, edema, headache, dizziness, drowsiness, depression, skin irritation, weight gain/loss, heartburn, abdominal pain, diarrhea, flatulence, vomiting, constipation, gastritis, peptic ulcer, nausea, urinary tract infection, visual disturbances, tinnitus.

Dose and Administration: *Oral:*

Adult: 400 mg 3 times /day; usual dose: 600 mg to 1.8 g/day; maximum; 2 g/day

Child \geq 2 years:

Anti-inflammatory: initial: 20 mg/kg/day in 3 divided doses, then 15-30 mg/kg/day in 3 divided doses.

Analgesic: 5-7 mg/kg/dose every 6-8 hours.

6.2. Drugs used for gout

It is important to distinguish drugs for the treatment of acute attacks of gout from those used in the long-term control of the disease. The latter exacerbate and prolong the acute manifestations if started during attack.

Acute gout

Acute attacks of gout are usually treated with high doses of NSAIDs such as indomethacin (150 - 200 mg daily in divided doses), ibuprofen has weaker anti-inflammatory properties than other NSAIDs and is therefore unsuitable for treatment of gout. Salicylates, including acetylsalicylic acid are also not suitable because they may increase plasma-urate concentrations. Colchicine is an alternative for those patients in whom NSAIDs are contraindicated. Its use is limited by toxicity with high doses. It does not induce fluid retention and can therefore be given to patients with heart failure; it can also be given to patients receiving anticoagulants.

Chronic gout.

For long-term control of gout in patients who have frequent attacks, the xanthine oxidase inhibitor allopurinol may be used to reduce production of uric acid. It should not be used to treat an acute attack since it may prolong it indefinitely. Treatment for chronic gout should not be started until after an acute attack has completely subsided, usually 2 - 3 weeks. The initiations of allopurinol treatment may precipitate an acute attack therefore colchicines or a suitable NSAIDs should be used as a prophylactic and continued for at least one month after the hyperuricaemia has been corrected. If an acute attack develops during treatment for chronic gout, then allopurinol should continue at the same dosage and the acute attack should be treated in its own right. Treatment for chronic gout must be continued indefinitely to prevent further attacks of gout.

Note: - Administer, prophylactic colchicine or non-steroidal anti-inflammatory drugs (not aspirin or salicylates) until at least 1 month after hyperuricemia corrected, ensure adequate fluid intake (2 liters/day). In neoplastic conditions treatment with allopurinol should be commenced before cytotoxic drugs are given.

Allopurinol

Tablet, 100 mg

Indications: long-term management of hyperuricemia associated with primary or secondary gout; to control hyperuricemia secondary to blood dyscrasias such as polycythemia vera, myeloid metaplasia, or their treatment.

Note: - Allopurinol is not effective in the treatment of acute gout attacks because it has no anti-inflammatory action, and may intensify and prolong inflammation during the acute phase.

Cautions: renal and hepatic function impairment, diabetes mellitus, and hypertension

Drug interactions: coumarin or indandione derivative anticoagulants, mercaptopurine, alcohol, xanthines such as aminophylline, oxtriphylline, theophylline, furosemide, diazoxide, ethacrinic acid and thiazide diuretics.

Contraindications: - sensitivity to allopurinol, acute gout.

Side effects: dermatitis allergic (skin rash, hives or itching, agranulocytosis (chills, fever or sore throat), angitis (vasculitis), hypersensitivity (chills, fever, sore throat, muscle ache, pain or weakness, shortness of breath, troubled breathing, tightness in chest, wheezing), diarrhoea, drowsiness, headache.

Dose and Administration:

Adult: *Antigout:* Initial - *Oral*, 100mg once a day, to be increased by 100mg per day at one week intervals until the desired serum uric acid concentration is attained. Maximum - 800mg per day. Maintenance - *Oral*, 100 -200mg two or three times a day or 300mg as a single dose once a day.

Child: *Antihyperuricemic, in neoplastic disease therapy:*

Child (up to 6 years)- *Oral*, 50mg three times a day; 6-10 years of age, oral, 100mg three times a day or 300mg as a single dose once a day.

Note: - Drink large amounts of fluids.

Storage: at room temperature in a well-closed container.

Colchicine

Tablet, 0.5mg

Injection, 0.5 mg/ml in 2 ml ampoule

Indications: acute gout, short-term prophylaxis during initial therapy with allopurinol and uricosuric drugs; prophylaxis of familial Mediterranean fever (recurrent polyserositis).

Cautions: elderly, gastro-intestinal disease, cardiac, hepatic and renal impairment

Drug interactions: cyclosporin

Contraindications: pregnancy and breast-feeding

Side effects: most common are nausea, vomiting, and abdominal pain, excessive doses may also cause profuse diarrhea, gastro-intestinal hemorrhage, rashes, renal and hepatic damage. Rarely peripheral neuritis, myopathy, alopecia, and blood disorder with prolonged treatment.

Dose and Administration:

Acute gout: *Oral:* 0.5 - 1mg initially, followed by 500 micrograms every 2 - 3 hours until relief of pain is obtained, or vomiting or diarrhea occurs; maximum total dose 6 mg, the course should not be repeated within 3 days.

Prevention of gout attacks during initial treatment with allopurinol, 500 micrograms 2 - 3 times daily continuing for at least 1 month after hyperuricaemia has been corrected.

Storage: at room temperature. Protect from freezing. Protect from light.

Ibuprofen

Tablet, 200 mg, 400 mg

Indications: for relief of the pain and inflammation of acute gout arthritis.

Cautions, Drug Interactions, Contraindications, Side effects, Storage; See section 6.1 under Ibuprofen.

Dose and Administrations:

Treatment of acute migraine attack: Oral: preferably with or after food,

Adult: 400–600 mg at first sign of attack, may be repeated every 6–8 hours if necessary, maximum 2.4 g daily;

Children: 8–12 years 200 mg at first sign of attack, may be repeated every 6–8 hours if necessary

Indomethacin

Capsule, 25 mg

Suppository, 100 mg

Indications: for relief of the pain and inflammation of acute gouty arthritis.

Cautions, Drug interactions, Contraindications, Side effect, and Storage; see section 6.1, under indomethacin.

Dose and Administration:

Adult: *Antigout: Oral:* 100mg initially, then 50mg three times a day until pain is relieved, with the dosage then being reduced until medication is discontinued.

Rectal: the total daily dose may be given as 100mg in the morning and at night. The total daily combined dose by mouth and by rectum should not exceed 200mg. In acute gout the daily dose is 150-200mg in divided doses until all symptoms and signs subside. In Child dose not recommended.

Probenecid

Tablet, 500 mg

Indications: long-term management of hyperuricemia associated with chronic gout.

Note: - It is not effective in the treatment of acute gout attacks and does not eliminate the need to use colchicine or non-steroidal anti-inflammatory drugs to relieve an attack.

Cautions: children (younger than 2 years of age), in patients with peptic ulceration, renal function impairment, blood dyscrasias.

Drug interactions: antineoplastic (rapidly cytolytic), zidovudine, indomethacin, ketoprofen, aspirin or other salicylates (including bismuth subsalicylate), cephalosporines or penicillines, heparin, and nitrofurantoin.

Contraindications: probenecid is contraindicated in any condition in which there is an increased risk of uric acid renal calculi formation or urate

nephropathy such as cancer chemotherapy with rapidly cytolytic antineoplastic agents, radiation therapy for malignancy, moderate to severe renal function impairment, history of blood dyscrasias nephrolithiasis, porphyria, acute gout attacks.

Side effects: acute gout, arthritis attack (joint pain, redness, swelling) headache, loss of appetite, nausea or vomiting (mild), dizziness, flushing or redness of face, urinary frequency, sore gums, aplastic anaemia, nephrotic syndrome (cloudy urine, swelling of face).

Dose and Administration:

Adult: *Antigout:* *Oral:* Initial - 250mg two times a day for one week

Maintenance - 500mg two times a day.

Child: dosage has not been established.

Storage: at room temperature in a well-closed container.

6.3. Skeletal Muscle Relaxants

Centrally acting muscle relaxants have a selective action on the central nervous system and are used in the management of spasticity due to neuromuscular and musculoskeletal disorders and for relief of painful muscle spasm. Diazepam and baclofen are effective for the control of muscle spasm in a variety of disorders. The efficacy of agents such as methocarbamol and orphenadrine is controversial; they may be no more clinically useful than adequate analgesia alone. Significant adverse effects (e.g. sedation, hepatotoxicity, immunological reactions) may occur.

Dantrolene acts uniquely outside the CNS and used in the treatment of malignant hyperthermia and in selected instances of skeletal muscle spasticity.

Muscle relaxants should be used with caution if muscle spasticity plays a role in sustaining upright posture and balance. A reduction in muscle tone may cause a loss of the splinting action of the spastic muscles and lead to increased disability and instability.

Baclofen

Tablet, 5mg, 10mg

Indications: relief of muscle spasticity due to spinal cord injury or disease, especially multiple sclerosis; pain relief in trigeminal neuralgia; stiff - man syndrome.

Cautions: epilepsy, peptic ulcer disease, renal impairment, cerebrovascular disease or pre - existing psychiatric disturbances.

Drug interactions: other CNS depressants; antihypertensive agents.

Contraindications: hypersensitivity to baclofen.

Side effects: drowsiness, dizziness, ataxia, nausea, constipation or diarrhea, confusion, hypotension, allergic skin reactions; psychiatric disturbances (e.g. depression, hallucinations, euphoria) occur occasionally in the elderly or in patients with psychiatric or brain disorders.

Dose and Administration: *Oral:*

Adult: initially 5mg 3 times daily; preferably with meals, increased by 5mg /dose every 3 days until the desired response is obtained, usually with 30 - 75mg/day. Maximum 100 mg/day.

Child: 1 - 1.5mg/kg daily. Maximum doses: 2 - 7 years, 30 - 40 mg/day; over 8 years, 60mg/day.

Storage: store at room temperature.

Dantrolene sodium

Capsule, 25mg, 50mg

Indications: treatment of spasticity associated with spinal cord injury, stroke, cerebral palsy, or multiple sclerosis; treatment of malignant hyperthermia.

Cautions: impaired cardiac function or pulmonary functions; hepatic disease.

Drug interactions: estrogens, CNS depressants, MAO inhibitors, phenothiazines, clindamycin, verapamil, warfarin, clofibrate, tolbutamide, azole antifungals, ciprofloxacin, clarithromycin, diclofenac, doxycycline, erythromycin, aminoglutethimide, carbamazepine, nafcillin, nevirapine, phenobarbital, phenytoin and rifamycins.

Contraindications: active hepatic disease; should not be used where spasticity is used to maintain posture or balance.

Side effects: drowsiness, dizziness, lightheadedness, fatigue, rash, diarrhea, vomiting, muscle weakness, chills, fever, headache, insomnia, nervousness, mental depression, constipation, anorexia, stomach cramps, blurred vision, respiratory depression.

Dose and Administration: *Oral:*

Spasticity:

Adult: 25mg/day to start, increase frequency to 2 - 4 times/day, then increase dose by 25mg every 4 - 7 days to a maximum of 100mg 2 - 4 times / day or 400mg/day.

Child: initial 0.5mg/kg/dose twice daily, increase frequency to 3 - 4 times/day at 4 - 7 day intervals, then increase dose by 0.5mg/kg to a maximum of 3mg/kg /dose 2 - 4 times/day up to 400mg/day.

Malignant hyperthermia:

Adult and Child: *preoperative prophylaxis:*

4 - 8 mg/kg/day in 4 divided doses, begin 1 – 2 days prior to surgery with last dose 3 - 4 hours prior to surgery.

Storage: store at room temperature.

Diazepam

Tablet, 2 mg, 5 mg, 10 mg

Syrup, 2 mg / 5 ml

Injection, 10 mg/ml, in 2 ml ampoule

Indications: muscle spasm of varied etiology, including tetanus; other indications (section 4.2, section 4.4).

Cautions: see section 4.2; special precautions for intravenous injection.

Contraindications, Side effects, see section 4.2; also hypotonia.

Dose and Administration:

Oral: 2 - 15 mg daily in divided doses, increased if necessary in spastic conditions to 60 mg daily according to response.

Cerebral spasticity in selected cases: **Child:** 2 - 40 mg daily in divided doses.

IM or slow IV injection (into a large vein at a rate of not more than 5 mg/minute), in acute muscle spasm, 10 mg repeated if necessary after 4 hours.

Note: Only use IM route when oral and IV routes not possible.

Tetanus: **Adult and Child:** *IV injection:* 100 - 300 micrograms/kg repeated every 1 - 4 hours; *IV infusion (or by nasoduodenal tube):* 3 - 10 mg/kg over 24 hours, adjusted according to response.

Methocarbamol

Injection, 1g in 10ml vial

Tablet, 500mg

Indications: treatment of muscle spasm associated with acute painful musculo skeletal conditions; supportive therapy in tetanus.

Cautions: renal or hepatic impairment, seizures.

Drug interactions: CNS depressants, ethanol.

Contraindications: hypersensitivity to methocarbamol.

Side effects: flushing of face, bradycardia, hypotension, syncope, drowsiness, dizziness, lightheadedness, convulsion, vertigo, headache, fever, amnesia, confusion, insomnia, sedation, allergic dermatitis, urticaria, pruritus, rash, nausea, vomiting, metallic taste, dyspepsia, leukopenia, jaundice, thrombophlebitis, blurred vision, renal impairment, conjunctivitis and nasal congestion.

Dose and Administration: *Muscle spasm:*

Adult and Child \geq 16 years:

Oral: 1.5g 4 times /day for 2 -3 days (up to 8g/day may be given in severe conditions) then decrease to 4 - 4.5 g /day in 3 - 6 divided doses.

I.M, I.V: 1 g every 8 hours if oral not possible; injection should not be used for more than 3 consecutive days. If condition persists, may repeat course of therapy after a drug-free interval of 48 hours.

Elderly: *oral:* initial: 500mg 4 times /day.

Storage: Store at controlled room temperature.

Orphenadrine Citrate

Tablet, 100 mg

Drop, 2.5 mg/ml

Injection, 30 mg/ml

Indications: to relieve pain due to spasm of skeletal muscle (see notes above).

Cautions, Drug interactions, Contraindications, Side effects; see section 4.5 under orphenadrine hydrochloride.

Dose and Administration:

Adult: *Oral:* 100 mg twice daily

IM or slow IV (over a period of 5 minutes) injection in a dose of 60 mg which is repeated every 12 hours, as needed.

Storage: at room temperature, protect from light and freezing.

Other centrally acting muscle relaxants include:

Orphenadrine citrate + Paracetamol

Tablet, 35mg + 450mg

Indications: generalised pain and the relief of muscle spasm associated with acute painful musculo-skeletal conditions.

Cautions: cardiac disease or arrhythmias, especially tachycardia.

Drug interactions: orphenadrine may increase central nervous system depression if taken concurrently with alcohol or central nervous system depressants. Anticholinergic effects may be intensified if orphenadrine is taken concurrently with anticholinergics or medication with anticholinergic effects.

Contraindications: hypersensitivity to any of the ingredients; severe liver function impairment; prostatic enlargement, achalasia, bladder neck obstruction, glaucoma, myasthenia gravis, peptic ulcer or stenosing and pyloric or duodenal obstruction; safety in pregnancy and lactation has not been established; porphyria.

Side effects: see under individual preparations.

Dose and Administration: Adult: 2 tablets 3 times a day. Do not exceed the recommended dosage.

Storage: store below 25°C. Protect from light.

Chlormezanone + Paracetamol

Tablet, 100mg + 450mg

Indications: relief of generalized pain associated with tension.

Cautions: do not use continuously for more than 10 days without consulting your doctor; liver or kidney disease.

Drug interactions: other tranquilizers or antidepressants.

Contraindications: sensitivity to Paracetamol. Safety in pregnancy and lactation has not been established.

Side effects: sensitivity reactions resulting in reversible skin rash or blood disorders; drowsiness, weakness, nausea, dizziness, flushing of the skin, excitement, depression, skin rash, confusion, dryness of the mouth and difficulty in micturition; cholestatic jaundice may occur. The patient should not drive a vehicle or operate machinery, if dizziness or drowsiness occurs.

Dose and Administration: Adult: 1 tablet 3-4 times daily as required

Child 9-12 years: ½ tablet 3 - 4 times daily as required

Not for children under 9 years of age.

Storage: store below 25°C. Protect from light.

6.4. Cholinergic and Anticholinesterase Agents

Parasympathomimetics may be classified into 2 distinct pharmacological groups. Cholinergic agonists, such as bethanechol, which act directly on effector cells to mimic the effects of acetylcholin. Anticholinesterases (neostigmine, pyridostigmine and edrophonium) which inhibit the enzymic hydrolysis of acetylcholin by acetylcholinesterase and other cholinesterases, thereby prolonging and enhancing its actions in the body.

Bethanechol

Tablet, 10mg, 25mg

Injection (chloride), 5 mg/ml in 1 ampoule

Indications: nonobstructive urinary retention and retention due to neurogenic bladder.

Cautions: hyperthyroidism, peptic ulcer disease, epilepsy, obstructive pulmonary disease, bradycardia, vasomotor instability, atrioventricular conduction defects, hypotension, or Parkinsonism.

Drug interactions: procainamide, quinidine, atropine, antihistamines, TCAs, phenothiazines.

Contraindications: hypersensitivity to bethanechol; mechanical obstruction of the GI or GU tract.

Side effects: hypotension, tachycardia, bradycardia, flushed skin, head ache, malaise, abdominal cramps, diarrhea, nausea, vomiting, salivation, eructation, urinary urgency, lacrimation, miosis, asthmatic attacks, branchial constriction, diaphoresis.

Dose and Administration:

Adult: *urinary retention, neurogenic bladder, and/or bladder atony:*

Oral: initial, 10 – 50 mg 2- 4 times/day. To determine effective dose, may initiate at a dose of 5 - 10mg, with additional doses of 5 - 10 mg hourly until an effective cumulative dose is reached.

SC: Initial: 2.575mg, may repeat in 15 - 30 minutes; (maximum cumulative initial dose: 10.3mg); subsequent doses may be given 3 - 4 times daily as needed.

Storage: store at room temperature.

Edrophonium

Injection, 10mg/ml in 1ml ampoule

Indications: diagnosis of myasthenia gravis, differentiation of cholinergic crises from myasthenia crises, reversal of non depolarizing neuromuscular blockers, adjunct treatment of respiratory depression caused by curare overdose.

Cautions: bronchial asthma and those receiving a cardiac glycoside; atropine sulfate should always be readily available as an antagonist.

Drug interactions: digoxin, succinylcholine, decamethonium, pancuronium, vecuronium, acetazolamide, neostigmine, physostigmine, atropin, nondepolarizing muscle relaxants, procainamide, and quinidine.

Contraindications: hypersensitivity to edrophonium, GI or GU obstruction.

Side effects: bradycardia, hypotension, decreased carbon monoxide, tachycardia, convulsions, dizziness, loss of consciousness, drowsiness, headache, skin rash, thrombophlebitis, urticaria, hyperperistalsis, nausea, vomiting, salivation, diarrhea, stomach cramps, dysphagia, flatulence, urinary urgency, muscle cramps, spasms, small pupils, lacrimation, increased bronchial secretions, laryngospasm, respiratory muscle paralysis, dyspnea, bronchospasm.

Dose and Administration:

Adult: *Diagnosis:*

IV: 2 mg test dose administered over 15 - 30 seconds; 8 mg given 45 seconds later if no response is seen; test dose may be repeated after 30 minutes.

IM: Initial: 10mg, if no cholinergic reaction occurs; administer 2mg 30 minutes later. Titration of oral anticholinesterase therapy: 1 - 2mg 1 hour after oral dose of anticholinesterase.

Reversal of non-depolarizing neuromuscular blocking agents:

I V: 10mg over 30 - 45 seconds, may repeat every 5 - 10 minutes up to 40mg.

Termination of paroxysmal atrial tachycardia: IV rapid injection: 5- 10mg.

Differentiation of cholinergic from myasthenic crisis: IV: 1mg; may repeat after 1 minute.

Child: *Diagnosis:*

Initial; 0.04 mg/kg over 1 minute followed by 0.16 mg/kg if no response, to a maximum total dose of 5mg for children < 34kg, or 10mg for children > 34kg

Titration of oral anticholinesterase therapy: 0.04 mg/kg once given 1 hour after oral intake of the drug being used in treatment.

Infant: *IM:* 0.5 - 1 mg

I.V: Initial 0.1 mg, followed by 0.4mg if no response; total dose = 0.5mg.

Storage: protect from light.

Neostigmine

Tablet (Bromide), 15 mg

Injection (Methylsulphate), 0.5 mg/ml, 2.5 mg/ml in 1 ml ampoules

Indications: in the treatment of conditions such as myasthenia gravis and to reverse muscle relaxation produced by competitive (non-depolarizing) muscle relaxant.

Cautions, Contraindications, Drug interactions, Side effects; see section 5.3 under neostigmine.

Dose and Administrations:

Oral: as neostigmine bromide,

Adult: 15 - 30 mg at suitable intervals throughout day, total daily dose 75 - 300 mg; but doses above 180 mg daily not usually tolerated.

Child: up to 6 years, initially 7.5 mg, 6 - 12 years, initially 15 mg, total daily dose usually 15 - 90 mg in divided doses at appropriate intervals.

SC or IM injection: *as neostigmine methylsulphate,*

Adult: 0.5 - 2.5 mg as required, total daily dose 5 - 20 mg;

Neonate: 50 - 250 micrograms 30 minutes before feeds (not usually required beyond 8 weeks of age);

Child: 200 - 500 micrograms as required.

Pyridostigmine bromide

Tablet, 10mg, 25mg, 60mg, 180mg (sustained release)

Injection, 1mg/ml, 5mg/ml in 1ml ampoule

Indications: myasthenia gravis.

Cautions: asthma, urinary tract infection, cardiovascular disease including arrhythmias, hypotension, peptic ulcer, epilepsy, parkinsonism, avoid intravenous injection, renal impairment, pregnancy and breastfeeding.

Drug interactions: alcuronium, atropine, biperiden, chloroquine, clindamycin, gentamicin, lithium, procainamide, propranolol, quinidine, streptomycin, suxamethonium, vecuronium.

Contraindications: recent intestinal or bladder surgery, mechanical intestinal or urinary tract obstruction, after suxamethonium, pneumonia, and peritonitis.

Side effects: muscaranic effects generally weaker than with neostigmine, increased salivation and bronchial secretions, sweating, nausea and vomiting, abdominal cramps, diarrhoea, miosis, muscle spasm, bradycardia, bronchospasm, allergic reactions, hypotension, cholinergic crisis on overdosage, thrombophlebitis, rash associated with bromide salt.

Dose and Administration:

Oral: Adult: 30 - 120mg at 4 - 6 hourly intervals, total daily dose 120 - 720mg, adjusted to individual response.

Child: 7mg/kg day in 5-6 divided doses.

I.M. Adult: 2mg every 2 - 3 hours;

Neonate: 50 - 150 micrograms before feeds (but neostigmine usually preferred)

Child: total daily dose 1 - 12 mg given in divided doses at appropriate intervals.

Storage: store at room temperature and protect from light.

6.5. Drugs for the relief of soft tissue inflammation

Enzymes

Hyaluronidase is used to render the tissues more easily permeable to injected fluids, e.g. for introduction of fluids by subcutaneous infusion (termed hypodermoclysis).

Hyaluronidase

Powder for injection, 1500 units in ampoule

Indications: enhance permeation of subcutaneous or intramuscular injections, local anesthetics and subcutaneous infusions; promote resorption of excess fluids and blood.

Cautions: infants or elderly (control speed and total volume and avoid overhydration especially in renal impairment).

Contraindication: do not be apply direct to cornea; avoid sites where infection or malignancy; not for anaesthesia in unexplained premature labour; not to be used to reduce swelling of bites or stings; not for intravenous administration.

Drug interactions: anticoagulants, antiplatelet.

Side effects: edema, flushing, hypotension, dizziness, headache, itching, rash, local (erythema, pain, rash, swelling).

Dose and Administration: *SC or IM:* 1500 units dissolved directly in solution to be injected (ensure compatibility)

With local anaesthetics, 1500 units mixed with local anaesthetic solution (ophthalmology, 15 units/mL)

Hypodermoclysis, 1500 units dissolved in 1 mL water for injections or 0.9% sodium chloride injection, administered before start of 500-1000mL infusion fluid

Extravasation or haematoma, 1500 units dissolved in 1mL water for injections or 0.9% sodium chloride injection, infiltrated into affected area (as soon as possible after extravasation)

Storage: store at 2° C to 8° C.

7. ANTI-INFECTIVE

7.1. Antibacterials

7.1.1. Penicillins

Penicillins can be classified into four broad categories, each covering a different spectrum of activity. The natural penicillins (penicillin G and penicillin V) have activity against many gram-positive organisms, gram-negative cocci and some other gram-negative organisms. The aminopenicillins (ampicillin, amoxicilline, bacampicillin, and pivampicillin) have activity against penicillin-sensitive gram-positive bacteria, as well as *Escherichia coli*, *Proteus mirabilis*, *Salmonella sp.*, *Shigella sp.* and *Haemophilus influenza*. The antistaphylococcal penicillins (cloxacillin, dicloxacillin, etc) are also active against beta – lactamase – producing staphylococci. The antipseudomonal penicillins have less activity against gram-positive organisms than the natural penicillins or aminopenicillins.

Benzylpenicillin can be considered the parent compound of the penicillins and is inactivated by penicillinase – producing bacteria and because of its instability in gastric acid it is usually injected. Long-acting preparations include procaine penicillin and benzathine penicillin which slowly release benzylpenicillin after injection. Phenoxymethyl penicillin is acid – stable and therefore given by mouth but it is also inactivated by penicillinase. It is generally used for relatively mild infections.

The isoxazolyl penicillins such as cloxacillin are resistant to penicillinase and gastric acid.

Ampicillin has a broader spectrum of activity than benzylpenicillin; although generally less active against gram-positive bacteria, some gram-negative organisms including *Escherichia coli*, *Haemophilus influenzae*, and *Salmonella spp.* are sensitive although resistance is being reported increasingly, *Pseudomonas spp.* are not sensitive. Ampicillin is acid stable and can be given by mouth but is destroyed by penicillinase. Amoxycillin, only differs from ampicillin by the addition of a hydroxyl group, but is better absorbed from the gastro-intestinal tract.

The most important side effect of the penicillins is hypersensitivity which cause rashes and anaphylaxis, which can be fatal. Individuals who have experienced anaphylaxis, urticaria, or rash immediately after penicillin administration are at increased risk of immediate hypersensitivity to penicillin; these individuals should not receive a beta-lactam antibiotic. Patients who are allergic to one penicillin will be allergic to all because the hypersensitivity is related to the basic penicillin structure. Individuals who develop a minor rash or a rash that occurs more than 72 hours after penicillin administration are probably not allergic to penicillin and in these individuals a penicillin should not be withheld.

unnecessarily on serious infections ; the possibility of an allergic reaction should, however, be borne in mind.

A rare but serious toxic effect of the penicillins is encephalopathy due to cerebral irritation. This may result from excessively high doses or in patients with severe renal failure. The penicillins should not be given by intrathecal injection because they can cause encephalopathy which may be fatal.

Another problem relating to high doses of penicillin, or normal dose given to patients with renal failure, is the accumulation of electrolyte since most injectable penicillins contain either sodium or potassium.

Diarrhea frequently occurs during oral penicillin therapy. It is most common with broad- spectrum penicillins, which can also cause antibiotic associated colitis.

Amoxicilline

Capsule, 250 mg, 500 mg

Tablet, 500 mg

Injection, 250 mg, 500 mg in vial

Syrup, 125mg/5ml, 250 mg/5ml

Indications: urinary tract infections, upper respiratory tract infections, bronchitis; pneumonia; otitis media; dental abscess; osteomyelitis; Lyme disease in children; endocarditis prophylaxis; post-splenectomy prophylaxis; gynaecological infections; gonorrhoea; *Helicobacter pylori* eradication (section 1.2)

Cautions, Drug interactions, Contraindications and Side effects; see under Ampicillin

Dose and Administrations:

Infections due to sensitive organisms: Oral:

Adult and Child over 10 years, 250 mg every 8 hours, doubled in severe infections; **Child** up to 10 years, 125mg every 8 hours, doubled in severe infections.

*Severe or recurrent purulent respiratory-tract infections: Oral: **Adult:** 3 g every 12 hours*

*Pneumonia: Oral: **Adult:** 0.5 – 1 g every 8 hours*

Short Course Oral therapy

*Dental abscess: **Adult:** 3 g repeated after 8 hours*

*Urinary tract infections: **Adult:** 3 g repeated after 10 – 12 hours.*

*Otitis media: **Child** 3 – 10 years, 750 mg twice daily for 2 days.*

*IM: 500 mg every 8 hours; **Child,** 50 – 10 mg/kg daily in divided doses*

IV injection or infusion: 500 mg every 8 hours increased to 1g every 6 hours;

Child, 50 – 100 mg/kg daily in divided doses

Meningitis (in combination with another antibiotic if necessary): IV infusion: 2 g every 4 hours for at least 5 days in meningococcal disease or for 10 – 14 days in listerial meningitis.

Enterococcal endocarditis (in combination with another antibiotic if necessary): IV infusion: 2 g every 4 hours.

Storage: at room temperature in a tight container; oral suspension remains stable for 14 days at room temperature or if refrigerated.

Note: Reconstitution and Administration: According to manufacturer's directions

Amoxicilline and Clavulanic acid

Tablet (Chewable), 125 mg + 31.25 mg; 250mg +62.5 mg; (film coated); 250 mg + 125 mg; 500 mg + 125 mg; 1gm

Oral Suspension, 125 mg + 31.25 mg in each 5 ml; 250 mg + 62.5 mg in each 5 ml; 228mg/5ml; 457mg/5ml

Injection, 500 mg + 100mg; 1 g + 200 mg

Indications: infection due to beta-lactamase-producing bacteria (where amoxicilline alone not appropriate) including respiratory tract infections, genitor-urinary and abdominal infections, cellulites, animal bites, severe dental infections, and surgical prophylaxis.

Cautions: during pregnancy, hepatic impairment and nursing women, history of allergy, renal impairment, erythematous rashes common in glandular fever, chronic lymphatic leukemia & HIV infection.

Drug interactions: allopurinol, disulfiram, probenecid, anticoagulants, anti-inflammatory drugs, platelet aggregation inhibitor, contraceptives, heparin, thrombolytic agents, sulfinpyrazone.

Contraindications: penicillin hypersensitivity, history of amoxicilline + clavulanic acid – associated or penicillin – associated jaundice or hepatic dysfunction.

Side effects: diarrhea, nausea, vomiting, abdominal discomfort, anorexia and flatulence, rash and urticaria, pseudomembraneous colitis, headache, dizziness.

Dose and Administration:

Note: All doses expressed as amoxicillin

Infections due to susceptible beta-lactamase producing organisms: Oral:

Adult and Child over 12 years, 250mg every 8 hours, doubled in severe infections; **Child** under 1 year, 20mg/kg daily in 3 divided doses; **Child** 1-6 years, 125mg every 8 hours; 6-12 years, 250mg every 8 hours.

Severe dental infections: Oral: Adult 250mg every 8 hours for 5 days

Infections due to susceptible beta-lactamase producing organisms: slow IV injection:

Adult and Child over 12 years, 1g every 8 hours, increased to 1g every 6 hours in severe infections; **Neonate** and **Premature Infant** 25mg/kg every 12 hours; **Infant** up to 3 months, 25mg/kg every 8 hours; **Child** 3 months to 12 years, 25mg/kg every 8 hours increased to 25 mg/kg every 6 hours in more severe infections.

Surgical prophylaxis: IV injection: Adult 1g at induction, with up to 2-3 further doses of 1g every 8 hours (if increased risk of infection)

Storage: commercially available amoxicilline and clavulanate potassium film coated tablets, chewable tablets, and powder for oral suspension should be stored in tight containers at a temperature less than 24°C; exposure to excessive humidity should be avoided.

Following reconstitution, oral suspension of amoxicilline and clavulanate potassium should be stored at 2 – 8 °C, and any unused suspension should be discarded after 10 days.

Ampicillin

Capsule, 250 mg, 500 mg

Oral suspension; 125 mg/5ml, 250 mg/5ml

Drop, 100 mg/ml

Injection, (sodium), 250 mg, 500 mg, 1 g in vial

Indications: broad-spectrum activity against several Gram-positive organisms, Gram-negative cocci and some bacilli. Used in respiratory tract infections, cholecystitis and gastrointestinal tract infections, including typhoid.

Cautions: history of allergy, renal impairment, erythematous rashes common in glandular fever, chronic lymphatic leukaemia, and possibly HIV infection.

Drug interactions: probenecid (except in cases of gonorrhea and other STD), allopurinol, oral contraceptives, methotrexate, warfarin.

Contraindications: known hypersensitivity (allergy) to any penicillines.

Side effects: allergic reaction, specifically anaphylaxis (bronchospasm, sudden or severe decrease in blood pressure), skin rash, joint pain, fever, GIT reaction (mild diarrhoea, nausea, vomiting), oral candidiasis (sore mouth or tongue), pseudomembranous colitis (severe abdominal or stomach cramps and pain, abdominal tenderness, watery and severe diarrhoea).

Dose and Administration:

Adult: *Oral:* 250-500mg 6 hourly (up to 1g 6 hourly for severe infections).

IM: 500mg 6 hourly

IV: by slow injection or infusion over 30-60 minutes, 500mg 4-6 hourly (up to 12g daily for severe infections).

Meningitis/septicaemia: IV: 1-2g 3-4 hourly; maximum 300 mg/kg/day or 16g.

Renal impairment: GFR 10-50ml/min, dose interval 6-12 hours; GFR <10ml/min, 12-24 hours.

Child: *Oral, IM or IV:* under 20kg, 10-25 mg/kg/dose 6 hourly; over 20kg, as for adults.

Meningitis or severe infections: IV: 50mg/kg dose 6 hourly

Neonates: *IM or IV:* 50mg/kg/dose (meningitis 100mg/kg/dose) 12 hourly in the first week of life, 8 hourly from 1-3 weeks old, 6 hourly thereafter.

Storage: at room temperature; after reconstitution oral suspension is stable for 7 days at room temperature or for 14 days under refrigeration.

Note: Reconstitution and Administration: According to manufacturer's directions.

Ampicillin sodium and sulbactam sodium

Injection, 1 g + 0.5g, 2 g + 1 g

Indications: in the treatment of intra-abdominal infections such as abscess, female pelvic infections & infections caused by ampicilline – susceptible organisms and as a secondary agent in the treatment of genito-urinary tract

infections, skin and soft tissue infections, including burn wound infections, and bone and joint infections.

Cautions: renal function impairment, congestive heart failure, and gastrointestinal disease.

Drug interactions: see notes under amoxicilline and clavulanic acid.

Contraindications: Allergy of penicillines, infectious mononucleosis.

Side effects: allergic reactions, specially anaphylaxis; serum sickness – like reactions (skin rash, joint pain, fever), chest pain pseudomembraneous colitis, oral candidiasis, vaginal candidiasis, clostridium difficile colitis, dysuria, edema, erythemamultiforme, hepatic dysfunction, glossitis, leukopenia, platelet dysfunction and seizures.

Dose and Administration:

Adult: *IM or IV:* 1.5 to 3 grams (1 to 2 grams [Ampicilline] and 500 mg to 1 gram [sulbactam]) every six hours.

Gonorrhea: *IM:* 1.5 grams (1 gram of Ampicilline and 500 mg of sulbactam) as a single dose with 1 gram of oral probenecid.

Note: Adults with impaired renal function may require a reduction in dose.

Usual adult prescribing limits: up to a maximum of 4 grams (sulbactam) daily.

Child: Dosage has not been established in children up to the age of 12 years. However, doses of 200 to 400mg per kg of body weight of ampicillin and 100 to 200 mg per kg of body weight of sulbactam per day, administered in divided doses, have been used.

Storage: Prior to reconstitution, do not store above 30 °C (86 °F), unless otherwise specified by the manufacturers.

Carbenicillin

Tablet (Indanyl sodium), 382 mg

Injection 1g, 5 g in vial

Indications: treatment of serious urinary tract infections and prostatitis caused by susceptible gram-negative aerobic bacilli.

Cautions: impaired renal and/or hepatic function.

Drug interactions: heparin or oral anticoagulants, aminoglycosides, methotrexate probenecid, disulfiram, tetracyclines.

Contraindications: hypersensitivity to carbenicillin, penicillins, or any component of the formulation.

Side effects: diarrhea, nausea, bad taste, vomiting, flatulenc, glossitis, anemia, epigastric distress, headache, hematuria, hypersensitivity reactions, hyperthermia, hypokalemia, rash, thrombocytopenia and urticaria.

Dose and Administration:

Urinary tract infections:

Oral: Adult: 1 - 2 tablets every 6 hours for urinary tract infections or 2 tablets every 6 hours for prostatitis.

Child: 30 - 50 mg/kg/day divided every 6 hours; maximum dose: 2 - 3 g/day.

IM: Adult: 1to 2g every 6 hours.

Child: 50-100mg/kg daily in divided doses.

Storage: tablets at a temperature not exceeding 30 °C and injections at 2-8 °C.

Cloxacilline sodium

Capsule, 250mg, 500mg

Syrup, 125mg, 250mg in each 5ml

Injection, 250mg, 500mg in vial

Indications: infections due to beta-lactamase-producing staphylococci including impetigo, cellulitis and other soft-tissue infections; staphylococcal endocarditis, septicaemia, pneumonia and osteomyelitis.

Cautions: history of allergy, renal and hepatic function impairment, GIT disease especially ulcerative colitis, regional enteritis, antibiotic associated colitis, heart failure; pregnancy and breastfeeding.

Drug interactions: probenecid, chloramphenicol, erythromycin, sulfonamide, and tetracyclines.

Contraindications: known hypersensitivity or allergy to penicillines.

Side effects: nausea and vomiting, diarrhea, hypersensitivity reactions including urticaria, fever, joint pain, rashes, angioedema, anaphylaxis, serum sickness-like reactions, haemolytic anaemia, interstitial nephritis; neutropenia, thrombocytopenia, coagulation disorders; antibiotic-associated colitis; hepatitis and cholestatic jaundice - may be delayed in onset; electrolyte disturbances; pain, inflammation, phlebitis or thrombophlebitis at injection sites.

Dose and Administration:

Adult: *Oral:* 250 to 500mg (base) every six hours. Maximum dose up to 6 gm (base) a day.

IV - 250 to 500mg (base) every six hours maximum - 6gms (base) daily

Child: Infants and children up to 20kg of body weights: *Oral:* 6.25 to 12.5mg (base) per kg of body weight every six hours or *IV:* 6.25 to 12.5mg (base) per kg of body weight every six hours.

Note: - continue medicines for full time of treatment and take on empty stomach.

Storage: store at room temperature. After reconstitution, solutions retain their potency for 14 days if refrigerated.

Flucloxacillin

Capsule, 250 mg, 500 mg

Injection, 250 mg, 500 mg in vial

Syrup, 125 mg/5ml

Indications: for treatment of infections due to staphylococci resistant to benzylpenicillin these include bone and joint infections, endocarditis, peritonitis, pneumonia, skin infections, surgical infection and toxic shock syndrome.

Cautions: older patients and those receiving flucloxacillin for more than 2 weeks.

Drug interactions: as for benzylpenicillin.

Side effects: hepatitis, cholestatic jaundice, agranulocytosis and neutropenia occur.

Dose and Administration: Adult: *Oral, IM:* 250mg four times daily.

It is given intravenously in a dose of 0.25 to 1 g four times daily by slow injection over 3 to 4 minutes or by IV infusion.

Storage: store at room temperature.

Mezlocillin

Powder for injection, 0.5 g, 1g, 2 g, 3 g, 4 g, / vial

Intravenous (IV) infusion, 2 g, 3 g, 4 g

Indications: treatment of infections caused by susceptible gram-negative aerobic bacilli (*Klebsiella*, *Proteus*, *Eschericia coli*, *Enterobacter*, *Pseudomonas aeruginosa*, *Serratia*) involving the skin and skin structure, bone and joint, respiratory tract, urinary tract, gastrointestinal tract, as well as septicemia.

Cautions: hypersensitivity to mezlocillin, any component, or penicillins.

Drug interactions: as for benzylpenicillin. Clavulanic acid, methotrexate, probenecid.

Side effects: as for carbenicillin.

Dose and Administration: Adult:

Serious infection: IV: 200 to 300mg/kg daily in divided doses, for life-threatening infections, up to 350mg/kg daily may be used, but total dose should not exceed 24g.

Urinary- tract infection: IM or IV: 1.5 to 2g every 6 hours.

Storage: store in airtight container.

Penicillin G, Benzathine

Injection, 0.6, 1.2, 2.4 million IU in Vial.

600 000 units equivalent to 450 mg

Indications: streptococcal pharyngitis; diphtheria carrier state; syphilis and other treponemal infections (yaws, pinta, bejel); rheumatic fever prophylaxis.

Cautions: history of allergy (see notes above); renal failure; pregnancy and breast feeding

Drug interactions: methotrexate

Contra indications: see under penicillin G, sodium crystalline; and neurosyphilis

Side effects: see under penicillin G, sodium crystalline

Dose and Administrations: *deep IM injection:*

Streptococcal pharyngitis; primary prophylaxis of rheumatic fever:

Adult and Child over 30 Kg body-weight, 900 mg as a single dose;

Child under 30 Kg body – weight, 450 – 675 mg as a single dose.

Secondary prophylaxis of rheumatic fever:

Adult and Child over 30 Kg body-weight, 900 mg once every 3 – 4 weeks;

Child under 30 Kg body-weight, 450 mg once every 3 – 4 weeks.

Early syphilis: **Adult** 1.8 g as a single dose, divided between 2 sites.

Late syphilis: **Adult** 1.8 g divided between two sites, once weekly for 3 consecutive weeks.

Congenital syphilis (where no evidence of CSF involvement): **Child** up to 2 years, 37.5 mg/kg as a single dose.

Yaws, Pinta, and bejel: **Adult:** 900 mg as a single dose; **Child** 450 mg as a single dose.

Reconstitution and Administration. According to manufacturer's directions.

Storage: store between 2 and 8°C.

Penicillin G, Sodium crystalline

Injection, 1 million IU, 10 million IU, 20 million IU in vial

1 million unit equivalent to 600 mg

Indications: throat infections, pneumonia, otitis media, lyme disease in children; streptococcal endocarditis; meningococcal disease; necrotizing enterocolitis, necrotizing fascitis; leptospirosis, neurosyphilis, anthrax; actinomycosis; brain abscess; gas gangrene; cellulitis; osteomyelitis.

Cautions: history of allergy (see notes above); renal failure; heart failure; pregnancy and breastfeeding.

Drug interactions: methotrexate, probenecid (decrease renal tubular secretion of the penicillins), aminoglycosides (inactivated by high doses of IV benzylpenicillin; should not be administered in same giving set).

Contraindications: penicillin hypersensitivity (see notes above); avoid intrathecal route

Side effects: hypersensitivity reactions including urticaria, fever, joint pains, rashes, angioedema, anaphylaxis, serum sickness – like reactions, hemolytic anemia and interstitial nephritis; neutropenia, thrombocytopenia, coagulation disorders and central nervous system toxicity including convulsions reported (especially with high doses or in severe renal impairment), paraesthesia with prolonged use; diarrhea and antibiotic associated colitis; see also notes above.

Dose and Administration:

Mild to moderate infections due to sensitive organisms: IM or slow IV injection or infusion:

Adult: 0.6 – 2.4 g daily in 2 – 4 divided doses, with higher doses in severe infections and duration of treatment depending on disease;

Neonate: 50 mg/kg daily in 2 divided doses;

Infant 1 to 4 weeks, 75 mg/kg daily in 3 divided doses;

Child 1 month to 12 years, 100 mg/kg daily in 4 divided doses, with higher doses in severe infections.

Bacterial endocarditic. slow IV injection or infusion: **Adult** up to 7.2g daily in 6 divided doses.

Meningococcal meningitis: slow IV injection or infusion:

Adult up to 14.4 g daily in divided doses;

Premature infant and Neonate 100 mg/kg daily in 2 divided doses;

Infant 150 mg/kg daily in 3 divided doses

Child 1 month to 12 years, 180 – 300 mg/kg daily in 4 – 6 divided doses.

Suspected meningococcal disease (before transfer to hospital): IM or slow IV injection:

Adult and Child over 10 years, 1.2 g; **Child** 1 to 9 years, 600 mg; **Child** less than 1 year, 300 mg.

Neurosyphilis: slow IV injection: **Adult:** 1.8 – 2.4 g every 4 hours for 2 weeks.

Congenital syphilis, IM or slow IV injection: **Child** up to 2 years, 30 mg

/kg daily in 2 divided doses for 10 days, **Child** over 2 years, 120 – 180 mg/Kg (to maximum of 1.44g) daily in divided doses for 14 days.

Reconstitution and Administration: According to manufacturer's directions

Storage: at room temperature. Prior to reconstitution.

Phenoxymethyl Penicillin

Tablet, 125 mg, 250 mg, 500,000 IU

Oral suspension, 125 mg/5ml, 50000 IU/ml

250mg = 400,000 units

Indications: streptococcal pharyngitis; otitis media; erysipelas; mouth infection; secondary prophylaxis of rheumatic fever; post-splenectomy prophylaxis.

Cautions, Contraindications, Drug interactions, Side effects; see under penicillin G, sodium crystalline

Dose and Administration:

Infections due to sensitive organisms: Oral:

Adult: 500 mg every 6 hours increased up to 1 g every 6 hours in severe infections;

Child up to 1 year, 62.5 mg every 6 hours; **Child** 1 – 5 years, 125 mg every 6 hours; **Child** 6 – 12 years, 250 mg every 6 hours.

Secondary prophylaxis of rheumatic fever: Oral: **Adult:** 500 mg twice daily; **Child** 1 – 5 years, 125 mg twice daily; **Child** 6 – 12 years, 250 mg twice daily.

Patient advice. Phenoxymethyl penicillin should be taken at least 30 minutes before or 2 hours after food.

Storage: at room temperature in a tight container.

Phenoxymethyl penicillin, potassium

Tablet, 390 mg

Suspension, 195 mg/5ml

See under Phenoxymethyl penicillin

Piperacillin

Powder for injection (as sodium salt), 1g, 2g in vial

Indications: infections due to *P. aeruginosa* - usually in combination with an aminoglycoside for synergistic effect.

Cautions: known hypersensitivity to any penicillin or cephalosporin.

Drug interactions: probenecid, aminoglycosides, oral contraceptives.

Side effects: the high sodium content may cause fluid retention and hypokalaemia. Piperacillin has a potential for provoking a bleeding diathesis. Neutropenia, leucopenia and thrombocytopenia have been reported. Other effects include thrombophlebitis at the injection site, neuromuscular excitability with high doses, cholestatic jaundice, bloody diarrhea, and reversible elevation of serum urea and creatinine levels.

Dose and Administration: Adult:

IV: usually 2-4g, 6 - 8 hourly, injected over 3-5 minutes, or infused over 20 - 40 minutes; maximum 24 g/day.

IM: 2g, 8 - 12 hourly (i.e. 4 - 6 g/day).

Single doses over 2g must be given intravenously; the IV route is preferred in severe infections.

Child: IV: 2 months - 12 years, 50 - 100mg/kg/dose 6-8 hourly (Maximum dose 2 – 4g). Give 12 hourly in the first week of life.

Storage: store in airtight containers.

Procaine Penicillin, Fortified

Injection (buffered), 4,000,000 IU in Vial, Dry Powder.

Penicillin G sodium -1,000,000 IU

Penicillin G procaine -3,000,000 IU

Indications: for the treatment of respiratory infections (e.g. pneumonia), acute otitis media, skin structure infections, uncomplicated urogenital gonorrhea, and syphilis.

Cautions: same as penicillin G benzathine and also caution in the treatment of gonococcal infections during pregnancy and in children.

Drug interactions: see under penicillin G, sodium crystalline

Contraindications: known hypersensitivity to any penicillin and/ or procaine.

Side effects: hypersensitivity reactions such as skin rash, fever, joint pains, edema and anaphylaxis may occur.

Dose and Administration: IM injection only.

Adult:

Gonorrhea (acute, uncomplicated): 4,800,000 IU (2,400,000 IU in each buttock). Repeat the same dose next day.

Syphilis– Primary, secondary, or latent (of not more than 2 years duration): 600,000 IU daily for 8 days. Tertiary (2 year and more)- 600,000 IU daily for 10-15 days.

Note: Remember to treat always the sexual partner.

Pneumonia, acute otitis media, skin or skin structure infections:

Adult and child (12 years and over): 600,000-1,200,000 IU daily for 5- 7days. Maximum dose –100,000 IU of penicillin G /kg of body weight in divided doses.

Child (below 12 years): Treatment is given daily for 5 –7 days, 1-5 months (3-5kg) –100,000 IU daily, 6-12 months (6-10kg) –200,000 IU daily, 1- 6 years (11-20kg) –300,000 IU daily, 1-5 years (21-30kg) – 400,000 IU daily.

Storage: At room temperature. After reconstitution, it should be used within 14 days provided it is stored between 2-4°C or within 4 days at about 20°C.

Sultamicillin (Ampicillin Sodium and Sulbactam Sodium)

Tablet, 375 mg, 750mg

Indications; Cautions; Drug interactions; Contraindications; Side effects: see under Ampicillin sodium + Sulbactam sodium.

Dose and Administration: Oral: 375-750mg twice daily.

7.1.2. Other Antibacterials

Cephalosporins

The cephalosporins are bactericidal and, similarly to the penicillins, they act by inhibiting synthesis of the bacterial cell wall. The most widely used system of classification of cephalosporins is by generations and is based on the general features of their antibacterial activity.

First- generation cephalosporin

It has good activity against a wide spectrum of Gram-positive bacteria including penicillinase-producing, but not meticillin-resistant, *staphylococci*; *enterococci* are, however, resistant. Its activity against Gram-negative bacteria is modest.

Cefadroxil and cefalexin are available in oral formulations, while cefazolin is administered parenterally and widely used for surgical prophylaxis.

Second- generation cephalosporin

It has similar or slightly less activity than first generation against Gram-positive bacteria, but greater stability to hydrolysis by beta lactamases produced by Gram-negative bacteria and enhanced activity against many of the *Enterobacteriaceae* and *Haemophilus influenzae*.

Cefaclor, cefprozil and Cefuroxime are second-generation cephalosporins. Cefaclor and cefprozil are orally administered cephalosporins.

Third- generation cephalosporin

It is sometimes referred to as extended-spectrum cephalosporins. Compared with the earlier generations of cephalosporins they have a wider spectrum and greater potency of activity against Gram-negative organisms, including most clinically important *Enterobacteriaceae*. Their activity against Gram-positive bacteria is said to be less than that of the first-generation drugs, but they are very active against *streptococci*.

Cefotaxime has good activity against most Gram-positive and Gram-negative organisms. It is useful in treating infection due to *H. influenzae* (including beta-lactamase-producing strains), *Salmonella spp* and *N. gonorrhoeae*. It is ineffective against *P.aeruginosa*. Ceftazidime is effective against many strains of *P.aeruginosa*. It is not adequate for *S.pneumoniae* or other streptococci. Ceftriaxone has activity similar to that of cefotaxime. Its longer half-life allows once or twice daily dosing. Cefixime and cefpodoxime are third-generation cephalosporins that can be administered orally. There is concern that widespread use of these agents could lead to increasing resistance, particularly among pneumococci.

Cephalosporin first generation

Cefadroxil

Tablet, 500mg, 1gm

Oral suspension, 125mg/5ml, 250mg/5ml

Indications: treatment of susceptible bacterial infections, including those caused by group A beta-hemolytic *Streptococcus*; prophylaxis against bacterial endocarditis in patients who are allergic to penicillin and undergoing surgical or dental procedures.

Cautions: severe renal impairment, history of penicillin allergy.

Drug interactions: probenecid, anticoagulants.

Contraindications: hypersensitivity to cefadroxil or other cephalosporins.

Side effects: diarrhea, abdominal pain, agranulocytosis, anaphylaxis, angioedema, arthralgia, cholestasis, dyspepsia, erythema multiforme, fever, nausea, neutropenia, pruritus, pseudomembranous colitis, rash, serum sickness, Stevens-Johnson syndrome, thrombocytopenia, transaminases increased, urticaria, vaginitis, vomiting.

Dose and Administration: *Oral:*

Adult: 1-2 g/day in 2 divided doses.

Child: 30 mg/kg/day divided twice daily up to a maximum of 2g/day.

Prophylaxis against bacterial endocarditis:

Adult: 2g 1 hour prior to the procedure.

Child: 50mg/kg 1 hour prior to the procedure.

Storage: store at room temperature.

Cephalexin

Capsule, 250 mg, 500 mg

Syrup, 125 mg/5ml

Indications: treatment of susceptible bacterial infections including respiratory tract infections, otitis media, skin and skin structure infections, bone infections and genitourinary tract infections, including acute prostatitis, alternative therapy for acute bacterial endocarditis prophylaxis.

Cautions: severe renal impairment, penicillin allergy.

Drug interactions: probenecid, aminoglycosides.

Contraindications: hypersensitivity to cephalexin or other cephalosporins.

Side effects: agitation, confusion, dizziness, fatigue, hallucinations, headache, angioedema, erythema multiforme, rash, Stevens-Johnson syndrome, urticaria, abdominal pain, diarrhea, dyspepsia, gastritis, pseudomembranous colitis, genital pruritus, genital moniliasis, vaginitis, vaginal discharge, thrombocytopenia; arthritis, joint-disorder.

Dose and Administration: *Oral:*

Adult: 250 - 1000 mg every 6 hours; maximum: 4 g/day.

Streptococcal pharyngitis, skin infections: 500 mg every 12 hours.

Uncomplicated cystitis: 500 mg every 12 hours for 7 - 14 days.

Prophylaxis of bacterial endocarditis: 2g 1 hour prior to procedure.

Child > 1 year: 25 - 50 mg/kg/day every 6 - 8 hours, more severe infections; 50 - 100 mg/kg/day in divided doses every 6-8 hours; maximum: 4 g/24 hours.

Otitis media: 75-100mg/kg/day in 4 divided doses.

Streptococcal pharyngitis, skin infections: 25-50 mg/kg / day divided every 12 hours.

Uncomplicated cystitis: **Child >15 years:** Refer to Adults dosing.

Prophylaxis of bacterial endocarditis: 50 mg/kg 1 hour prior to procedure (maximum: 2 g).

Storage: store capsules and powder for oral suspension at room temperature. After reconstitution of oral suspension store in airtight containers at 2-8 °C and discard if not used within 2 weeks.

Cephazoline Sodium

Injection, 250 mg, 500 mg, 1g in vial.

Indications: treatment of respiratory tract, skin and skin structure, genital, urinary tract, biliary tract, bone and joint infections, septicemia, preoperative prophylaxis.

Cautions: severe renal impairment, history of penicillin allergy.

Drug interactions: probenecid, aminoglycosides, warfarin.

Contraindications: hypersensitivity to cefazolin sodium or other cephalosporins.

Side effects: fever, seizure, rash, pruritus, Stevens-Johnson syndrome, diarrhea, nausea, vomiting, abdominal cramps, anorexia, pseudomembranous colitis, oral candidiasis, vaginitis, hepatitis, eosinophilia, neutropenia, thrombocytopenia, leukopenia, thrombocytosis, pain at injection site, phlebitis, renal failure; BUN increased, serum creatinine increased.

Dose and Administration: *IM, IV:*

Adult: 250 mg to 2 g every 6 - 12 (usually 8) hours, depending on severity of infection; maximum dose: 12g/day.

Child >1 month: 25 - 100 mg/kg/day divided every 6 - 8 hours; maximum: 6 g/day.

Storage: store intact vials at room temperature and protect from temperature exceeding 40°C.

Cephadrine

Capsule, 250 mg, 500 mg

Intravenous (I.V) Infusion, 2g, 4g/100ml

Powder for injection, 250mg, 500mg, 1g/vial

Syrup, 125 mg/5ml; 250 mg/5ml

Indications: treatment of infections when caused by susceptible strains in respiratory, genitourinary, gastrointestinal, skin, bone and joint infections; treatment of susceptible gram-positive bacilli and cocci; some gram-negative bacilli.

Cautions: renal impairment, penicillin allergy.

Drug interactions: probenecid, aminoglycosids.

Contraindications: hypersensitivity to cephradine or other cephalosporins.

Side effects: dizziness, rash, pruritus, diarrhea, nausea, pseudomembranous colitis, leukopenia, neutropenia, eosinophilia, joint pain, BUN increased, creatinine increased.

Dose and Administration:

Adult: *Oral:* 250 - 500 mg every 6 - 12 hours.

In severe infection: deep IM or IV by slow injection over 3-5 minutes or by infusion, in doses of 2-4 g daily in 4 divided doses; up to 8g daily.

Child ≥ 9 months: *Oral:* Usual dose: 25 - 50 mg/kg/day in divided doses every 6 hours. *Otitis media:* 75 -100 mg/kg/day in divided doses every 6 or 12 hours (maximum: 4g/day).

Injection: 50-100mg/kg daily may be given in 4 divided doses, increasing to 300mg/kg daily in severe infections.

Storage: store at controlled room temperature.

Cephalosporin second generation

Cefaclor

Capsules, 250 mg, 500 mg

Suspension, 125 mg/5ml, 250 mg/5ml.

Indications: treatment of susceptible bacterial infections including otitis media, lower respiratory tract infections, acute exacerbations of chronic bronchitis, pharyngitis and tonsillitis, urinary tract infections, skin infections.

Cautions: severe renal impairment, history of penicillin allergy.

Drug interactions: probenecid, furosemide, aminoglycosides.

Contraindications: hypersensitivity to cefaclor or other cephalosporins.

Side effects: rash, diarrhea, vaginitis, eosinophilia, transaminases increased, agitation, agranulocytosis, anaphylaxis, angioedema, aplastic anemia, cholestatic jaundice, CNS irritability, confusion, dizziness, hallucinations, hemolytic anemia, hepatitis.

Dose and Administration: *Oral:*

Adult: 250 - 500 mg every 8 hours

Child >1 month: 20 - 40 mg/kg/day divided every 8 - 12 hours;

Maximum dose: 1 g/day.

Otitis media: 40 mg/kg/day divided every 12 hours

Pharyngitis: 20 mg/kg/day divided every 12 hours.

Storage: store at controlled room temperature. Refrigerate suspension after reconstitution and discard after 14 days. Do not freeze.

Cefprozil

Oral solution, 125mg/5ml, 250mg/5ml

Indications: treatment of otitis media, infections involving respiratory tract and skin and skin structure; active against methicillin –sensitive staphylococci, many streptococci, and various gram-negative bacilli including *E.coli*, some *Klebsiella*, *P. mirabilis*, *H. influenzae* and *Moraxella*.

Cautions: severe renal impairment, history of penicillin allergy.

Drug interactions: probenecid, furosemide, aminoglycosides.

Contraindications: cephalosporin hypersensitivity.

Side effects: dizziness, diaper rash, diarrhea, nausea, vomiting, abdominal pain, vaginitis, transaminases increased, and superinfection.

Dose and Administration: *Oral:*

Pharyngitis/tonsillitis:

Adult and Child >13 years: 500 mg every 24 hours for 10 days.

Children 2-12 years: 7.5-15 mg/kg/day divided every 12 hours for 10 days; maximum: 1 g/day.

Uncomplicated skin and skin structure infections:

Adult and Child >13 years: 250mg every 12 hours, or 500 mg every 12-24 hours for 10 days.

Child 2-12 years: 20mg/kg every 24 hours for 10 days; maximum: 1 g/day.

Secondary bacterial infection of acute bronchitis or acute bacterial exacerbation of chronic bronchitis: 500mg every 12 hours for 10 days.

Infants and Child > 6 months to 12 years: Otitis media: 15mg/kg every 12 hours for 10 days.

Storage: store at room temperature.

Cefuroxime

Tablet, 125 mg, 250 mg

Powder for injection, 250 mg/vial, 750 mg/vial, 1.5 g/vial

Oral suspension, 125mg/ml

Indications: used in the treatment of bone and joint infections; upper respiratory tract infections (pneumonia or bronchitis) caused by *S.Pyogenes*; *H.influenza* (beta-lactamase negative and beta-lactamase positive strains); sinusitis caused by *M. Catarrhalis*, *S.Pneumonia* or *H.Influenzae*; Lower respiratory tract infections (pneumonia or bronchitis) caused by *S.Pneumonias*, *H.Influenzae*, *H.parainfluenzae*, *K.Pneumoniae* or *M.Catarrhalis*; skin structure infections caused by *S.Aureus*, *S.Pyogenes* or *S.Agalactiae*; Gonorrhea caused by *N. Gonorrheae*.

Cautions: penicillin sensitivity; renal impairment; pregnancy and breast feeding (but appropriate to use); false positive urinary glucose (if tested for reducing substances) and false positive coombs' test.

Drug interactions: anticoagulants

Contraindications: cephalosporin hypersensitivity; porphyria.

Side effects: diarrhea and rarely antibiotic associated colitis, nausea and vomiting, abdominal discomfort, headache; allergic reactions including rashes, pruritus, urticaria, serum sickness – like reactions with rashes, fever and arthralgia, and anaphylaxis; erythema multiforme, toxic epidermal necrolysis reported; disturbances in liver enzymes, transient hepatitis and cholestatic jaundice; other side-effects reported include eosinophilia and blood disorders (including thrombocytopenia, leucopenia, agranulocytosis, aplastic anaemia and hemolytic anaemia); reversible interstitial nephritis, hyperactivity, nervousness, sleep disturbances, confusion, hypertonia, and dizziness.

Dose and Administration:

Oral: (as cefuroxime axetil), 250 mg twice daily in most infections including mild to moderate lower respiratory – tract infections (e.g. bronchitis); doubled for more severe lower respiratory-tract infections or if pneumonia suspected.

Urinary-tract infection, 125 mg twice daily, doubled in pyelonephritis.

Gonorrhoea, 1 g as a single dose; **Child** over 3 months, 125 mg twice daily, if necessary doubled in child over 2 years with otitis media.

Lyme disease, Adult and Child over 12 years, 500 mg twice daily for 20 days.

IM or IV injection or infusion: 750 mg every 6 – 8 hours; 1.5 g every 6 – 8 hours in severe infections; single doses over 750 mg intravenous route only. Child usual dose 60 mg/kg daily (range 30 – 100 mg/Kg daily) in 3- 4 divided doses (2- 3 divided doses in neonates).

Gonorrhoea, 1.5 g as a single dose by intramuscular injection (divided between 2 sites)

Surgical prophylaxis, 1.5 g by intravenous injection at induction; may be supplemented with 750mg intramuscularly 8 and 16 hours later (abdominal, pelvic, and orthopedic operations) or followed by 750 mg intramuscularly every 8 hours for further 24 – 48 hours (cardiac, pulmonary, oesophageal, and vascular operations).

Meningitis, 3 g intravenously every 8 hours; **Child**, 200 – 240 mg/kg daily (in 3 – 4 divided doses) reduced to 100 mg/kg daily after 3 days or on clinical improvement; Neonate, 100 mg/kg daily reduced to 50 mg/kg daily.

Storage: at room temperature.

Cephalosporin third generation

Cefixime

Tablet, 200mg, 400mg

Indications: treatment of urinary tract infections, otitis media, respiratory infections due to susceptible organisms; uncomplicated cervical/urethral gonorrhea due to *N. gonorrhoeae*.

Cautions: severe renal impairment, history of penicillin allergy.

Drug interactions: probenecid, furosemide, aminoglycosides, warfarin.

Contraindications: cephalosporin hypersensitivity.

Side effects: diarrhea, abdominal pain, nausea, dyspepsia, flatulence, loose stools, acute renal failure, anaphylactic reactions, angioedema, dizziness, drug fever, headache, rash, seizure, Stevens-Johnson syndrome.

Dose and Administration: *Oral:*

Adult and Child > 50kg or >12 years: 400mg/day divided every 12-24 hours.

Uncomplicated cervical/urethral gonorrhea due to N. gonorrhoeae: 400mg as a single dose

Child ≥ 6 months: 8mg/kg/day divided every 12-24 hours.

Cefotaxime

Injection, as sodium, 0.5 g, 1 g in vial

Indications: treatment of susceptible infection in respiratory tract, skin, bone and joint, urinary tract, gynecologic as well as septicemia, and documented or suspected meningitis. Active against most gram-negative bacilli, gram-positive cocci and many penicillin-resistant pneumococci.

Cautions: severe renal impairment, patients with colitis, a history of penicillin allergy.

Drug interactions: probenecid, furosemide, aminoglycosides.

Contraindications: hypersensitivity to cefotaxime or other cephalosporins.

Side effects: rash, pruritus, diarrhea, nausea, vomiting, colitis, pain at injection site, anaphylaxis, arrhythmia, candidiasis, fever, headache, interstitial nephritis, neutropenia, Stevens-Johnson syndrome, thrombocytopenia, urticaria, vaginitis, agranulocytosis, aplastic anemia, cholestasis, hemolytic anemia, hemorrhage, renal dysfunction, seizure, superinfection, toxic nephropathy.

Dose and Administration:

Adult and Child >12 years:

Uncomplicated infections: I.M, I.V: 1 g every 12 hours.

Moderate/severe infections: I.M, I.V: 1 - 2 g every 8 hours.

Infections commonly needing higher doses (e.g. septicemia): I.V: 2 g every 6 - 8 hours.

Life-threatening infections: I.V: 2 g every 4 hours.

Preop: I.M, I.V: 1 g 30 - 90 minutes before surgery.

C-section: 1 g as soon as the umbilical cord is clamped, then 1g I.M, I.V at 6 and 12 hour intervals.

Infants and Child 1 month to 12 years: *I.M, I.V: <50 Kg: 50 - 180 mg/kg/day in divided doses every 4 - 6 hours.*

Meningitis: 200 mg/kg/day in divided doses every 6 hours.

Storage: store at a temperature not exceeding 8 °C.

Cefpodoxime

Tablet, 100mg

Indications: treatment of susceptible acute, community acquired pneumonia caused by *S. pneumoniae* or nonbetalactamase producing *H.influenzae*; acute uncomplicated gonorrhea caused by *N. gonorrhoeae*; uncomplicated skin and skin structure infections caused by *S. aureus* or *S.pyogenes*; acute otitis media caused by *S.pneumoniae*, *H.influenzae* or *M.catarrhalis*; pharyngitis or tonsillitis; and uncomplicated UTI caused by *E.coli*, *Klebsiella*, and *Proteus*.

Cautions: renal impairment, prolonged use may result in superinfection, use with caution in patients with a history of penicillin allergy especially IgE-mediated reactions (eg anaphylaxis, urticaria)

Drug interactions: probenecid, furosemide, aminoglycosides, antacids and H2-receptor antagonists.

Contraindications: hypersensitivity to cephalosporins

Side effects: diaper rash, diarrhea in infants, headache, rash, nausea, abdominal pain, vomiting.

Dose and Administration: *Oral:*

Adult and Child ≥ 12 years: *Acute community-acquired pneumonia and bacterial exacerbations of chronic bronchitis:* 200 mg every 12 hours for 14 days and 10 days, respectively

Acute maxillary sinusitis: 200mg every 12 hours for 10 days

Skin and skin structure: 400mg every 12 hours for 7-14 days

Uncomplicated gonorrhea (male and female) and rectal gonococcal infections (female): 200mg as a single dose

Pharyngitis/tonsillitis: 100mg every 12 hours for 5-10 days

Uncomplicated urinary tract infection: 100mg every 12 hours for 7 days

Child 2 months to 12 years:

Acute otitis media: 10mg/kg/day divided every 12 hours (400mg/day) for 5 days (maximum: 200mg/dose)

Acute maxillary sinusitis: 10mg/kg/day divided every 12 hours for 10days (maximum: 200mg/dose)

Pharyngitis/tonsillitis: 10mg/kg/day in 2 divided doses for 5-10 days (maximum: 100mg/dose)

Ceftazidime

Injection, 0.5 g, 1 g, 2 g in vial

Indications: infections due to sensitive bacteria, especially those due to pseudomonas spp. and including those resistant to aminoglycosides.

Cautions: penicillin sensitivity, renal impairment, pregnancy and breast-feeding, false positive urinary glucose and false positive coombs' test.

Drug interactions: contraceptives (oral), furosemide, warfarin.

Contraindications: cephalosporin hypersensitivity; porphyria.

Side effects: diarrhea, nausea, vomiting, abdominal discomfort, headache, rarely, antibiotic - associated colitis (particularly with higher doses); allergic reactions including rashes, pruritus, urticaria, serum sickness like reaction, fever and arthralgia, and anaphylaxis, erythema multiforme, toxic epidermal necrolysis reported; disturbances in liver enzymes, transient hepatitis, cholestatic jaundice eosinophilia and blood disorders (including thrombocytopenia, leukopenia, agranulocytosis, aplastic anaemia, and haemolytic anaemia); reversible interstitial nephritis, nervousness, sleep disturbances, confusion, hypertonia, and dizziness.

Dose and Administration:

Adult: *IM, IV:* 500mg to 2g every 8-12 hours

Urinary tract infections: 250-500mg every 12 hours.

Infants and Child 1 month to 12 years: *IV:* 30-50mg/kg/dose every 8 hours; maximum dose: 6g/day.

Storage: store between (-25) and (-10) °C unless otherwise specified by manufacturer. After thawing, solutions retain their potency for 24 hours at room temperature or for 7 days if refrigerated.

Ceftriaxone

Injection, 0.25g, 0.5 g, 1 g, 2 g in vial

Indications: serious infections due to sensitive bacteria, including septicaemia, pneumonia, and meningitis, surgical prophylaxis, prophylaxis of meningococcal meningitis, gonorrhea.

Cautions: penicillin sensitivity; renal and hepatic impairment; premature neonates, may displace bilirubin from serum albumin; pregnancy and breast feeding; false positive urinary glucose and false positive coombs' test.

Drug interactions: contraceptives (oral), furosemide, and warfarin.

Contraindications: cephalosporin hypersensitivity, porphyria, neonates with jaundice, hypoalbuminaemia, acidosis or impaired bilirubin binding.

Side effects: diarrhea, nausea and vomiting, abdominal discomfort, headache, antibiotic-associated colitis, allergic reactions including rashes, pruritus, urticaria, serum sickness - like reactions, fever and arthralgia, and anaphylaxis, erythema multiforme, toxic epidermal necrolysis, disturbances in liver enzymes, transient hepatitis and cholestatic jaundice, eosinophilia and blood disorders, reversible interstitial nephritis, hyperactivity, nervousness, sleep disturbances, confusion, hypertonia and dizziness, calcium ceftriaxone precipitates in urine or in gall bladder - consider discontinuation if symptomatic, rarely prolongation of prothrombin time, pancreatitis.

Dose and Administration:

Infections due to susceptible organisms: IM, IV injection (over 3 - 4 minutes) or IV infusion:

Adult: 1 g daily; severe infections 2 - 4 g daily.

Infant and Child: 20 - 50 mg/kg daily, up to 80 mg/kg daily in severe infections; by *IV infusion* (over 60 minutes).

Neonate: 20 - 50 mg/kg daily.

Uncomplicated gonorrhea: IM: Adult: 250 mg as a single dose.

Surgical prophylaxis: IM, IV injection (over at least 2 - 4 minutes), 1 g as a single dose.

Colorectal surgery (with antibacterial active against anaerobes), IM or IV (over at least 2 - 4 minutes), or by *IV infusion*, 2 g as a single dose.

Storage: prior to reconstitution, store at room temperature. Premixed solution store at -20°C; once thawed, solutions are stable for 3 days at room temperature of 25°C or for 21 days refrigerated at 5°C. Do not refreeze.

Macrolides

The macrolides are bacteriostatic or bactericidal, depending on the concentration and type of micro-organism, and are thought to interfere with bacterial protein synthesis. Their antimicrobial property is similar to benzylpenicillin but they are also active against such organisms as *Legionella pneumophila*, *Mycoplasma pneumoniae*, and some *rickettsias*, *chlamydias*, and *chlamydophilas*. Macrolides and related drugs have a postantibiotic effect: that is, antibacterial activity persists after concentrations have dropped below the minimum inhibitory concentration.

Azithromycin

Capsule, 250 mg

Powder for oral suspension, 200 mg/5ml

Indications: treatment of acute otitis media, pharyngitis/tonsillitis, mild to moderate upper and lower respiratory tract infections, infections of the skin, community - acquired pneumonia, pelvic inflammatory disease, sexually-transmitted diseases (urethritis/cervicitis), genital ulcer, acute bacterial exacerbations of chronic obstructive pulmonary disease (COPD), acute bacterial sinusitis.

Cautions: hepatic and renal dysfunction, prolonged cardiac repolarization.

Drug interactions: pimozide, phenytoin, ergot alkaloids, alfentanil bromocriptine, carbamazepine, cyclosporine, digoxin, disopyramide, triazolam; nelfinavir, aluminium and magnesium - containing antacids.

Contraindications: hypersensitivity to azithromycin.

Side effects: diarrhea, nausea, abdominal pain, cramping, vomiting, acute renal failure, allergic reaction, aggressive behaviour, anaphylaxis, angioedema, arrhythmia, cholestatic jaundice, deafness, enteritis, erythema multiforme, headache, hearing loss, hepatic necrosis.

Dose and Administration: *Oral:*

Adolescents ≥ 16 years and Adults:

Respiratory tract, skin and soft tissue infections: 500 mg on day 1 followed by 250 mg/day on days 2 – 5.

Alternative regimen: Bacterial exacerbation of COPD: 500 mg/day for a total of 3 days.

Bacterial sinusitis: 500 mg/day for a total of 3 days.

Urethritis / cervicitis: Due to C.trachomatis: 1 g as a single dose

Due to N.gonorrhoeae: 2 g as a single dose

Chancroid due to H-ducreyi: 1 g as a single dose

Child ≥ 6 months:

Community - acquired pneumonia: 10 mg/kg on day 1 followed by 5 mg/kg/day once daily on days 2 - 5.

Bacterial Sinusitis: 10 mg/kg once daily for 3 days.

Otitis media: 1- day regimen: 30 mg/kg as a single dose

3-day regimen: 10 mg/kg once daily for 3 days.

5 - day regimen: 10 mg/kg on day 1 followed by 5 mg/kg/day once daily on days 2 – 5.

Child ≥ 2 years: *pharyngitis, tonsillitis:* 12 mg/kg/day once daily for 5 days.

Storage: Suspension: store dry powder below 30°C; following reconstitution, store suspension at 5°C to 30°C.

Clarithromycin

Granules for oral suspension, 125 mg/5ml, 250 mg/5 ml

Tablet, 250 mg, 500 mg

Powder for IV infusion, 500 mg/vial

Indications: respiratory-tract infections, mild to moderate skin and soft tissue infections; adjunct in the treatment of duodenal ulcers by eradication of *Helicobacter pylori* (see section 1.2). It is the drug of choice for *Mycobacterium avium* infections, in combination with ethambutol.

Cautions: severe renal impairment.

Drug interactions: cisapride, pimozone, sparfloxacin, thioridazine, benzodiazepines, calcium channel blockers, cyclosporine, quinidine, sildenafil, midazolam, triazolam, cisapride, ergot alkaloids, neuromuscular - blocking agents and warfarin, amprenavir, azole antifungals, ciprofloxacin, diclofenac, doxycycline, erythromycin, isoniazid, nefazodone, propofol.

Contraindications: hypersensitivity to clarithromycin, or any macrolide antibiotics; use with ergot derivatives, pimozone, cisapride.

Side effects: headache, rash, diarrhea, vomiting, nausea, abnormal taste, heartburn, abdominal pain, prothrombin time increased, BUN increased.

Dose and Administration:

Adult: *Oral:* 250-500mg twice daily. *IV infusion* over 60 minutes, 500mg twice daily. *M.avium complex (MAC) infections in AIDS:* 500mg twice daily plus ethambutol.

H. pylori: *Oral:* 500 mg twice daily, in combination regimens only.

Child: *Oral:* 7.5-15 mg/kg/dose (maximum 500 mg) 12 hourly.

Storage: store at room temperature.

Erythromycin*Tablet (stearate), 250mg, 500mg**Capsule, 250mg**Oral suspension, 125mg/5ml, 200mg/5ml, 250mg/5ml**Injection, 50mg/ml in 2ml ampoule*

Indications: for treatment of conjunctivitis in newborns, genitourinary tract infection during pregnancy, pneumonia in infants, prophylaxis of bacterial endocarditis, gonorrhea, legionnaires disease, pharyngitis, sinusitis and for long term prophylaxis of rheumatic fever, syphilis.

Cautions: pregnancy and breast-feeding, in patients with renal and hepatic function impairment, cardiac arrhythmias (prolongation of QT interval), porphyria.

Drug interactions: alfentanil, carbamazepine, chloramphenicol, itraconazole, cyclosporins, terfenadin, warfarin, xanthines such as aminophylline, caffeine, oxtriphylline, and theophylline.

Side effects: GIT disturbance (Nausea, Vomiting, diarrhoea, abdominal or stomach cramping and discomfort), reversible loss of hearing, recurrent fainting, sudden death (rare), hypersensitivity (skin rash, redness or itching), cholestatic jaundice (dark or amber urine, pale stools, stomach pains), inflammation or phlebitis at injection site (for parenteral erythromycin).

Dose and Administration:**Adult:**

Antibacterial (systemic): Oral: 250mg (base) every 6 hours, or 500mg every 12 hours if twice a day dosage is required. Maximum: - up to 4 grams (base) daily.

IV infusion: 250-500mg (base) every 6 hours. Maximum - up to 4 grams.

Endocarditis (prophylaxis): In patients with heart disease or rheumatic or other acquired valvular heart disease who undergo dental procedures or surgical procedure of the upper respiratory tract, Oral, 1gm (base) one hour prior to the procedure, and 500mg 6 hours following the procedure.

Genitourinary tract infection, including chlamydial: Oral: 500mg (base) every six hours for at least seven days. For patients unable to tolerate the higher dosage regimen, the dosage may be halved and given for at least fourteen days.

Legionnaires' disease: Oral: 500mg (base) to 1gm(base) every six hours.

Streptococcal (prophylaxis) - continuous prophylaxis of streptococcal infections in patients with a history of rheumatic heart disease: Oral: 250mg (base) every twelve hours.

Child:

Antibacterial (systemic): oral: 7.5to 12.5 (base) per kg of body weight every 6 hours, or 17 to 25mg per kg of body weight every 12 hours

Severe infection: 15 to 25mg (base) per kg of body weight every six hours.

Antibacterial (systemic): IV infusion, 3.75 to 5mg (base) per kg of body weight every 6 hours.

Conjunctivitis, chlamydial: oral: 12.5mg (base) per kg of body weight every 6 hours for at least two week.

Endocarditis prophylaxis: in patients with heart disease are rheumatic or other acquired valvular heart disease who undergo dental procedures or surgical procedures of the upper

respiratory tract: Oral: 20mg (base) per kg of body weight one hour prior to the procedure, and 10mg per kg of body weight six hours following the procedure.

Pertusis: oral: 10 to 12.5mg (base) per kg of body weight every 6 hours for 14 days.

Pneumonia, chlamydial: oral: 12.5mg (base) per kg of body weight every 6 hours for two weeks.

Streptococcal pharyngitis: oral: 5-12.5mg (base) per kg of body weight every 6 hours for at least 10 days.

Note: - For oral dosage- continue medicine for full time of treatment

Storage: at room temperature in tight container.

Aminoglycosides

The aminoglycosides, such as amikacin, gentamicin, neomycin and tobramycin have a similar antimicrobial spectrum and appear to act by interfering with bacterial protein synthesis, possibly by binding irreversibly to the 30S and to some extent the 50S portions of the bacterial ribosome. The manner in which they bring about cell death is not fully understood. They are most active against Gram-negative rods. Aminoglycosides show enhanced activity with penicillins against some enterococci and streptococci.

Amikacin

Injection, (as sulphate), 50 mg/ml, 250 mg/ml in 2 ml vial.

Indications: treatment of serious infections due to organisms resistant to gentamicin and tobramycin.

Cautions: renal impairment, drug should be discontinued if signs of ototoxicity, nephrotoxicity.

Drug interactions: amphotericin, neuromuscular blocking agents.

Contraindications: hypersensitivity to amikacin sulfate.

Side effects: neurotoxicity, ototoxicity, nephrotoxicity, allergic reaction, dyspnea, eosinophilia.

Dose and Administration:

Adult: *I.M or slow I.V over 30 minutes*, 15mg/kg/day as a single daily dose. Maximum 1.5g/day.

Child: *IV or IM*, 1week-10 years, 25mg/kg/dose daily on first day, then 18mg/kg/dose daily; over 10 years, 20mg/kg/dose daily on first day, then 15mg/kg/dose daily. Maximum dose 360mg daily.

Neonates: 15mg/kg/dose daily (all gestations). Measure trough levels before the third dose. If trough level >5mg/L, increase dosage interval to 36-48 hours and measure after 2 further doses given..

Storage: stable for 24 hours at room temperature and 2 days at refrigeration when mixed in DW, DNS, NS, LR.

Gentamicin

Injection, 40mg/ml ; 80mg/ 2ml

Indications: biliary tract infection, bone and joint infection, meningitis, ventriculitis, urinary tract infection, peritonitis, bacterial septicemia.

Cautions: pregnancy and breast-feeding, in premature infants and neonates, elderly, patients with renal function impairment or dehydration, and in those with eighth-cranial nerve impairment. Prolonged use should be avoided.

Drug interactions: avoid concurrent and /or sequential use of two or more aminoglycosides or aminoglycosides with capreomycin, antimysthenic, methoxyflurane or polymyxin, cephalosporins, ciclosporin, cisplatin, neostigmine, pyridostigmine, suxamethonium, vecuronium, furosemide, penicillines and indomethacin.

Contraindications: pregnancy, myasthenia gravis, previous allergic reaction to one aminoglycoside.

Side effects: nephrotoxicity (greatly increased or decreased frequency of urination or amount of urine; increased thirst, loss of appetite, nausea or vomiting); neurotoxicity (muscle twitching, numbness, seizures, tingling); ototoxicity, auditory damage (loss of hearing, ringing or buzzing a feeling of fullness in the ears), vestibular damage (clumsiness, dizziness, nausea, vomiting, unsteadiness)

Dosage and Administration:

Adult:

Antibacterial (systemic): IM or IV infusion: 1-1.7mg (base) per kg of body weight every eight hours for seven to ten days or more.

Urinary tract infection (bacterial, uncomplicated): IM or IV infusion: Adults (< 60kg body weight) - 3mg (base) per kg of body weight once a day, or 1.5mg per kg of body weight every 12 hours. Adults (\geq 60kg of body weight)- 160mg (base) once a day, or 80mg every 12 hours.

Usual adult prescribing limit - up to 8mg (base) per kg of body weight daily in severe, life threatening infections.

Child:

Antibacterial (systemic): IM or IV infusion: premature or full term neonates up to 1 week of age: 2.5mg (base) per kg of body weight every 12 or 24 hours for seven to ten days or more.

Older neonates and infants: 2.5mg (base) per kg of body weight every 8 to 16 hours for 7-10 days or more.

Child: 2 to 2.5mg (base) per kg of body weight every 8 hours for 7-10 days or more.

Storage: store at room temperature and protect from freezing.

Neomycin

Tablet, 500 mg

Indications: Orally to prepare GI tract for surgery; treatment of diarrhea caused by *E. Coli*; adjunct in the treatment of hepatic encephalopathy; bladder irrigation, ocular infections.

Cautions: renal impairment, pre-existing hearing impairment, neuromuscular disorders.

Drug interactions: oral anticoagulants, digoxin, methotrexate.

Contraindications: hypersensitivity to neomycin or other aminoglycosides.

Side effects: nausea, diarrhea, vomiting, irritation or soreness of the mouth or rectal area, dyspnea, eosinophilia, nephrotoxicity, neurotoxicity, ototoxicity.

Dose and Administration: *Oral:*

Preoperative intestinal antisepsis:

Adult: 1 g each hour for 4 doses then 1 g every 4 hours for 5 doses, or 1 g at 1 PM, 2 PM, and 11 PM on day preceding surgery as an adjunct to mechanical cleansing of the bowel and oral erythromycin; or 6g/day divided every 4 hours for 2-3 days.

Child: 90 mg/kg/day divided every 4 hours for 2 days; or 25 mg/kg at 1 PM, 2 PM and 11 PM on the day preceding surgery as an adjunct to mechanical cleansing of the intestine and in combination with erythromycin base.

Hepatic encephalopathy:

Adult: 500-2000mg every 6-8 hours or 4-12g/day divided every 4-6 hours for 5 - 6 days.

Child: 50 - 100 mg/kg/day in divided doses every 6 - 8 hours or 2.5 - 7 g/m²/day divided every 4 - 6 hours for 5 - 6 days not to exceed 12 g/day.

Chronic hepatic insufficiency: **Adult:** 4 g/day for an indefinite period.

Storage: store in airtight containers and at room temperature.

Tobramycin

Injection, 40 mg/ml in 1 and 2 ml ampoules

Indications: treatment of documented or suspected infections caused by susceptible gram-negative bacilli including *Pseudomonas aeruginosa*.

Cautions: renal impairment, pre-existing auditory or vestibular impairment, patients with neuromuscular disorders.

Drug interactions: penicillins, neuromuscular blockers, amphotericin B, cephalosporins, and loop diuretics.

Contraindications: hypersensitivity to tobramycin and other aminoglycosides, pregnancy.

Side effects: confusion, disorientation, dizziness, fever, headache, lethargy, vertigo, exfoliative dermatitis, itching, rash, urticaria, serum calcium, magnesium, potassium, and/or sodium decreased, diarrhea, nausea, vomiting, anemia, eosinophilia, granulocytopenia, leukocytosis, leukopenia, thrombocytopenia, hearing loss, tinnitus, ototoxicity, roaring in the ears, BUN increased, serum creatinine increased, oliguria, proteinuria.

Dose and Administration: *I.M., I.V.:*

Adult: *Severe life - threatening infections:*

Conventional dosing: 2 - 2.5 mg/kg/dose.

High dose: some clinicians suggest a daily dose of 4 - 7 mg/kg for all patients with normal renal function.

Urinary tract infection: 1.5 mg/kg /dose.

Infant and Child <5 years: 2.5 mg/kg/dose every 8 hours.

Children > 5 years: 2 - 2.5 mg/kg/dose every 8 hours.

Cystitis/fibrosis: 2.5 - 3.3 mg/kg every 6 - 8 hours.

Storage: store at room temperature.

Quinolones

Nalidixic acid and Norfloxacin are effective in uncomplicated urinary – tract infections.

Ciprofloxacin is active against both Gram-Positive and Gram – Negative bacteria. It is particularly active against Gram – negative bacteria, including *Salmonella*, *Shigella*, *Campylobacter*, *Neisseria*, and *Pseudomonas*, Ciprofloxacin has only moderate activity against Gram-positive bacteria such as *Streptococcus pneumoniae* and *Enterococcus faecalis*; it is not the drug of first choice for *Pneumococcal pneumonia*. It is active against *Chlamydia* and some mycobacteria. Most anaerobic organisms are not susceptible. Uses for ciprofloxacin include infections of the respiratory tract (but not for *Pneumococcal pneumonia*) and of the urinary tract, and of the gastro-intestinal system (including typhoid fever), and gonorrhoea and septicaemia caused by sensitive organisms.

Sparfloxacin is a fluoroquinolone antibacterial agent similar to ciprofloxacin. It has been reported to be more active in vitro than ciprofloxacin against some organisms, including staphylococci and mycobacteria, and has a much longer plasma half-life.

Cautions – Quinolones should be used with caution in patients with a history of epilepsy or conditions predisposing to seizures; convulsions may be induced in patients with or without a history of convulsions; also, use with caution in G6PD deficiency, pregnancy or breast feeding; use in children or adolescents is generally not recommended (quinolones cause arthropathy in weight – bearing joints in young animals), although in some specific circumstances, shorter use may be justified. Exposure to sunlight should be avoided (discontinue if photosensitivity occurs).

Side effects– Adverse effects of quinolones include nausea, vomiting, dyspepsia, abdominal pain, diarrhoea, and rarely antibiotic associated colitis; headache, dizziness, sleep disorders, rash (rarely Stevens – Johnson Syndrome and toxic epidermal necrolysis), and pruritus; less commonly, anorexia, transient disturbances in liver enzymes and bilirubin and increases in blood urea and creatinine; drowsiness, restlessness, depression, confusion, hallucinations, convulsions, paraesthesia; photosensitivity; hypersensitivity reactions including fever, urticaria, angioedema, arthralgia, myalgia, and anaphylaxis, blood disorders; disturbances in vision, taste, hearing, and smell; isolated reports of tendon inflammation and damage; if psychiatric, neurological, or hypersensitivity reactions occur –discontinue the drug.

Drug interactions –Quinolones may interact with the various compounds including analgesics, anticoagulants, ciclosporin (increased risk of nephrotoxicity) and theophylline.

Ciprofloxacin

Tablet (as hydrochloride), 250 mg

Injection Infusion (as lactate), 2 mg/ml in 50 ml and 100 ml bottle

Indications: gastroenteritis—including cholera, shigellosis, travellers' diarrhoea, campylobacter and salmonella enteritis; typhoid; gonorrhoea; chancroid;

legionnaires' disease; meningitis (including meningococcal meningitis prophylaxis); respiratory-tract infections—including pseudomonal infections in cystic fibrosis, but not pneumococcal pneumonia; urinary-tract infections; bone and joint infections; septicaemia; anthrax; skin infections; prophylaxis in surgery

Cautions: history of epilepsy or conditions that predispose to seizures, G6PD deficiency, myasthenia gravis (risk of exacerbation), pregnancy, breastfeeding, children or adolescents (see below); avoid exposure to excessive sunlight (discontinue if photosensitivity occurs); rarely, tendon damage—discontinue at first sign of pain or inflammation and rest affected limb; hepatic impairment; renal failure; avoid excessive alkalinity of urine and ensure adequate fluid intake as risk of crystalluria

USE IN CHILDREN. Ciprofloxacin causes arthropathy in the weight-bearing joints of immature *animals* and is therefore generally not recommended in children and growing adolescents. However, the significance of this effect in humans is uncertain and in some specific circumstances short-term use of ciprofloxacin in children may be justified. Ciprofloxacin is used for pseudomonal infections in cystic fibrosis (for children over 5 years), and for treatment and prophylaxis of anthrax

SKILLED TASKS. May impair ability to perform skilled tasks, for example operating machinery, driving

Drug interactions: see notes above

Contraindications: Absolut- Known allergy to ciprofloxacin or other quinolones.

Relative- patients under 18 years, pregnancy and lactation.

Side effects: nausea, vomiting, dyspepsia, abdominal pain, diarrhoea (rarely antibiotic-associated colitis), headache, dizziness, weakness, sleep disorders, rash (rarely erythema multiforme (Stevens-Johnson syndrome) and toxic epidermal necrolysis), and pruritus; less frequently anorexia, increase in blood urea and creatinine; metabolic acidosis; drowsiness, restlessness, asthenia, depression, confusion, hallucinations, convulsions, paraesthesia, raised intracranial pressure, cranial nerve palsy; photosensitivity, hypersensitivity reactions including fever, urticaria, angioedema, arthralgia, myalgia, and anaphylaxis; blood disorders (including eosinophilia, leukopenia, thrombocytopenia); disturbances in vision, taste, hearing and smell; also isolated reports of tendon inflammation and damage (especially in the elderly and in those taking corticosteroids); haemolytic anaemia, renal failure, interstitial nephritis, and hepatic dysfunction (including hepatitis and cholestatic jaundice); if psychiatric, neurological or hypersensitivity reactions (including severe rash) occur discontinue.

Dose and Administration: Adult: Oral:

Infections due to susceptible organisms: 250 – 750 mg twice daily.

Acute uncomplicated cystitis: 100 mg twice daily for 3 days

Chronic prostatitis: 500 mg twice daily for 28 days.

Gonorrhea, chancroid, shigellosis, or cholera: 500 mg as a single dose

Pseudomonal lower respiratory– tract infection in cystic fibrosis: 750 mg twice daily;

Child 5 – 17 years, up to 20 mg/kg twice daily (max. 1.5 g daily).

Most other infections: 500 – 750 mg twice daily

Surgical prophylaxis: 750 mg 60- 90 minutes before procedure.

IV infusion (over 30 – 60 minutes ; 400 mg over 60 minutes), 200–400 mg twice daily pseudomonal lower respiratory –tract infection in cystic fibrosis, 400 mg twice daily; Child 5-17 years, up to 10mg/kg 3 times daily (max. 1.2g daily)

Urinary tract infections: 100 mg twice daily

Gonorrhoea: 100 mg as a single dose

Note: Child not recommended (see cautions and contraindications above) but where benefit outweighs risk, by mouth, 10 – 30 mg/kg daily in 2 divided doses or by intravenous infusion, 8-16 mg/kg daily in 2 divided doses.

Storage: Tablet: store below 30°C in a well-closed container.

Injection: Store in a cool place (between 8 and 15°C) or at controlled room temperature (between 20 and 25°C). Protect from light and freezing.

Levofloxacin

Tablet, 250mg, 500mg

Indications: treatment of mild, moderate, or severe infections caused by susceptible organisms. Includes the treatment of community-acquired pneumonia, including multidrug resistant strains of *S.pneumoniae* (MDRSP); nosocomial pneumonia; chronic bronchitis (acute bacterial exacerbation); acute maxillary sinusitis; urinary tract infection (uncomplicated or complicated), including acute pyelonephritis caused by *E.coli*; prostatitis (chronic bacterial); skin or skin structure infections (uncomplicated or complicated); prevention of inhalational anthrax (postexposure).

Cautions: not recommended in children < 18 years of age. CNS disorders or renal dysfunction.

Drug interactions: warfarin, class Ia and class III antiarrhythmics, erythromycin, cisapride, antacids, oral electrolyte supplements, quinapril, sucralfate and some didanosine formulations

Contraindications: hypersensitivity reactions.

Side effects: dizziness, fever, headache, insomnia, abdominal pain, dyspepsia, nausea, vomiting, diarrhea, constipation, decreased vision, pharyngitis, dyspnea.

Dose and Administration: Adult: Oral:

Chronic bronchitis (acute bacterial exacerbation): 500mg every 24 hours for at least 7 days

Inhalational anthrax: 500mg every 24 hours for 60 days, beginning as soon as possible after exposure

Maxillary sinusitis (acute): 500mg every 24 hours for 10-14 days

Pneumonia:

Community-acquired: 500mg every 24 hours for 7-14 days or 750mg every 24 hours for 5 days (efficacy of 5-day regimen for MDRSP not established)

Nosocomial: 750mg every 24 hours for 7-14 days

Prostatitis (chronic bacterial): 500mg every 24 hours for 28 days

Skin infections:

Uncomplicated: 500mg every 24 hours for 7-10 days

Complicated: 750mg every 24 hours for 7-14 days

Urinary tract infections:

Uncomplicated: 250mg once daily for 3 days

Complicated, including acute pyelonephritis: 250mg every 24 hours for 10 days

Storage: store at room temperature.

Nalidixic acid

Tablet, 500 mg

Oral suspension 300 mg/vial

Indications: urinary – tract infections; shigellosis.

Cautions: see notes above; avoid in porphyria; liver disease; renal impairment; false positive urinary glucose (if tested for reducing substances); monitor blood counts, renal and liver function if treatment exceeds 2 weeks.

Drug interactions: see notes above

Side effects: see notes above; also reported toxic psychosis, weakness, increased intracranial pressure, cranial nerve palsy, and metabolic acidosis.

Dose and Administration:

Urinary tract infections: Oral:

Adult: 1g every 6 hours for 7 days, reduced in chronic infections to 500 mg every 6 hours;

Child over 3 months: maximum 50 mg/kg daily in divided doses, reduced in prolonged treatment to 30 mg/Kg daily.

Shigellosis: Oral: Adult: 1 g every 6 hours for 5 days

Child over 3 months: 15 mg/kg every 6 hours for 5 days

Patient Advice – Take on an empty stomach, preferably one hour before a meal

Storage: store at room temperature (up to 25°C) in a tight container. Protect from freezing.

Norfloxacin

Tablet, 400 mg

Indications: uncomplicated urinary tract infections and cystitis caused by susceptible gram-negative and gram-positive bacteria; sexually transmitted disease (eg, uncomplicated urethral and cervical gonorrhea) caused by *N.gonorrhoeae*; prostatitis due to *E. coli*.

Cautions: see notes above; renal impairment.

Drug interactions: see notes above.

Side effects: see notes above, also reported euphoria, anxiety, tinnitus, polyneuropathy, exfoliative dermatitis, pancreatitis, and vasculitis.

Dose and Administration:

Urinary-tract infections: 400 mg twice daily for 7 – 10 days (for 3 days in uncomplicated lower urinary tract infections)

Chronic relapsing urinary tract infections: 400 mg twice daily for up to 12 weeks; may be reduced to 400 mg once daily if adequate suppression within first 4 weeks.

Uncomplicated gonorrhea: 800 mg as a single dose.

Chronic prostatitis: 400 mg twice daily for 28 days.

Storage: at room temperature in a tight container

Ofloxacin

Tablet, 200 mg, 400 mg

Injection, 200 mg/100ml

Indications: quinolone antibiotic for the treatment of acute exacerbations of chronic bronchitis, community-acquired pneumonia, skin and skin structure infections (uncomplicated), urethral and cervical gonorrhea (acute, uncomplicated), urethritis and cervicitis (nongonococcal), mixed infections of the urethra and cervix, pelvic inflammatory disease (acute), cystitis (uncomplicated), urinary tract infections (complicated), prostatitis.

Cautions: epilepsy or other CNS diseases, renal or hepatic impairment.

Drug interactions: see notes above.

Side effects: chest pain, headache, insomnia, dizziness, fatigue, somnolence, sleep disorders, nervousness, pyrexia, rash/pruritus, diarrhea, vomiting, GI distress, abdominal cramps, flatulence, abnormal taste, xerostomia, decreased appetite, nausea, constipation, vaginitis, external genital pruritus in women, visual disturbances, pharyngitis, trunk pain.

Dose and Administration: Adult:

Chronic bronchitis (acute exacerbation), community-acquired pneumonia, skin and skin structure infections (uncomplicated): 400 mg every 12 hours for 10 days

Urethral and Cervical gonorrhea (acute, uncomplicated): 400 mg as a single dose

Cervicitis/Urethritis (nongonococcal) due to C.trachomatis, mixed infection of urethra and cervix due to C.trachomatis and N.gonorrhoeae: 300 mg every 12 hours for 7 days

Pelvic inflammatory disease (acute): 400 mg every 12 hours for 10-14 days

Cystitis (uncomplicated):

Due to E.coli or K.pneumoniae: 200 mg every 12 hours for 3 days

Due to other organisms: 200 mg every 12 hours for 7 days

UTI (complicated): 200 mg every 12 hours for 10 days

Prostatitis: 200 mg every 12 hours for 6 weeks

Storage: store tablets at room temperature.

Sparfloxacin

Tablet, 100 mg, 200 mg

Indications: bacterial exacerbation of chronic bronchitis, community acquired pneumonia.

Cautions: see notes above, renal impairment, cerebral arteriosclerosis, epilepsy.

Drug interactions: medications that prolong the QTc, interval and see notes above.

Contraindications: in patients with history of photosensitivity, not recommended for patients with ongoing proarrhythmic conditions; patients younger than 18 years of age, breast-feeding.

Side effects: see notes above and also phototoxicity, QTc – interval prolongation (irregular or slow heart rate; recurrent fainting); vaginitis.

Dose and Administrations:

Oral: Adult: 400 mg on the first day, then 200 mg every twenty four hours for a total of ten days of therapy.

Note: The recommended dose for patients with renal function impairment (creatinine clearance less than 40 ml per minute) is 400 mg on the first day, then 200 mg every forty-eight hours for a total of nine days of therapy.

Child up to 18 years of age – use is not recommended in infants, children, or adolescents since fluoroquinolones cause arthropathy in immature animals.

Storage: at room temperature.

Tetracyclines

Tetracyclines all have a broad spectrum of activity which includes Gram-positive and Gram-negative bacteria. Unlike the penicillins and aminoglycosides they are usually bacteriostatic at the concentrations achieved in the body but act similarly to the aminoglycosides by interfering with protein synthesis in susceptible organisms.

Doxycycline is a tetracycline and is a broad-spectrum antibiotic effective for conditions caused by Chlamydia, rickettsia, brucella and spirochaete, Borrelia burgdorferi (Lyme disease). It is a preferred tetracycline since it has a more favourable pharmacokinetic profile than tetracycline.

Doxycycline

Tablet, 100mg

Capsule, 100mg

Indications: respiratory-tract infections, including pneumonia and chronic bronchitis; urinary-tract infections; syphilis; chlamydia, mycoplasma, and rickettsia; prostatitis; lymphogranuloma venereum; pelvic inflammatory disease (with metronidazole); Lyme disease; brucellosis (with rifampicin); leptospirosis, scrub typhus and travellers' diarrhoea; psittacosis; cholera; melioidosis; plague; anthrax; Q fever; malaria.

Cautions: hepatic function impairment.

Drug interactions: antacids, carbamazepine, ciclosporin, oral contraceptives, ergotamine, ferrous salts, phenobarbital, phenytoin, rifampicin and warfarin.

Contraindications: pregnancy, and breast-feeding, in infants and children up to 8 years of age.

Side effects: nausea, vomiting, diarrhoea, erythema, headache, visual disturbance, hepatotoxicity, pancreatitis, pseudomembrane colitis, discolouration of infants and children's teeth, photosensitivity.

Dose and Administration: *Infections due to susceptible organisms:* Oral:

Adult and Child over 8 years: 200 mg on first day then 100 mg daily; in severe infections, 200 mg daily

Syphilis: Oral: 200–300 mg daily in 1–2 divided doses

Uncomplicated genital chlamydia, non-gonococcal urethritis: Oral: 100 mg twice daily

Louse and tick-borne relapsing fevers: Oral: 100 mg or 200 mg as a single dose

Cholera: Oral: **Adult:** 300 mg as a single dose; **Child:** over 8 years, 100 mg as a single dose.

Malaria prophylaxis: Oral: **Adult:** 100mg once a day. **Children older than 8 years of age:** 2mg per kg of body weight, up to 100mg, once a day. Prophylaxis should begin one to two days before travel to the malarious area and be continued daily during travel and for four weeks after the traveler leaves the malarious area.

Patient Advice. Capsules should be swallowed whole with plenty of fluid while sitting or standing to prevent oesophageal irritation. May be given with food to counter gastric irritation

Storage: at room temperature in a tight, light-resistant container.

Tetracycline hydrochloride

Capsules, 250mg, 500mg

Tablet, 250 mg, 500 mg (coated)

Injection, 100 mg, 250 mg, 500 mg in vial

Indications: exacerbations of chronic bronchitis; brucellosis, chlamydia, mycoplasma, and rickettsia; acne vulgaris, rosacea, typhus, gonorrhea, chancroid, syphilis, and cholera.

Cautions: caution in patients with renal function impairment.

Drug interactions: aluminium and/or magnesium containing antacids, laxatives, calcium (e.g. milk or other dairy products, eggs) and/or iron supplements, penicillines, or streptomycin.

Contraindications: pregnant or nursing women, infants and children under 8 years of age (it may also depress bone growth and cause permanent discolouration of the teeth).

Side effects: nausea, vomiting, epigastric burning and distress, flatulence and diarrhoea occur most frequently due to gastric irritation. Rarely photosensitivity, skin discoloration, blood dyscrasias may occur.

Dose and Administration: *Orally*, given 1 hour before or 2 hours after meals with adequate amounts of fluid.

Reduce dosage in renal and hepatic function impairment.

Adult:

Rickettsial infection (e.g. typhus): 1-2g daily in 2-4 divided doses for 7-10 days.

Gonorrhea (uncomplicated or disseminated) in penicillin allergies: 500mg every 6 hours daily for at least 7 days.

Chancroid: 1-2g daily in 2-4 divided doses for 7 days.

Syphilis (in penicillin allergies):

Early syphilis (of not more than 2 years duration) and Late syphilis (2 years and more): 500mg every 6 hours daily for 15 days.

Cholera: 1-2g daily in 2-4 divided doses for 48 – 72 hours.

Child (8 years and over): usually, *oral*, 25 – 50mg/ml of body weight daily in 2-4 divided doses.

Relapsing fever-

Adult: 500mg – 1g every twelve hours.

Child (8 years and over): 6.25 – 12.5mg/kg of body weight every six hours.

Adult and Child: *IV or IM:* administration given in two to four divided doses at dose levels of 2.5 to 5 mg/kg/day for patients with normal renal function depending on the severity of the infection.

Storage: at room temperature, in a tight, light-resistant container.

Note: outdated and decomposed tetracycline are toxic and may cause nephrotoxicity and skin lesion.

Chloramphenicols

Chloramphenicol was the first broad-spectrum antibacterial to be discovered; it acts by interfering with bacterial protein synthesis and is mainly bacteriostatic. Its range of activity is similar to that of tetracycline and includes *Gram-positive* and *Gram-negative* bacteria, *Rickettsia* spp., and *Chlamydiae*.

It is associated with serious haematological adverse effects and should be reserved for the treatment of severe infections, particularly those caused by *Haemophilus influenzae* and typhoid fever.

Chloramphenicol

Capsules, 250mg

Suspension, oral (palmitate), 125mg/5ml; 60ml.

Injection (sodium succinate), 1 g in vial

Indications: severe life-threatening infections, particularly those caused by *Haemophilus influenzae*, and typhoid fever; also, cerebral abscess; mastoiditis; relapsing fever; gangrene; granuloma inguinale; listeriosis; severe melioidosis; plague; psitticosis; tularaemia; Whipple disease; septicaemia; empirical treatment of meningitis

Cautions: it should not be used for the treatment of minor and undefined infections, or as a prophylaxis. Caution in patients with hepatic function impairment, blood disorder, in neonates and infants, in pregnant women, particularly those near term or in labour, and in nursing women.

Drug interactions: phenobarbital, oral contraceptives (estrogen containing), tolbutamide, chlorpropamide, penicillins, or streptomycin.

Contraindications: known hypersensitivity and/or toxic reactions to chloramphenicol.

Side effects: nausea, vomiting diarrhoea, and bone-marrow depression may occur.

Dose and Administration:

Note: A high initial dosage should not be given in the treatment of typhoid fever as sensitivity like reaction occurs. Reduce dose in hepatic and/or renal impairment.

Typhoid Fever: **Adult:** 500mg every 6 hours daily for 14 days. **Child:** 11-30kg, 250mg every 6 hours daily for 14 days. 6-10kg, 125mg every 8 hours daily for 14 days.

Typhus: **Adult:** 500mg every 6 hours for 10 days. **Child:** 50 – 75 mg/kg of body weight daily in divided doses every 6 hours for 10 days.

Meningitis: *I.V.*: infants > 30 days and **Child:** 50 - 100 mg/kg/day divided every 6 hours.

Other infections: I.V.:

Adult: 50 - 100 mg/kg/day in divided doses every 6 hours; maximum daily dose: 4 g/day.

Infant > 30 days and **Child:** 50 - 75 mg/kg/day divided every 6 hours; maximum daily dose: 4 g/day.

Storage: at room temperature, in a tight container.

Thiamphenicol

Capsule, 250 mg

Tablet, 250 mg

Indications, Cautions, Drug interactions and Side effects see under chloramphenicol.

Dose and Administration: *Oral:*

Adult: 1.5g daily; up to 3g daily has been given initially in severe infections.

Child: 30-100mg/kg daily.

Gonorrhoea: oral dose ranged from 2.5g daily for 1 or 2 days through to 2.5g on the first day followed by 2g daily on each of 4 subsequent days.

Miscellaneous**Clindamycin**

Capsule, 75 mg, 150 mg

Injection, 150 mg/ml in ampoule

Oral solution, 15 mg/ml

Indications: staphylococcal bone and joint infections; peritonitis, endocarditis prophylaxis; alternate treatment for toxoplasmosis (see section 7.4.5).

Cautions: discontinue immediately if diarrhea or colitis develop; hepatic and renal impairment, neonates and infants; elderly; pregnancy; breastfeeding.

Drug interactions: alcuronium, neostigmine, pyridostigmine, vecuronium.

Contraindications: hypersensitivity to clindamycin.

Side effects: diarrhea, nausea, vomiting, abdominal discomfort, antibiotic - associated colitis, rashes, urticaria, and rarely anaphylaxis, erythema multiforme, exfoliative and vesiculobullous dermatitis, jaundice and altered liver function tests; neutropenia, eosinophilia, agranulocytosis, and thrombocytopenia, pain, indurations, and abscess after IM injection; thrombophlebitis after IV injection.

Dose and Administration: *Osteomyelitis or peritonitis:*

Oral:

Adult: 150 - 300 mg every 6 hours; up to 450 mg every 6 hours in severe infections.

Child: 3 - 6 mg/kg every 6 hours.

IM or IV infusion:

Adult: 0.6 - 2.7 g daily in 2 - 4 divided doses, increased up to 4.8 g daily in life-threatening infections; single doses over 600 mg by IV infusion only; single doses by IV infusion not to exceed 1.2 g;

Neonates: 15 - 20 mg/kg daily.

Child over 1 month: 15 - 40 mg/kg daily in 3 - 4 divided doses; severe infections, at least 300 mg daily, regardless of weight.

Endocarditis prophylaxis (for procedures under local or no anaesthetic):

Oral:

Adult: 600 mg, 1 hour before procedure.

Endocarditis prophylaxis (for procedures under general anaesthetic):

IV infusion:

Adult: 300 mg over at least 10 minutes, at induction or 15 minutes before procedure, then 150 mg 6 hours later by mouth or infusion.

Storage: store at room temperature.

Metronidazole

Tablet, 250mg

Intravenous infusion, 5mg/ml in 100ml

Indications: treatment of anaerobic infection, bone and joint infection, meningitis, bacterial endocarditis, prophylaxis of perioperative infection during colorectal surgery, lower respiratory tract infection including pneumonia, empyema and lung abscess, bacterial septicemia, skin and soft tissue infection, inflammatory bowel disease, antibiotic associated colitis, *Helicobacter pylori* associated duodenal ulcer; see also section 1.2.

Cautions: disulfiram like reaction with alcohol; hepatic impairment and hepatic encephalopathy, pregnancy; breastfeeding; clinical and laboratory monitoring in courses lasting longer than 10 days; see also interactions.

Note: - Avoid Alcohol. The drug may cause dizziness.

Drug interactions: phenytoin, coumarin or indandion derivative anticoagulant, warfarin, disulfiram, alcohol, cimetidine, fluorouracil, lithium, phenobarbitone.

Contraindications: chronic alcohol dependence

Side effects: nausea, vomiting, unpleasant metallic taste, furred tongue and gastrointestinal disturbances; rarely headache, drowsiness, dizziness, ataxia, darkening of urine, erythema multiform, pruritus, urticaria, angioedema, and anaphylaxis; abnormal liver function tests, hepatitis, jaundice, thrombocytopenia, aplastic anaemia, myalgia, arthralgia, peripheral neuropathy, epileptiform seizures, leucopenia, on prolonged or high dosage regimens

Dose and Administration:

Adult:

Antibacterial (systemic), anaerobic infections: Oral: 7.5mg (base) per kg of body weight up to a maximum of 1 gm, every 6 hours for 7 days or longer; *IV-infusion*, 15mg (base) per kg of body weight initially, then 7.5mg per kg of body weight up to a maximum of 1gm, every six hours for seven days or longer;

Inflammatory bowel disease: Oral: 500mg (base) four times a day.

Antibiotic associated colitis: Oral: 500mg (base) three or four times a day.

Helicobacter - pylori associated gastritis or duodenal ulcer: Oral: 500mg (base) three times a day with amoxicillin for one to two weeks.

Perioperative infections, colonic (prophylaxis): IV infusion: 15mg (base) per kg of body weight one hour prior to start of surgery and 7.5mg per kg of body weight six and twelve hours after the initial dose.

Child:

Anaerobic infection: Oral: 7.5mg (base) per kg of body weight every 6 hours, or 10mg per kg of body weight every 8 hours.

Anaerobic infection - for preterm infants: IV infusion: 15mg per kg of body weight (base) as an initial dose, then 7.5mg per kg of body weight every 12 hours starting 48 hours after the initial dose. Term infants, *IV infusion*, 15mg (base) per kg of body weight as an initial dose, then 7.5mg per kg of body weight every 12 hours starting 24 hours after the initial dose. Infants greater than 7 days of age and children - *IV infusion*, 15mg (base) per kg of body weight as an initial dose, then 7.5 mg per kg of body weight every 6 hours.

Storage: at room temperature, in a well closed, light resistant container. Protect from freezing

Nitrofurantoin

Tablet, 50mg, 100mg

Capsule (macrocrystal), 50mg, 100mg

Oral suspension, 0.5%

Indications: prophylaxis and treatment of urinary tract infection.

Cautions: hypersensitive to nitrofurantoin, diabetes mellitus, electrolyte imbalance, vitamin B and folate deficiency, pulmonary disease, hepatic impairment, peripheral neuropathy.

Drug interactions: hemolytic, neurotoxic medication, probenecid, sulfapyrazone.

Contraindications: impaired renal function; infants less than 3 months, pregnancy, during breastfeeding; glucose 6 phosphate dehydrogenase (G6PD) deficiency; porphyria.

Side effects: pneumonitis (chills, chest pain, cough, fever, troubled breathing, abdominal or stomach pain or upset, diarrhoea, loss of appetite, nausea, vomiting), hematology reactions, specifically granulocytopenia (sore throat and fever) or megaloblastic anemia (unusual tiredness or weakness), neurotoxicity (dizziness, drowsiness, headache, unusual tiredness or weakness), polyneuropathy (numbness or tingling, or burning of face or mouth, unusual muscle weakness, haemolytic anaemia (pale skin, unusual tiredness or weakness), hepatitis (yellow eyes or skin), hypersensitivities (skin rash, itching, arthralgia, fever, chills), rust yellow to brown discoloration of urine.

Dose and Administration: *Oral:*

Adult: 50 to 100mg every 6 hours. Maximum up to 600 mg daily, or up to 10mg per kg of body weight daily.

Note: - Prophylaxis – 50 to 100mg once a day at bedtime.

Child: infants and children 1 month of age and over, 0.75 to 1.75mg per kg of body weight every 6 hours.

Note: - Prophylaxis - 1mg per kg of body weight once a day at bedtime. Continue medicine for full time of treatment.

Storage: store at room temperature in a tight, light resistant container.

Pentamidine Isethionate

Nebulizer solution, 300 mg/vial

Indications: treatment and prevention of pneumonia caused by pneumocystis carinii (PCP).

Cautions: diabetes mellitus, renal or hepatic dysfunction; hypertension or hypotension; leukopenia, thrombocytopenia, asthma, hypo/hyperglycemia.

Drug interactions: delavirdine, flunconazole, fluvoxamine, gemfibrozil, isoniazid, omeprazole, and ticlopidine, cisapride, sparfloxacin, pimozide, and type Ia and type III antiarrhythmics.

Contraindications: hypersensitivity to pentamidine isethionate.

Side effects: chest pain, rash, wheezing, dyspnea, cough, pharyngitis, bitter or metallic taste, hypoglycemia, and renal insufficiency.

Dose and Administration: *prevention of PCP pneumonia: Inhalation:*

Adult: 300 mg every 4 weeks via Respigard[®] II nebulizer.

Child: (aerosolized pentamidine in children ≥ 5 years): 300 mg/dose given every 3 - 4 weeks via inhaler (8 mg/kg dose has also been used in children < 5 years).

Storage: store intact vials at controlled room temperature and protect from light.

Sodium Fusidate

Powder for Injection (as Diethanolamine Fusidate), 580 mg in vial.

Indications: treatment of severe staphylococcal infections (osteomyelitis, pneumonia, septicaemia), in combination with another antistaphylococcal agent, such as cloxacillin, to prevent the emergence of resistance.

Cautions: neonates, pregnancy and breast-feeding.

Drug interactions: hydrocortisone.

Contraindications: hepatic dysfunction.

Side effects: hepatotoxicity, vomiting, diarrhea, epigastric pain, anorexia, skin rashes and pruritus.

Dose and Administration: *IV: Adult:* over 50kg, 500mg 8 hourly; under 50kg, 18-21mg/kg/day in 3 divided doses.

Child: *IV*, infused over 2-8 hours, 6-7mg/kg/dose (maximum dose 500mg) 8 hourly.

Storage: store at temperature of 2-8 °C. Protect from light.

Spectinomycin

Injection, 2g in vial

Indications: uncomplicated and disseminated gonorrhoea; adult and neonatal gonococcal conjunctivitis; chancroid

Note: - It is not indicated for pharyngeal gonorrhea.

Cautions: renal impairment, pregnancy and breastfeeding.

Drug interactions: lithium, botulinum toxin.

Contraindications: hypersensitive to spectinomycin.

Side effects: hypersensitivity (chills, fever, itching or redness of the skin), dizziness, nausea, vomiting, abdominal cramp.

Dose and Administration:

Uncomplicated gonococcal infections and chancroid: deep IM injection: Adult: 2g as a single dose (may be increased to 4g as a single dose divided between 2 injection sites in difficult to treat cases and where there is known antibiotic resistance)

Disseminated gonococcal infections: deep IM injection: Adult: 2g twice daily for 7 days.

Neonatal gonococcal conjunctivitis: deep IM injection: Neonate 25 mg/kg (maximum 75mg) as a single dose.

Storage: at room temperature.

Sulphamethoxazole and Trimethoprim

Tablet (pediatric), 100mg + 20mg; (adult), 400mg + 80mg, 800mg+160mg

Mixture, 200mg + 40mg in each 5ml

Injection, 400mg + 80mg in each 5ml ampoule

Indications: prophylaxis and treatment of *Pneumocystis carinii* infections. Treatment of nocardiosis, and of urinary tract, respiratory tract and prostatic infections caused by susceptible organisms. Also used in treatment of typhoid/paratyphoid fevers, and in the treatment and prophylaxis of toxoplasmosis and *Isospora belli* diarrhea.

Cautions: elderly, renal and hepatic function impairment, photosensitivity, Glucose-6-phosphate dehydrogenase (G6PD) deficiency; maintain adequate fluid intake (to avoid crystalluria); avoid in blood disorders (unless under specialist supervision); monitor blood counts and discontinue immediately if blood disorder develops; rash – discontinue immediately; predisposition to folate deficiency; asthma; pregnancy; breastfeeding.

Drug interactions: coumarin or indandione derivative anticoagulant, hydantoin, oral hypoglycemics, hemolytics, hepatotoxic medication, methenamine, methotrexate, folate antagonists.

Contraindications: infants up to two months of age, in patients who are allergy to sulfonamide, furosemide, thiazide diuretics, sulfonylureas, carbonic anhydrase inhibitors or trimethoprim.

Side effects: hypersensitivity (fever, itching, skin rash), photosensitivity (increased sensitivity of skin to sunlight), blood disorder (sore throat, fever, pale skin), unusual bleeding or bruising, unusual tiredness or weakness), hepatitis (yellow eyes or skin), Steven's Johnson syndrome, aching joints and muscles, redness, blistering, peeling, or loosening of the skin, unusual tiredness or weakness, toxic epidermal necrosis (difficulty in swallowing, redness, blistering, peeling, loosening of the skin), dizziness, headache, GIT disturbance, loss of appetite, nausea or vomiting.

Dose and Administration:

Adult:

Oral: 160mg of trimethoprim and 800mg of sulphamethoxazole every 12 hours may be increased to 320/1600 mg 12 hourly in severe infections.

IV infusion: 160/800 mg 12 hourly. Each 80/400mg (5ml) to be diluted in 125ml 5% glucose or 0.9% sodium chloride solution or infused over 1-1.5 hours.

Cerebral toxoplasmosis: 320/1600mg twice daily for 4 weeks, then 160/800 mg twice daily for 3 months.

Isospora belli: 160/800 mg 6 hourly for 10 days.

Primary prophylaxis in HIV-infection: *Oral:* 160/800 mg daily. Lower doses (80/400 mg daily or 160/800 mg 3 times a week) have been shown to be effective for *Pneumocystis pneumonia* and are better tolerated.

Child:

Oral: 2 months to 5 months, 20/100mg; 6months -5 years, 40/200 mg; 6-12 years, 80/400mg, 12 hourly.

IV infusion: 6/30 mg/kg/day in 2 divided doses, increased to 9/45 mg/kg/day in severe infections.

Pneumocystis carinii pneumonia:

Treatment: *Oral or IV infusion: Adult and Child:* sulphamethoxazole up to 100mg/kg daily with trimethoprim up to 20mg/kg daily in 2-4 divided doses for 14-21 days.

Prophylaxis: *Oral: Adult and Child:* sulphamethoxazole 25mg/kg with trimethoprim 5 mg/kg in 2 divided doses on alternate days (3 times a week).

Note: - For oral, continue medicine for full time of treatment, avoid too much sun or use of sun lamp. Avoid IM administration.

Storage: at room temperature, in a tight, light-resistant container, protect from freezing.

Sulphasalazine

Tablet (e/c), 500 mg

See section 6.1

Trimethoprim

Injection, 20 mg/ml

Tablet, 100 mg, 200 mg

Suspension, 50 mg/ml

Indications: acute uncomplicated urinary tract infections, respiratory tract infections and chronic prostatitis. Alternative to co-trimoxazole for *Pneumocystis* pneumonia, in combination with dapsone.

Cautions: impaired renal or hepatic function or with possible folate deficiency.

Drug interactions: digoxin, phenytoin or phenobarbital, oral contraceptives, zidovudine and lamivudine.

Contraindications: use in neonates.

Side effects: skin rashes, pruritus, nausea, epigastric pain and glossitis, hyperkalaemia, bone marrow depression (with leukopenia, thrombocytopenia and megaloblastic anaemia).

Dose and Administration: *Oral:*

Adult: 100 mg every 12 hours or 200 mg every 24 hours for 10 days; longer treatment periods may be necessary for prostatitis (i.e, 4 - 16 weeks); in the treatment of pneumocystis carinii pneumonia; dose may be as high as 15 - 20 mg/kg/day in 3 - 4 divided doses.

Child: 4 mg/kg/day in divided doses every 12 hours.

IV: Acute infection: **Adult:** 200mg every 12 hours.

Child under 12 years: 8mg/kg daily in 2-3 divided doses.

Storage: store at room temperature and protect from light

Vancomycin

Injection, 500 mg in vial

Indications: generally reserved for the treatment of infections due to cloxacillin - resistant staphylococci and enterococci; also as an alternative agent for prophylaxis and treatment of endocarditis in penicillin allergic patients.

Cautions: renal impairment.

Drug interactions: ototoxic and nephrotoxic agents, e.g. aminoglycosides.

Contraindications: hearing abnormalities.

Side effects: nephrotoxicity including renal failure and interstitial nephritis, ototoxicity (discontinue if tinnitus occurs); blood disorders; nausea, chills, fever, eosinophilia, anaphylaxis, rashes, including exfoliative dermatitis, Stevens Johnson syndrome, and vasculitis; phlebitis; on rapid infusion, severe hypotension (with shock, cardiac arrest), wheezing, dyspnoea, urticaria, pruritus, flushing of the upper body ('red man' syndrome), pain and muscle spasm of back and chest.

Dose and Administration: *IV infusion:*

Adult: over at least 1 hour, 500 mg 6 hourly or 1 g 12 hourly.

Child: over at least 1 hour, 10 mg/kg 6 hourly or 20 mg/kg 12 hourly.

Neonates: under 1 week old, initially 15 mg/kg followed by 10 mg/kg 12 hourly; 1 week - 1 month old, 15 mg/kg followed by 10 mg/kg 8 hourly.

Storage: vancomycin reconstituted IV solutions are stable for 14 days at room temperature or refrigeration.

7.1.3. Antituberculars

Tuberculosis is a chronic infectious disease caused primarily by *Mycobacterium tuberculosis* or sometimes *M. bovis*; the closely related form *M. africanum* has occasionally been implicated as a cause of human tuberculosis. Infection is usually due to inhalation of infected droplet nuclei, and the lung is generally the first organ affected, but the primary infection is usually asymptomatic.

Drug treatment for clinical infection always involves multi drug regimens, chosen to provide early bactericidal activity (activity against actively dividing mycobacteria), and sterilizing activity (activity against non-dividing, semi-dormant organisms), and to prevent resistance. Treatment is divided into 2 phases, an initial intense phase involving daily administration of 3 or more drugs for 8 weeks, followed by a continuation phase for 4 or more months usually 2 drugs are used in the continuation phase and they may be administered daily or 2 or 3 times per week. The continuation phase may be extended beyond 4 months when treating extrapulmonary tuberculosis or AIDS – associated tuberculosis.

Direct observation of therapy (DOT) is considered essential to ensure compliance in the initial phase and also useful in the continuation phase if patients are receiving rifampicin. The six antituberculosis drugs, isoniazid, rifampicin, pyrazinamide, streptomycin, (which are bactericidal) ethambutol and thioacetazone (which are bacteriostatic) are used in various combinations as part of WHO recommended treatment regimens

In supervised regimens change of drug regimen should be considered only if the patient fails to respond after 5 months of DOTS.

Isoniazid, rifampicin, and Pyrazinamide are components of all antituberculosis drug regimens currently recommended by WHO. Unsupervised and alternative regimens as set out in the following tables may be administered as specified.

Recommended 6-month treatment regimens for tuberculosis^a

Drug	Initial phase (2 months)	Continuation phase (4 months)
Isoniazid	5mg/kg daily	5mg/kg daily
Rifampicin	10mg/kg daily	10mg/kg daily
Pyrazinamide	25mg/kg daily	
together with		
Streptomycin	15mg/kg daily	
Or		
Ethambutol	<u>15mg/kg daily</u>	
Isoniazid	10mg/kg 3 times weekly	10mg/kg 3 times weekly
Rifampicin	10mg/kg 3 times weekly	10mg/kg 3 times weekly
Pyrazinamide	35mg/kg 3 times weekly	
together with		
Streptomycin	15mg/kg 3 times weekly	
Or		
Ethambutol	30 mg/kg 3 times weekly ^c	

Recommended 8-month treatment regimen for tuberculosis^a

Drug	Initial phase (2 months)	Continuation phase (6 months)
Isoniazid	5mg/kg daily	5mg/kg daily
Rifampicin	10mg/kg daily	
Pyrazinamide	30mg/kg daily	
Thioacetazone		2.5mg/kg daily
together with		
Streptomycin	15mg/kg daily	
Or		
Ethambutol	25mg/kg daily ^b	

^aUnless otherwise indicated, doses are suitable for both adults and children

^b15mg/kg for children

^cNot suitable for children

World wide, an important predisposing cause of immuno suppression leading to tuberculosis is human immunodeficiency virus (HIV) infection. It increases susceptibility to primary infection and increases the reactivation rate of tuberculosis. Preventative antituberculosis therapy for such persons is recommended.

Chemoprophylaxis with isoniazid can prevent the development or clinically apparent disease in persons in close contact with infectious patients, and in other persons at high risk particularly those who are immuno deficient.

Monitoring: since isoniazid, rifampicin and Pyrazinamide are associated with liver toxicity, hepatic function should be checked before treatment with these

drugs. Those with preexisting liver disease or alcohol dependence should have frequent checks particularly in the first 2 months. If there is no evidence of liver disease (and pre-treatment liver function is normal), further checks are only necessary if the patient develops fever, malaise, vomiting, jaundice or unexplained deterioration during treatment.

Renal function should be checked before treatment with antituberculous drugs and appropriate dosage adjustments made. Streptomycin or Ethambutol should preferably be avoided in patients with renal impairment, but if used, the dose should be reduced and the plasma – drug concentration monitored. Visual acuity should be tested before Ethambutol is used.

Isoniazid is cheap and highly effective. It should always be indicated in any antituberculous regimen unless there is a specific contraindication. Its only common side effect is peripheral neuropathy which is more likely to occur where there are pre-existing risk factors such as diabetes, alcohol dependence, chronic renal failure, malnutrition and HIV infection. In these circumstances pyridoxine 10 mg daily (or 20 mg daily if suitable product not available) should be given prophylactically from the start of treatment. Other side effects such as hepatitis and psychosis are rare.

Rifampicin, a rifamycin, is a key component of any antituberculous regimen. Like isoniazid it should always be included unless there is a specific contraindication. During the first two months (initial phase) of rifampicin administration transient disturbance of liver function with elevated serum transaminases is common but generally does not require interruption of treatment. Occasionally more serious liver toxicity requires a change of treatment particularly in those with preexisting liver disease (important: see monitoring above). Rifampicin induces hepatic enzymes which accelerate the metabolism of several drugs including oestrogens, corticosteroids, phenytoin, sulphonylureas, and anti-coagulants. The effectiveness of oral contraceptives is reduced and alternative family planning advice should be offered.

Pyrazinamide is a bactericidal drug only active against intracellular dividing forms of *Mycobacterium tuberculosis*; it exerts its main effect only in the first two or three months. It is particularly useful in tuberculous meningitis because of good meningeal penetration. It is not active against *M. Bovis*. Serious liver toxicity may occasionally occur.

Ethambutol is included in a treatment regimen if isoniazid resistance is suspected, it can be omitted if the risk of resistance is low.

Side effects of Ethambutol are largely confined to visual disturbances in the form of loss of acuity, colour blindness, and restriction of visual fields. These toxic effects are more common where excessive dosage is used or if the patient's renal function is impaired. Early discontinuation of the drug is almost always followed by recovery of eyesight. Patients who cannot understand warnings about visual side effects should, if possible, be given an alternative drug. In particular, Ethambutol should be used with caution in children until they are at least 5 years old and capable of reporting symptomatic visual changes accurately.

Rifabutin, ethionamide, cycloserine and capreomycin considered as a second-line agent for use in multiple-drug regimens for the treatment of active tuberculosis. Rifabutin is a broad-spectrum, semisynthetic rifamycin antibiotic, similar to rifampicin. It is active against *M. tuberculosis* and is also used in the treatment of infections with non-tuberculous mycobacteria. A high degree of cross-resistance exists between rifampicin and rifabutin. Rifabutin is a less potent hepatic enzyme inducer than rifampicin, and may be preferred in patients on certain antiretroviral therapy, e.g. protease inhibitors.

Ethionamide although chemically related to isoniazid, cross-resistance does not occur. It penetrates the CNS well and may be bacteriostatic or bactericidal, depending on the concentration at the site of infection.

Cycloserine is bacteriostatic and is used in combination with other second-line agents, as it does not share cross-resistance with other tuberculosis drugs.

Capreomycin

Powder for injection, 1 g/vial

Indications: treatment of tuberculosis in conjunction with at least one other antituberculosis agent.

Cautions: renal insufficiency or pre-existing auditory impairment, elderly, use with non-antituberculous drugs (i.e., aminoglycoside antibiotics).

Contraindications: hypersensitivity to capreomycin sulfate.

Drug interactions: aminoglycosides (e.g., Streptomycin).

Side effects: ototoxicity, tinnitus, nephrotoxicity, eosinophilia, acute tubular necrosis, Bartter's syndrome, hypersensitivity (urticaria, rash, fever), hypokalemia, leukocytosis, pain, induration, and bleeding at injection site, vertigo.

Dose and Administration: *IM, I.V.*

Adult: 1 g/day (not to exceed 20 mg/kg/day) for 60 - 120 days, followed by 1g 2 - 3 times/week.

Infant and Child: 15 - 30 mg/kg/day, up to 1g/day maximum

Storage: store at room temperature.

Cycloserine

Capsule, 250 mg

Indications: in combination with other second- line drugs for treating tuberculosis resistant to first- line agents.

Cautions: epilepsy, depression, severe anxiety, psychosis, severe renal insufficiency, chronic alcoholism.

Drug interactions: alcohol, isoniazid, ethionamide and phenytoin.

Contraindications: hypersensitivity to cycloserine.

Side effects: cardiac arrhythmia, drowsiness, headache, dizziness, vertigo, seizure, confusion, psychosis, paresis, coma, rash, vitamin B12 deficiency, folate deficiency, liver enzymes increased, tremor.

Dose and Administration: *Oral:*

Adult: Initial: 250 mg every 12 hours for 14 days, then administer 500 mg to 1g/day in 2 divided doses for 18 - 24 months (maximum daily dose: 1 g).

Child: 10 - 20 mg/kg/day in 2 divided doses up to 1000 mg/day for 18 - 24 months.

Storage: store at room temperature.

Ethambutol

Tablet, 100mg, 400mg

Indications: tuberculosis, in combination with other drugs (see notes and tables above)

Cautions: visual disturbances - ocular examination recommended before and during treatment; reduce dose in renal impairment and monitor plasma concentration: elderly; pregnancy; breastfeeding.

Contraindications: optic neuritis, poor vision, children under at least 6 years of age.

Side effects: optic neuritis, red/green colour blindness, peripheral neuritis, rarely rash, pruritus, urticaria, and thrombocytopenia.

Dose and Administration:

Tuberculosis (initial phase of combination therapy; see notes and tables above):

Oral: **Adult** 15mg/kg daily or 30 mg/kg 3 times a week; **Child** 15mg/kg daily.

Storage: at room temperature, in a well-closed containers. Protect from light, moisture, and excessive heat.

Ethionamide

Tablet, 250 mg

Indications: tuberculosis therapy in combination with other agents.

Cautions: depression, psychiatric illness, chronic alcoholism, epilepsy, hypothyroidism, diabetes.

Drug interactions: isoniazide, cycloserine and terizidone.

Contraindications: hypersensitivity, severe hepatic disease.

Side effects: nausea, vomiting, anorexia, metallic taste, abdominal discomfort, diarrhoea and weight loss, seizures, pellagra-like encephalopathy responsive to niacin, acute psychosis, anxiety and depression, optic neuritis, and peripheral neuropathy responsive to pyridoxine, hepatotoxicity.

Dose and Administration: *Oral:*

Adult: 15 - 20 mg/kg/day as a single dose; Maximum 1 g/day.

Child: over 10 years, as for adults. Under 10 years, 10 mg/kg/day, increased gradually to 15 mg/kg/day, up to 20 mg/kg/day (maximum 750mg daily).

Storage: store at room temperature.

Isoniazid

Tablet, 100mg, 300mg

Injection, 100mg/ml in 10ml ampoule

Indications: tuberculosis treatment, in combination with other drugs (see notes and tables above); tuberculosis prophylaxis.

Cautions: hepatic impairment; renal impairment; slow acetylator status (increased risk of side effects); epilepsy; history of psychosis; alcohol dependence, malnutrition, diabetes mellitus, HIV infection (risk of peripheral neuritis); pregnancy and breast-feeding; porphyria

Drug interactions: carbamazepine, ethosuximide, Phenytoin.

Contraindications: drug induced hepatic disease.

Side effects: nausea, vomiting, constipation, dry mouth; peripheral neuritis with high doses (pyridoxine prophylaxis, see notes above), optic neuritis, convulsions, psychotic episodes, vertigo; hypersensitivity reactions including fever, erythema multiforme, purpura; blood disorders including agranulocytosis, haemolytic anaemia, aplastic anaemia; hepatitis (especially over age of 35 years); systemic lupus erythematosus-like syndrome, pellagra, hyperreflexia, difficulty with micturation, hyperglycaemia, and gynaecomastia reported.

Dose and Administration:

Tuberculosis, treatment (combination therapy; see also notes and tables): Oral: **Adult** and **Child:** 5mg/kg (4-6 mg/kg) daily (maximum, 300 mg daily), or 10mg/kg 3 times weekly.

Tuberculosis, treatment in critically ill patients unable to take oral therapy (combination therapy): IM: **Adult:** 200 - 300 mg as single daily dose; **Child:** 10 - 20 mg/kg daily.

Tuberculosis, prophylaxis: Oral: **Adult:** 300mg daily for at least 6 months; child 5mg/kg daily for at least 6 months.

Note: - isoniazid should be taken on an empty stomach; if taken with food to reduce gastrointestinal irritation, oral absorption and bioavailability may be impaired.

Storage: at room temperature, in a well closed, light resistant containers.

Isoniazid +Ethambutol

Tablet, 150mg + 400mg

Indications: tuberculosis, in combination with other drugs (see notes and tables above)

Cautions: see ethambutol and isoniazid

Drug interactions: see ethambutol and isoniazid

Contraindications: preparation not suitable for use in children; see ethambutol and isoniazid.

Side effects: see ethambutol and isoniazid

Dose and Administration:

*Tuberculosis, continuation phase of 8-month regimen in place of thioacetazone with isoniazid (see notes and tables): Oral: **Adult:** ethambutol hydrochloride 800mg and isoniazide 300 mg daily.*

Storage: at room temperature, in a well closed, light resistant container.

Pyrazinamide

Tablet, 500mg

Indication: tuberculosis, in combination with other drugs (see notes and tables above)

Cautions: hepatic impairment (monitor hepatic function); renal impairment; diabetes mellitus (monitor blood glucose - may change suddenly); increased uric acid level in urine; breast-feeding.

Note: - Patients or their carers should be told how to recognize signs of liver disorders and advised to discontinue treatment and seek immediate medical attention if symptoms such as persistent nausea, Vomiting, malaise or jaundice develop.

Drug interactions: uricosurics (probenecid, sulfinpyrazone)

Side effects: hepatotoxicity including fever, anorexia, hepatomegaly, jaundice, liver failure; nausea, vomiting; arthralgia; gout; sideroblastic anaemia; urticaria; skin flushing.

Contraindications: severe hepatic impairment; porphyria.

Dose and Administration:

Tuberculosis (initial phase of combination therapy; see notes and tables above): Oral:

Adult and child 25-mg/kg daily or 35 mg/kg 3 times weekly.

Storage: at room temperature, in a well closed container.

Rifabutin

Capsule, 150 mg.

Indications: treatment of pulmonary tuberculosis in combination with other agents. Prophylaxis of *M. avium-intracellulare complex (MAC)*; treatment of non-tuberculous mycobacteria.

Cautions: severe hepatic or renal dysfunction.

Drug interactions: clarithromycin, azithromycin, ciprofloxacin, fluconazole, isoniazid, indinavir, nelfinavir, ritonavir, nevirapine and efavirenz.

Contraindications: hypersensitivity to rifamycins.

Side effects: rash, gastrointestinal intolerance (nausea, vomiting, anorexia, abdominal pain and diarrhea), headache, and hematological effects (leucopenia, neutropenia, thrombocytopenia and anemia), hepatotoxicity. Hypersensitivity reactions (flu-like syndrome, chest pain, eosinophilia, bronchospasm, shock) are reported rarely.

Dose and Administration: Oral: Adult:

Tuberculosis, in combination with other antituberculosis agent: 300 - 450 mg daily.

Non- tuberculous mycobacteria treatment: 450 - 600 mg daily.

Non-tuberculous mycobacteria prophylaxis: 300 mg daily.

Storage: store at a temperature not exceeding 40 °C.

Rifampicin

Capsule, 150mg, 300mg, 600mg

Syrup, 20mg/5ml

Powder for injection (sodium) 300mg, 600mg in vial

Indications: tuberculosis, in combination with other drugs (see notes and tables above); leprosy.

Cautions: reduce dose in hepatic impairment, liver function tests and blood counts required in liver disorders, elderly, and on prolonged therapy; renal impairment (if dose above 600 mg daily); pregnancy; breastfeeding; porphyria; discolour soft contact lenses.

Note: Advise patients on oral contraceptives to use additional means.

Resumption of rifampicin treatment after a long interval may cause serious immunological reactions, resulting in renal impairment, haemolysis, or thrombocytopenia. Discontinue permanently if serious adverse effects occur.

Patients or their carers should be told how to recognize signs of liver disorders and advised to discontinue treatment and seek immediate medical attention if symptoms such as persistent nausea, vomiting, malaise or jaundice develop.

Drug interactions: azathioprine, ciclosporin, contraceptives, dexamethasone, fluconazole, fludrocortisone, glibenclamide, haloperidol, hydrocortisone, indinavir, levonorgestrel, lopinavir, medroxyprogesterone, nelfinavir, nifedipine, norethisterone, phenytoin, prednisolone, guanidine, saquinavir, verapamil, warfarin.

Contraindications: hypersensitivity to rifamycins, jaundice.

Side effects: severe gastrointestinal disturbances including anorexia, nausea, vomiting and diarrhea (antibiotic associated colitis reported); rashes, fever, influenza-like syndrome and respiratory symptoms, collapse, shock, haemolytic anaemia, acute renal failure, and thrombocytopenic purpura-more frequent with intermittent therapy; alterations of liver function jaundice and potentially fatal hepatitis (dose related; do not exceed maximum dose of 600 mg daily); stains body fluid (urine, tears, saliva, and sputum) orange - red.

Dose and Administration:

*Tuberculosis (combination therapy; see notes and tables above): Oral: **Adult and Child** 10mg/kg daily or 3 times weekly (maximum dose, 600mg daily)*

Note: - take dose at least 30 minutes before a meal, as absorption is reduced when taken with food.

Storage: below 40, in a tight, light - resistant container.

Rifampicin + Isoniazid

Tablet, 150mg + 100mg, 300mg + 150mg

Capsule, 150mg + 100mg

Indications: tuberculosis (see notes and tables above)

Cautions: preparation not suitable for use in children; see under rifampicin, and isoniazid

Drug interactions, Contraindications, Side effects; see under rifampicin, and isoniazid

Dose and Administration:

Tuberculosis, 6 - month regimen (combination therapy; see notes and tables): Oral:

Adult: 10mg/kg (rifampicin) and 5mg/kg (isoniazid) daily.

*Tuberculosis, 6-month regimen (combination therapy; see notes and tables): Oral: **Adult***

10mg/kg (rifampicin) and 10mg/kg (isoniazid) 3 times a week.

Rifampicin + Isoniazid + Pyrazinamide

Tablet, 150mg + 75mg + 400mg

Indications: tuberculosis, in combination with other drugs (see notes and tables above)

Cautions; Side effects, Drug interactions; see Rifampicin, Isoniazid, and Pyrazinamide

Contraindications: preparations not suitable for use in children; see rifampicin, isoniazid, and Pyrazinamide.

Dose and Administration:

Tuberculosis, initial phase of 6 - month treatment regimens (see notes and tables above):

*Oral: **Adult:*** rifampicin 10mg/kg, isoniazid 5mg/kg, and Pyrazinamide 25 mg/kg daily or rifampicin 10mg/kg, isoniazid 10mg/kg and Pyrazinamide 35mg/kg 3 times a week.

Rifampicin + Isoniazid + Pyrazinamide + Ethambutol

Tablet, 150mg + 75mg + 400mg + 275mg

Indications: tuberculosis (see notes and tables above)

Cautions, Side effects, Drug interactions, Contraindications; see rifampicin, isoniazid, Pyrazinamide and Ethambutol.

Dose and Administration:

Tuberculosis, induction phase of 6-month regimen (see notes and tables above): Oral:

Adult: rifampicin 10mg/kg, isoniazid 5mg/kg, Pyrazinamide 25mg/kg, and Ethambutol hydrochloride 15mg/kg daily.

Streptomycin Sulphate

Powder for injection, 1g, 5g bases in vial

Indications: tuberculosis, in combination with other drugs (see notes and tables above)

Cautions: children - painful injection, avoid use if possible, renal impairment, infants, and elderly (dosage adjustment), and monitor renal, auditory, and vestibular function, and plasma streptomycin concentrations.

Drug interactions: alcuronium, ciclosporin, cisplatin, furosemide, neostigmine, pyridostigmine, suxamethonium, and vecuronium.

Contraindications: hearing disorders; myasthenia gravis, pregnancy.

Side effects: vestibular and auditory damage; nephrotoxicity; hypersensitivity reactions - withdraw treatment; paraesthesia of mouth, rarely, hypomagnesaemia on prolonged therapy; antibiotic associated colitis; also

nausea, vomiting, rash; rarely, haemolytic anaemia, aplastic anaemia, agranulocytosis, thrombocytopenia; pain and abscess at injection site.

Dose and Administration:

Tuberculosis (initial phase of combination therapy; see notes and table above): deep IM injection, Adult and child 15mg/kg daily or 3 times a week (patients over 60 years or those weighing less than 50kg may not tolerate doses above 500 - 750mg daily)

Storage: at room temperature protect from light.

Note: Reconstituted solutions may vary in colour from colourless to yellow and may darken on exposure to light but potency is not affected for 48 hours at room temperature and for up to 14 days when refrigerated.

7.1.4. Antileprotics

Leprosy (Hansen's disease) is a chronic disease caused by *Mycobacterium leprae*; it affects the peripheral nervous system, the skin, and some other tissues. It is transmitted from person to person when bacilli are shed from the nose and skin lesions of infected patients, but most individuals are naturally immune, and symptoms are suppressed. For treatment purposes patients may be classified as having paucibacillary (PB) or multibacillary (MB) leprosy. The 2 forms may be distinguished by skin smears, but facilities are not always available to process them and their reliability is often doubtful.

Drugs recommended are dapsone, rifampicin and clofazimine.

A three - drug regimen is recommended for multibacillary leprosy (lepromatous, borderline-lepromatous, and borderline leprosy) and a two - drug regimen for paucibacillary leprosy (borderline tuberculoid, tuberculoid, and indeterminate).

Any patient with a positive skin smear should be treated with the multidrug therapy regimen for MB leprosy. The regimen for PB leprosy should never be given to a patient with MB leprosy. If diagnosis in a particular patient is not possible the multi drug therapy regimen for MB leprosy must be used.

Multibacillary leprosy (3 - drug regimen)

Rifampicin 600mg once-monthly, supervised (450mg for adults weighing less than 35kg)

Dapsone 100mg daily, self administered (50mg daily or 1 - 2 mg/kg daily for adults weighing less than 35kg)

Clofazimine 300mg once - monthly, supervised, and 50mg daily (or 100mg on alternate days), self-administered.

Multibacillary leprosy should be treated for at least 2 years. Treatment should be continued unchanged during both type I (reversal) or type II (erythema nodosum leprosum) reactions. During reversal reactions neuritic pain or weakness can herald the rapid onset of permanent nerve damage. Treatment with prednisolone (initially 40 - 60mg daily) should be instituted at once. Mild type II reactions may respond to aspirin or chloroquine. Severe type II reactions

may require corticosteroids; thalidomide is also useful in men and post menopausal women who have become corticosteroid dependent, but it would be used under specialist supervision and it should never be used in women of child bearing potential (significant teratogenic risk). Increase doses of clofazimine 100mg 3 times daily for the first month with subsequent reductions, are also useful but may take 4 - 6 weeks to attain full effect.

Paucibacillary leprosy (2 - drug regimen)

Rifampicin 600mg once - monthly, supervised (450mg for those weighing less than 35kg)

Dapsone 100mg daily, self - administered (50mg daily or 1-2 mg/kg daily for adults weighing less than 35kg)

Paucibacillary leprosy should be treated for 6 months. If treatment is interrupted the regimen should be recommended where it was left off to complete the full courses.

Neither the multibacillary nor the paucibacillary antileprosy regimen is sufficient to treat tuberculosis.

Clofazimine

Capsule, 50mg, 100mg

Indications: multibacillary (MB) leprosy; type II lepra reactions.

Cautions: pre-existing gastrointestinal symptoms (reduce dose, increase dose interval or discontinue if symptoms develop during treatment); liver and renal impairment; pregnancy and breast-feeding; may discolour soft contact lenses.

Note: -Patients should be warned that Clofazimine might cause a reddish - brown discolouration of skin, conjunctiva, tears, sputum, sweat, urine, and faces.

Side effects: reversible discoloration of skin, hair, cornea, conjunctiva, tears, sweat, sputum; symptoms including pain, nausea, vomiting and diarrhoea; severe mucosal and submucosal oedema with prolonged treatment with high doses - may be severe enough to cause sub acute small bowel obstruction.

Dose and Administration:

Leprosy, see notes above

Lepromatous lepra reactions, dosage increased to 300mg daily for max. of 3 months.

Dapsone

Tablet, 25mg, 50mg, 100mg

Injection, 20% in 50ml ampoule

Indications: paucibacillary (PB) and multibacillary (MB) leprosy (see notes above)

Cautions: cardiac or pulmonary disease; anaemia (treat severe anaemia before starting); G6PD deficiency (including breastfeeding affected infants); pregnancy; breast-feeding; porphyria.

Note: - on long term treatment patients and their carers should be told how to recognize blood disorders and advised to seek immediate medical attention if symptoms such as fever, sore throat, rash, mouth ulcers, purpura, bruising or bleeding develop.

Drug interactions: rifamycins, amprenavir, and probenecid.

Contraindications: hypersensitivity to sulfones; severe anaemia.

Side effects: (dose-related and uncommon at doses used for leprosy), haemolysis, methaemoglobinaemia, neuropathy, allergic dermatitis (rarely including toxic epidermal necrolysis and Stevens-Johnson syndrome), anorexia, nausea, vomiting, tachycardia, headache, insomnia, psychosis, hepatitis, agranulocytosis; dapsone syndrome (rash with fever and eosinophilia)-discontinue immediately (may progress to exfoliative dermatitis, hepatitis, hypoalbuminaemia, psychosis and death)

Dose and Administration:

Leprosy: 1 - 2mg/kg daily, see notes above

Storage: at room temperature, in a well - closed, light - resistant containers.

Rifampicin

Capsule, 150mg, 300mg, and 600mg

Indications: Paucibacillary leprosy; multibacillary leprosy; tuberculosis (section 7.1.3)

Cautions, Drug interactions, Side effects, Contraindications; see under section 7.1.3.

Dose and Administrations: see notes above.

7.2. Antifungals

Fungal infections may be classified as superficial, affecting only the skin, hair, nail, or mucous membranes, or systemic, affecting the body as a whole; systemic infections tend to occur more frequently in immunocompromised individuals such as those with AIDS.

Drugs used in fungal infections:

Polyene antifungals - The polyene antifungals include amphotericin and Nystatin; neither drug is absorbed when given by mouth. They are used for oral, oropharyngeal, and perioral infections by local application in the mouth.

Nystatin is used principally for candida albicans infections of the skin and mucous membranes, including esophageal and intestinal candidiasis.

Amphotericin B is active against most fungi and yeasts. It is the drug of choice for most serious systemic mycotic infections.

Imidazole Antifungals, among the imidazole antifungal, Ketoconazole is better absorbed by mouth than other imidazoles. It has been associated with fatal hepatotoxicity; prescribers should weigh the potential benefits of ketoconazole treatment against the risk of liver damage and should carefully monitor patients both clinically and biochemically. It should not be used for superficial fungal infections.

Miconazole is grouped in imidazole antifungals. Miconazole can be used locally for oral infections; it is also effective in intestinal infections. Systemic absorption may follow use of miconazole oral gel and may result in significant drug interactions.

Triazole Antifungals. Fluconazole is very well absorbed after oral administration. It also achieves good penetration into the cerebrospinal fluid to treat fungal meningitis. Itraconazole is indicated for mucocutaneous candidiasis and in dermatomycoses unresponsive to conventional therapy. It is also used in the treatment of histoplasmosis, blastomycosis and invasive aspergillosis.

Other Antifungals. Griseofulvin is effective for widespread or intractable dermatophyte infections but has been superseded by newer antifungals, particularly for nail infections. It is usually well tolerated and is licensed for use in children. Duration of therapy is dependent on the site of the infection and may be required for a number of months.

Flucytosine is a synthetic fluorinated pyrimidine with a narrow spectrum of antifungal activity, particularly against *Cryptococcus* and *Candida* spp. In susceptible fungi, it is converted to fluorouracil by cytosine deaminase. Flucytosine is myelosuppressive and plasma concentrations above 75mcg/ml are associated with myelotoxicity.

Amphotericin B

Powder for injection, 10mg, 50mg in vial

Lozenges, 10mg

Liposomal injection, 50mg in 15ml and 30ml vial

Indications: the drug of choice for most severe systemic mycoses such as disseminated candidiasis, cryptococcosis, mucormycosis, histoplasmosis, extracutaneous sporotrichosis and blastomycosis. Also used in leishmaniasis (see section 7.4.3)

Cautions: when given parenterally, toxicity common (close supervision necessary and test dose required); renal impairment; hepatic and renal function test, blood counts, and plasma electrolyte monitoring required; corticosteroids (avoid except to control reactions); pregnancy and breast-feeding; avoid rapid infusion (risk of arrhythmias); see also interactions.

Drug interactions: cardiac glycosides, ciclosporin, corticosteroids, tacrolimus.

Contraindications: hypersensitivity to amphotericin.

Side effects: when given parenterally, anorexia, nausea and vomiting, diarrhea, epigastric joint pain, anaemia; disturbances in renal function (including arrhythmias), blood disorders, neurological disorders (including hearing loss, diplopia, convulsions, peripheral neuropathy), abnormal liver function (discontinue treatment), rash, anaphylactoid reactions; pain and thrombophlebitis at injection site.

Dose and Administration: Adult:

The dose and duration of therapy depend on the infecting organism. The daily dose must not exceed 1.5mg/kg. The following have been suggested.

Extrapulmonary cryptococcosis: IV infusion: 0.7 mg/kg/day for 4-8 weeks.

Invasive candidiasis: IV infusion: 0.6 mg/kg/day; duration of therapy should be 2 weeks after resolution of clinical features and candidaemia, but longer courses are recommended for neutropenic patients and endocarditis.

Candidaemia (in patients without neutropenia): IV infusion: 0.5-0.6mg/kg/day until at least 14 days after resolution of signs/last positive deep-site culture.

Mucormycosis or invasive aspergillosis: IV infusion: 1-1.5 mg/kg/day; total dose 2.5-3g.

Lozenges: Suck 1, slowly, 4 times daily; up to 8 times daily in severe conditions.

Fluconazole

Capsule/tablet, 50mg, 100mg, and 200mg

Suspension, 50mg /5ml, 200mg /5ml

IV infusion in sodium chloride 2mg/ml

Indications: vaginal and oropharyngeal candidiasis not responding to topical therapy; oesophageal and systemic candidiasis; cryptococcal meningitis and maintenance therapy to prevent relapse of cryptococcal disease in patients with AIDS.

Cautions: renal or hepatic impairment.

Drug interactions: enzyme-inducing agents (e.g rifampicin), hydrochlorothiazide, phenytoin, sulphonylureas, hypoglycemic agents, cyclosporin, nortriptyline, and zidovudine, terfenadine, oral anticoagulants and theophylline.

Contraindications: hypersensitivity to other azole antifungals.

Side effects : nausea, abdominal discomfort, diarrhoea, flatulence, headache, rash (discontinue treatment or monitor closely if infection invasive or systemic); less frequently dyspepsia, vomiting, taste disturbance, abnormalities of liver enzymes, angioedema, dizziness, seizures, alopecia, pruritus, toxic epidermal necrolysis, and Stevens Johnson syndrome reported, severe cutaneous reactions in AIDS patients also reported.

Dose and Administration:

Adult: *Vaginal candidiasis: Oral:* 150mg as a single dose.

Oropharyngeal candidiasis: Oral: 50-100mg daily for 7-14 days.

Oesophageal candidiasis: Oral: 100-200mg daily for 14-28 days.

Systemic candidiasis: Oral or IV: 400mg daily.

Cryptococcal meningitis: Oral or IV: 400mg daily for 8-10 weeks, prevention of relapse in patients with AIDS, 200mg daily.

Child: *Oropharyngeal candidiasis: Oral or IV:* 3-6 mg/kg on the first day, then 3 mg/kg/day.

Systemic candidiasis, cryptococcal meningitis: Oral or IV: 6-12mg/kg/day daily.

Prevention of fungal infections in immunocompromised patients following cytotoxic chemotherapy or radiotherapy; 3-12 mg/kg/day, depending on extent and duration of neutropenia.

Storage: store tablets and powder for oral suspension below 30°C. Reconstituted suspension and fluconazole injection should be stored at 5°C - 30°C. Do not freeze reconstituted suspension or intravenous infusion.

Flucytosine

IV infusion, 10 mg/ml

Solution for Injection, 2.5 g /250 ml

Capsule, 250mg, 500mg

Indications: adjunct to amphotericin B (or fluconazole) in cryptococcal meningitis and in systemic candidosis.

Cautions: elderly, renal impairment, pregnancy and breast-feeding.

Drug interactions: amphotericin, cytarabine.

Contraindications: hypersensitivity to flucytosine.

Side effects: rash, nausea, vomiting, diarrhea, alterations in liver function tests; less frequently, confusion, hallucinations, convulsions, headache, sedation, vertigo, blood disorders including leukopenia, potentially fatal thrombocytopenia and aplastic anemia.

Dose and Administration:

Adult and Child:

Systemic candidosis and cryptococcosis: IV infusion: (over 20 - 40 minutes), 200 mg/kg daily in 4 divided doses, for usually no more than 7 days (at least 4 months in cryptococcal meningitis); extremely sensitive organisms, 100 - 150 mg/kg daily in 4 divided doses.

Systemic candidosis: initial treatment or after IV therapy, *Oral:* 50 - 150 mg/kg daily in 4 divided doses.

Storage: store in airtight containers and protect from light. I.V infusion should be stored between 18 and 25 °C.

Griseofulvin

Tablet, 125mg, 250mg, 500mg

Suspension, 125mg / 5ml

Indications: dermatophyte infections of the skin, scalp, hair and nail where topical therapy has failed or is inappropriate.

Cautions: rarely aggravation or precipitation of systemic lupus erythematosus; breast-feeding; griseofulvin may impaired the ability to drive or operate machinery, see also drug interaction.

Drug interactions: phenobarbitone, coumarin anticoagulants and oral contraceptives, aspirin.

Contraindications: patients with porphyria and liver failure, lupus erythematosus and related conditions, pregnancy (avoid pregnancy during and for 1 month after treatment, men should not father children with in 6 months of treatment)

Side effects: side effects are usually mild and transient and consist of headache, skin rashes, dryness of the mouth an altered sensation of taste, and gastrointestinal disturbances; angioedema, erythemamultiforme, toxic epidermal necrolysis, proteinuria, leucopenia and other blood dyscrasias, candidaisis, paraesthesia, photosensitization, and severe headache have been reported occasionally. Depression, confusion, dizziness, insomnia, and fatigue. Griseofulvin may precipitate or aggravate systemic lupus erythematosus.

Dose and Administration:

Adult: *Oral:* 500mg daily, in divided doses or as a single dose, in severe infection dose may be doubled reducing when response occurs;

Child: 10mg/kg daily in divided doses or as a single dose.

Storage: at room temperature, in a tight container.

Itraconazole

Capsule, 100 mg, 200 mg

Oral solution, 10 mg/ml.

Indications: vulvovaginal, oropharangeal or oesophageal candidiasis and dermatomycoses, not responding to conventional therapy. Useful for endemic mycoses, e.g. histoplasmosis, and may be an effective alternative to amphotericin B for aspergillosis.

Cautions: hepatic disease.

Drug interactions: antacids, sucralfate, H₂-receptor antagonists (cimetidine), didanosine, carbamazepine, phenytoin, rifampicin, ciclosporin, cisapride, terfenadine, digoxin, indinavir, ritonavir, midazolam, triazolam, warfarin.

Contraindications: hypersensitivity to any azole antifungal.

Side effects: skin rash, gastrointestinal disturbances (nausea, diarrhea, abdominal pain, dyspepsia, vomiting, constipation, anorexia) and headache; transient increase in liver enzymes and rarely, hepatitis.

Dose and Administration: *Oral:*

Adult: *Vulvovaginal candidiasis:* 200 mg morning and evening for 1 day.

Oropharyngeal candidiasis: 100 mg (200 mg in AIDS or neutropenia) daily for 15 days.

Oropharyngeal and Oesophageal candidiasis in HIV infection: solution: 200 mg daily (given as 1 or 2 doses) for 1 -2 weeks; solution held in the mouth before swallowing. Dose may be doubled in resistant cases.

Systemic mycoses: 200 - 400 mg daily in single or 2 divided doses.

Tinea Corporis, tinea cruris: 100 mg daily for 15 days.

Tinea pedis, tinea manuum: 100 mg daily for 30 days.

Storage: Capsule: store at room temperature; protect from light and moisture. Oral solution: store at $\leq 25^{\circ}\text{C}$; do not freeze.

Ketoconazole

Tablet, 200mg

Syrup, 20mg /5ml

Indications: in chronic mucocutaneous candidiasis, fungal infections of the gastro intestinal tract, and dermatophyte infections of the skin and fingernails. It is also used for the treatment of systemic blastomycosis, candidiasis, coccidioidomycosis, histoplasmosis, & aracoccidioidomycosis.

Cautions: during breast-feeding, in pediatrics and geriatrics, alchlorhydria, hypochlorhydria, alcoholism, renal function impairment

Drug interactions: antimuscarinic agents, antacids H₂ - receptors antagonists (*** patients should be advised to take these medications at least 2 hours after taking ketoconazole); rifampicin, isoniazid, phenytoin, astemizole, terfenadine, cisapride, corticosteroids, cyclosporin, oral anticoagulants, alcohol, oral contraceptives, tolbutamide, sucralfate, midazolam and triazolam, didanosin, digoxin and indinavir.

Contra indications: pre-existing liver disease, pregnancy; concurrent use of astemizole, cisapride and terfenadine with ketoconazole is contra indicated; hypersensitivity to azole antifungals

Side effects: gastro intestinal disturbance, gynaecomastia, impotence, menstrual irregularities, oligospermia, azoospermia, decreased male libido, liver toxicity, and adrenal cortex suppression.

Dose and Administration: Oral:**Adult:**

Candidiasis, vulvovaginal: 200 to 400mg once a day for five days.

Carcinoma, prostatic: 400mg three times a day.

Cushing's syndrome: 600 mg to 1.2 grams a day.

Paronychia: 200 to 400 mg once a day.

Pityriasis versicolor: 200 mg once a day for five to ten days.

Pneumonia, fungal or septicemia, fungal: 400 mg to 1 gram once a day.

For all other antifungal indications: 200 to 400 mg once a day.

Child:

Candidiasis, vulvovaginal: **Child 2 years of age and older:** 5 to 10 mg per kg of body weight once a day for five days.

Infants and Child up to 2 years of age: Dosage has not been established.

Paronychia or Penicillin marneffeii infection or pneumonia, fungal or septicemia, fungal: children 2 years of age and older: 5 to 10 mg per kg of bodyweight once a day.

Infants and Child up to 2 years of age: Dosage has not been established.

For all antifungal indications: **Child 2 years of age and older:** 3.3 to 6.6 mg per kg of body weight once a day.

Note: Advise the patient to take the medication with food to increase absorption, and to avoid alcoholic beverages.

Storage: in a well –closed container at room temperature.

Miconazole

Tablet, 250 mg

Oral Gel, 25mg /ml

Intravenous infusion, 10 mg/ml in 20 ml

Indications: in the treatment of mucocutaneous candidiasis, dermatophytosis, and pityriasis versicolor.

Cautions: pregnancy and breast feeding; avoid in porphyria, haematocrit, haemoglobin and serum electrolytes and lipids should be monitored regularly; see also interactions.

Drug interactions: oral anticoagulants, sulphonylurea hypoglycaemic drugs, or phenytoin (miconazole enhance the activity of these drugs); amphotericin

Contraindications: hepatic impairment

Side effects: nausea, vomiting and diarrhea (usually on long-term treatment); rarely allergic reactions; isolated reports of hepatitis.

Dose and Administration:

Prevention and treatment of oral and intestinal fungal infections 125 to 250 mg as tablet or 5 - 10 ml oral gel in the mouth after food 4 times daily, keep in oral cavity near lesions before swallowing; child under 2 years, 62.5mg as tablet or 2.5ml twice daily; 2 - 6 years 125mg of tablet or 5ml oral gel twice daily; over 6 years, 125mg of tablet or 5ml oral gel 4 times daily.

Systemic fungal infections:

Adult: IV: range from 0.2 to 1.2 g three times daily. Each dose must be diluted in at least 200 mL of sodium chloride 0.9% or glucose 5% and infused slowly over 30 to 60 minutes.

Child: *IV*: 20 to 40 mg/kg body-weight daily (intravenously) but not more than 15 mg/kg of miconazole should be given at each infusion.

Storage: at room temperature.

Nystatin

Tablet, 500,000IU

Indications: prophylaxis and treatment of candidiasis of skin and mucous membranes.

Side effects: nausea, vomiting, and diarrhea; Steven Johnson syndrome, irritation.

Dose and Administration: *Oral:*

Adult: *intestinal candidiasis:* 500, 000 unit every 6 hours, doubled in severe infections;

Child: 100,000 units 4 times daily prophylaxis, 1 million units once daily

Neonate: 100,000 units once daily.

Storage: at room temperature in a tight light resistant container.

7.3. Antivirals

7.3.1. Anti-Retroviral (ARV) Agents

Currently available antiretroviral drugs inhibit the reverse transcriptase and protease enzymes of the human immunodeficiency virus (HIV) thus suppressing viral replication. Highly active antiretroviral therapy (HAART) is the use of a combination of three or more antiretrovirals to achieve durable suppression of replication.

As HIV mutates rapidly and there is a high viral turnover; inappropriate drug prescribing may cause rapid development of drug resistance.

Response to therapy may be measured virologically (by serial monitoring of viral load), immunological (by serial monitoring of CD4 or total lymphocyte count) or clinically. Viral load monitoring is the only way to detect the emergence of resistance.

The Ethiopian HIV guideline suggests that treatment should be commenced in a symptomatic HIV-positive patient (WHO stage 3 or 4) or in patients with a CD4 count of < 200 cells/mm³.

Post Exposure prophylaxis (PEP)

To be effective treatment has to commence as soon as possible (within 1 to 2 hours, post-exposure). However, the maximum delay for initiation of treatment, which would prevent infection, is not known in humans. In most developed countries, PEP is commenced within 2 - 4 hours post exposure. Prophylaxis is sometimes given empirically up to 2 weeks in case of severe exposure when the delay has been unavoidable. Prophylaxis is to be given for 28 days.

Mother To Child Transmission (MTCT)

ARV has been shown to prevent transmission from mother to infant. Several antiretroviral regimens - using zidovudine, zidovudine plus lamivudine, nevirapine, or HAART have been shown to reduce perinatal transmission. In contrast to treating established infection, the short-term use of monotherapy is

effective in this setting. Combination therapy is more effective and may delay the emergence of resistance. Non-drug measures that reduce transmission (including elective caesarean section and avoiding breast feeding) add to the benefit of antiretroviral therapy.

HAART, ideally initiated in the second trimester, is the most effective MTCT prophylaxis, and is recommended if the viral load is more than 1000 copies/ml, together with elective caesarean section. A zidovudine - containing regimen is recommended. Efavirenz is teratogenic and must be avoided in early pregnancy. The combination of didanosine and stavudine should be avoided in pregnancy due to the high risk of lactic acidosis. Only if the mother fulfils the adult criteria for initiation of HAART should she continue antiretroviral therapy after delivery.

- If the viral load is less than 1000 copies/ml, zidovudine monotherapy, 300 mg twice daily, may be prescribed (for at least 4 weeks, and ideally for the last 12 weeks of pregnancy). During labour, zidovudine 300 mg 3 hourly should be administered.
- Dual therapy with zidovudine and lamivudine is more effective than monotherapy, but lamivudine resistance commonly develops.
- With any of the above regimens, zidovudine 2 mg/kg 6 hourly for 6 weeks should be prescribed for the baby.
- A single dose of nevirapine 200 mg is given to the mother in labour and a single dose (2 mg/kg) to the baby within 72 hours of birth. Resistant viral mutations may emerge, particularly if the maternal nevirapine dose is repeated, which may limit further treatment options for the mother and the baby.
- The mother should be offered the option of formula feeding if this is practical and affordable for her. If not, exclusive breast-feeding should be recommended (breast milk only-no water, juice or other milk) for 3 months, followed by rapid weaning. Mixing formula feeding and breast-feeding results in a much higher risk of HIV transmission.

Nucleoside Reverse Transcriptase Inhibitors

Nucleoside reverse transcriptase inhibitors (NRTIs) are nucleoside analogues, which act as false substrates for reverse transcriptase and terminate the DNA chain. Currently available NRTIs are abacavir (ABC), didanosine (ddI), lamivudine (3TC), stavudine (d4T), zalcitabine (ddc) and zidovudine (AZT). Dual NRTI is the conventional backbone of triple therapy. Selection of a dual NRTI combination must avoid cross-resistance and antagonism.

- Avoid the use of 2 analogues of the same nucleoside, e.g. stavudine and zidovudine, both thymidine analogues.
- If possible, do not prescribe 2 nucleoside analogues with similar adverse effects, e.g. zalcitabine and stavudine-both cause peripheral neuropathy; didanosine and stavudine may increase the risk of lactic acidosis.

Abacavir (ABC)

Tablets, 300mg (as sulphate)

Indications: treatment of HIV infection, in combination with other antiretrovirals.

Cautions: hepatic and renal impairment, pregnancy, breastfeeding.

Drug interactions: the potential for clinically significant drug interactions is low.

Contraindications: prior hypersensitivity to the drug.

Side effects: hypersensitivity reactions, nausea, vomiting, diarrhoea, anorexia, lethargy, fatigue, fever, headache, pancreatitis, lactic acidosis.

Dose and Administration: *Oral:*

Adult: 300mg 12 hourly;

Child: 3 months - 16 years, 8mg/kg twice daily.

Storage: store at room temperature.

Didanosine (DDI, ddI)

Tablet, 25mg, 150mg

Chewable / dispersible tablet, 100mg

Indications: treatment of HIV infection, in combination with at least two other antiretroviral drugs.

Cautions: peripheral neuropathy or hyperuricaemia; renal and hepatic impairment; pregnancy and breast-feeding; dilated retinal examinations recommended every 6 months, or if visual changes occur.

Drug interactions: drugs in which absorption is impaired by increased gastric pH, e.g. fluoroquinolones, some protease inhibitors, dapsone: take at least 2 hours before or 2 hours after didanosine.

Contraindications: history of pancreatitis, alcoholism; conditions requiring sodium restriction.

Side effects: pancreatitis, peripheral neuropathy especially in advanced HIV infection suspend (reduced dose may be tolerated when symptoms resolve), hyperuricaemia (suspend treatment if significant elevation), diarrhea; nausea, vomiting, dry mouth, asthenia, headache, hypersensitivity reactions, retinal and optic nerve changes (especially in children), diabetes mellitus, raised liver enzymes, liver failure.

Dose and Administration:

Adult: *Oral:* ≥ 60 kg, 200 mg 12 hourly or 400 mg daily; < 60 kg, 125 mg 12 hourly or 250 mg daily. Half hr pre-meals or 1hr after meal.

Child: *Oral:* 240 mg/m² daily or 120 mg/m² 12 hourly.

Storage: store at room temperature.

Emtricitabine

Capsule, 200mg

Indications: Treatment of HIV infection in combination with at least two other antiretroviral agents.

Cautions: lactic acidosis, severe hepatomegaly, hepatic failure, renal impairment.

Drug interactions: concomitant use of nucleoside analogues.

Contraindications: hypersensitivity to emtricitabine.

Side effects: headache, dizziness, insomnia, rash, diarrhea, nausea, abdominal pain, skeletal weakness, cough, rhinitis.

Dose and Administration: *Oral:* **Adult:** 200mg once daily.

Storage: store at room temperature.

Emtricitabine + Tenofovir

Tablet, 200mg + 300mg

Indications: Treatment of HIV infection in combination with other antiretroviral agents.

Dose and Administration: *Oral:* **Adult:** one tablet (emtricitabine 200mg and tenofovir 300mg) once daily.

Lamivudine (3TC)

Tablet, 150mg

Oral solution, 10mg/ml

Indications: HIV infection; reduction of perinatal transmission of HIV; post-exposure prophylaxis; only in combination with other antiretrovirals. Chronic hepatitis B infection (off-label use).

Cautions: renal impairment, hepatic disease, pregnancy and breastfeeding.

Drug interactions: co-trimoxazole, trimethoprim component of co-trimoxazole.

Contraindications: significant anaemia or neutropenia, known hypersensitivity to the drug.

Side effects: nausea, vomiting, diarrhoea, abdominal pain, cough; headache, insomnia, malaise, fever, rash, alopecia, muscle disorders, nasal symptoms; peripheral neuropathy; rarely pancreatitis (discontinue); neutropenia, anaemia and thrombocytopenia; lactic acidosis; raised liver enzymes and serum amylase reported.

Dose and Administration: *Oral:*

Adult: 150 mg 12 hourly; < 50 kg, 2 mg/kg 12 hourly.

Chronic hepatitis B infection: 100-150mg once daily. In patients with concomitant HIV infection, use the dose for HIV treatment.

Child: 3 months-12 years: 4 mg/kg (maximum 150mg) twice daily.

Neonates < 30 days old: 2 mg/kg twice daily.

Storage: store at 2 - 25 °C temperature.

Stavudine (d4T)

Capsules, 15mg, 20mg, 30mg, 40mg

Powder for oral solution, 1mg/mL

Indications: treatment of HIV infection, in combination with other antiretrovirals.

Cautions: peripheral neuropathy and pancreatitis or concomitant use with other drugs associated with pancreatitis; hepatic disease, renal impairment, pregnancy and breastfeeding.

Drug interactions: zidovudine, didanosine, zalcitabine, dapsone, ethambutol, ethionamide and isoniazid, pentamidine, valproate.

Side effects: peripheral neuropathy, pancreatitis, headache, gastrointestinal intolerance (diarrhoea, nausea, anorexia), neutropenia, thrombocytopenia, myalgia, elevated liver enzymes, lactic acidosis.

Dose and Administration: *Oral:*

Adult: >60kg, 40mg 12 hourly; <60kg, 30mg 12 hourly

Renal impairment: creatinine clearance 26-50ml/min, half dose 12 hourly; creatinine clearance <25 ml/min, half dose 24 hourly.

Child: > 3 months and ≤ 30kg, 1mg/kg 12 hourly; > 30 kg, as for adults.

Storage: store capsules and powder for oral solution at room temperature. Following reconstitution, oral solution should be stored at 2-8°C for up to 30 days.

Zalcitabine (ddC, DDC)

Tablet, 375 mcg, 750mcg

Indications: treatment of HIV infection, in combination with other antiretrovirals.

Cautions: peripheral neuropathy, history of pancreatitis; known hypersensitivity to the drug.

Drug interactions: aminoglycosides, amphotericin B and foscarnet; antacids, cimetidine, didanosine, drugs associated with peripheral neuropathy (e.g. stavudine, chloramphenicol); drugs associated with pancreatitis (e.g. alcohol), metoclopramide, probenecid.

Side effects: these tend to be dose related and may be difficult to distinguish from the underlying disease. They tend to be more frequent and severe in advanced disease. Dose-related peripheral neuropathy, oral ulcers, pancreatitis, hepatitis, arthralgia and gastrointestinal disturbances. Pharyngitis, headache, dizziness, rash, pruritus, weight loss, fatigue, chest pain, leucopenia, thrombocytopenia, rigors and sweating. Oesophageal ulcers, hypersensitivity reactions.

Dose and Administration: Adult: *Oral:* 0.75mg 8 hourly.

Storage: store at room temperature.

Zidovudine / Azidothymidine (ZDV, AZT,)

Capsules, 100 mg, 250 mg

Tablets, 150 mg, 300 mg

Syrup, 50 mg/5ml

IV infusion, 10 mg/ml

Indications: HIV infection; reduction of perinatal transmission of HIV; Post-exposure prophylaxis. Usually in combination with other antiretrovirals.

Cautions: haematological toxicity; vitamin B12 deficiency (increased risk of neutropenia); reduce dose or interrupt treatment according to product literature if anaemia or myelosuppression, renal impairment; hepatic impairment; risk of lactic acidosis.

Drug interactions: ganciclovir, myelosuppressive agents, probenecid.

Contraindications: abnormally low neutrophil counts or haemoglobin; neonates either with hyperbilirubinaemia requiring treatment other than phototherapy or with raised transaminase.

Side effects: haematological effects include anaemia and leucopenia or neutropenia. Platelet count may rise initially after starting therapy. Nausea, headache, myalgia, insomnia, and rarely, myopathy, lactic acidosis, seizures, confusion, mania, and hepatotoxicity.

Dose and Administration:

Adult:

Oral: 300 mg 12 hourly, Dose may be reduced to 250 mg 12 hourly if needed.

IV infusion: over 1 hour, 1-2 mg/kg 4 hourly, in 5% glucose to give a zidovudine concentration 2 or 4 mg/ml. The IV route is used only until oral therapy can be given.

PMTCT:

Adult: *Oral:* 300mg 12 hourly for at least the last 4 weeks of pregnancy; from onset of labour to delivery, 300 mg 3 hourly.

Child: *Oral:* 3 months - 12years, 180 mg/m² 12 hourly; maximum 800mg/day.

Neonates: for prevention of MTCT, initiated within 12 hours of birth and given for the first 6 week of life: *Oral:* 2 mg/kg 6 hourly

IV: 1-5 mg/kg 8 hourly

Premature infants: *Oral:* 1.5 mg/kg 12 hourly for 2 weeks, then 2 mg/kg 6 hourly. IV, as for term infants.

Storage: store at room temperature.

Zidovudine and Lamivudine combinations (Combivir)

Tablets, zidovudine 300mg, lamivudine 150mg

Dose and Administration:

Adult and Child >12 years: *Oral:* one tablet twice daily.

Nucleotide Reverse Transcriptase Inhibitors

Tenofovir disoproxil fumarate (TDF) is a prodrug of tenofovir, a nucleotide analogue of adenosine. It interferes with the HIV viral RNA dependent DNA polymerase resulting in inhibition of viral replication. TDF is first converted intracellularly by hydrolysis to tenofovir and subsequently phosphorylated to the active tenofovir diphosphate; nucleotide reverse transcriptase inhibitor.

Tenofovir

Tablet, 300mg

Indications: treatment of HIV infection, in combination with other antiretrovirals.

Cautions: co-infection with hepatitis B (severe acute exacerbation of hepatitis reported on discontinuation); renal impairment, porphyria.

Drug interactions: didanosine, drugs that reduce renal function or compete for active tubular secretion (aciclovir, valaciclovir, ganciclovir), lopinavir-ritonavir, other nephrotoxic agents.

Side effects: mild to moderate gastrointestinal effects, such as nausea, diarrhoea, vomiting and flatulence. Tenofovir is nephrotoxic and cause renal impairment (including acute renal failure), proteinuria and Fanconi syndrome (renal tubular injury with severe hypophosphataemia). Reduction in bone mineral density may occur. Rare – hypersensitivity reactions; hyperlactataemia and hepatic steatosis.

Dose and Administration: Adult: *Oral:* 300 mg once daily.

Renal impairment: Increase dose interval. Creatinine clearance 30 – 50 ml/min, 48 hours; 10 – 30 ml/min, twice weekly; < 10 ml/min, not recommended.

Non - Nucleoside Reverse Transcriptase Inhibitors

Non-nucleoside reverse transcriptase inhibitors (NNRTIs) inhibit reverse transcriptase activity directly. They potently suppress HIV replication. High-level resistance develops rapidly and they must always be used in combination, usually with 2NRTIs. Cross-resistance within the class occurs. Hypersensitivity rashes are common. Currently available NNRTIs include nevirapine and efavirenz.

Efavirenz (EFV, EFZ)

Capsules, 50mg, 100mg, 200mg

Indications: treatment of HIV infection, in combination with other antiretrovirals.

Cautions: hepatic and renal impairment, breast feeding, elderly; history of mental illness or substance abuse.

Drug interactions: efavirenz may either induce or inhibit metabolism of other hepatically metabolised drugs. Cisapride, midazolam, triazolam, ergot alkaloids, terfenadine, rifampicin, phenytoin, carbamazepine, phenobarbitol, warfarin, protease inhibitors, oral contraceptives.

Contraindications: pregnancy (teratogenic); substitute nevirapine for efavirenz in pregnant women or women for whom effective contraception cannot be assured.

Side effects: rash including Stevens Johnson Syndrome, dizziness, headache, insomnia, somnolence, abnormal dreams, fatigue, impaired concentration (administration at bed time in the first 2 - 4 weeks reduces CNS effects); nausea; less frequently vomiting, diarrhoea, hepatitis, depression, anxiety, psychosis, amnesia, ataxia, stupor, vertigo; raised serum cholesterol, elevated liver enzymes (especially if seropositive for hepatitis B or C), pancreatitis.

Dose and Administration: *Oral:*

Adult: 600mg once daily as a single dose at night.

Child: administered once daily, preferably at bedtime: over 40kg, 600mg; 32.5 - 40kg, 400mg; 25-32.5kg, 350mg; 20 - 25kg, 300mg; 15-20kg, 250mg; 13-15kg, 200mg.

Not recommended for children under 3 years or under 13kg.

Storage: store at room temperature.

Nevirapine (NVP)

Tablet, 200 mg

Suspension, 50 mg/5ml

Indications: treatment of HIV infection, in combination with other antiretrovirals; reduction of perinatal transmission of HIV.

Cautions: hepatic and renal impairment.

Drug interactions: oral contraceptives; rifampicin and rifabutin; protease inhibitors.

Contraindications: hypersensitivity to the drug.

Side effects: rash including Stevens-Johnson syndrome and rarely, toxic epidermal necrolysis, hepatitis or jaundice reported; nausea, vomiting, abdominal pain, diarrhoea, headache, drowsiness, fatigue, fever; hypersensitivity reactions; anaphylaxis, angioedema, urticaria also reported.

Dose and Administration: *Oral:*

Adult: 200 mg daily for 14 days, followed by 200 mg 12 hourly.

PMTCT: 200 mg to the mother at the onset of labour; 2 mg/kg to the infant within 72 hours.

Child: 2 months - 8 years, 4mg/kg once daily for 2 weeks, then 7mg/kg twice daily; ≥ 8 years, 4mg/kg once daily for 2 weeks, then 4mg/kg twice daily. Maximum 400mg/day.

Storage: store at room temperature.

Nevirapine + Lamuvidine + Stavudine

Tablet, 200mg + 150mg + 30mg/40mg, 50mg+30mg+6mg, 100mg+60mg+12mg

Indications: for the treatment of HIV infection, once patients have been stabilized on the maintenance regimen of nevirapine 200 mg bd, and have demonstrated adequate tolerability to nevirapine.

Cautions: it should not be administered to patients who have just initiated therapy with nevirapine. This is because an initial lead-in dosing of 200 mg nevirapine once daily for 2 weeks is recommended. Following this lead-in dose, a dose escalation (maintenance dose) to 200 mg nevirapine bd may be carried out in the absence of any hypersensitivity reactions.

Dose and Administration: **Adult:**

200mg + 150mg + 30mg: 1 tablet twice daily for patients weighing < 60 kg.

200mg + 150mg + 40mg: 1 tablet twice daily for patients weighing > 60 kg.

Protease Inhibitors

Protease inhibitors inhibit the HIV protease enzyme. Inhibition of this enzyme prevents cleavage of viral polyproteins, and results in immature, non-infectious HIV viral particles.

Protease inhibitors cause potent suppression of HIV replication. They must always be used in combination, and are usually reserved for second-line therapy if the initial treatment regimen of 2 NRTIs + 1NNRTI fails.

Currently available protease inhibitors include amprenavir, indinavir, lopinavir, nelfinavir, ritonavir and saquinavir. There is cross-resistance between some of these. They undergo hepatic cytochrome P450 metabolism and some, especially ritonavir, are potent hepatic enzyme inhibitors. This is exploited therapeutically

by using subtherapeutic doses of ritonavir to reduce metabolism of other protease inhibitors, allowing the use of lower doses and/or increased dosing intervals. Drug interactions are common.

Lipodystrophy and metabolic disorders

Abnormal fat distribution, with increased abdominal girth, dorsocervical fat deposition, breast enlargement and peripheral fat wasting (lipo-atrophy) has been associated with HAART. The protease inhibitors are most strongly associated with fat accumulation.

Protease inhibitors may also cause metabolic abnormalities, such as hypercholesterolaemia, hypertriglyceridaemia and insulin resistance. These may occur with or without lipodystrophy.

Atazanavir

Tablet, 100mg, 150mg, 200mg

Indications: treatment of HIV-1 infections in combination with at least two other antiretroviral agents.

Note: In patients with prior virologic failure, coadministration with ritonavir is recommended.

Cautions: patients with pre-existing conduction abnormalities or with medications which prolong AV conduction; hepatic dysfunction.

Drug interactions: cisapride, ergot derivatives, sildenafil, antiarrhythmics, ciprofloxacin, clarithromycin, diclofenac, doxycycline, erythromycin, isoniazid, protease inhibitors, quinidine, verapamil.

Contraindications: do not use in children <3 months of age due to potential for kernicterus; hypersensitivity to atazanavir.

Side effects: hyperglycemia, facial atrophy, breast enlargement, rash, nausea, depression, dizziness, fatigue, fever, headache, insomnia, pain, peripheral neuropathy, lipodystrophy, vomiting, diarrhea, jaundice, myalgia.

Dose and Administration: *Oral: Adult:*

Antiretroviral-naïve patients: 400mg once daily; administer with food

Antiretroviral-experienced patients: 300mg once daily plus ritonavir 100mg once daily; administer with food

Coadministration with efavirenz:

Antiretroviral-naïve patients: it is recommended that atazanavir 300mg plus ritonavir 100mg be given with efavirenz 600mg (all as a single daily dose); administer with food

Antiretroviral-experienced patients: recommendations have not been established.

Indinavir (IDV)

Capsule, 200mg, 400mg

Indications: treatment of HIV infection, in combination with two Nucleoside reverse transcriptase inhibitors and usually with low-dose ritonavir booster.

Cautions: hepatic impairment; ensure adequate hydration to reduce risk of nephrolithiasis; diabetes mellitus; haemophilia; pregnancy; breast feeding, metabolism of many drugs inhibited if administered concomitantly.

Drug interactions: carbamazepine, dexamethasone, efavirenz, ergotamine, nelfinavir, nevirapine, Phenobarbital, phenytoin, rifampicin, ritonavir, saquinavir.

Side effects: nephrolithiasis, unconjugated hyperbilirubinaemia, lipodystrophy, hypercholesterolaemia, hypertriglyceridaemia and insulin resistance. Nausea, vomiting, diarrhoea, hair loss, dry skin and skin rashes may occur. Allergic reactions include anaphylaxis, erythema multiforme and Stevens – Johnson syndrome. Acute haemolytic anemia and decreased neutrophil counts have been reported.

Dose and Administration: *Oral:*

Adult: 800 mg 8 hourly, 1 hour before or 2 hours after a meal; alternatively indinavir 800 mg plus ritonavir 100 -200 mg 12 hourly (independent of meals).

Child: 4-17 years, 500 mg/m² (maximum 800 mg) 8 hourly.

Note. Administer 1 hour before or 2 hours after a meal; may be administered with low-fat, light meal; when given with didanosine tablets, allow 1 hour between the drugs (antacids in didanosine reduce absorption of indinavir)

Storage: store at room temperature and in a tight container.

Nelfinavir (NFV)

Tablet, 250 mg

Oral powder, 50 mg/ml

Indications: HIV infection in combination with two other antiretroviral drugs.

Cautions: hepatic and renal impairment; diabetes mellitus; haemophilia.

Drug interactions: carbamazepin, contraceptives, ergotamine, phenobarbital, quinidine, ritonavir, saquinavir.

Side effects: diarrhoea, nausea, vomiting, flatulence, abdominal pain; rash, reports of elevated creatine kinase, hepatitis, pancreatitis, neutropenia, hypersensitivity reactions including bronchospasm, fever, pruritus and facial oedema, lipodystrophy and metabolic effects.

Dose and Administration: *Oral:*

Adult: 1.25g twice daily or 750mg 3 times daily.

Child: under 1 year, 40 - 50mg/kg 3 times daily or 65 - 75mg/kg twice daily; 1-13 years, 55 - 65 mg/kg twice daily.

Note: Administer with or after food, powder may be mixed with water, milk, formula feeds or pudding; it should not be mixed with acidic foods or juices owing to its taste.

Storage: store at room temperature and in tight containers.

Ritonavir (RTV)

Capsule, 100 mg

Oral Solution, 80 mg/ml

Indications: treatment of HIV infection and as a booster to increase effect of indinavir, lopinavir or saquinavir and in combination with two other antiretroviral drugs.

Cautions: hepatic impairment; diabetes mellitus; haemophilia.

Drug interactions: amiodarone, cisapride, clozapine, dextro-propoxyphene, pethidine, pimozide, quinidine and terfenadine; ergot alkaloids and derivatives; sedatives and hypnotics; HMG CoA reductase inhibitors; rifabutin; anticonvulsants; ketoconazole, macrolides; oral contraceptives; protease inhibitors.

Contraindications: severe hepatic impairment.

Side effects: gastrointestinal intolerance (nausea, vomiting and diarrhoea), vasodilation, orthostatic hypotension and syncope, hypertriglyceridaemia, pancreatitis, lipodystrophy, dyspepsia, oral ulceration, dry mouth, hyperaesthesia. Hypersensitivity reactions, including anaphylaxis.

Dose and Administration: *Oral:*

Adult: 600 mg 12 hourly. Gradual dose escalation may provide relief if nausea occurs or initiation: 300mg 12 hourly for 1 day, 400mg 12 hourly for 2 days, 500mg 12 hourly for 1 day, then 600mg 12 hourly.

Child: Over 2 years, initially (to minimise nausea) 250mg/m² 12 hourly, increased gradually over a week to 350mg/m² 12 hourly upto a maximum of 600mg 12 hourly.

As a booster with other antiretroviral drugs:

Adult: 100 mg twice daily.

Child 6 months – 13 years: 57.5 mg/m² twice daily (or 3 – 5 mg/kg twice daily) (maximum 100 mg twice daily)

Storage: liquid-filled capsules should be stored at 2 - 8 °C but may be stored at a temperature lower than 25 °C for up to 30 days. Store oral solution at room temperature.

Saquinavir (SQV)

Capsule, 200 mg

Tablet, 500 mg

Indications: HIV infection in combination with two other antiretroviral drugs and usually with low - dose ritonavir booster.

Cautions: hepatic and renal impairment; diabetes mellitus, haemophilia, pregnancy and breastfeeding.

Drug interactions: indinavir, nevirapine, phenobarbital, phenytoin, rifampicin, ritonavir.

Contraindications: hypersensitivity to the drug.

Side effects: diarrhoea, buccal and mucosal ulceration, abdominal discomfort, nausea, vomiting; headache, peripheral neuropathy, paraesthesia, dizziness, insomnia, mood changes, ataxia, musculoskeletal pain, asthenia; fever, pruritus, rash and other skin eruptions, rarely Stevens - Johnson syndrome; other rare adverse effects include thrombocytopenia and other blood disorders, seizures, liver damage, pancreatitis and nephrolithiasis; reports of elevated creatine

kinase, raised liver enzymes and neutropenia when used in combination therapy; lipodystrophy and metabolic effects.

Dose and Administration: Adult: Oral:

HIV infection (in combination with nucleoside reverse transcriptase inhibitors and low-dose ritonavir booster): saquinavir 1g and ritonavir 100 mg twice daily;

HIV infection (in combination with other antiretroviral drugs but without ritonavir booster): 1.2g every 8 hours after a meal.

Child under 16 years, safety and efficacy not established.

Note: Administer with or after food.

Storage: saquinavir liquid-filled capsules should be stored at 2 - 8 °C in airtight container but may be stored at a temperature lower than 25 °C for upto 3 months. For tablets store at room temperature.

7.3.2. Other Antivirals

Acyclovir

Tablet, 200mg, 400mg

Powder for injection, 250mg, 500mg in vial

Indications: treatment of primary genital herpes; disseminated varicella-zoster (chickenpox) in immunocompromised patients; herpes simplex encephalitis and herpes zoster.

Cautions: renal impairment, maintain adequate hydration; pregnancy and breast-feeding.

Drug interactions: probenecid, any nephrotoxic drugs.

Contraindications: hypersensitivity to acyclovir.

Side effects: nausea, vomiting, abdominal pain, diarrhea, headache, fatigue, rash urticaria, pruritus, photosensitivity; rarely hepatitis, jaundice, dyspnoea, angioedema, anaphylaxis, neurological reactions (including dizziness, confusion, hallucinations and drowsiness); acute renal failure, decreases in hematological indices; on intravenous infusion, severe local inflammation (sometimes leading to ulceration), fever, and rarely agitation, tremors, psychosis and convulsions.

Dose and Administration:

Adult:

Treatment of primary genital herpes: Oral: 200mg 5 times daily for 7-10 days or 400 mg 3 times daily for 7-10 days.

Prevention of recurrence of genital herpes: Oral: 400 mg twice daily

Disseminated varicella-zoster (chickenpox) in immunocompromised patients: IV infusion: 10 mg/kg 3 times daily for 7 days.

Herpes simplex encephalitis: IV infusion: 10 mg/kg 3 times daily for 10 days.

Herpes zoster: 800mg every 4 hours (5 times/day) for 7-10 days.

Child: Up to 12 years, IV infusion (over at least 1 hour), 250 mg/m²

8 hourly for 5-7 days. This may be doubled in herpes encephalitis and in varicella-zoster in immunocompromised patients.

Varicella (chickenpox): 20mg/kg (maximum 800mg/dose) 4 times daily for 5 days, initiated within 24 hours of appearance of the rash.

Storage: store at controlled room temperature.

Adenine Arabinoside

Injection, 500 mg in vial

Vidarabine was formerly used intravenously in the treatment of severe and disseminated herpes simplex infections and herpeszoster but aciclovir is preferred.

Amantadine

Capsule, amantadine hydrochloride, 100mg.

Syrup, 50mg/5ml

Indications: parkinson's disease (not for drug induced parkinson - like syndromes) (See section 4.5) ; influenza prophylaxis.

Cautions: epilepsy, serious mental disorders, a history of eczematoid rashes, congestive heart failure and/ or peripheral oedema, or orthostatic hypotension.

Drug interactions: agents with anticholinergic effects, alcohol, CNS stimulants, hydrochlorothiazide and triamterene, levodopa.

Contraindications: hypersensitivity to amantadine.

Side effects: livedo reticularis (skin discolouration) mainly of the legs; oedema of the legs. CNS reactions like psychotic episodes, convulsions and nausea. Headache, constipation, insomnia and nervousness, urinary retention, dry mouth, blurred vision as well as neutropenia and skin rashes have occurred.

Dose and Administration: *Oral:*

Adult: *Influenza A viral infection:* 100mg twice daily; initiate within 24-48 hours after onset of symptoms; discontinue as soon as possible based on clinical response (generally within 3-5 days or within 24-48 hours after symptoms disappear).

Influenza A prophylaxis: 100mg twice daily.

Parkinson's disease: 100mg twice daily as sole therapy; may increase to 400mg/day if needed with close monitoring.

Child: *Influenza A treatment:*

1-9 years: 5mg/kg/day in 2 divided doses. ≥ 10 years and < 40 kg: 5mg/kg/day; maximum dose: 150 mg/day. 10-12 years and ≥ 40 kg: 100 mg twice daily.

Storage: store at 15-30 °C; protect from freezing.

Famciclovir

Tablet, 125mg, 250mg, 500mg

Indications: treatment of herpes zoster, acute genital herpes simplex and suppression of recurrent genital herpes.

Cautions: renal impairment; pregnancy and breastfeeding.

Drug interactions: see under acyclovir

Side effects: nausea, vomiting, headache, rarely dizziness, confusion,

hallucinations, rash, abdominal pain and fever have been reported in immunocompromised patients.

Dose and Administration: **Adult:** *Oral: herpes zoster:* 250mg 3 times daily for 7 days or 750mg once daily for 7 days (in immunocompromised, 500mg 3 times daily for 10 days)

Genital herpes, first episode, 250mg 3 times daily for 5 days; recurrent infection, 125mg twice daily for 5 days (in immunocompromised, all episodes, 500mg twice daily for 7 days)

Genital herpes, suppression, 250mg twice daily (in HIV patients, 500mg twice daily) interrupted every 6-12 months.

Child: not recommended.

Foscarnet Sodium

Capsule, 250 mg, 500 mg

Intravenous infusion, 24 mg/ml

Powder for intravenous infusion, 500 mg/vial

Indications: treatment of cytomegalovirus retinitis in AIDS patients when ganciclovir fails or is contraindicated, also for aciclovir resistant herpes simplex virus infection.

Cautions: renal impairment.

Drug interactions: ciprofloxacin, cyclosporin, amphotericin B, I.V pentamidine, aminoglycosides, ritonavir, and saquinavir.

Contraindications: hypersensitivity to foscarnet.

Side effects: fever, headache, seizure, nausea, diarrhea, vomiting, anemia, nephrotoxicity, fatigue, dizziness, depression, confusion, rash, anorexia, granulocytopenia, leukopenia, vision abnormalities, coughing, dyspnea.

Dose and Administration: **Adult:** *CMV retinitis: I.V:*

Induction treatment: 60 mg/kg/dose every 8 hours or 100 mg/kg every 12 hours for 14-21 days.

Maintenance therapy: 90-120 mg/kg/day as a single infusion.

Acyclovir-resistant HSV induction treatment: I.V: 40 mg/kg/dose every 8-12 hours for 14-21 days.

Storage: store injection at room temperature.

Ganciclovir

Capsules, 250mg, 500mg

Powder for IV infusion, 500 mg/vial (as sodium salt)

Indications: treatment of slight or life threatening cytomegalovirus (CMV) infections in immuno-compromised patients, and for the prevention of CMV disease in transplant recipients.

Cautions: thrombocytopenia, impaired renal function.

Drug interactions: zidovudine; agents that inhibit renal tubular secretion; antineoplastic agents, co-trimoxazole.

Contraindications: hypersensitivity to ganciclovir.

Side effects: myelosuppression, neutropenia, thrombocytopenia, CNS effects, fever, skin rash, GI disturbances; liver function abnormalities; phlebitis. Fertility may be impaired.

Dose and Administration: Adult: *CMV retinitis:*

IV infusion: initially 5mg/kg 12 hourly infused at a constant rate over 1 hour (10mg/kg/day) for 14 - 21 days.

Maintenance: IV infusion 6mg/kg/day for 5 days /week; or 5mg/kg/day for 7 days/week.

Oral: maintenance therapy (in HIV - infected patients, when retinitis is stable): 1g 3 times daily, or 500mg 6 times daily, with food.

Storage: store intact vials at room temperature and capsules at 5-25°C.

Ribavirin

Tablet, 200mg

Indications: in combination with peginterferon alfa-2a injection for the treatment of chronic hepatitis C in patients with compensated liver disease who were previously untreated with alpha interferons.

Cautions: monitor for anemia 1-2 weeks after initiation; cardiac, pulmonary, and elderly patients; paediatric patients < 3 years of age.

Drug interactions: nucleoside analogues (didanosine, lamivudine, stavudine, zidovudine).

Contraindications: hypersensitivity to ribavirin; women of childbearing age who will not use contraception reliably; pregnancy; male partners of pregnant women; hemoglobinopathies; as monotherapy for treatment of chronic hepatitis C; patients with autoimmune hepatitis; anemia, severe heart disease.

Side effects: dizziness, headache, fatigue, fever, insomnia, irritability, depression, emotional lability, impaired concentration, alopecia, rash, pruritus, nausea, anorexia, vomiting, dyspepsia, decreased hemoglobin, myalgia, dyspnea, flu-like syndrome.

Dose and Administration: Oral: Adult:

Chronic hepatitis C, genotype 1,4 (in combination with peginterferon alfa-2a):

<75kg: 1000mg/day in 2 divided doses for 48 weeks

≥75kg: 1200 mg/day in 2 divided doses for 48 weeks

Chronic hepatitis C, genotype 2,3 (in combination with peginterferon alfa-2a):

800mg/day in 2 divided doses for 24 weeks.

Tablet: Should be administered with food.

Storage: store at room temperature.

Valaciclovir

Tablet, 500mg

Indications: treatment of herpes zoster and of herpes simplex infections of the skin and mucous membranes including initial and recurrent genital herpes.

Cautions: maintain adequate hydration; renal impairment; pregnancy and breast-feeding.

Drug interactions: see acyclovir.

Side effects: as a prodrug of acyclovir it is anticipated that side effects will be comparable; nausea and headache reported.

Dose and Administration: *herpes zoster*: 1g 3 times daily for 7 days

Herpes simplex, first episode, 500mg twice daily for 5 days (up to 10 days if severe); recurrent infection, 500mg twice daily for 5 days.

Child: not recommended.

7.4. Antiprotozoals

7.4.1 Antimalarials

Malaria is one of the most serious protozoal infections, which is transmitted by anopheline mosquitoes and rarely by congenital transmission, transfusion of infected blood or use of contaminated syringes among drug addicts. It is caused by infection by any of four species of plasmodium. *Plasmodium vivax* is the most extensively distributed and cause much debilitating disease. *P. falciparum* is also widespread, and causes the most severe infections, which are responsible for nearly all malarial - related deaths. *P. Ovale* is mainly confined to Africa and is less prevalent, while *P. malariae*, which causes the least severe but most persistent infections also occur widely.

Certain tissue forms of *P. vivax* and *P. ovale* which persist in the liver for many months and even years are responsible for the relapses characteristic of malaria such latent forms are not generated by *P. falciparum* or *P. malariae*. Recrudescence of these infections results from persistent blood forms in inadequately treated or untreated patients.

Management of malaria involves vector control, protection from bites, prophylaxis with drugs, and treatment of any infection that develops. It is now recognized that for many countries vector eradication is an unrealistic aim.

Treatment of Malaria

Blood Schizontocides are the mainstay of the treatment of acute malaria and some are used for prophylaxis. They include the 4- aminoquinolines (chloroquine), the related arylaminoalcohols (quinine and mefloquine), and artemisinin and its derivatives (artemether and artesunate). They suppress malaria by destroying the asexual blood forms of the parasites but, because they are not active against intrahepatic forms, they do not eliminate infections by *P. vivax* and *P. ovale*.

Some antimetabolites act synergistically when given in combination. For example, pyrimethamine in combination with a sulfonamide or sulfone (sulfadoxine); and some antibiotics (tetracyclines particularly doxycycline). Because they act more slowly these substances are of little value when used alone. The tetracyclines are used primarily as adjuncts to quinine where multi-drug resistant *P. falciparum* is prevalent.

Chloroquine, a rapidly acting schizontocide, is well tolerated, safe and inexpensive. It should be used to treat malaria wherever the parasites remain susceptible. *P. malariae* and *P. ovale* remain fully sensitive to chloroquine where as wide spread chloroquine resistance strains of *P. falciparum* have been reported in

many countries. Resistance in *P. vivax* has also become established in several parts of the world. Infections acquired in areas of known or unknown chloroquine resistance are treated now with quinine followed by pyrimethamine and sulfadoxine. Parenteral administration of chloroquine may be used when there is no expectation of resistance in cases of severe and complicated malaria, when the patient is unable to take oral medication and when neither quinine nor quinidine is available.

If subsequent relapse occurs in *P. ovale* and *P. vivax* infections primaquine should be administered, after a second course of chloroquine, to eliminate the intrahepatic infection. The combination of pyrimethamine with sulfadoxine is recommended for therapeutic use only in areas of high chloroquine resistance. A single dose of pyrimethamine with sulfadoxine is usually sufficient to eliminate infection; quinine should also be given for 3 days in patients in whom quinine may accelerate reduction of parasitaemia and in those patients with risk of fulminating disease. Because sulfonamides can induce hypersensitivity in pregnant women and possible kernicterus in the newborn, quinine should be used, whenever possible, to treat chloroquine resistant malaria during pregnancy.

Quinine, given orally, should be reserved for *P. falciparum* infections likely to be unresponsive to other drugs. Resistance to quinine was, until recently, rare. Doxycycline, which is an effective oral schizontocide should be given in combination with quinine except in pregnant women and children under 8 years.

Mefloquine remains effective except in certain areas of resistance. No parenteral preparations are currently available, and is thus suitable only for patients who can take drugs by mouth. It is generally well tolerated, although, some adverse effects have been reported. However, because of the danger of the emergence of mefloquine-resistant strains of *P. falciparum* and because of its potential toxicity, it should be used only following either microscopic or careful clinical diagnosis of *P. falciparum* infections that are known or strongly suspected to be resistant to chloroquine or sulfadoxine with pyrimethamine.

In multi-drug resistant malaria, preparations of artemisinin or its derivatives (artemether or artesunate) offer the only prospect of cure. They should not be used in the first trimester of pregnancy. For the treatment of multiresistant falciparum malaria oral artesunate may be an effective antimalarial. It should always be given in combination with mefloquine. Parenteral artemether, whose use is restricted, is effective alternative to quinine for the treatment of severe falciparum malaria and are preferred in areas where decreased efficacy of quinine has been documented. To ensure radical cure following parenteral treatment with artemether or oral treatment with artesunate, a full therapeutic dose of mefloquine should be given. A fixed-dose oral formulation of artemether with lumefantrine has recently become available and is recommended for the treatment of uncomplicated falciparum malaria in areas with significant resistance. The combination is not for use in pregnancy or breastfeeding.

Pregnancy: malaria is especially dangerous during pregnancy and the seriousness of the disease usually outweighs any potential risk from treatment.

For falciparum malaria, the adult treatment doses of oral and intravenous quinine can safely be given to pregnant women. Doxycycline should be avoided in pregnancy.

The adult treatment doses of chloroquine can be given for benign malaria. In the case of *P.vivax* or *P.ovale*, however, the radical cure with primaquine should be postponed until the pregnancy is over; instead chloroquine should be continued at a dose of 600mg each week during the pregnancy.

Prophylaxis against malaria

No drug regimen gives assured protection to everybody, and indiscriminate use of existing antimalarials increases the risk of inducing resistance.

Chloroquine, which is usually well tolerated at the required dosage, is preferred where *P.falciparum* remains fully sensitive. The recommended prophylactic regimen has been employed effectively even in areas of marginal resistance. However, it must be started 1 week before exposure, and be maintained in pregnant women until after delivery and for at least 4 weeks after the last risk of exposure in the case of non-immune individuals. This is sufficient to ensure elimination of *P.falciparum* and *P.malaria*, but not of *P.vivax* and *P.ovale* whose residual hepatic forms survive.

Mefloquine may be used for prophylaxis in areas of high risk or where multiple-drug resistance has been reported. Where possible prophylaxis should be started 2-3 weeks before travel to enable any adverse reactions to be identified before exposure (over three-quarters of adverse reactions occur by the third dose) and should be continued for 4 weeks after the second and third trimesters. It should be used in early pregnancy only if alternative drugs are either not available or unlikely to be effective and when it is impracticable for the woman to leave the endemic area.

Proguanil, a predominantly tissue schizontocide with little blood schizontocidal activity, is a causal prophylactic agent since it is active against pre-erythrocytic intrahepatic forms, particularly of *P.falciparum*. The latent persistent liver forms of *P.ovale* and *P.vivax* are unresponsive. However, there is evidence that it may be effective against *P.vivax* only immediately after the initial infection. *P.falciparum* resistance to proguanil and related compounds may occur in malaria endemic areas and particularly where it has been employed in mass prophylaxis. Proguanil is used for prophylaxis with chloroquine in areas where there is resistance to chloroquine but a low risk of infection as it may give some protection against *P.falciparum* and may alleviate symptoms if an attack occurs.

Pregnancy: -travel to malarious areas should be avoided during pregnancy; if travel is unavoidable, effective prophylaxis must be used. Chloroquine and proguanil may be given in usual doses in areas where *P.falciparum* strains are sensitive; in the case of proguanil, folic acid 5mg daily should be given.

Artemether

Injection, 80 mg/ml, 20 mg/ml

Suppository, 40 mg

Oral suspension, 40 mg/0.5ml, 80mg/ml

Indications: treatment of severe *P.falciparum* malaria in areas where evidence that quinine is ineffective.

Contraindications: first trimester of pregnancy.

Side effects: headache, nausea, vomiting, abdominal pain, diarrhoea; dizziness, tinnitus, neutropenia, elevated liver enzyme values; cardiotoxicity; neurotoxicity – in animal studies.

Dose and Administration:

Adult and Child over 6 months: *IM*: loading dose of 3.2 mg/kg, then 1.6 mg/kg daily until patient can tolerate oral medication or to maximum of 7 days; this is followed by a single dose of mefloquine 15 mg/kg (or occasionally, if necessary 25 mg/kg) to effect a radical cure.

Artemether seems to be as effective as IV quinine when given rectally to infants in coma from cerebral malaria. The initial dose for babies weighing less than 9 kg was 40 mg (one suppository). For those weighing more than this it was 80 mg. All then received a 40 mg suppository once a day for 6 days.

Artemether + Lumfantrine

Tablet, 20mg + 120mg

Indications: treatment of uncomplicated malaria due to *P.falciparum* and acute *P.vivax*.

Cautions: electrolyte disturbances, concomitant administration of drugs that prolong QT interval; severe renal or hepatic impairment.

Drug interactions: amiloride, amitriptyline, azithromycin, chloroquine, chlorpromazine, ciprofloxacin, clomipramine, erythromycin, fluconazole, fluphenazine, furosemide, grapefruit juice, hydrochlorothiazide, mefloquine, naldixic acid, ofloxacin, procainamide, pyrimethamine, quinidine, quinine, spironolactone, sulfadoxine + pyrimethamine.

Contraindications: pregnancy, breastfeeding, history of arrhythmias, of clinically relevant bradycardia, and congestive heart failure accompanied by reduced left ventricular ejection fraction.

Side effects: abdominal pain, anorexia, diarrhoea, nausea and vomiting; headache, dizziness, sleep disorders; palpitations; arthralgia, myalgia; cough; asthenia; fatigue; pruritus, rash.

Dose and Administration: *Oral*:

Adult: 35-65kg, artemether 80mg and lumefantrine 480mg, repeated after 8 hours, then twice daily on the following 2 days (i.e. 3-day course of 6 doses). Over 65 kg, as for 35-65 kg, but with closer monitoring for treatment failure / recrudescence.

Child: 5 - < 15kg, 1 tablet; 15 - < 25kg, 2 tablets; 25 - < 35kg, 3 tablets; 35 - 65 kg, 4 tablets, repeated after 8 hours, then twice daily on the following 2 days (i.e. a 3-day course of 6 doses).

Storage: store at room temperature.

Artesunate

Tablet, 100mg, 200mg

Indications: treatment of uncomplicated *P. falciparum* malaria in areas of multiple-drug resistance.

Cautions: risk of recurrence if used alone in non-immune patients.

Contraindications: first trimester of pregnancy.

Side effects: headache, nausea, vomiting, abdominal pain, diarrhoea, dizziness, tinnitus, neutropenia, elevated liver enzyme values; ECG abnormalities, including prolongation of QT interval; temporary suppression of reticulocyte response and induction of blackwater fever, reported.

Dose and Administration: *Oral:*

Adult and Child over 6 months: 4 mg/kg daily for 3 days; a single dose of mefloquine 15 mg/kg (or occasionally 25 mg/kg, if necessary) is given on day 2 or 3 to effect a radical cure; if artesunate used alone, 4 mg/kg on day 1, then 2 mg/kg daily for 6 days.

Chloroquine Phosphate

Tablets, 250mg (equivalent to 150 mg chloroquine base)

Syrup, 80mg/5ml (equivalent to 50 mg chloroquine base)

Injection, 250mg/5ml; 5ml (equivalent to 150 mg chloroquine base)

Indications: prophylaxis and treatment of acute attacks of malaria.

Cautions: patients should avoid alcoholic beverages while taking chloroquine.

Side effects: gastro-intestinal disturbances, headache, also convulsions, visual disturbances, depigmentation or loss of hair, skin reactions (rashes, pruritus); rarely, bone-marrow suppression; other side effects (not usually associated with malaria prophylaxis or treatment).

Drug interactions: carbamazepine, ciclosporin, digoxin, ethosuximide, mefloquine, phenytoin and valproic acid.

Dose and administration: Orally with meals or milk and intramuscularly. Where chloroquine syrup is not available the tablets can be given to children by crushing and mixing with sweetened milk on spoon. Chloroquine phosphate injection is very dangerous and should be used only in severe malaria and in comatose or vomiting patients. Always check if patients have not taken chloroquine tablet before giving the injection.

For prophylaxis –

Adult: *Oral*, 500mg (300mg base) once weekly.

Child: *Oral*, 8.3mg/kg (5mg/kg base) of body weight once weekly, not to exceed 500mg/week (300mg base) regardless of weight.

The tablets are taken on the same day of the week, beginning 1–2 weeks before travel into a malarious area until 6 weeks after leaving it. If therapy has not been started 2 weeks prior to exposure –

Adult: Initially, 1g (600mg base).

Child: Initially, 16.7mg/kg (10mg base/kg) of body weight.

Note: The initial dose is given in 2 equally divided doses 6 hrs apart followed by the usual dosage.

Counselling. Warn travellers about importance of avoiding mosquito bites, importance of taking prophylaxis regularly, and importance of immediate visit to doctor if ill within 1 year and especially within 3 months of return.

For treatment –

Oral treatment of cases with chloroquine dose table for 150mg base/tablet or 50mg base/5ml syrup—

Age group in year	Chloroquine Dosage (Expressed in mg base and in tablets)	
Under 1 year	75mg ½ tab 40 mg ¼ tab 75mg ½ tab 75mg ½ tab	STAT 6 hours later 2 nd . Day 3 rd . day
1 -5 years	150mg 1 tab 75mg ½ tab 75mg ½ tab 75mg ½ tab	STAT 6 hours later 2 nd . Day 3 rd . day
6 – 9 years	300mg 2 tab 150mg 1 tab 150mg 1 tab 150mg 1 tab	STAT 6 hours later 2 nd . Day 3 rd . day
10 -15 years	450mg 3 tab 225 mg 1 ½ tab 225 mg 1 ½ tab 225 mg 1 ½ tab	STAT 6 hours later 2 nd . Day 3 rd . day
ADULT (16 years and over)	600mg 4 tab 300 mg 2 tab 300 mg 2 tab 300 mg 2 tab	STAT 6 hours later 2 nd . Day 3 rd . day

For the treatment of comatose or vomiting patient and severe malaria, *intramuscular injection*, 5.8mg (3.5mg base)/kg of body weight. May be repeated if necessary after 6 hours. Continue treatment with tablet or syrup as soon as the patient can swallow until a total dose of 25mg/kg of chloroquine base.

Note: resistance should be considered if a good response is not noted in 2 or 3 days.

Storage: at room temperature.

Dihydroartemisinin

Tablet, 60mg

Dihydroartemisinin appears to offer no advantage over artesunate or artemether for the treatment of uncomplicated or severe malaria. However, it may be used in the absence of micro-scopic diagnosis if the compound is the recommended first-line treatment.

Dose and Administration: 4 mg/kg in a divided loading dose on the first day followed by 2 mg/kg daily for 6 days.

Mefloquine*Tablet, 250mg*

Indications: treatment of uncomplicated malaria due to multiple-resistant *P. falciparum*; treatment of severe and complicated malaria, after quinine; adjunct to treatment with artemisinin and derivatives; prophylaxis of malaria for travelers to areas where high risk of multiple-resistant *P. falciparum*.

Cautions: pregnancy, cardiac conduction disorders; avoid for prophylaxis in severe hepatic impairment and in epilepsy; breastfeeding, infants under 3 months.

Drug interactions: artemether + lumfantrine, atenolol, carbamazepine, chloroquine, digoxin, ethosuximide, nifedipine, phenytoin, propranolol, quinidine, quinine, timolol, valproic acid, verapamil.

Contraindications: neuropsychiatric disorders including depression or convulsions; hypersensitivity to quinine.

Side effects: nausea, vomiting, diarrhoea, abdominal pain, anorexia, headache, dizziness, loss of balance, somnolence, insomnia and abnormal dreams; neurological and psychiatric disturbances including sensory and motor neuropathies, tremor, ataxia, visual disturbances, tinnitus, vestibular disorders; convulsions, anxiety, depression, confusion, hallucinations, panic attacks, emotional instability, aggression, agitation and psychoses; circulatory disorders, tachycardia, bradycardia, cardiac conduction disorders; muscle weakness, myalgia, arthralgia; rash, urticaria, pruritus, alopecia; disturbances in liver function tests, leukopenia, leucocytosis, thrombocytopenia; rarely, Stevens-Johnson syndrome, atrioventricular block and encephalopathy.

Dose and Administration: **Adult** and **Child:** *Oral:* 15mg/kg (up to a maximum of 1g) as a single dose (increased to 25mg/kg in areas of resistance)

Adult: *Prophylaxis of malaria:* 250mg once a week; **Child** over 15kg once a week; prophylaxis should start 1-3 weeks departure and continue for 4 weeks after last exposure.

Primaquine phosphate*Tablet, 7.5mg (base), 15mg (base)*

Indications: For the prevention of relapses (radical cure) of malaria caused by *Plasmodium vivax* and *Plasmodium ovale*. It is also effective against the gametocytes of *Plasmodium falciparum* (after routine therapy with a blood schizontocide).

Cautions: G6PD deficiency, history of acute hemolytic anemia, systemic disease associated with agranulocytopenia (e.g. rheumatoid arthritis), and in those patients who are hypersensitive to Primaquine. Caution is also required during breast-feeding.

Drug interactions: bone marrow depressants, and other drugs that cause hemolysis (e.g. dapsone).

Contraindications: during pregnancy and in patients with Glucose 6 phosphate dehydrogenase (G6PD) deficiency.

Side effects: haemolytic anemia especially in G6PD deficiency, leucopenia, abdominal pain or cramps, nausea, vomiting, methemoglobinemia (cyanosis -

bluish fingernails, lips, or skin, dizziness or light headedness, difficult breathing, unusual tiredness or weakness).

Dose and Administration:

Adult: *Malaria:* Oral: 26.3mg (15mg base) once a day for 14 days or 45 mg base once weekly for 8 weeks

Child: *Malaria:* Oral: 0.68mg (0.39mg base) per kg of body weight once a day for 14 days.

Gametocytocidal treatment of P.falciparum (after routine blood schizontocide therapy),

Oral: **Adult and Child:** 500 – 750 mcg/kg as a single dose.

Note: - Continue medicine for full time of treatment.

Storage: at room temperature in a well closed, light-resistant container.

Proguanil Hydrochloride

Tablet, 100mg (scored)

Indications: chemoprophylaxis of malaria.

Cautions: pregnancy and in renal impairment.

Drug interaction: - anticoagulants.

Side effects: mild gastric intolerance and diarrhoea, occasional mouth ulcers and stomatitis, skin reaction and hair loss.

Dose and Administration: *Prophylaxis of malaria:* Oral:

Adult: 200mg daily, after food;

Child under 1 year, 25mg daily; 1-4 years, 50mg daily; 5-8 years, 100mg daily; 9-14 years, 150mg daily.

Note:- Warn travelers about importance of avoiding mosquito bites, importance of immediate visit to doctor if ill within 1 year and especially within 3 months of return.

Quinine Dihydrochloride

Tablet, (Dihydrochloride or sulphate), 300mg, 600mg

Injection, 300mg/ml in 1ml ampoule

Indications: quinine is indicated concurrently with tetracycline, doxycycline, clindamycin, pyrimethamine plus sulfadiazine, or pyrimethamine + sulfadoxine in the treatment of chloroquine resistant malaria.

Cautions: during pregnancy and breast feeding, in patients with atrial fibrillation, conduction defects, heart block and glucose 6 phosphate dehydrogenase (G6DP) deficiency.

Drug interactions: mefloquine, quinidine, cimetidine, halofantrine, digoxin, antacids, other hemolytics.

Contraindications: haemoglobinuria, optic neuritis and in patients hypersensitive to quinine or quinidine.

Side effects: cinchonism (blurred vision or change in colour vision, severe headache, nausea or vomiting, ringing or buzzing in ears or transient loss of hearing), GIT disturbances (abdominal or stomach cramps or pain, nausea, vomiting, diarrhoea), confusion, hypersensitivity reaction (fever, angioedema, blood disorder including thrombocytopenia and intravascular coagulation), acute renal failure, hypoglycemia.

Dose and Administration:

Treatment of multiple-drug resistant Plasmodium falciparum malaria:

Oral:

Adult: 600 mg (quinine sulfate) every 8 hours for 3, 7, or 10 days;

Child: 10 mg/kg (quinine sulfate) every 8 hours for 3, 7, or 10 days; duration of treatment depends on local susceptibility of *P. falciparum* and whether or not additional antimalarials also used.

Patient Advice. If all or part of a dose is vomited within one hour, the same amount must be readministered immediately.

Treatment of multiple-drug resistant Plasmodium falciparum malaria (in patients unable to take quinine by mouth): Slow IV infusion (over 4 hours):

Adult: 20 mg/kg (quinine dihydrochloride) followed by 10 mg/kg (quinine dihydrochloride) every 8 hours;

Child: 20 mg/kg (quinine dihydrochloride) followed by 10 mg/kg (quinine dihydrochloride) every 12 hours;

Initial dose should be halved in patients who have received quinine, quinidine or mefloquine during the previous 12 – 24 hours.

Storage: at room temperature in a well closed container (for tablet).

Sulfadoxine and Pyrimethamine

Tablet, 500mg + 25mg

Injection, 500mg + 25mg in 2.5ml ampoule

Indications: treatment of malaria due to susceptible *P. falciparum* in areas of high chloroquine resistance and in patients who have not responded to chloroquine; additionally quinine may be given for 3 days (see notes above)

Note: - It is not recommended for prophylaxis use for severe occurrence of side effects.

Cautions: anemia, bone marrow depression, hepatic and renal function impairment. Women of child bearing potential who travel to areas where chloroquine resistant malaria is endemic should be warned not to become pregnant.

Drug interaction: anticoagulants (cumarine or indandione derivatives), hydantoin, bone marrow depressants, other haemolytics, hepatotoxic medications.

Contraindication: breastfeeding; infants under two months of age; pregnancy; allergy to sulfonamides, pyrimethamine, furosemide, thiazide diuretics, sulfonylureas, carbonic anhydrase inhibitors.

Side effects: atrophic glossitis (pain, burning, or inflammation of the tongue, change in or loss of taste) due to folic acid deficiency with high doses, blood dyscrasias, specifically agranulocytosis (fever, sore throat), megaloblastic anaemia (usual tiredness or weakness), or thrombocytopenia (unusual bleeding or bruising), hypersensitivity (skin rash, fever), photosensitivity (increased sensitivity of skin to sunlight), hepatitis (yellow eyes or skin), Stevens' Johnson syndrome (aching of joints and muscles, redness, blistering, peeling, or loosening of skin, unusual tiredness or weakness).

Dose and Administration:

Treatment of malaria due to susceptible P. falciparum: Oral:

Adult: sulfadoxine 1.5g with pyrimethamine 75 mg (3 tablets) as a single dose

Child: 5 – 10 kg, half tablet; 11 – 20 kg, 1 tablet; 21 – 30 kg, 1½ tablets; 31 – 45 kg, 2 tablets; 31 – 45 kg, 2 tablets, as a single dose.

Storage: at room temperature in a well closed, and light-resistant containers.

7.4.2. Amoebicides and Antigiardial Agents

Metronidazole is a 5-nitroimidazole derivative with activity against protozoa and anaerobic bacteria. In amoebiasis, metronidazole acts as an amoebicide at all sites of infection with *Entamoeba histolytica*. Because of its rapid absorption it is probably less effective against parasites in the bowel lumen and is therefore used in conjunction with a luminal amoebicide such as **diloxanide furoate** or diiodohydroxyquinoline in the treatment of amoebic dysentery and in extra-intestinal amoebiasis, including hepatic amoebiasis.

Tinidazole has the antimicrobial actions of metronidazole and usually administered as a single dose by mouth with or without food.

Dehydroemetine, a synthetic derivative of emetine, is a tissue amoebicide with similar actions and uses, although probably of lower toxicity.

Chloroquine Phosphate

Tablet, 150mg base

Syrup, 50mg base / 5ml

Injection, 150mg base in 5ml ampoule

Indications: treatment of extraintestinal amebiasis, usually in combination with an effective intestinal amebicide. However, it is not considered a primary drug. See also under section 7.4.1.

Cautions: pregnancy and breast-feeding, severe blood disorders, hepatic function impairment; severe neurological disorders, retinal or visual field changes. See also under section 7.4.1.

Drug interactions: mefloquine, antiepileptics, cardiac glycosides, and cyclosporin.

Side effects: see chloroquine phosphate under section 7.4.1.

Dose and Administration:

Extraintestinal amebiasis:

Adult: 1g/day (600mg base) for 2 days followed by 500 mg/day (300 mg base) for at least 2 – 3 weeks

Child: 10 mg/kg (base) once daily for 2 – 3 weeks (up to 300 mg base/day)

Storage: Store in a well-closed container and at room temperature.

Dehydroemetine

Injection, 30 mg/ml in 1 and 2 ml ampoules

Indications: treatment of intestinal amoebiasis.

Cautions: breast-feeding, pregnancy, severe disease of any organ.

Contraindications: cardiac, renal, or neuromuscular disease.

Side effects: nausea, vomiting, diarrhoea, weakness, low blood pressure, irregular heartbeats, pain at the injection site

Dose and Administration: Adult: *IM*: 1mg/kg daily (maximum daily dose of 60 mg), generally for up to 4 – 6 day, but no more than 5 days in children. Elderly or severely ill patients, 0.5 mg/kg

Storage: store at room temperature.

Diloxanide Furoate

Tablet, 500mg

Indications: chronic amoebiasis, intestinal amoebiasis. It is a drug of choice for asymptomatic patients with *E.histolytica* cysts in the faces.

Side effects: flatulence, vomiting, urticaria, pruritus

Dose and Administration: Oral:

Adult: 500mg 3 times daily for 10 days

Child over 25 kg, 20mg/kg daily in 3 divided doses for 10 days; course may be repeated if necessary.

Metronidazole

Tablet, 250mg

Syrup 4% w/v, 250mg/5ml

Suspension (oral), 125mg/5ml

Intravenous infusion, 5mg / ml in 100ml

Indications: invasive amoebiasis and giardiasis, trichomoniasis, tissue nematode infections, bacterial infections (section 7.1.2); *Helicobacter pylori* eradication.

Cautions, Drug interactions, Contraindications, Side effects -see section 7.1.2 under metronidazole.

Dose and Administration:

Invasive amoebiasis: Oral: Adult and Child: 30mg/kg daily in 3 divided doses for 8 - 10 days; subsequent course of luminal amoebicide.

Invasive amoebiasis (if oral administration not possible): IV infusion: Adult and Child: 30 mg/kg daily in 3 divided doses (until patient able to complete course with oral drugs), subsequent course of luminal amoebicide.

Giardiasis: Oral: Adult: 2g once daily for 3 days,

Child: 15mg/kg daily in divided doses for 5 - 10 days.

Urogenital trichomoniasis: Oral: Adult: 2g as a single dose or 400 – 500 mg twice daily for 7 days; sexual partners should be treated concomitantly.

Note. In amoebiasis and giardiasis, various dosage regimens are used and definitive recommendations should be based on local experience.

Patient Advice: Metronidazole tablets should be swallowed whole with water, during or after a meal; metronidazole suspension should be taken one hour before a meal.

Storage: at room temperature, in a well closed, light resistant container.

Tinidazole

Tablet, 150mg, 500mg

Indications: in the treatment of susceptible protozoal infections and in the treatment and prophylaxis of anaerobic bacterial infections.

Cautions: see under metronidazole; avoid porphyria

Drug interactions: alcohol

Side effects: see under metronidazole

Dose and Administration:

Intestinal amoebiasis, 2gm daily for 2 - 3 days; **Child:** 50 - 60 mg/kg daily for 3 days

Amoebic involvement of liver, 1.5 - 2gm daily for 3 - 6 days, **Child:** 50 - 60mg/kg daily for 5 days.

Urogenital trichomoniasis and giardiasis, single 2gm dose (repeated once if necessary); **Child:** single dose of 50 - 75 mg/kg.

7.4.3. Leshmaniacides

Leishmaniasis is caused by the protozoa leishmania. It can be categorized as visceral, cutaneous or mucocutaneous. It may be a self-limiting localized skin lesion but may range from this to disseminated progressive disease. In endemic areas there is usually a reservoir of disease in a mammalian host and the usual vectors are sand flies.

Sodium Stibogluconate, an organic pentavalent antimony compound, is the treatment of choice for visceral leishmaniasis. The dose is 20mg/kg daily (max. 850 mg) for at least 20 days by intramuscular or intravenous injection; the dosage varies with different geographical regions and expert advice should be obtained. Skin lesions are treated for 10 days.

Amphotericin is used with or after an antimony compound for visceral leishmaniasis unresponsive to the antimonial alone; side effects may be reduced by using liposomal amphotericin at a dose of 1-3mg/kg daily for 10 - 21 days to a cumulative dose of 21- 30mg/kg.

Pentamidine Isethionate has been used in antimony resistant visceral leishmaniasis, but although the initial response is often good, the relapse rate is high; it is associated with serious side effects.

Amphotericin B

Powder for injection, 50mg in vial

Liposomal injection, 50mg in 15ml and 30ml vial

Indications: leishmaniasis

Cautions, Drug interactions, and Side effects (see section 7.2).

Dose and Administration: Adult:

IV infusion: 0.25 mg/kg/day, increased gradually to 0.5-1mg/kg/day; total dose 1-3g.

Liposomal injection: treatment of visceral leishmaniasis:

Immunocompetent patients: 3 mg/kg/day on days 1-5, and 3 mg/kg/day on days 14 and 21; a repeat course may be given in patients who do not achieve parasitic clearance.

Immunocompromised patients: 4 mg/kg/day on days 1-5, and 4 mg/kg/day on days 10, 17, 24, 31, and 38.

Pentamidine Isethionate

Powder for injection, 200mg in vial

Indications: pentamidine is used parenterally in the treatment of early African Trypanosomiasis, of various forms of leishmaniasis, and of pneumonia due to pneumocystis carinii.

Cautions: avoid rapid intravenous administration of pentamidine. Patients should remain supine during administration and their blood pressure should be monitored. Pentamidine should be used under close supervision and great care. Caution should be taken during pregnancy, breastfeeding (breast-feeding is not recommended during pentamidine therapy because of the potential risks to the new born), and in geriatric patients. Patients should be instructed in proper oral hygiene during treatment, including caution in use of regular toothbrushes, dental floss, and toothpicks. Pentamidine Isethionate should be used with caution when the following medical problems exist: bleeding disorder; bone marrow depression, cardiac disease or arrhythmias, dehydration, renal function impairment, diabetes mellitus, hypoglycemia, & hypotension.

Drug interactions: bone marrow depressants, radiation therapy, and didanosine, foscarnet, nephrotoxic medications.

Contra indications: previous allergic reaction to pentamidine.

Side effects: nephrotoxicity, leucopenia, anaemia, thrombocytopenia, raised liver enzyme, hypoglycaemia followed by hyperglycaemia and insulin dependent diabetes mellitus, hypotension, the IM administration often causes pain, swelling, sterile abscess formation, and muscle necrosis at the site of injection.

Dose and Administrations:

*** Pentamidine is toxic when given by injection and can affect the kidney, liver, blood and pancreas but systemic effects are rare following inhalation.

Adult:

Leishmaniasis visceral:

Intravenous infusion, 2 to 4 mg per Kg of body weight, administered over one to two hours, once a day for up to fifteen days. Administration may be repeated in one to two weeks if required.

Leishmaniasis, cutaneous:

Intravenous infusion, 2 to 4 mg per kg of body weight, administered over one to two hours, once or twice a week until the lesions heal.

Trypanosomiasis, African (without CNS involvement):

Intravenous infusion, 4 mg per Kg of body weight, administered over one to two hours, once a day for ten days.

Pneumonia, Pneumocystis carinii:

Intravenous infusion, 4 mg per Kg of body weight, administered over one to two hours. Once a day for fourteen to twenty-one days, depending on clinical response.

Usual **adult** prescribing limits:

Trypanosomiasis, African –3 to 5 mg per Kg of body weight a day

Child: See adult dose

Storage: Prior to reconstitution, store between 2°C and 8°C (36°F and 80°F), unless other wise specified by manufacturer. Protect dry powder and reconstituted solution from light.

Sodium Stibogluconate

Injection, 33% w/v in 2 and 6ml ampoule

Indications: a primary agent in the treatment of Leishmaniasis. It is treatment of choice for visceral leishmaniasis.

Cautions: hepatic impairment, pregnancy, IV injection must be given slowly over 5 minutes (to reduce risk of local thrombosis) and stopped if coughing and substernal pain, mucocutaneous disease, heart-disease occur. Treat intercurrent infections (e.g. Pneumonia)

Contraindications: significant renal impairment, breast-feeding.

Side effects: anorexia, nausea, vomiting, abdominal pain, headache, lethargy, myalgia, raised liver enzyme, coughing and substernal pain, rarely anaphylaxis, fever, sweating, flushing, vertigo, bleeding from nose and gum, jaundice, rash, pain and thrombosis on IV administration, IM injections is also painful.

Dose and Administration: See notes above.

7.4.4. Trypanocides

African trypanosomiasis, or sleeping sickness, is a protozoan infection transmitted by *Glossina Spp.* (tsetse flies). Two subspecies of *Trypanosoma brucei* - *T. brucei gambiense* and *T. brucei rhodesiense* - produce distinctive clinical forms of the diseases.

The early stage of African Trypanosomiasis results from infection of the blood stream and lymph nodes. The late meningoencephalitic stage results from infection of the central nervous system.

The drugs used for treatment are pentamidine, suramin and melarsoprol.

Treatment of early-stage infections of *T.b. rhodesiense* with suramin sodium and *T.b. gambiense* with Pentamidine Isethionate can be curative if started before the central nervous system has become involved. In areas where pentamidine resistance occurs, suramin sodium may be used for *T.b. gambiense* infection. Melarsoprol is used for confirmed cases of *T.b. rhodesiense* and *T.b. gambiense* with meningoencephalitic involvement.

Melarsoprol

Injection, 36 mg/ml in ampoule

Indications: treatment of meningoencephalitic stage of *T.b. gambiense* or *T.b. rhodesiense* infections.

Cautions: episodes of reactive encephalopathy, pneumonia and malaria, malnutrition; G6PD deficiency, leprosy.

Contraindications: pregnancy, influenza epidemics.

Side effects: fatal reactive encephalopathy characterized by headache, tremor, slurred speech, convulsions and ultimately coma, myocardial damage, albuminuria, hypertension, hypersensitivity reactions, agranulocytosis, dose-related renal and hepatic impairment, hyperthermia, urticaria, headache, diarrhoea and vomiting - in late stage of treatment.

Dose and Administration: Adult and Child:

Slow IV injection: gradually increased from 1.2 mg/kg to maximum of 3.6 mg/kg daily in courses of 3 - 4 days with intervals of 7 - 10 days between courses or 2.2 mg/kg daily for 10 days.

Storage: store at room temperature.

Melarsonyl potassium

Powder for injection, 200mg in vial

Melarsonyl potassium is a water-soluble derivative of melarsoprol which was formerly used as an alternative to melarsoprol but was probably more toxic and less effective.

Pentamidine Isethionate

Indications, Cautions, Drug interactions, Contraindications, Side effects, see under leishmaniacides (section 7.4.3)

Dose and Administration:

Treatment of haemolympathic stage of T.b.gambiense infection: IM injection: Adult and Child: 4 mg/kg daily or on alternative days for a total of 7 - 10 doses.

Treatment of meningoencephalitic stage of T.b.gambiense (prior to melarsoprol): IM injection: Adult and Child: 4mg/kg daily on days one and two.

Reconstitution and Administration. According to manufacturer's directions, Pentamidine Isethionate is toxic; care is required to protect personnel during handling and administration.

Suramin sodium

Powder for injection - 1gm in vial

Indications: Suramin is a trypanocide used in the treatment of the early stages of African trypanosomiasis.

Cautions, Contraindications, Side effects; see under suramin sodium, section 7.5.1

Dose and Administration: Suramin is not used as a sole therapy for late stage infection with central nervous involvement. Because of the danger of severe reaction, a test dose of 100 - 200mg should be given before initial treatment.

Adult: *IV* if test dose tolerated - 20mg per kg of body weight of suramin up to maximum of 1gm in adults given every 5 or 7 days, usually to a total of 5 injections and not exceeding of injections.

7.4.5. Drugs for Toxoplasmosis

Toxoplasmosis is caused by infection with the protozoan parasite *Toxoplasma gondii*. Toxoplasmosis in immunocompetent individuals is usually asymptomatic and if symptomatic infection does occur it is usually self-limiting. Very rarely myocarditis or encephalitis may occur. Patients with impaired immunity may develop serious complications such as encephalitis, myocarditis, and pneumonitis.

The treatment of choice is a combination of pyrimethamine and sulphadiazine.

Calcium folinate should also be given every third day during treatment to counteract megaloblastic anaemia. Treatment is ideally continued for several weeks after clinical cure. Prolonged even life long, maintenance therapy should be considered for AIDS patients since the tissue cyst forms of *T.gondii* will not have been affected by the initial treatment.

Congenital toxoplasmosis is not a problem in women who have toxoplasma antibody before conception but primary toxoplasmosis during early pregnancy is serious because of the risk of transplacental transmission, which may result in foetal death or congenital toxoplasmosis.

Clindamycin has some antiprotozoal actions, and has been used, usually with other antiprotozoals, in various infections including toxoplasmosis. Clindamycin with pyrimethamine has been used for treatment of toxoplasmosis instead of the more usual treatment with pyrimethamine plus sulfadiazine, in patients unable to tolerate sulfonamides.

Clindamycin

Capsule, 75 mg, 150 mg

Injection, 150 mg/ml in ampoule

Oral solution, 15 mg/ml

Indications: treatment for toxoplasmosis.

Cautions, Drug interactions, Contraindications, Side effects and Storage see section 7.1.2.

Dose and Administrations: *patients with AIDS and toxoplasmic encephalitis:* Oral: Clindamycin 600mg every 6 hours for at least 3 weeks, maintenance, 1200mg daily; patients also received pyrimethamine **or** Clindamycin 600mg four times daily together with pyrimethamine 75mg daily for 6 weeks.

Acute therapy with pyrimethamine and clindamycin 600mg four times daily by mouth or 1200mg every 6 hours intravenously.

Pyrimethamine

Tablet, 25mg

Indications: pyrimethamine is indicated in combination with sulfapyrimidine - type sulfonamide in the treatment of toxoplasmosis caused by *Toxoplasma gondii*.

Cautions: pregnancy and breast-feeding, hepatic function impairment and in those patients hypersensitive to pyrimethamine.

Drug interactions - bone marrow depressants, folate antagonists.

Contraindications: pregnancy (14 or 16 weeks), hypersensitivity, history of seizures disorders, anaemia and bone marrow depression.

Side effects: Atrophic glossitis (pain, burning, or inflammation of the tongue, change in or loss of taste), blood dyscrasias, specifically agranulocytosis (fever, sore throat), megaloblastic anaemia (unusual tiredness, or weakness), or thrombocytopenia (unusual bleeding or bruising), GIT disturbance (anorexia, Nausea, vomiting, diarrhoea), Hypersensitivity (skin rash).

Dose and Administration:

Toxoplasmosis (in second and third trimesters of pregnancy): Oral: Adult: 25mg daily for 3-4 weeks

Toxoplasmosis in neonates: Oral: 1 mg/kg daily; duration of treatment depends on whether neonate has overt disease-continue for 6 months, or is without overt disease but, born to mother infected during pregnancy-treat for 4 weeks, followed by further courses if infection confirmed.

Toxoplasmosis in immunodeficiency: Oral: Adult: 200mg in divided doses on first day, then 75-100mg daily for at least 6 weeks, followed by a suppressive dose of 25-50mg daily.

Chorioretinitis: Oral: Adult: 75mg daily for 3 days then 25mg daily for 4 weeks; in unresponsive patients, 50 mg daily for a further 4 weeks

Note: for the treatment of toxoplasmosis, pyrimethamine must always be taken with sulfadiazine. Take with meals and continue medicine with full time of treatment.

Storage: at room temperature in a tight, light-resistant container.

Spiramycin

Tablet, 3 mega unit

Indications: for treatment of toxoplasmosis.

Caution, Drug interactions and Side effects see erythromycin (section 7.1.2).

Dose and Administration: *Oral: Adult:* 6-9 million units daily, in 2 or 3 divided doses. Doses of up to 15 million units have been given daily in divided doses for severe infections.

Storage: store at room temperature.

Sulphadiazine

Tablet, 500mg

Indications: toxoplasmosis (with pyrimethamine); rheumatic fever

Cautions: hepatic and renal impairment; maintain adequate fluid intake (to avoid crystalluria); avoid in blood disorders (unless under specialist supervision); monitor blood counts and discontinue immediately if blood disorder develops; rashes - discontinue immediately; elderly; asthma, G6PD deficiency; pregnancy - avoid in first trimester, but may be given thereafter if danger of congenital transmission; breast feeding; see also interactions.

Drug interactions: ciclosporin, glibenclamide, pyrimethamine & co-trimoxazole (increased risk of antifolate effect), Warfarin

Contraindications: hypersensitivity to sulfonamides, severe renal failure or severe hepatic impairment, porphyria.

Side effects: nausea, vomiting, diarrhea, headache, hypersensitivity reactions including rashes, pruritus, photosensitivity reactions, exfoliative dermatitis, and erythema nodosum; rarely, erythema multiforme and toxic epidermal necrolysis; crystalluria resulting in haematuria, oliguria, anuria, blood disorders including granulocytopenia, agranulocytosis, aplastic anaemia, purpura - discontinue immediately, liver damage, pancreatitis, antibiotic - associated colitis, eosinophilia, cough and shortness of breath, pulmonary infiltrates, aseptic meningitis, depression, convulsions, ataxia, tinnitus, and electrolyte disturbances .

Dose and Administrations:

Toxoplasmosis (in second and third trimesters of pregnancy): Oral: Adult: 3g daily in 4 divided doses.

Toxoplasmosis in neonates: Oral: 85mg/kg daily in 2 divided doses; duration of treatment depends on whether the neonate has overt disease continue for 6 months, or is without overt disease but born to mother infected during pregnancy - treat for 4 weeks, followed by further courses, if infection confirmed.

Toxoplasmosis in immunodeficiency: Oral: Adult: 4 - 6g daily in 4 divided doses for at least 6 weeks, followed by a suppressive dose of 2 - 4g daily.

Note: - For the treatment of toxoplasmosis, Sulfadiazine must always be taken with pyrimethamine.

Storage: below 30°C in a tight container, protect from light.

7.5. Anthelmintics

7.5.1. Filaricides

Filarial nematode infections are endemic in large areas of the tropics and produce considerable morbidity. These are loiasis (arises from infections with *loa loa*), lymphatic filariasis (by *wuchereria bancrofti*, *brugia malayi*, or *B.timori*), onchocerciasis (river blindness, is caused by infection with the filarial nematode *onchocerca volculus*), mansonella infections.

Diethylcarbamazine is effective against microfilariae and adults of *loa loa*, *Wuchereria bancrofti*, and *Brugia malayi*. To minimise reactions, treatment is commenced with a dose of diethylcarbamazine citrate 1 mg/kg on the first day and increased gradually over 3 days to 6mg/kg daily in divided doses; this dosage is maintained for 21 days and usually gives a radical cure for these infections. Close medical supervision is necessary particularly in the early phase of treatment. In heavy infections there may be a febrile reaction, and in heavy *loa loa* infection there is a small risk of encephalopathy. In such cases treatment must be given under careful in-patient supervision and stopped at the first sign of cerebral involvement. (And specialist advice sought).

Ivermectin is very effective in onchocerciasis and it is now the drug of choice. A single dose of 150 micrograms/kg by mouth produces a prolonged reduction in microfilarial levels. Retreatment at intervals of 6 to 12 months depending on symptoms must be given until the adult worms die out. Reactions are usually slight and most commonly take the form of temporally aggravation of itching and rash.

Suramin is the only macrofilaricide that is currently available for use against *Onchocera volvulus*. Administered intravenously over a period of several weeks suramin also kills microfilariae.

It is, however, one of the most toxic substances used in clinical medicine and should always be given under medical supervision in a hospital. A careful assessment must always be made of the patient's capacity to withstand the effects of suramin treatment both before and during administration.

Diethyl Carbamazine Citrate

Tablet, 50 mg

Indications: in the treatment of lymphatic filariasis due to *Wuchereria bancrofti* (bancroftian filariasis), *Brugia malayi*, or *B. timori*. It is also used in loiasis due to *Loa loa* and also for toxocariasis.

Cautions: treatment with diethyl carbamazine should be closely supervised since hypersensitivity reactions are common and may be severe, especially in patients with onchocerciasis or loiasis.

Avoid mass treatment schedules for infants, pregnant women, the elderly, and debilitated patients, especially those with cardiac or renal disease. Caution if dizziness, loss of vision, night blindness, or tunnel vision occurs. Diethyl carbamazine should be administered with caution (eg. Gradually increasing doses) to prevent or minimize allergic reactions.

Side effects: itching and sweating of face, especially eyes; fever, lymphadenopathy; skin rash and visual disturbances; nausea; vomiting; headache; dizziness, drowsiness.

Dose and Administration: *Oral:*

Lymphatic filariasis (bancroftian):

Adult and Child over 10 years: 6mg/kg daily, preferably in divided doses after meals, for 21 days; **Child** under 10 years, half the adult dose; mass treatment program, **Adult and Child** over 10 years, 6mg/kg in divided doses over 24 hours, once a year; **Child** under 10 years, half the adult dose.

Lymphatic filariasis (brugian): **Adult and Child** over 10 years, 3-6mg/kg, preferably in divided doses after meals, for 6-12 days; **Child** under 10 years, half the adult dose; mass treatment control program, **Adult and Child** over 10 years, 3-6mg/kg in divided doses over 24 hours, 6 times at weekly or monthly intervals; **Child** under 10 years, half the adult dose

Occult filariasis: **Adult:** 8mg/kg daily for 14 days, repeated as necessary if symptoms return.

Loiasis, treatment: **Adult:** 1mg/kg as a single dose on the first day, doubled on two successive days, then adjusted to 2-3mg/kg 3 times daily for a further 18 days

Loiasis, prophylaxis: **Adult:** 300mg weekly for as long as exposure occurs

Note: Diethyl Carbamazine should be taken immediately after meals.

Storage: in airtight containers at room temperature.

Ivermectin

Tablet, 3mg, 6mg (scored)

Indications: suppressive treatment of onchocerciasis; as a secondary agent in the treatment of bancroftian filariasis caused by wucheria bancrofti.

Cautions: breast-feeding (avoid treating mother until infant is 1 week old).

Contraindications: pregnancy (delay treatment until after delivery), hypersensitivity to ivermectin.

Side effects: Mazotti like reaction, specifically arthralgia or myalgia (joint or muscle pain), dizziness, fever, headache, lymphadenopathy (painful and tender nodes in necks, armpits, or groin), skin rash or itching - due to death of microfilaria in skin; or unusual tiredness or weakness; postural hypotension (light headedness while standing).

Dose and Administration:

Bancroftian filariasis: **Oral: Adult:** 200mcg (0.2mg) per kg of body weight as a single dose.

Suppression of microfilariae: **Oral: Adult and Child** over 5 years (and weighing over 15kg), 150mcg/kg as a single dose once a year.

Note: - avoid food or alcohol for at least 2 hours before and after a dose.

Storage: at room temperature in a well-closed container.

Suramin Sodium

Powder for injection, 1gm in vial

Indications: curative treatment of onchocerciasis; trypanosomiasis (sec. 7.4.4)

Cautions: administer only under close medical supervision in hospital and with general condition of patient improved as far as possible before treatment (see notes above); first dose - possible loss of consciousness (see under dosage, below); maintain satisfactory food and fluid intake during treatment; urine tests before and weekly during treatment - reduce dose if moderate albuminuria, discontinue immediately if severe albuminuria or casts in urine.

Contraindications: previous anaphylaxis or suramin sensitivity, pregnancy (delay treatment until after delivery); severe liver or renal function impairment; elderly or debilitated; total blindness (unless required for relief from intensely itchy lesions).

Side effects: nausea, vomiting, shock, loss of consciousness reaction such as urticaria and pruritis, and later paraesthesia, hyperaesthesia of the palms and soles, skin eruptions, fever, photophobia and lachrymation, albuminuria, haematuria.

Dose and Administration:

Curative treatment of onchocerciasis: slow IV injection: **Adult** 3.3mg/kg as a single dose (see first (test) dose administration, below), followed at weekly intervals by incremental doses of 6.7 mg/kg, 10.0mg/kg, 13.3 mg/kg, 16.7 mg/kg, and 16.7mg/kg on weeks 2 to 6 respectively (total dose 66.7 mg/kg over 6 weeks)

Reconstitution of injection. Reconstitute in water for injections to produce a final concentration of 10%.

First (test) dose. Administer first dose with particular caution; wait at least 1 minute after injecting the first few microlitres; inject the next 0.5ml over 30 seconds and wait 1 minute; inject the remainder over several minutes.

7.5.2. Schistosomicides

Schistosomiasis, a waterborne parasitic infection, is caused by several species of trematode worms (blood flukes).

Intestinal schistosomiasis is caused principally by *Schistosoma mansoni* as well as *S.japonicum*, *S.mekongi*, and *S.intercalatum*. Urinary schistosomiasis is caused by *S.haematobium*. The latter is an important predisposing cause of squamous cell cancer of the bladder.

Praziquantel is used for the treatment of chronic schistosomiasis and is effective against all species of schistosomes.

Metrifonate and **oxamniquine** are also used but are only effective against *S.haematobium* and *S.mansoni* respectively. Antischistosomal drugs may cause clinical deterioration if used during the acute phase of infection; treatment is either delayed or given in conjunction with a corticosteroid.

Metrifonate

Tablet, 100mg

Indications: urinary schistosomiasis due to *S.haematobium*.

Cautions: avoid for those recently exposed to insecticides or other agricultural chemicals with anticholinesterase activity; pregnancy.

Drug interactions: depolarizing muscle relaxants such as suxamethonium (avoid for at least 48 hours), organophosphorus insecticides.

Side effects: cholinergic side effects, nausea, vomiting, abdominal pain, diarrhea, headache, dizziness, and weakness.

Dose and Administration:

Oral: 7.5mg/kg in three doses at intervals of 2 weeks.

Storage: Store at a temperature not exceeding 25°C.

Oxamniquine

Capsule, 250mg

Suspension, 250ml/5ml

Indications: intestinal schistosomiasis due to *Schistosoma mansoni* (acute stage and chronic hepatosplenic disease)

Cautions: epilepsy, pregnancy, breast-feeding. May impair ability to perform skilled tasks, for example operating machinery, driving.

Side effects: dizziness and drowsiness, headache, vomiting, diarrhea, intense reddish discoloration of urine occur commonly; rarely, urticaria, hallucinations, epileptiform convulsions; raised liver enzyme values; transient fever, eosinophilia.

Dose and Administration:

Intestinal Schistosomiasis due to S.mansoni (East and central Africa, Arabian peninsula):

Oral: **Adult** and **Child** 30mg/kg in 2 divided doses.

Storage: at room temperature in a tight container.

Praziquantel

Tablet, 600mg

Indication: treatment of schistosomiasis; intestinal tapeworm infections (*T. solium*, *T. saginata*, *D. latum* and *H. nana*); cysticercosis caused by *T. solium*.

Cautions: moderate to severe liver disease and in those hypersensitive to praziquantel; pregnancy and breast-feeding, nursing mothers (discontinue breast-feeding on the day of therapy and for 72 hours thereafter). The drug causes drowsiness that patients are to be advised not to drive vehicles or operate machineries.

Side effects: CNS effects (dizziness, drowsiness, headache, malaise), fever, GIT effects (abdominal cramps or pain, loss of appetite, nausea or vomiting, bloody diarrhoea), increased sweating, skin rash, hives or itching.

Dose and Administration: **Oral:** **Adult** and **Child** (above 4):

S. haematobium, *S.mansoni*: **Oral:** 20mg per kg of body weight two times a day for 1 day. *S.Japonium*, *S. mekongi*: **Oral:** 20mg per kg of body weight 3 times a day for 1 day.

T. solium, *T. saginata*, infections: 5-10mg/kg as a single dose

H. nana infection: 15-25 mg/kg as a single dose

D. latum infection: 10-25mg/kg as a single dose

Cysticercosis: 50mg/kg daily in 3 divided doses for 14 days with prednisolone (or similar corticosteroid) given 2-3 days before and throughout treatment period.

Storage: store below 30°C

7.5.3. Other Anthelmintics

Albendazole

Tablet, 200mg

Oral Suspension, 100mg/5ml

Indications: for the treatment of single or mixed intestinal nematode infection such as ascariasis, enterobiasis, hookworm infection, or trichuriasis and strongyloidiasis. Also for treatment of hydatid disease caused by *Echinococcus granulosus*.

Cautions: breast-feeding. Exclude pregnancy before starting treatment.

Contraindications: pregnancy.

Side effects: GIT disturbances, headache, dizziness, changes in liver enzyme, rarely reversible alopecia (loss of hair), rash, fever, blood disorders, including leucopenia and pancytopenia.

Dose and Administration:

Adult and **Child over 2 years:** **Oral:**

Single or mixed intestinal parasites: **Oral:** 400 mg as a single dose (given for 3 days in heavy mixed infestations involving *Trichuris* or *Taenia* spp.). Repeated after 3 weeks if required.

Strongyloidiasis: 400mg given once or twice daily for 3 consecutive days. May be repeated after 3 weeks.

Giardiasis: 400 mg once daily for 5 days

Hydatid: <60 kg: 15mg/kg/day in 2 divided doses (maximum: 800mg/day)

: ≥ 60 kg: 400mg twice daily

(Administer dose for three 28-day cycles with a 14-day drug-free interval in between).

Storage: at room temperature.

Levamisole

Tablet, 40mg

Indications: treatment of ascariasis, hookworm and mixed ascariasis with hookworm infections; with fluorouracil for the treatment of colorectal carcinoma after complete resection of primary tumour.

Cautions: sensitive to levamisole

Drug interactions: anticoagulants (cumarine and indandione), bone marrow depressants.

Contraindications: advanced liver or kidney disease, pre-existing blood disorders.

Side effects: nausea, vomiting, abdominal pain, dizziness and headache.

Dose and Administration: *Oral:*

Adult: 120mg (3 tablets) as a single dose

Child: 3mg per kg of body weight as a single dose.

Mebendazole

Tablets, 100mg, 500mg

Syrup, 100mg/5ml

Indications: For the treatment of whipworm (*trichuris trichuria*), pinworm (*Enterobius Vermicularis*), roundworm (*Ascaris Lumbricoids*), hookworm (*Ancylostoma duodenale*, *Nectar americanus*), and capillariasis in single or mixed infections.

Cautions: ulcerative colitis, liver diseases, hypersensitivity, treatment of intestinal worm is recommended in children over 1 year of age, there is limited data to assess the risk-benefit in those under one year. During pregnancy and in nursing women. In hookworm and whipworm infections iron supplements may be required as anemia may occur.

To prevent reinfection all other infected member of the family should be treated. Personal hygiene and sanitation should be observed and all bedding and nightclothes washed after treatment, especially in pinworm infection.

Side effects: transient abdominal pain or upset, nausea, vomiting, diarrhoea, dizziness, headache, skin rash and itching may occur occasionally in cases of massive infection and expulsion of worms.

Dose and Administration: Oral:**Adult and Child over 1 year:**

Ascariasis: 500mg as a single dose or 100mg twice daily for 3 days.

Hookworm infections, trichuriasis: 100mg twice daily for 3 days; if eggs persist in the faeces, second course after 3-4 weeks; alternatively 500mg as a single dose.

Adult and Child over 2 years:

Enterobiasis: 100mg as a single dose, repeated after interval of 2-3 weeks; all household members over 2 years should be treated at the same time.

Capillariasis: 200mg daily for 20-30 days; for mass treatment control programmes, 500mg as a single dose 4 times a year.

Roundworm, Whipworm, Hookworm mixed infection: 100mg twice daily, morning and evening, for 3 consecutive days. May be repeated in 2- 3 weeks if required.

Tapeworm (Taenia spp.): 100 mg twice daily for 6 days. There are reports of high success rates with higher doses for shorter periods (200mg twice daily for 4 days or 300mg twice daily for 3 days). Repeat after 3 weeks if necessary.

Storage: at room temperature, in well-closed containers.

Niclosamide

Tablet (chewable), 500mg.

Indications: eradication of tapeworm and *H.nana*.

Cautions: caution in patients with hypersensitivity to niclosamide, in children under 2 years and during pregnancy.

Side effects: nausea or vomiting, stomach pain, bad taste in mouth, dizziness, drowsiness, skin rash and itching may rarely occur.

Dose and Administration: Oral: preferably after a light meal or breakfast. Tablets should be crushed or chewed thoroughly and washed down with a small amount of water.

For small children tablets should be grounded as finely as possible and mixed with small amount of water.

In those with chronic constipation a mild laxative may be given before or after administering the drug.

A second course of niclosamide may be given if proglotides and /or ova persist for 7 – 14 days after treatment.

Adult: tapeworm: 2g

H.nana: 2 g on the first day, followed by 1 g for the following 6 days.

Child: 1 –5 years: 500mg; 6-12 years: 1g

Note: The dose may be given once as a single dose or half the dose first and the other half 1 hour later.

Storage: At room temperature, in a tight container, away from heat and direct light.

Piperazine

Tablet (Adipate), 300mg

Elixir (Citrate), 500mg/5ml, 622.5mg/5ml, 750mg/5ml, 706mg/5ml, 937.5mg/5ml, 1gm/5ml

Indications: for the treatment of round worm (*Ascaris Lumbricoids*) and pinworm (*Enterobius*) infections.

Cautions: caution in patients with epilepsy, impaired renal or hepatic function, and hypersensitivity. Supportive therapy should be given for anemic, dehydrated or malnourished patients prior to administration of the drug. Treat other members of the family paying attention to personal hygiene.

Drug interactions: chlorpromazine.

Side effects: nausea, vomiting, mild diarrhoea, abdominal cramps, headache, and dizziness may occur occasionally.

Dose and Administration: *Oral:* in constipated patients a purgative should be given to ease expulsion of the worm. A single dose is usually enough to treat roundworms. However, the dose may be repeated in 2 days if a patient has large number of roundworms.

Roundworm infection (Ascariasis):

Adult: 3- 4g (30 – 40ml) or 75mg/kg of body weight as a single dose.

Child: 75mg/kg of body weight as a single dose. Or, 1 –5 years –1g (10ml) as a single dose. 6 –12 years –2g (20ml) as a single dose.

Pinworm Infection (Enterobiasis, oxyuriasis):

Adult: 2g (20ml) or 65mg/kg of body weight every 12 hours daily for 7 days.

Child: 65 mg/kg of body weight as a single dose for 7 days. Or, 1 –5 years 750 mg (7.5ml) once daily for 7days. 6 –12 years –1½ g (15ml) once daily for 7days. Maximum – 2.5 g once daily.

Storage: at room temperature, in tight containers, protected from light.

Pyrantel Pamoate

Tablet, 125mg base

Oral suspension, 250mg base in each 5ml

Indications: treatment of Ascariasis, enterobiasis (pinworm infection), helminth infection (multiple), hookworm infection

Cautions: pre-existing liver dysfunction, severe malnutrition or anaemia.

Drug interactions: piperazine

Contraindications: hypersensitivity to the drug

Side effects: nausea, vomiting, tenesmus, anorexia, diarrhoea drowsiness, headache, trouble in sleeping, hypersensitivity (skin rash)

Dose and Administration:

Adult:

Ascariasis: Oral: 11mg (base) per kg of body weight as a single dose may be repeated in 2 or 3 weeks if required.

Enterobiasis: Oral: 11mg (base) per kg of body weight as a single dose. Repeat in 2 or 3 weeks

Hookworm (infection): Oral: 11mg (base) per kg of body weight once a day for three days.

Trichostrongyliasis: Oral: 11mg (base) per kg of body weight as a single dose. Maximum - up to 1 gm (base)

Child 2 years and over same as adults

Storage: at room temperature in a tight, light resistant container.

Thiabendazole*Tablet, 500mg**Oral suspension, 500mg/ml*

Indications: for treatment of strongyloidiasis, cutaneous and visceral larva migrans, dracontiasis, symptoms of trichinosis. It is also used as secondary treatment for threadworm when mixed with above infestations, adjunct in hookworm, whipworm or roundworm (but not suitable for mixed infection involving round worms due to risk of migration). It is not used for prophylactic purpose

Cautions: hepatic and renal function impairment, in elderly. Discontinue if hypersensitivity reaction occur, correct anemia, dehydration or malnutrition preferably before treatment.

Drug interactions: theophylline.

Contraindications: pregnancy, breast-feeding.

Side effects: anorexia, nausea, vomiting, diarrhoea, dizziness, headache, pruritus, drowsiness, hypersensitivity reaction (fever, chills, angioedema, rashes), visual disorder.

Dose and Administration: Adult: Oral:

Cutaneous Larva migrans: 25mg per kg of body weight two times a day for two days. May be repeated two days after completion of treatment if active lesions are still present.

Visceral Larva migrans: 25mg per kg of body weight 2 times a day for 5-7 days may be repeated in 4 weeks if required

Strongyloidiasis:

- *Uncomplicated infection:* 25mg per kg of body weight 2 times a day for two days.

- *Hyper infection syndrome:* 25mg per kg of body weight 2 times a day for 5-7 days may be repeated if required.

Trichinosis: 25mg per kg of body weight two times a day for 2-4 days based on patient response. Maximum - up to 3 grams daily

Child: (children 13.6kg of body weight and above) - same as adults dose

Note: - Continue medicines for full time of treatment and take after meals.

Storage: at room temperature in a tight container.

8. DRUGS USED IN ENDOCRINE DISORDERS AND CONTRACEPTIVES

8.1. Pituitary Hormone Preparations

Vasopressin, also known as antidiuretic hormone, is used in the treatment of pituitary diabetes insipidus, chiefly as desmopressin. It has documented efficacy in the short-term management of bleeding oesophageal varices and colonic diverticular bleeding.

Desmopressin, a synthetic analogue of vasopressin, differs from vasopressin in being longer-acting and in evoking minimal vasoconstrictor effects. It is used for diagnosis and treatment of diabetes insipidus. Intravenous injection may be used when intranasal or oral administration is considered unsuitable.

Desmopressin Acetate

Tablet, 100 mcg, 200 mcg

Injection, 4 mcg/ml

Nasal spray, 100 mcg/ml, 10 mcg/metered spray

Indications: diagnosis and treatment of diabetes insipidus; management of mild to moderate haemophilia.

Cautions: renal failure and hypertension; elderly; cystic fibrosis.

Contraindications: cardiac insufficiency and other conditions treated with diuretics.

Side effects: fluid retention and hyponatraemia; abdominal pain, headache, nausea, vomiting, epistaxis.

Dose and Administration:

Adult: *Diabetes insipidus:* *Oral:* initially 0.1 mg 3 times daily, adjusted to a maximum of 1.2 mg/day in 3 divided doses.

Intranasal: 10- 20 mcg (0.1- 0.2 ml) 1 - 2 times daily.

IV: 1 - 4 mcg (0.25 - 1 ml) 1 - 2 times daily.

Enuresis: *Oral:* under 65 years, 0.2 mg at bedtime; may be increased to 0.4 mg if necessary.

Child: *Diabetes insipidus:* *Oral:* initially 0.1 mg 3 times a day, adjusted to a maximum of 1.2mg/day in 3 divided doses.

Intranasal: 5-10 mcg (0.05-0.1ml) 1-2 times daily.

I.V: over 1 year, 0.4 - 1mcg 1-2 times daily; under 1 year, 0.2 - 0.4mcg 1-2 times daily.

Enuresis: *Intranasal:* over 5 years, 10-40mcg (0.1-0.4ml) given before sleep.

Oral: over 5 years, initially 0.2mg at bedtime; may be increased to 0.4 mg if necessary.

Storage: store tablets at room temperature; Injection at 2 - 8°C.

Nasal solution of desmopressin acetate preserved with benzalkonium chloride should be stored at 20 - 25 °C, nasal solutions preserved with chlorobutanol should be refrigerated at 2-8°C.

Vasopressin

Injection, 20 units/ml in 1 ml ampoule

Indications: treatment of diabetes insipidus, prevention and treatment of postoperative abdominal distention.

Cautions: chronic nephritis, asthma, epilepsy, migraine, heart failure, or other conditions which might be aggravated by water retention.

Drug interactions: cimetidine, chlorpropamide, clofibrate, carbamazepine, fludrocortisone, urea, or tricyclic antidepressants, lithium, heparin, demeclocycline, noradrenaline and alcohol.

Side effects: large parenteral doses cause headache, sweating, tremor, nausea, vomiting, diarrhoea, cramp. In women, cause uterine cramps of a menstrual character. Hyponatraemia with water retention. Hypersensitivity reactions (urticaria and bronchial constriction). Cardiovascular effects (hypertension, arrhythmias).

Dose and Administration:

Diabetes insipidus:

SC or I.M. Adult: 5-10 units 2-4 times/day as needed.

Child: 2.5-10 units 2-4 times/day as needed.

Abdominal distention: Adult: I.M: 5 units stat, 10 units every 3-4 hours.

Storage: store in airtight containers at 2° to 8°C.

8.2. Corticosteroidal Preparations

The corticosteroids are used in physiological (low) doses for replacement therapy in adrenal insufficiency. In pharmacological (high) doses, glucocorticoids decrease inflammation, suppress the immune response, stimulate erythroid cells of the bone marrow, promote protein catabolism, reduce intestinal absorption, increase blood glucose, and elevate blood pressure, increase renal excretion of calcium and promote redistribution of fat and development of cushingoid features.

Systemic administration of corticosteroids is contraindicated in patients with peptic ulcer, osteoporosis, psychoses, or severe psychoneuroses, and they should be used only with great caution in the presence of congestive heart failure or hypertension, in patients with diabetes mellitus, epilepsy, glaucoma, infectious diseases, chicken pox and severe herpeszoster, ocular herpes simplex, chronic renal failure and uremia in elderly persons. Patients with active or doubtfully quiescent tuberculosis should not be given corticosteroids except, very rarely, as adjuncts to treatment with tubercular drugs. Corticosteroids are usually contraindicated in the presence of acute infections, because of the interference with inflammatory and immunological response during long courses of corticosteroid therapy. Patients should be examined regularly and in particular, checked for hypertension, glucosuria, hypocalcaemia, gastric discomfort, and mental changes. Sodium intake may need to be reduced and potassium supplements may be necessary. Monitoring of the fluid intake and output, and daily weight records may give early warning of fluid retention.

Corticosteroids should not be administered concurrently with barbiturates, carbamazepine, phenytoin, primidone, or rifampicin; potassium depleting diuretics such as thiazide, anticoagulants, antidiabetics antihypertensives, salicylates, antimuscarinics, somatotropin, somatrem & vaccines, live virus, or other immunizations.

Signs of potential side effects upon using of corticosteroid are diabetes mellitus; burning, numbness, pain, or tingling at or near injections site; congestive heart failure (in susceptible individuals); generalized allergic reaction; local allergic reaction or infection at injection site; psychic disturbances; sudden blindness generalized anaphylaxis; cardiac arrhythmias; flushing of face or cheeks; seizures, acne; adrenal suppression; a vascular necrosis; cataracts, posterior subcapsular; Cushing's syndrome effects; cutaneous or subcutaneous tissue atrophy; ecchymosis; fluid and sodium retention; glaucoma with possible damage of optic nerves; growth suppression (in children); hypokalemic syndrome; impaired wound healing; increased intracranial pressure; secondary fungal or viral ocular infection; osteoporosis or bone fractures; pancreatitis; peptic ulceration or intestinal perforation; scarring at injection site; steroid myopathy; tendon rupture; and thin fragile skin.

Note: The risk of adverse effects with pharmacologic doses of corticosteroids generally increases with the duration of therapy and frequency of administration and to a lesser extent, with dosage.

Withdrawal of systemic corticosteroids.

Gradual withdrawal should be considered in those whose disease is unlikely to relapse and who have:

- Recently received repeated courses with in 1 year of stopping long-term therapy
- Other possible causes of adrenal suppression
- Received more than 40mg daily prednisolone (or equivalent)
- Been given repeat doses in the evening
- Received more than 3 weeks' treatment

Abrupt withdrawal may be considered in those whose disease is unlikely to relapse and who have received treatment for 3 weeks or less and are not included in the patient groups described above.

During corticosteroid withdrawal the dose may be reduced rapidly down to the physiological dosage (equivalent to 7.5mg prednisolone daily) and then reduced more slowly. Assessment of the disease may be needed during withdrawal to ensure that relapse does not occur.

Corticosteroid cover during stress.

Patients who are unable to take the dose by mouth should receive parenteral corticosteroid cover.

For patients requiring surgery, parenteral hydrocortisone should be administered as follows:

- 200mg hydrocortisone intramuscularly with premeditation.
- 100mg hydrocortisone by intravenous infusion in 5000ml 0.9% sodium chloride during surgery.

- 100mg hydrocortisone intramuscularly every 6 hours for 72 hours after surgery. For patients requiring minor surgical procedures.
- 100mg by hydrocortisone intramuscularly shortly before and after intervention.

Betamethasone

Tablet, 0.5mg

Indications: inflammatory dermatoses such as seborrheic or atopic dermatitis, neurodermatitis, anogenital pruritus, psoriasis, and inflammatory phase of xerosis.

Cautions, Drug interactions, Contraindications and Side effects: - see notes above

Dose and Administration:

Adult: *Oral:* 2.4 - 4.8 mg/day in 2-4 doses; range: 0.6-7.2 mg/day.

Child: *Oral:* 0.0175-0.25 mg/kg/day divided every 6-8 hours or 0.5-7.5 mg/m²/day divided every 6-8 hours.

Storage: store at 2-30 °C.

Dexamethasone

Tablet, 0.5mg, 0.75mg, 1mg, 2mg

Injection, 4mg/ml, 25mg/ml, 50mg/ml

Indications: suppression of inflammatory and allergic disorders; shock; diagnosis of Cushing's disease, congenital adrenal hyperplasia; cerebral oedema; nausea and vomiting with chemotherapy; rheumatic disease; see also notes above.

Cautions, Contraindications, Drug interactions and Side effects; see notes above

Side effects: see notes above; perineal irritation may follow intravenous administration of the phosphate ester.

Dose and Administration:

Oral: usual range 0.5-10mg daily

IM injection or slow IV injection or infusion (as dexamethasone phosphate), initially 0.5-20mg; **Child** 200-500 micrograms/kg daily

Cerebral oedema (as dexamethasone phosphate), intravenous injection, 10mg initially, then 4mg by intramuscular injection every 6 hours as required for 2-10 days.

Shock (as dexamethasone phosphate), intravenous injection or infusion, 2-6mg/kg, repeated in necessary after 2-6 hours.

Note: Dexamethasone 1mg \approx dexamethasone phosphate 1.2mg \approx dexamethasone sodium phosphate 1.3 mg

Storage: at room temperature.

Fludrocortisone Acetate

Tablet, 0.1mg, 0.3 mg

Indications: partial replacement therapy for primary and secondary adrenocortical insufficiency in Addison's disease; treatment of salt-losing adrenogenital syndrome.

Cautions, Contraindications, Drug interactions and Side effects; see notes above.

Dose and Administration: *Oral:*

Adult: 0.1-0.2 mg/day with ranges of 0.1 mg 3 times/week to 0.2 mg/day.

Addison's disease: initial: 0.1mg/day; if transient hypertension develops, reduce the dose to 0.05 mg/day. Preferred administration with cortisone (10-37.5 mg/day) or hydrocortisone (10-30mg/day).

Infant and Child: 0.05-0.1mg/day

Storage: store in well-closed container and at room temperature.

Hydrocortisone

Tablet (Acetate), 5mg, 10 mg

Injection (sodium succinate), 50mg/ml in 2ml ampoule, 125mg/ml

Powder for injection, 25mg/amp, 500mg in vial

Indications: adrenocortical insufficiency; hypersensitivity reactions including anaphylactic shock inflammatory bowel disease.

Cautions, Drug interactions, Contraindications and Side effects; see notes above

Dose and Administration:

Replacement therapy in adrenocortical insufficiency: Oral: **Adult:** 20 - 30mg daily in divided doses (usually 20 mg in the morning and 10 mg in early evening), **Child,** 10 - 30mg.

Acute adrenocortical insufficiency: Slow IV injection or IV infusion: **Adult:** 100 – 500 mg, 3 - 4 times in 24 hours or as required; Slow IV injection, Child up to 1 year 25mg, 1-5 years 50mg, 6 - 12 years 100mg.

Reconstitution and Administration. According to manufacturer's directions.

Storage: At room temperature, in a tight, light resistant container, protect from freezing.

Note: Reconstituted solutions should be used only if it is clear and should be discarded after 3 days.

After reconstitution, protect the solution from light.

Methylprednisolone Acetate

Injection (aqueous suspension), 40 mg/ml in 1 and 2ml ampoules

Indications: treatment of rheumatoid arthritis, osteoarthritis, bursitis and other non-infectious inflammatory conditions. Anti-inflammatory effects may be evident within 12-24 hours and usually last 3-4 weeks.

Cautions, Contraindications, Drug interactions and Side effects; see notes above.

Dose and Administration: *Intra-articular, large joints (knees, ankles, shoulders)* 20-80mg; *medium joints (elbows, wrists)* 10-40mg; *small joints (metacarpophalangeal, interphalangeal, sternoclavicular, acromioclavicular)* 4-10 mg. Soft-tissue injection, up to 60 mg, depending on the amount of inflamed tissue.

Storage: store at room temperature.

Prednisolone

Tablet, 1mg, 3.5mg, 5mg, 10mg

Injection (Sodium Phosphate), 10mg/ml, 25mg/ml in 2ml ampoule

Indications: suppression of inflammatory and allergic disorders; inflammatory bowel disease, asthma, and rheumatic disease, for the treatment of adrenocortical insufficiency and as immune suppression.

Cautions, Contraindications, and Drug interactions and Side effects; see notes above.

Intra articular injection of prednisolone is contraindicated in patients with arthroplasty of joint; blood clotting disorders, intra articular fracture, current or history of periarticular infection, osteoporosis & unstable joint.

Note: -owing to its less pronounced mineralocorticoids activity prednisolone is less likely than hydrocortisone to cause sodium retention, electrolyte imbalance, and oedema.

Dose and Administration:

Suppression of inflammatory and allergic disorders: Oral: Adult: initially up to 10 - 20mg daily (severe disease, up to 60mg daily), preferably taken in the morning after breakfast: dose can often be reduced within a few days, but may need to be continued for several weeks or months: maintenance, 2.5 - 15mg daily or higher; cushingoid features are increasingly likely with doses above 7.5mg daily; **Child:** fractions of adult dose may be used (for example, at 1 year 25% of adult dose, at 7 years 50%, and at 12 years 75%) but clinical factors must be given due weight.

Storage: store in a tight container at room temperature. Protect from freezing and light.

Triamcinolone Acetonide

Tablet, 4mg

Injection, 10mg/ml, 40mg/ml in 1ml vial

Indications: suppression of inflammatory and allergic disorders; rheumatic disease.

Cautions; Drug interactions, Contraindications, Side effects see notes above. Anorexia, weight loss, flushing, depression, and muscle wasting are reported to have been particularly associated with Triamcinolone.

Dose and Administration

Oral: 4 - 48mg daily although daily doses over 32mg are seldom indicated.

deep intramuscular injection, into gluteal muscle, 40mg of Acetonide for depot effect, repeated at intervals according to the patient's response, max. single dose 100mg.

Storage: at room temperature. Protect from freezing and light.

8.3. Thyroid Hormones and Antithyroid Agents

Thyroid agents are natural or synthetic agents containing levothyroxine (thyroxine) or liothyronine (tri-iodothyronine). The principal effect is to increase the metabolic rate. They also exert a cardio stimulatory effect which may be the result of a direct action on the heart. The main agent for thyroid replacement and described in this section is thyroxine. It is used in hypothyroidism (myxoedema) and also in diffuse non-toxic goiter, Hashimoto thyroiditis (lymphadenoid goiter) and thyroid carcinoma. Neonatal hypothyroidism requires prompt treatment for normal development.

Thyroxine Sodium (Levothyroxine Sodium) is the treatment of choice for maintenance therapy. It is almost completely absorbed from the gastrointestinal tract but the full effects are not seen for up to 1 to 3 weeks after beginning therapy; there is a slow response to dose change and effects may persist for several weeks after withdrawal. Dosage of thyroxine sodium in infants and children for congenital hypothyroidism and juvenile myxoedema should be titrated according to clinical response, growth assessment and measurement of plasma thyroxine and thyroid stimulating hormone.

Antithyroid drugs are used for hyperthyroidism either to prepare patients for thyroidectomy or for long-term management.

Antithyroid agents are used to achieve euthyroidism in patients with thyrotoxicosis. Propylthiouracil and carbimazole, interfere with thyroxine synthesis in the thyroid gland and are used mainly to prepare patients for surgery or irradiation, or in the long-term management of hyperthyroidism associated with Grave's disease.

Antithyroid drugs do not block the release of stored thyroid hormones and it is only when the performed hormones are depleted and concentrations of circulating hormones decline that clinical effects become apparent. An additional action of propylthiouracil is inhibition of the peripheral deiodination of thyroxine to tri-iodothyronine.

Propylthiouracil is given in a dose of 200 to 400mg daily in adults and this dose is maintained until the patient becomes euthyroid; the dose may then be gradually reduced to a maintenance dose of 50 to 150mg daily.

Antithyroid drugs only need to be given once daily because of their prolonged effect on the thyroid. Over-treatment with the rapid development of

hypothyroidism is not uncommon and should be avoided particularly during pregnancy because it can cause fetal goiter.

Pregnancy and breastfeeding:

Propylthiouracil cross the placenta and in high doses may cause fetal goiter and hypothyroidism- the lowest dose that will control the hyperthyroid state should be used (requirements in Graves disease tend to fall during pregnancy).

Propylthiouracil appears in breast milk but this does not preclude breastfeeding as long as neonatal development is closely monitored and the lowest effective dose is used.

Iodine has been used as an adjunct to antithyroid drugs for 10 to 14 days before partial thyroidectomy; however, there is little evidence of a beneficial effect. Iodine should not be used for long-term treatment because its antithyroid action tends to diminish. In patients in whom drug therapy fails to achieve long-term remissions definitive treatment with surgery or (increasingly) radioactive iodine is preferable.

Propranolol is useful for rapid relief of thyrotoxic symptoms and may be used in conjunction with antithyroid drugs or as an adjunct to radioactive iodine. Beta-blockers are also useful in neonatal thyrotoxicosis and in supraventricular arrhythmias due to hyperthyroidism. Propranolol has been used in conjunction with iodine to prepare mildly thyrotoxic patients for surgery but it is preferable to make the patient euthyroid with carbimazole. Laboratory tests of thyroid function are not altered by beta-blockers. Most experience is treating thyrotoxicosis has been gained with propranolol but nadolol is also used.

Carbimazole

Tablet, 5 mg

Indications: hyperthyroidism.

Cautions: impaired liver function, tracheal obstruction.

Drug interactions: oral anticoagulants and heparin.

Contraindications: hypersensitivity to carbimazole.

Side effects: pruritus, skin rashes, non-specific gastrointestinal disturbances, headache, mild arthralgia, urticaria, alopecia, drug-induced agranulocytosis, cholestatic hepatitis with jaundice, blood dyscrasias and "drug-fever" reactions.

Dose and Administration: *Oral:*

Adult: Initially 20 - 60 mg daily until there is euthyroidism.

Maintenance: 5 - 15 mg as a single daily dose.

Child: the usual initial daily dose is 15mg per day.

Storage: do not store above 25°C. Store in the original container.

Iodine + Potassium Iodide (Aqueous Iodine oral solution or Lugol's solution)

Solution, 5% + 10%

Indications: thyrotoxicosis (pre-operative).

Cautions: pregnancy, children; not for long-term treatment.

Contraindications: breastfeeding.

Side effects: hypersensitivity reactions including Coryza - like symptoms, headache, lacrimation, conjunctivitis, pain in salivary glands, laryngitis, bronchitis, rashes; on prolonged treatment depression, insomnia, impotence; goiter in infants of mothers taking iodides.

Dose and Administration: 0.3ml 3 times daily well diluted with milk or water.

Propranolol

Injection, 1mg/ml in 1ml ampoule

Tablet, 10mg, 40mg

See notes above and section 2.3 under propranolol

Propylthiouracil

Tablet, 25mg, 100mg

Indications: hyperthyroidism

Cautions: liver disorders, pregnancy, breast-feeding, reduce dose in renal impairment.

Side effects: nausea, mild gastrointestinal disturbances headache, rashes and pruritus, arthralgia; rarely alopecia, bone marrow suppression, urticaria, leucopenia; rarely coetaneous viscosities, thrombocytopenia, aplastic anaemia, hepatitis, lupus erythematosus - like syndromes.

Dose and Administrations: see notes above

Storage: at room temperature.

Thyroxin Sodium

Tablet, 0.05mg, 0.1mg

Indications: hypothyroidism

Cautions: cardiovascular disorders (myocardial insufficiency or ECG evidence of myocardial infarction); hypopituitarism or predisposition to adrenal insufficiency (must be corrected by corticosteroid prior to initial levothyroxine); elderly, long-standing hypothyroidism, diabetes insipidus, diabetes mellitus (may need to increase dose of insulin or oral antidiabetic drug); pregnancy; breast feeding.

Drug interactions: warfarin.

Contraindications: thyrotoxicosis, cholestyramine or colestipol, sympathomimetics.

Side effects: (usually with excessive dose) anginal pain, arrhythmias, palpitations, tachycardia, skeletal muscle cramps, diarrhea, vomiting, tremors, restlessness, excitability, insomnia, headache, flushing, sweating, excessive loss of weight and muscular weakness.

Dose and Administration:

Hypothyroidism: Oral: Adult: initially 50 - 100micrograms daily (25-50 micrograms for: those over 50 years) before breakfast, increased by 25 - 50 micrograms every 3 - 4 weeks until normal metabolism maintained (usual maintenance dose, 100 - 200 micrograms daily); where there is cardiac disease,

initially 25 micrograms daily or 50 micrograms on alternate days, adjusted in steps of 25 micrograms every 4 weeks.

*Congenital hypothyroidism and juvenile myxoedema: Oral: **Child:** up to 1 month, initially 5 - 10 micrograms/kg daily, adjusted in steps of 25 micrograms every 2 - 4 weeks, until mild toxic symptoms appear, then reduce dose slightly.*

Storage: at room temperature store in a tight light resistant container.

8.4. Insulin and oral antidiabetic agents

Diabetes mellitus is a disorder of carbohydrate metabolism in which the action of insulin is diminished or absent through altered secretion, decreased insulin activity, or a combination of both factors. There are two principal classes of diabetes (and many sub types not listed here):

Type I diabetes: Type I diabetes, also referred to as insulin dependent diabetes mellitus (IDDM), is due to a deficiency of insulin following autoimmune destruction of pancreatic beta cells. Patients with type I diabetes require administration of insulin.

Type II diabetes: Type II diabetes, also referred to as non-insulin dependent diabetes (NIDDM), is due to reduced secretion of insulin or to peripheral resistance to the action of insulin. Although patients may be controlled on diet alone, many require administration of oral antidiabetic drugs or insulin to maintain satisfactory control.

The aim of treatment is to achieve the best possible control of plasma glucose concentration and prevent or minimize complications including microvascular complications (retinopathy, albuminuria, neuropathy).

Diabetes mellitus is a strong risk factor for cardiovascular disease. Other risk factors such as smoking, hypertension, obesity and hyperlipidaemia should also be addressed.

Management of diabetes mellitus

Insulin: Insulin plays a great role in the regulation of carbohydrate, fat and protein metabolism. It is a polypeptide hormone of complex structure. There are differences in the amino acid sequence of animal insulin's, human insulin's and the human insulin analogues.

Insulin may be of beef or pork origin or it may be human insulin produced by gene technology or by modification of porcine insulin.

All insulin preparations are to a greater or lesser extent immunogenic in man but immunological resistance to insulin action is uncommon. Human and Porcine insulin are less immunogenic than bovine insulin and where possible most newly diagnosed IDDM patients are now given human insulin.

Insulin of whatever origin is formulated to provide a range of preparations offering: -

- Short duration which have a relatively rapid onset of action, namely soluble insulin, insulin lispro and insulin aspart.
- Intermediate action, e.g isophane insulin and insulin zinc suspension; and
- Long action which have a relatively slower in onset, e.g. Crystalline insulin Zinc suspension

For those who require administration of insulin, appropriate combinations of insulin therapy will have to be worked out for the individual patient. In pregnancy insulin requirements should be monitored frequently.

Examples of recommended insulin regimens

- Short - acting insulin mixed with intermediate - acting insulin: twice daily (before meals)
- Short - acting insulin mixed with intermediate acting insulin before breakfast
Short - acting insulin before evening meal
Intermediate - acting insulin: at bed time
- Short - acting insulin: three times daily (before breakfast, midday and evening meal)
Intermediate - acting insulin at bedtime
- Intermediate - acting insulin with or without short-acting insulin once daily either before breakfast or at bedtime suffices for some patients with type II diabetes who need insulin, sometimes in combination with oral hypoglycemic drugs.

Insulin is inactivated by gastro-intestinal enzymes, and must therefore be given by injection; the subcutaneous route is ideal in most circumstances. It is usually injected in to the upper arms, thighs, buttocks, or abdomen; there may be increased absorption from a limb site if the limb is used in strenuous exercise following the injection. Generally subcutaneous insulin injections cause few problems; fat hypertrophy does however occur but can be minimized by rotating

the injection site. Local allergic reactions are now rare. The various types of insulin may also be given intramuscularly when the onset of action is faster than with the subcutaneous route. An even faster onset may be achieved with intravenous administration, but this route is only suitable for fast-acting or soluble insulin.

Hypoglycemia: The most frequent complications of insulin therapy is hypoglycemia and patients taking insulin should be educated about its cause, symptoms, and treatment. Most patients can recognize the early warning signs of hypoglycemia and by taking sugar immediately they can prevent more serious symptoms developing. Comatose patients should be given intravenous glucose or, if this is not practicable, subcutaneous or intramuscular glucagons.

Hypoglycemia can also develop in patients taking oral hypoglycemic, notably the sulphonylureas. Some patients may no longer be able to recognize the warning signs of hypoglycemia after transferring from animal to human insulin and these patients, if appropriate, should be transferred back to porcine insulin.

Car drivers need to be particularly careful to avoid hypoglycemia. They should check their blood glucose concentrations before driving and, on long journeys, at intervals of approximately two hours; they should ensure that a supply of sugar is always readily available. If hypoglycemia occurs the driver should switch off the ignition until recovery is complete (may be 15 minutes or longer). Driving is not permitted when hypoglycemic awareness has been lost. For sporadic physical activity departing from the patients usual daily routine extra carbohydrate may need to be taken to avert hypoglycemia. Blood glucose should be monitored before, during and after exercise.

Diabetic Ketoacidosis. Diabetic ketoacidosis results from a lack of insulin due to a number of factors and the onset may be over hours or days. It is characterized by hyperglycemia, hyperketonaemia, and acidaemia and is a medical emergency which should be treated promptly with fluid and electrolyte replacement and insulin. However, over vigorous fluid replacement without severe dehydration carries the risk of precipitating cerebral oedema.

Surgery: Insulin dependent diabetics who require surgery should be managed with a continuous intravenous insulin infusion. Insulin is given as normal the night before operation, and switched to either a variable rate infusion via a syringe pump, together with a 10% glucose drip, or to a combined insulin-glucose infusion, on the day of operation. Subsequent conversion back to subcutaneous insulin should be undertaken before breakfast, giving the first subcutaneous dose 30 minutes before stopping continuous infusion. Non - insulin dependent patients should have any oral treatment omitted on the day of operation, and may be given insulin by a similar regimen if control is poor or deteriorates as can happen with major surgery.

Soluble insulin is a short - acting form of insulin. When injected subcutaneously it has a rapid onset of action (after 30 - 60 minutes), a peak action between 2 and 4 hours, and duration of action up to 8 hours when injected intravenously, soluble insulin has a very short half - life of only about 5 minutes.

When administered subcutaneous, intermediate-acting insulin's have an onset of action of approximately 1 - 2 hours, a maximal effect at 4 - 12 hours and duration of action of 16 - 24 hours. They can be given twice daily together with short - acting insulin or once daily, particularly in elderly patients. They can be mixed with soluble insulin in the syringe, essentially retaining properties of each component.

The duration of action of different insulin preparations varies considerably from one patient to another and this needs to be assessed for every individual. The type of insulin used and its dose and frequency of administration depend on the needs of each patient. For patients with acute onset diabetes mellitus, treatment should be started with soluble insulin given 3 times daily with medium acting insulin at bedtime. For those less seriously ill, treatment is usually started with a mixture of premixed short and medium acting insulin given twice daily. The proportions of soluble insulin can be increased in patients with excessive post-prandial hyperglycaemia. Patients should remain on the same insulin throughout treatment. Regimens should be developed by each country.

Biphasic Insulin (BP)⁺

Injection (highly purified), 100 units/ml in 10ml vial

Indications: diabetes mellitus (intermediate acting)

Cautions; Drug interactions, Side effects: see notes above and under soluble insulin; Protamine may cause allergic reactions

Dose and Administrations:

By subcutaneous injection, according to requirements

Storage: store at 2⁰ C to 8⁰ C. Do not allow freezing protect from light.

Note: It should be gently shaken before use.

Biphasic Isophane Insulin (soluble/Isophane Mixture)

Injection, 50/50, 30/70, 100 units/ml in 10ml vial

Indications: diabetes mellitus (intermediate acting)

Cautions, Drug interactions, Side effects; see notes above and under soluble insulin; protamine may cause allergic reactions.

Dose and Administration:

By subcutaneous injection, according to requirements

Storage: Store at 2⁰ C to 8⁰ C. Do not allow freezing protect from light.

Note: It should be gently shaken before use.

Insulin lispro

100u/ml (equivalent to 3.5 mg insulin lispro) in 10 ml vial solution for injection

⁺ BP stands for Bovine and porcine

Insulin lispro 25% + Insulin lispro protamine 75% sus.

Injection, 100u/ml (equivalent to 3.5 mg insulin lispro) in 3ml vial

Insulin lispro 50% + Insulin lispro protamine 50% sus.

Injection, 100u/ml (equivalent to 3.5 mg insulin lispro) in 3ml vial

Insulin lispro protamine sus.

Injection, 100u/ml (equivalent to 3.5 mg insulin lispro) in 3ml vial

Insulin soluble /Neutral (HPB)*

Injection 100 units/ml in 10ml vial

Indications: diabetes mellitus; diabetic emergencies and at surgery; diabetic ketoacidosis or coma.

Cautions: see notes above; reduce dose in renal impairment; occasionally insulin resistance necessitating large doses; pregnancy and breastfeeding; see also interactions.

Drug interactions: analgesics, antibacterials, antifungals, uricosurics.

Side effects: hypoglycaemia in overdose; localized and rarely generalized, allergic reactions; lipoatrophy at injection site; insulin resistance.

Dose and Administration:

Diabetes mellitus: SC, IM, IV injection or infusion: Adult and Child according to individual requirements

Storage: store at 2⁰ C to 8⁰ C. Do not allow to freeze protect from light.

Insulin Zinc suspension/Insulin Lente (HPB)*

Injection 100 units/ml in 10ml vial

Indications: diabetes mellitus (long acting)

Cautions, Drug interactions, Side effects: see notes above and under soluble insulin.

Dose and Administrations

By subcutaneous injection, according to requirements

Storage: store between 2⁰ C and 8⁰ C protect from freezing.

Isophane/NPH insulin (HPB)*

Injection, 100units/ml in 10ml vial

Indications: diabetes mellitus

* HPB stands for Human, porcine, and Bovine

Cautions, Drug interactions, Side effects; see notes above and under soluble insulin; Protamine may cause allergic reactions

Dose and Administrations

By subcutaneous injection, according to requirements.

Intravenous injection is contraindicated.

Storage: unopened vials of insulin should be stored at 2°C to 8°C and should not be subjected to freezing. The vial in use may be stored at room temperature; exposure to extremes in temperature or direct sunlight should be avoided.

Oral antidiabetic drugs

If patients with NIDDM have not achieved suitable control after about 3 months old dietary modification and increased physical activity, then oral hypoglycemic may be tried.

The two major classes of oral hypoglycemic agents are the sulphonylureas and the biguanides. Sulphonylureas act mainly by increasing endogenous insulin secretion, whilst biguanides act chiefly by decreasing hepatic gluconeogenesis and increasing peripheral utilization of glucose. Both types of agents only function in the presence of some endogenous insulin production.

Oral treatment of NIDDM is usually begun with a sulphonylureas. Chlorpropamide has more adverse effects than the other sulphonylureas. It has a long half life and hence is considered to have an increased tendency to cause hypoglycaemia, although a recent large study reported that hypoglycaemic episodes were less frequent with chlorpropamide than Glibenclamide. Use of chlorpropamide is therefore inadvisable in the elderly; Glibenclamide is also best avoided for the same reason.

A sulphonylurea with a short half-life, such as tolbutamide, should be used instead in such patients. Unfortunately sulphonylureas can cause weight gain so severely obese patients may be treated with the biguanide metformin rather than a sulphonylurea. Metformin is as effective as the sulphonylurea in terms of blood glucose control but has a rare tendency to cause lactic acidosis in patients with renal failure and should therefore be avoided in patients at risk. Patients with NIDDM who cannot be controlled adequately by oral therapy and diet need to be given insulin either in addition to the existing treatment or in place of the oral therapy.

Contraindications: sulphonylureas should be avoided where possible in severe hepatic and renal impairment and in porphyria. They should not be used while breast feeding and insulin therapy should be substituted during pregnancy.

Insulin therapy should also be instituted temporarily during intercurrent illness (such as myocardial infarction, coma, infection, and trauma). Oral antidiabetic drugs should be omitted on the morning of surgery; insulin is often required because of the ensuing hyperglycaemia in these circumstances. Sulphonylureas are contraindicated in the presence of ketoacidosis.

Side effects: side effects of sulphonylureas are generally mild and infrequent and include gastro-intestinal disturbances such as nausea, vomiting, diarrhoea and constipation.

They can occasionally cause a disturbance in liver function, which may rarely lead to cholestatic jaundice, hepatitis and hepatic failure. Hypersensitivity

reactions can occur, usually in the first 6 - 8 weeks of therapy; they consist mainly of allergic skin reactions which progress rarely to erythema multiforme and exfoliative dermatitis, fever and jaundice; photosensitivity has rarely been reported with chlorpropamide. Blood disorders are also rare but may include leucopenia, thrombocytopenia, agranulocytosis, pancytopenia, haemolytic anaemia, and aplastic anaemia.

Chlorpropamide has appreciably more side effects, mainly because of its very prolonged duration of action and the consequent hazard of hypoglycaemia and it should generally no longer be used. It may also cause facial flushing after drinking alcohol; this effect does not normally occur with other sulphonylureas. Chlorpropamide may also enhance antidiuretic hormone secretion and very rarely cause hyponatraemia.

Biguanides

The biguanides are agents of first choice in the management of obese type 2 diabetics, but the small risk of lactic acidosis demands that they may be used with caution. Risk factors for lactic acidosis include: impaired renal or hepatic function, cardiopulmonary insufficiency, presence of infections, excessive alcohol intake, and certain systemic illnesses, e.g. leukaemia.

Metformin is useful in management of obese diabetics because it induces a mild anorexia and so helps to control weight gain. The biguanides include metformin.

Metformin

Tablet, 500mg, 850mg

Indications: type 2 diabetes mellitus.

Cautions: substitute insulin during severe infection, trauma, surgery; breastfeeding.

Drug interactions: alcohol, cimetidine & other cationic medication excreted by renal tubular transport (such as: amiloride, nifedipine, digoxin, morphine, procainamide, quinidine, quinine, ranitidine, triamterene, trimethoprim, vancomycin); Furosemide; vitamin B12.

Contraindications: renal impairment (withdraw if renal impairment suspected; hepatic impairment; heart failure; severe infections or trauma; dehydration; alcohol dependence; pregnancy).

Side effects: anorexia, nausea and vomiting, diarrhoea patients with renal failure (discontinue); decreased vitamin B12 absorption.

Dose and Administrations:

Oral: Adult: 500mg every 8 hours or 850mg every 12 hours with or after food (maximum 2g daily in divided doses).

Storage: Store at room temperature in a light resistant container, unless otherwise specified by manufacturer.

Sulphonamides, Urea Derivatives

Sulphonylureas act mainly by stimulating the release of endogenous insulin. Some pancreatic beta-cell responsiveness should remain intact for these agents to be effective. They may provide good control of blood glucose and have been shown to reduce the microvascular complications of diabetes. They are used in the management of type 2 diabetes not controlled by diet alone, and may be given together with a biguanide if necessary to achieve control. The sulphonylureas in common use include glibenclamide, glimepiride, glipizide, chlorpropamide and tolbutamide.

Chlorpropamide

Tablet, 100mg, 250mg

Indications: type II diabetes mellitus.

Cautions, Contraindications, Side effects; see notes above.

Drug interactions: see under Glibenclamide.

Dose and Administrations:

Initially 250mg daily with breakfast (Elderly 100 - 125 mg but avoid - see notes above), adjusted according to response; maximum 500 mg daily.

Storage: Store in a well-closed container at room temperature

Glibenclamide

Tablet, 5mg

Indications: type II diabetes mellitus

Cautions, Side effects, Contraindications: see notes above

Drug interactions: analgesics (azapropazone, phenylbutazone and possibly other NSAIDs enhance effect of sulphonylureas), antibacterial, antifungals, uricosurics.

Dose and Administrations: Initially 5mg daily with or immediately after breakfast (Elderly 2.5mg, but avoid - see notes above), adjusted according to response, maximum 15mg daily.

Glimepiride

Tablet, 1mg, 2mg, 4mg

Indications: management of type 2 diabetes mellitus (NIDDM).

Cautions, Contraindications and Side effects: see notes above.

Drug interactions: see under Glibenclamide.

Dose and Administration: Adult: Oral: initially 1 mg once daily, before breakfast. If necessary the dose may be increased by 1 mg at weekly intervals up to 6 mg daily, according to blood glucose levels; maximum 8 mg daily.

Glipizide

Tablet, 2.5 mg, 5 mg, 10 mg

Indications: management of type 2 diabetes mellitus (NIDDM).

Cautions, Contraindications and Side effects: see notes above.

Drug interactions: see under Glibenclamide.

Dose and Administration: Adult: Oral: initially, 2.5 - 5 mg daily, 15 - 30 minutes before breakfast (2.5 mg in the elderly and in liver impairment), gradually increased, if necessary, to a maximum of 40 mg/day. Amounts exceeding 15 mg/day should be given in divided doses.

Storage: store at controlled room temperature.

Pioglitazone

Tablet, 15mg, 30mg, 45mg

Indications:

Type 2 diabetes mellitus (NIDDM), monotherapy: Adjunct to diet and exercise, to improve glycemic control

Type 2 diabetes mellitus (NIDDM), combination therapy with sulfonyl urea, metformin, or insulin: when diet, exercise, and a single agent alone does not result in adequate glycemic control.

Cautions: should not be used in diabetic ketoacidosis; use in type 1 diabetes is not recommended; anemia; not for use in children < 18 years of age.

Drug interactions: delavirdine, fluconazole, gemfibrozil, ketoconazole, nicardipine, NSAIDs, sulfonamides, amiodarone, fluoxetine, glimepride, glipizide, phenytoin, sertraline, warfarin.

Contraindications: hypersensitivity reaction, active liver disease, patients who have experienced jaundice during therapy.

Side effects: serum triglycerides decreased, HDL-cholesterol increased, weight gain, upper respiratory tract infection, edema, headache, fatigue, hypoglycemia, anemia, myalgia, sinusitis, pharyngitis.

Dose and Administration: *Oral: Adult:*

Monotherapy: Initial: 15-30 mg once daily; if response is inadequate, the dosage may be increased in increments up to 45mg once daily; maximum recommended dose: 45mg once daily.

Combination therapy: Maximum recommended dose: 45mg/day

With sulphonylureas: Initial: 15-30 mg once daily;

With metformin: Initial: 15-30mg once daily

With insulin: Initial: 15-30mg once daily

Rosiglitazone maleate

Tablet, 1.32mg equ. 1mg base, 2mg

Indications: type 2 diabetes mellitus (noninsulin dependent, NIDDM):

Monotherapy: improve glycemic control as an adjunct to diet and exercise

Combination therapy: in combination with a sulfonylurea, metformin, or insulin when diet, exercise, and a single agent do not result in adequate glycemic control.

Cautions: diabetic ketoacidosis; use in type 1 diabetes; premenopausal, anovulatory women; anemia or depressed leukocyte count; edema.

Drug interactions: delavirdine, fluconazole, gemfibrozil, ketoconazole, nicardipine, NSAIDs, sulfonamides, amiodarone, fluoxetine, glimepride, glipizide, phenytoin, sertraline, warfarin.

Contraindications: active liver disease, patients who previously experienced jaundice during troglitazone therapy.

Side effects: weight gain, increase in total cholesterol, increased LDL-cholesterol, increased HDL-cholesterol, edema, headache, fatigue, hyperglycemia, hypoglycemia, diarrhea, anemia, back pain.

Dose and Administration: *Oral: Adult:*

Monotherapy: Initial: 4 mg daily as a single daily dose or in divided doses twice daily. If response is inadequate after 12 weeks of treatment, the dosage may be increased to 8 mg daily as a single daily dose or in divided doses twice daily.

Combination therapy:

With sulfonylureas: initial: 4 mg daily as a single daily dose or in divided doses twice daily; doses of sulfonylurea should be reduced if the patient reports hypoglycemia.

With metformin: initial: 4 mg daily as a single daily dose or in divided doses twice daily. If response is inadequate after 12 weeks of treatment, the dosage may be increased to 8 mg daily as a single daily dose or in divided doses twice daily.

With insulin: initial: 4 mg daily as a single daily dose or in divided doses twice daily. Doses of insulin should be reduced by 10% to 25% if the patient reports hypoglycemia or if the plasma glucose falls to < 100 mg/dl.

Thiazolidinediones

The thiazolidinediones, such as pioglitazone and rosiglitazone, improve glycaemic control by reducing cellular insulin resistance.

Tolbutamide

Tablet, 500mg

Indications: type II diabetes mellitus

Cautions, Contraindications: see notes above.

Side effects: see notes above, also headache, and tinnitus.

Drug interactions: see under Glibenclamide.

Dose and Administrations:

0.5 - 1.5g (max. 2g) daily in divided doses; with or immediately after breakfast.

Storage: store in a well-closed container at room temperature.

8.5. Female Sex hormones and Combination preparations

Therapeutically, oestrogens, progestogens and their derivatives are used alone or in combination:

- In oral contraceptives to suppress ovulation.
- To control abnormalities in ovarian hormone secretion in the treatment of dysfunctional uterine bleeding and primary dysmenorrhoea.
- Peri and postmenopausally to relieve symptoms and to prevent and possibly treat the long-term sequelae of the menopause.
- To induce normal pubertal development in Turner's syndrome and other hypo-oestrogenic states. Patients with delayed puberty should be managed by a specialist as injudicious use of oestrogen can cause abnormal breast development.

They are also used in high doses in the palliative treatment of advanced prostatic carcinoma.

Chorionic Gonadotrophin

Powder for injection, 1500 IU, 5000 IU

Indications: induces ovulation and pregnancy in anovulatory, infertile females; treatment of hypogonadotrophic hypogonadism, prepubertal cryptorchidism; spermatogenesis induction with follitropin alfa or follitropin beta.

Cautions: asthma, epilepsy, migraine, or cardiovascular disorders, including hypertension, or renal disorders.

Contraindications: hypersensitivity to the drug; prostatic carcinoma, precocious puberty.

Side effects: headache, tiredness, changes in mood, depression, restlessness, edema, (especially in males), and pain on injection, gynaecomastia, ovarian

hyperstimulation with marked ovarian enlargement or cyst formation, acute abdominal pain, ascites, pleural effusion, hypovolaemia, shock, and thromboembolic disorders in severe cases.

Dose and Administration: Adult: *I.M.:*

Induction of ovulation: 5000-10,000 units given to mimic the midcycle peak of luteinising hormone. Up to 3 repeat injections of up to 5000 units each may be given within the following 9 days to prevent insufficiency of the corpus luteum.

Prepubertal cryptorchidism (males): IM: 500-4000 units three times weekly.

Delayed puberty associated with hypogonadism in males: IM: 500-1500 units twice weekly.

Storage: store at 2° to 15 °C in airtight containers; protect from light.

Conjugated estrogens (equine)

Vaginal cream, 625 mcg/g

Tablet, 0.3mg, 0.45 mg, 0.625 mg, 0.9 mg, 1.25 mg, 2.5 mg

Indications: for replacement therapy in naturally occurring or surgically induced estrogen deficiency state associated with menopausal and postmenopausal symptoms; e.g. hot flushes, sleep disturbances and atrophic vaginitis; prostatic cancer, breast cancer, abnormal uterine bleeding.

Cautions: postmenopausal women, endometriosis, asthma, epilepsy, migraine, coronary heart disease, diabetes or renal disorders; gallbladder disease, cholestatic jaundice.

Drug interactions: hydrocortisone, anticoagulants, aminoglutethimide, carbamazepine, phenobarbital, rifampin, nafcillin, nevirapine, phenytoin, ethanol, rifamycins.

Contraindications: hepatic dysfunction; a history of estrogen dependent neoplasia such as breast or endometrial cancer, endometrial hyperplasia, undiagnosed vaginal bleeding, cerebrovascular accident; thrombosis or thromboembolic disorders; active thrombophlebitis, ophthalmic vascular disease; known or suspected pregnancy.

Side effects: there may be sodium and water retention with oedema, weight gain, tenderness and enlargement of the breasts, changes in libido, menstrual disorders and withdrawal bleeding, alterations in liver function, jaundice, gallstones, depression, headache, migraine, dizziness, a decrease in glucose tolerance, and decrease in tolerance of contact lenses. Nausea and vomiting and other gastro-intestinal disturbances. Skin reactions, cardiovascular effects (risk in blood pressure).

Dose and Administration: Adult:

Atrophic vaginitis:

Vaginal cream: PV or Topicaly: 1-2 g daily, on a cyclical basis; maximum 4 g/day.

Oral: initial: 0.3 mg/day; the lowest dose that will control symptoms should be used. May be given cyclically or daily, depending on medical assessment of patient.

In menopausal and postmenopausal symptoms: Oral: 0.3 to 1.25 mg daily is given in conjunction with a progestogen in women with a uterus.

Primary ovarian failure: Oral: 1.25 mg daily.

Female hypogonadism: Oral: 2.5 to 7.5 mg daily administered on a cyclical basis.

Palliative treatment of prostatic carcinoma: Oral: 1.25 to 2.5 mg three times daily.

Abnormal uterine bleeding: Oral: 1.25 mg, may repeat every 4 hours for 24 hours, followed by 1.25 mg once daily for 7-10 days.

Storage: store in airtight containers and at room temperature.

Conjugated estrogens (equine) (initial phase) Conjugated estrogens (equine) and Medroxyprogesterone acetate (second phase)

Biphasic tablet, conjugated estrogens 0.625mg and conjugated estrogens 0.625mg / medroxyprogesterone acetate 5mg.

Indications: women with an intact uterus; treatment of moderate to severe vasomotor symptoms associated with menopause; treatment of atrophic vaginitis; osteoporosis (prophylaxis).

Contraindications: pregnancy.

Dose and Administration: *Oral: Adult:*

One maroon conjugated estrogen 0.625mg tablet daily on days 1 through 14 and one light blue conjugated estrogen 0.625mg / MPA 5mg tablet daily on days 15 through 28.

Conjugated estrogens and Medroxyprogesterone acetate

Monophasic tablet, 0.3+1.5mg, 0.45+1.5mg, 0.625+2.5mg, 0.625+5mg

Dose and Administration: *Oral: Adult:*

One conjugated estrogen 0.3mg / MPA 1.5mg tablet daily; dose may be increased to one conjugated estrogen 0.625mg / MPA 5mg tablet daily.

Conjugated estrogens (equine) (initial phase) Conjugated estrogen (equine) + Norgestrel (= levonorgestrel) (second) phase

Biphasic tablets

Diensterol

Vaginal Cream 0.1%

Indications: treatment of atrophic vaginitis or other vaginal disturbances associated with hypoestrogenic conditions.

Cautions and Contraindications: abnormal vaginal bleeding, breast cancer, active/recent stroke or heart attack, asthma, diabetes, seizures, migraine headaches, liver disease, heart disease (e.g., high blood pressure, heart attacks, congestive heart failure), kidney disease, low thyroid hormone (hypothyroidism), abnormal calcium level in the blood, depression, high blood pressure during pregnancy (toxemia), cholestatic jaundice, uterine fibroids, endometriosis, cholesterol or lipid problems, gallbladder disease, excessive weight gain, certain blood disorder (porphyria), any allergies (especially peanut allergy).

Side effects: vaginal irritation, dizziness, lightheadedness, headache, stomach upset, bloating, nausea, weight changes, increased/decreased interest in sex, and breast tenderness, mental/mood changes (e.g., severe depression, memory loss), calf pain/swelling, sudden severe headache, chest pain, trouble

breathing, one-sided weakness, slurred speech, vision changes, breast lumps, swelling of hands or feet, changes in vaginal bleeding, unusual vaginal discharge/itching/odor, yellowing of the eyes or skin, rash, itching, swelling, severe dizziness, trouble breathing.

Dose and Administration: the usual dosage range is one or two applicatorful per day for one or two weeks, then gradually reduced to one half initial dosage for a similar period. A maintenance dosage of one applicatorful, one to three times a week, may be used after restoration of the vaginal mucosa has been achieved.

Storage: store at room temperature and away from light and moisture.

Estradiol Valerate

Tablets, 1 mg, 2 mg

Indications: treatment and prophylaxis of menopausal and postmenopausal disorders, and in menstrual symptoms arising from estrogen deficiency.

Cautions, Contraindications and Side effects: as for the estrogens in general.

Dose and Administration:

Adult: *Oral:* 1 - 2 mg daily, according to severity of symptoms and clinical response.

Storage: store at room temperature.

Estradiol + Estrinol + Estrone

Monophasic tablet, 600mcg + 270mcg + 1.4 mg

Dose and Administration:

Menopausal symptoms and Osteoporosis prophylaxis: 1 - 2 tablets daily, with cyclical progestogen for 12 - 14 days of each cycle in women with intact uterus.

Estradiol Valerate (initial phase) Estradiol valerate + Norethisterone (second phase)

Biphasic tablets

Estradiol Valerate (initial phase) Estradiol valerate + Medroxy progesterone acetate (second phase)

Biphasic tablets

Estradiol Valerate (initial phase) Estradiol valerate + dydrogesterone (second phase)

Biphasic tablets

Estradiol + dydrogesterone

Monophasic tablets

Estradiol

Tablet, 2mg

Intravaginal cream, 0.01 %

Pessary, 500 mcg

Indications: actions and uses similar to those described for the oestrogens in general.

Cautions, Contraindications and Side effects; similar to estrogens.

Dose and Administration:

Adult: *Oral:* initially 2-8 mg daily for 5-7 days; maintenance 2-4 mg daily, cyclically or continuously.

Atrophic vaginitis: PV, 1 applicator (0.5g) daily for 2-3 weeks, maintenance 1 application twice weekly.

Storage: stores in airtight containers.

Ethinyl estradiol

Tablets, 10 mcg,

Indications: hormone replacement for menopausal symptoms, osteoporosis prophylaxis; palliation in breast cancer in men and postmenopausal women; contraception in combination with a progestogen.

Cautions: progestogen may need to be added to regimen to reduce risk of endometrial cancer due to unopposed estrogen; migraine; history of breast nodules of fibrocystic disease; uterine fibroids may increase in size; symptoms of endometriosis may be exacerbated; predisposition to thromboembolism; presence of antiphospholipid antibodies; increased risk of gall bladder disease; porphyria.

Drug interactions: rifampicin, ritonavir, warfarin, doxycycline, nevirapine, phenytoin.

Contraindications: pregnancy; estrogen - dependent cancer; active thrombophlebitis or thromboembolic disorders; undiagnosed vaginal bleeding; breastfeeding; liver disease, Dubin Johnson and Rotot syndromes.

Side effects: nausea and vomiting, abdominal cramps and bloating; weight increase; breast enlargement and tenderness; premenstrual - like syndrome; sodium and fluid retention; changes in liver function; cholestatic jaundice; rashes and chloasma, changes in libido; depression, headache, migraine, dizziness, leg cramps; contact lenses may irritate.

Dose and Administration: *Oral: Adult:*

Hormone replacement (female): 10 - 20 mcg daily.

Palliation in breast cancer in postmenopausal women: 0.1- 1 mg 3 times daily.

Storage: store at room temperature

Hydroxyprogesterone Caproate

Injection, 250 mg/ml in 1 ml ampoule

Indications: used for recurrent miscarriage and various menstrual disorders.

Dose and Administration: *Recurrent miscarriage associated with proven progesterone deficiency: IM:* 250-500mg weekly given during the first half of pregnancy.

Norethisterone (Norethindrone)

Tablet, 5 mg

Indications: endometriosis; menorrhagia; severe dysmenorrhoea; contraception (section - 8.4.1); hormone replacement therapy (HRT).

Cautions: epilepsy; migraine; diabetes mellitus; hypertension; cardiac or renal disease and those susceptible to thromboembolism; depression; breast-feeding.

Drug interactions: carbamazepine, ciclosporine, dexamethasone, fludrocortisone, glibenclamide, griseofulvin, hydrocortisone, insulins, metformin, nevirapine, phenobarbital, phenytoin, prednisolone, rifampicin, warfarin.

Contraindications: pregnancy, undiagnosed vaginal bleeding; hepatic impairment or active liver disease; severe arterial disease, breast or genital tract cancer, porphyria; history in pregnancy of idiopathic jaundice, severe pruritus or pemphigoid gestations.

Side effects: acne, urticaria, fluid retention, weight increase, gastrointestinal disturbances, changes in libido, breast discomfort, premenstrual symptoms, irregular menstrual cycles, depression, insomnia, somnolence, alopecia, hirsutism, anaphylactoid - like reactions; exacerbation of epilepsy and migraine; rarely jaundice.

Dose and Administration: Adult: Oral:

Endometriosis: 10 mg daily starting on fifth day of cycle (increased if spotting occurs to 20 - 25 mg daily, reduced once bleeding has stopped).

Menorrhagia: 5 mg three times daily for 10 days to stop bleeding; to prevent bleeding 5 mg twice daily from day 19 to 26 of cycle.

Dysmenorrhoea: 5 mg 2 - 3 times daily from day 5 to 24 for 3 to 4 cycles.

Storage: protect from light.

Serum Gonadotrophin

Powder for injection, 400IU, 1000IU

8.6. Male sex hormone Preparations

Mesterolone

Tablet, 25 mg

Indications: replacement therapy for adult onset hypogonadism or following parenteral therapy after secondary sexual characteristics have developed.

Cautions, Contraindications, Drug interactions and Side effects; see under testosterone.

Dose and Administration:

Adult: Oral: initially 25 mg 3 times daily; maintenance 25 mg once or twice daily, depending on individual response.

Storage: protect from light.

Testosterone

Indications: hypogonadism; palliative treatment of advanced breast cancer in women.

Cautions: cardiac, renal or hepatic impairment; elderly, ischaemic heart disease, hypertension, epilepsy, skeletal metastases (risk of hypercalcaemia); regular examination of prostate during treatment; prepubertal boys.

Drug interactions: glibenclamide, insulins, metformin, warfarin.

Contraindications: breast cancer in men, prostate cancer, hypercalcaemia, pregnancy, breastfeeding, nephrosis, and history of primary liver tumours.

Side effects: prostate abnormalities and prostate cancer, headache, depression, gastrointestinal bleeding, nausea, cholestatic jaundice, changes in libido, gynaecomastia, anxiety, asthenia generalized paraesthesia, electrolyte disturbances including sodium retention with oedema and hypercalcaemia; increased bone growth; androgenic effects such as hirsutism, male pattern baldness, seborrhoea, acne, priapism, precocious sexual development and premature closure of epiphyses in pre-pubertal males, virilism in females, and suppression of spermatogenesis in men.

Storage: protect from light and store at room temperature.

Preparations include:

Testosterone propionate

Injection, 10 mg/ml, 100 mg/ml, 100 mg/ml, 250 mg/ml in 1 ml ampoule

Dose and Administration: IM: 50 mg two or three times weekly.

Testosterone + Chorionic Gonadotrophin

Injection, 10 mg + 1000 IU, 18 mg + 2000 IU

Testosterone Enanthate + Testosterone propionate

Injection (depot), 80 mg + 20 mg in each ml

Testosterone propionate + Testosterone phenyl propionate + Testosterone isocaproate + Testosterone decanoate

Injection, 30 mg + 60 mg + 60 mg + 100 mg

Dose and Administration: IM: usually 1 ml every 4 weeks.

8.7. Contraceptives

Hormonal Contraceptives

Hormonal contraceptives are only generally available for women although preparations for men are being evaluated. Oral contraceptives are divided into 2 main types: combined (containing an oestrogen and a progestogen) and progestogen - only. They produce a contraceptive effect mainly by suppressing the hypothalamic pituitary system resulting in prevention of ovulation. In addition changes in the endometrium make it unreceptive to implantation and changes in the cervical mucus may prevent sperm penetration.

Combined Oral Contraceptives

Oral contraceptives containing an oestrogen and a progestogen are the most effective preparations for general use.

Advantage of combined oral contraceptives include:

- Reliable and reversible.
- Reduced dysmenorrhoea and menorrhagia;
- Reduced incidence of premenstrual tension.
- Less symptomatic fibroids and functional ovarian cysts;
- Less benign breast disease
- Reduced risk of ovarian and endometrial cancer
- Reduced risk pelvic inflammatory disease, which may be a risk with intra uterine devices.

An association between the amount of estrogen and progestogen in oral contraceptives and an increased risk of adverse cardiovascular effects has been observed.

The oestrogen content ranges from 20 to 50 micrograms and generally a preparation with the lowest oestrogen and progestogen content which gives good cycle control and minimal side - effects in the individual woman is chosen.

The risk of hypertension increases with increasing duration of oral contraceptive use and they should be discontinued if the woman becomes hypertensive during use. Combined oral contraceptives are associated with an increased risk of thromboembolic and thrombotic disorders and an increase in risk of cerebrovascular disorders including stroke and subarachnoid hemorrhage.

Risk factors for venous Thromboembolism or Arterial disease: Risk factors for venous thromboembolism include family history of venous thromboembolism in first degree relative age under 45 years, obesity, long-term immobilization and varicose veins.

Risk factors for arterial disease: Risk factors for arterial disease include family history of arterial disease in first - degree relative age under 45 years, diabetes mellitus, hypertension, smoking, age over 35 years, obesity and migraine.

If 2 or more factors for either venous thromboembolism or arterial disease are present, combined oral contraceptives should be avoided. Combined oral contraceptives are contraindicated if there is severe or focal migraine

Estrogen - containing oral contraceptives should be discontinued four weeks prior to major elective surgery and all surgery to the legs. When discontinuation is not possible consideration, should be given to the prophylactic use of subcutaneous heparin.

Reasons to stop combined oral contraceptives immediately. Combined estrogen - containing oral contraceptives should be stopped immediately if any of the following symptoms occur.

- Sudden severe chest pain (even if not radiating to left arm):
- Sudden breathlessness (or cough with blood strained sputum):
- Severe pain in calf of one leg
- Severe stomach pain

- Serious neurological effects including unusual, severe, prolonged headache especially if first time or getting progressively worse or sudden partial or complete loss of vision or sudden disturbance of hearing or other perceptual disorders or dysphagia or bad fainting attack or collapse or first unexplained epileptic seizure or weakness, motor disturbances, very marked numbness suddenly affecting one side or one part of body:
- Hepatitis, jaundice, liver enlargement;
- Severe depression
- Blood pressure above systolic 160mmHg and diastolic 100mmHg;
- Detection of a risk factor.

Diarrhea and vomiting: Diarrhea and vomiting up to 3 hours after taking an oral contraceptive or very severe diarrhea can interfere with its absorption. Additional precautions should therefore be used during and for 7 days after recovery. If the vomiting and diarrhoea occurs during the last 7 tablets, the next pill - free intervals should be omitted (in the case of every day (ED) tablets the inactive ones should be omitted).

Interactions. The effectiveness of both combined and progestogen only oral contraceptives may be considerably reduced by interaction with drugs that induce hepatic enzyme activity (e.g carbamazepine, griseofulvin, modafinil, nelfinavir, nevirapine, oxcarbazepine, phenytoin, phenobarbital, primidone, ritonavir, topiramate, and above all, rifabutin and rifampicin); advice on the possibility of interaction with newer antiretroviral drugs should be sought from HIV specialists: some broad - spectrum antibiotics (eg. Ampicillin, doxycycline) may reduce the efficacy of combined oral contraceptives by impairing the bacterial flora responsible for recycling of ethinylestradiol from the large bowel.

Progestogen-only contraceptives

Progestogen only contraceptives, such as oral levonorgestrel may offer a suitable alternative when estrogens are contraindicated but the oral progestogen only preparations do not prevent ovulation in all cycles and have a higher failure rather than combined estrogen containing preparations. Progestogen - only contraceptives carry less risk of thromboembolic and cardiovascular disease than combined oral contraceptives and are preferable for women over 35 years, for heavy smokers, and for those with hypertension, valvular heart disease, diabetes mellitus, and migraine, they can be used as an alternative to estrogen containing combined preparations prior to major surgery. Menstrual irregularities (oligomenorrhoea, menorrhagia, amenorrhoea) are common. Injectable preparations of Medroxy progesterone acetate or norethisterone enantate may be given intramuscularly. They have prolonged action and should only be given with full counseling and manufacturer's information leaflet.

Interactions: effectiveness of oral progestogen - only preparations is not affected by broad-spectrum antibiotics but is reduced by enzyme inducing drugs.

Starting routine. One tablet daily, on a continuous basis, starting on day 1 of cycle and taken at the same time each day (if delayed by longer than 3 hours contraceptive protection may be lost). Additional contraceptive precautions are not necessary when initiating treatment.

Changing from a combined oral contraceptive: start on the day following completion of the combined oral contraceptive course without a break (or in the case of every day (ED) tablets omitting the inactive ones).

After childbirth: start any time after 3 weeks postpartum (increased risk of breakthrough bleeding if started earlier) - lactation is not affected.

Emergency contraception

Emergency contraception can be obtained using levonorgestrel, one tablet of 750 micrograms should be taken as soon as possible (within 72 hours) after unprotected intercourse followed 12 hours later by another one tablet. Under those circumstances it prevents about 86% of pregnancies that would have occurred if no treatment had been given. Adverse effects include nausea, vomiting, headache, dizziness, breast discomfort, and menstrual irregularities. If vomiting occurs within 2-3 hours of taking the tablets, replacement tablets can be given orally with an antiemetic.

It should be explained to the woman that her next period may be early or late; that she needs to use a barrier contraceptive method until her next period, and that she should return promptly if she has any lower abdominal pain or if the subsequent menstrual bleed is abnormally light, heavy, brief or absent. There is no evidence of harmful effects to the fetus if pregnancy should occur.

8.7.1. Combined Oral Contraceptives

*Tablet, levonorgestrel (D-Norgestrel)+Ethinylestradiol and Iron tablets**
(0.15mg + 0.03mg; 0.25mg + 0.05mg; 0.5mg + 0.005mg; 0.3mg + 0.003mg)

*Tablet, Norethindrone (Norethisterone) + Ethinylestradiol** (0.5mg + 0.03mg)

*Tablet, Norethindrone (Norethisterone) + Mestranol and iron tablets** (1mg + 0.05mg)

Indications: contraception, menstrual symptoms, endometriosis.

Cautions: risk factor for venous thromboembolism and arterial disease (see notes above); migraine; hyperprolactinaemia (seek specialist advice); some types of hyperlipidaemia; gallbladder disease; depression; long-term immobilization,

* Each iron Tablet contains: Ferrous fumarate 75 mg

sickle-cell disease; inflammatory bowel disease including crohn disease; see also interactions

Drug interactions: see notes above

Contraindications: pregnancy; twenty-one days postpartum; breastfeeding until weaning or for first 6 months postpartum; personal history of venous or arterial thrombosis, heart disease associated with pulmonary hypertension or risk of embolism; migraine; history of sub-acute bacterial endocarditis; ischaemic cerebrovascular disease; liver disease, including disorders of hepatic secretion such as Dubin - Johnson or Rotor syndromes, infections hepatitis (until liver function normal); porphyria; systemic lupus erythematosus; liver adenoma; history of cholestasis; gall stones: estrogen - dependent neoplasms; neoplasms of breast or genital tract; undiagnosed vaginal bleeding; history during pregnancy of pruritus, chorea, herpes, deteriorating otosclerosis; cholestatic jaundice; pemphigoid gestationis; diabetes mellitus (if either retinopathy, neuropathy or if more than 20 years duration); after evacuation of hydatidiform mole (until return to normal of urine and plasma gonadotrophin values)

Side effects: nausea, vomiting, headache, breast tenderness, increase in body weight, thrombosis, changes in libido, depression, chorea, skin reaction, chloasma, hypertension, impairment of liver function, 'spotting' in early cycles, absence of withdrawal bleeding, irritation of contact lenses; rarely, photosensitivity and hepatic tumours; breast cancer (small increase in risk of breast cancer during use which reduces during the 10 years after stopping; risk factor seems related to age at which contraceptive is stopped rather than total duration of use; small increase in risk of breast cancer should be weighed against the protective effect of the ovary and endometrium)

Dose and Administrations

Contraception (21 - day combined (monophasic) preparations), by mouth, Adult (female), 1 tablet ('pill') daily for 21 days; subsequent courses repeated after 7 - day pill - free interval (during which withdrawal bleeding occurs)

Administration each tablet (pill') should be taken at approximately the same time each day; if delayed by longer than 24 hours contraceptive protection may be lost. It is important to bear in mind that the critical time for loss of protection is when a pill is omitted at the beginning or end of a cycle (which lengthens the pill - free interval).

The following advice is recommended:

If you forget a pill, take it as soon as you remember, and the next one at the normal time. If you are 12 or more hours late, the pill may not work; as soon as you remember, continue normal pill - taking, but for 7 days an additional method of contraception such as the sheath will be required. If the 7 days run beyond the end of your packet, start the next packet when you have finished the present one - do not have a gap between packets.

Storage: - at room temperature, in a well - closed container.

Levonorgestrel + Ethinylestradiol

6 tablet 0.05mg + 0.03mg

5 tablet 0.075mg + 0.04mg

10 tablet 0.125mg + 0.03mg

8.7.2. Progestogen - only contraceptives

Indications: contraception

Cautions: heart disease, sex - steroid dependent functional ovarian cysts, active liver disease, recurrent cholestatic jaundice, history of jaundice in pregnancy; see also interactions

Drug interactions: see notes above under interaction and progestogen only contraceptives notes.

Contraindications: pregnancy, undiagnosed vaginal bleeding; severe arterial disease; liver adenoma, porphyria; after evacuation of hydatidiform mole (until return to normal of urine and plasma gonadotrophin values); see notes above

Side effects: menstrual irregularities (see also notes above); nausea, vomiting, headache dizziness, breast discomfort, depression, skin disorders, disturbance of appetite, weight changes, changes in libido.

Breast cancer: There is a small increase in the risk of having breast cancer diagnosed in women using or who have recently used, a progestogen - only contraceptive pill; this relative risk may wholly or partly be due to an earlier diagnosis. The most important risk factor appears to be the age at which the contraceptive is stopped rather than the duration of use; the risk disappears gradually during the 10 years after stopping and there is no excess risk by 10 years.

Dose and Administrations: See under preparation

Oral Preparations

Ethinodiol Diacetate

Tablet, 0.5mg

Levonorgestrel (D-Norgestrel)

Tablet, 0.03 mg, 0.75mg

Lynestrenol

Tablet 0.5mg

Norethindrone (Norethisterone)

Tablet, 0.35mg

Dose and Administration: 1 tablet daily at same time each days starting on day 1 of cycle then continuously; if administration delayed for 3 hours or more it should be regarded as a 'missed pill'.

Parental preparations

Medroxyprogesterone Acetate,

Injection (aqueous suspension), 150mg/ml in 1 ml vial

Dose and Administration: by deep intramuscular injection, 150mg within first 5 days of cycle or within first 5 days after parturition (delay until 6 weeks after parturition if breast-feeding); for long-term contraception, repeated every 12 weeks (if interval greater than 12 weeks and 5 days, exclude pregnancy before next injection and advise patient to use additional contraceptive measures (e.g barrier) for 14 days after the injection).

Norethindrone (Norethisterone) Enanthate

Injection (oily), 200mg/ml in 1 ml ampoule.

Dose and Administration: by deep intramuscular injection given very slowly into gluteal muscle, short-term contraception, 200mg with in first 5 days of cycle or immediately after parturition (duration 8 weeks); may be repeated once after 8 weeks (withhold breast-feeding for neonates with severe or persistent jaundice requiring medical treatment).

Implants

Etonogestrel

Implant (subdermal) 68 mg/capsule, pack of 1 capsule.

Dose and Administration: by subdermal implantation, no previous hormonal contraceptive, 1 implant inserted during first 5 days of cycle; parturition or abortion in second trimester, 1 implant inserted between days 21 - 28 after delivery or abortion (if inserted after 28 days additional precautions necessary for next 7 days); abortion in first trimester, 1 implant inserted immediately; changing from an oral contraceptive, consult product literature; remove within 3 years of insertion.

Levonorgestrel (D-Norgestrel)

Implant capsule (subdermal); 108mg/capsule pack of 2 capsules; 75mg/capsule pack of 2 capsules.

Dose and Administration: Implant capsule -by subdermal implantation, set of 6 implant capsules inserted within first 5 days of cycle (preferably on 1st day after 1st day additional precautions necessary for following 7 days) or 21st day after parturition (after this any additional, precautions necessary for following 7 days), remove within 5 years of insertion.

8.7.3. Contraceptive Devices, Barriers, and Spermicides

Condoms - Latex condoms

- Lamb CECUM condoms

Indications: as a primary method of contraception to prevent pregnancy at times when oral contraceptives or intrauterine devices may not be effective or are contraindicated or as an adjuvant to the periodic abstinence (rhythm) method of contraception.

Also for prevention (prophylactic) of Sexually transmitted diseases (STDs)

Cautions: in medical or psychosocial conditions where a critical need exists for highly effective contraception. Patients must be sufficiently counseled regarding the need for consistent and correct use of condoms if they are to be effective in preventing pregnancy.

Contraindication: sensitivity to latex condom

Side effect: burning, stinging, warmth, itching, other irritation of the Skin, penis, rectum, or vagina, vaginal dryness or malodor, allergic vaginitis, contact dermatitis.

Note: -Condoms should be completely unrolled into the penis before any genital contact occurs and remain intact throughout intercourse

Copper T 380 A

Indications: Copper T 380 A is an intra-uterine device used for prevention of pregnancy, most suitable in parous women but should be a last-resort contraceptive for young nulliparous women because of the increased risk of pelvic inflammatory disease and infertility.

Cautions: caution should be taken in those with anaemia, heavy menses, history of pelvic inflammatory disease, diabetes, valvular heart disease (antibiotic cover needed) - avoid if prosthetic valve or past attack of infective endocarditis; epilepsy, increased risk of expulsion if inserted before uterine involution; there should be gynaecological examination before insertion, 6 weeks after (or sooner if there is a problem), then after 6 months, then yearly. The IUD should be removed if pregnancy occurs.

Contraindications: Pregnancy, severe anaemia, known HIV infection very heavy menses, history of ectopic pregnancy or tubal surgery, distorted or small uterine cavity, genital malignancy, pelvic inflammatory disease, immunosuppressive therapy, copper allergy, Wilson's disease, medical diathermy.

Side effect: Uterine or cervical perforation, displacement, pelvic infection may be exacerbated, heavy menses, dysmenorrhoea, allergy, some pain on insertion (pain helped by giving NSAIDs half an hour before insertion) bleeding, occasionally, epileptic seizures, vasovagal attack.

Note: -Copper T 380A should be fitted into uterine cavity after the end of menstruation and before the calculated time of implantation.

An intrauterine device should not be removed in mid cycle unless an additional contraceptive was used for the previous 7 days.

Diaphragm with spermicides

Indications: Diaphragm is a mechanical barrier method of contraception designed to hold spermicides near the cervical os, which is particularly important in the event that the diaphragm is dislodged or does not form a complete seal around the cervix.

Cautions: Caution is required in cases where there was recent abortion or parturition, in chronic allergic conditions, in genital contact dermatitis.

Drug interactions: Avoid use of diaphragm (with spermicides) with vaginal or topical medications, and vaginal douch products.

Contraindications: Allergy to spermicides (Nonoxinol, octoxinol), menstruation, toxic-shock syndrome.

Side effects: Vulvovaginal candidiasis (thick, white or curd like vaginal discharge), toxic shock syndrome (dizziness, fever, lightheadedness, chills, sunburn-like rash followed by peeling of the skin, muscle aches, hypotension, unusual redness of the mucous membrane inside of the mouth, nose, throat, vagina or conjunctiva; confusion)

Dose and Administration:

Nonoxinol 9 vaginal cream with diaphragm: Intravaginal, Initially 1 applicatorful (approximately 1 teaspoonful of 0.5% cream placed into cup (diaphragm) and additional spermicides spread along the rim of diaphragm just before insertion of diaphragm and not longer than six hours prior to intercourse. An additional applicatorful should be inserted into the vagina just prior to each repeat act of intercourse or if intercourse occurs later than six hours after initial diaphragm placement.

Nonoxinol 9 vaginal foam with diaphragm: Intravaginal, initially 1 applicatorful placed into vagina and additional spermicide spread along the rim of diaphragm just before insertion of diaphragm and not longer than one hour prior to intercourse. An additional applicatorful should be inserted into vagina just prior to, and not longer than one hour before, each repeat of intercourse.

Nonoxinol 9 vaginal gel with diaphragm: Intravaginal, initially 2 teaspoonful of a 2% gel placed into cup and additional spermicide spread along the rim of diaphragm just before insertion of diaphragm and not longer than six hours prior to intercourse. An additional applicatorful should be inserted into vagina, just prior to each repeat act of intercourse or if intercourse takes place later than six hours after initial diaphragm placement.

Octoxinol 9 vaginal cream with diaphragm: Intravaginal, initially 2 teaspoonful placed into cup and additional spermicide spread along the rim of diaphragm just before insertion of diaphragm and not longer than six hours prior to intercourse. An additional applicatorful should be inserted into vaginal just prior to each repeat act of intercourse or if intercourse occurs later than six hours after initial diaphragm placement.

Octoxinol 9 vaginal jelly with diaphragm: Intravaginal, initially 1 applicatorful placed into cup and additional spermicide spread along the rim of diaphragm just before insertion of diaphragm and not longer than six hours prior to intercourse. An additional applicatorful should be inserted into vagina just prior to each repeat act of intercourse or if intercourse occurs later than six hours after initial diaphragm placement.

Storage: at room temperature.

Spermicides

(*Menfegol*), tablet (foaming), 60mg

(*Nonoxinol, octoxinol*), Creams, Foams, Gels

Indications: Vaginal spermicides are used as chemical barrier contraceptive for prevention of pregnancy.

Also used for prevention of sexually transmitted diseases when used in combination with latex condoms.

Cautions: Caution is required in chronic allergy (local), genital contact dermatitis, in medical or psychosocial conditions where a critical need exists for highly effective contraception. Caution should also be taken in recent parturition or abortion.

Drug interactions: vaginal or topical medication, especially those containing aluminium, citrate, cotton dressing, hydrogen peroxide, iodide, lanolin, nitrates, permanganates, salicylates, silver salts, sulfonamides. Avoid also use of spermicides with vaginal douche products or other vaginal or local cleansing products.

Contraindications: allergy to octoxinol, nonoxinol, and benealleonium chloride, menstruation, history of toxic-shock syndrome, Genital ulcer, vaginal epithelial irritation.

Side effects: burning, stinging, warmth, itching, or other irritation of the skin, penis, rectum, or vagina, vaginal discharge (transient), vaginal dryness or odor, Allergic vaginitis (persistent vaginal redness, irritation, rash, dryness, or whitish discharge), contact dermatitis (persistent skin rash, redness, irritation or itching), urinary tract infection (female) - due to change in vaginal flora.

Dose and Administration:

Nonoxinol 9 vaginal cream - Intravaginal, 1 applicatorful of 5% cream inserted just prior to intercourse. An additional applicatorful should be inserted into vagina just prior to each repeat act of intercourse.

Nonoxinol 9 vaginal Foam - Intravaginal, 1 applicatorful of inserted just prior to and not longer than one hour prior to each act of intercourse.

Nonoxinol 9 vaginal Gel - Intravaginal, 1 applicatorful of a 4% gel inserted just prior to and not longer than one hour prior to intercourse.

Storage: at room temperature, in a well-closed container (cream and gel), protect from freezing.

8.8. Drugs affecting Gonadotrophins

Danazol

Capsules, 100 mg, 200 mg

Indications: in the management of endometriosis, benign breast disorders such as fibrocystic disease, gynaecomastia and pre-pubertal breast hypertrophy; hereditary angioedema.

Cautions: seizure, migraine, or conditions influenced by edema.

Drug interactions: carbamazepine, cyclosporine, and warfarin.

Contraindications: undiagnosed genital bleeding; pregnancy; breast-feeding; porphyria; markedly impaired hepatic, renal, or cardiac function.

Side effects: greasy skin, acne, voice changes and possibly signs of virilisation (when therapy should be stopped immediately).

Dose and Administration: Adult: Oral:

Endometriosis: 200 - 800 mg daily in divided doses, adjusted according to

response, usually for 3 - 6 months (maximum 9 months).

Cyclical breast pain and nodularity: 100 mg twice daily for a maximum of 3 months.

Storage: store at room temperature.

8.9. Drugs used for impotence

The phosphodiesterase type 5 (PDE5) inhibitors, sildenafil, tadalafil are equally effective in mild to moderate erectile dysfunction. The choice of drug depends on the patient's requirements and the side-effect profile of the drug. Tadalafil is the longest lasting with efficacy up to 36 hours. Tadalafil can be taken with food and alcohol, whilst sildenafil has delayed and reduced absorption when taken with a high fat meal. Failure with one drug does not imply that the others will be ineffective as well. These drugs are strongly contraindicated in patients taking vasodilator nitrates.

Sildenafil is a phosphodiesterase type 5 inhibitor. The neurotransmitter produced in the penis as the result of erotic stimulation is nitric oxide, which promotes the production of cGMP causing vasodilation. By blocking the action of PDE5 (which breaks down cGMP), sildenafil allows the concentration of cGMP to build up during erotic stimulation. Sildenafil reacts to a lesser degree with other isoenzymes of PDE, which accounts for some of the side effects.

Sildenafil

Tablet, 25 mg, 50 mg, 100 mg

Indications: male erectile dysfunction.

Cautions: predisposition to priapism (e.g. sickle cell disease, leukaemia); hepatic or severe renal impairment, elderly.

Drug interactions: nitrates; agents that inhibit cytochrome P450 (eg. itraconazole, ketoconazole, erythromycin and cimetidine); other agents for erectile dysfunction.

Contraindications: concurrent use with nitrates or nitric oxide donors (combination can be fatal); severe ischaemic heart disease; retinitis pigmentosa (possible disorders of retinal PDE).

Side effects: cardiovascular effects related to vasodilation (headache, flushing, dizziness, hypotension); dyspepsia; mild and transient abnormal vision and sensitivity to light priapism has been reported.

Dose and Administration: Adult: Oral:

Initially 50 mg taken 1 hour before anticipated sexual activity. Titrate upwards to 100 mg if effect is inadequate, or downwards to 25 mg if severe side-effects occur. The maximum dosing frequent is once per day and maximum dose is 100mg.

Hepatic or renal impairment, the **elderly**, and concomitant use with agents known to inhibit cytochrome P450: Initially 25 mg.

Storage: store at room temperature.

Tadalafil

Tablet, 10mg

Indications, Cautions, Drug interactions, Contraindications and Side effects; See under sildenafil and notes above.

Dose and Administration: Adult: *Oral:* 20mg from 16 minutes to 36 hours before sexual activity. Maximum 20 mg once in 24 hours.

Mild to moderate hepatic impairment (avoid if severe): Maximum 10mg once daily.

8.10. Drug used in benign prostatic hyperplasia

Benign prostatic hyperplasia (BPH) is a common condition affecting men as they age. Stromal and glandular hyperplasia of the prostate gland occurs as a result of the changing hormonal environment in middle-aged men and is present in most men at 45 years of age; about 30% of these men will eventually require treatment if their BPH causes lower urinary tract symptoms. It is increasingly common for surgical treatment to be used only in cases of failure of medical treatment or because of patient preference.

Contraction of smooth muscle in the prostate and bladder neck accounts for up to 40% of bladder outlet resistance. Alpha₁ blockers treat the dynamic component of bladder outlet obstruction. Those available include alfuzosin and prazosin. They are short acting and are given twice daily.

Alfuzosin

Tablet, 2.5mg, 5mg, 10mg

Indications: treatment of the functional symptoms of benign prostatic hyperplasia (BPH).

Cautions: not intended for use as an antihypertensive drug. Renal and hepatic impairment.

Drug interactions: azole antifungals, ciprofloxacin, clarithromycin, diclofenac, doxycycline, erythromycin, isoniazid, propofol, protease inhibitors, quinidine, verapamil and other CYP3A4 inhibitors; aminoglutethimide, carbamazepine, nafcillin, nevirapine, phenobarbital, phenytoin, rifamycins, and other CYP3A4 inducers.

Contraindications: hypersensitivity reactions.

Side effects: dizziness, fatigue, headache, abdominal pain, constipation, dyspepsia, nausea, impotence, bronchitis, and pharyngitis.

Dose and Administration: Adult: *Oral:* 10 mg once daily.

Storage: store at room temperature and protect from light and moisture.

9. OBSTETRIC AND GYNAECOLOGICAL MEDICATIONS

Drugs used in obstetrics: Drugs may be used to modify uterine contractions. These include oxytocic drugs to stimulate uterine contractions both in induction of labour and to control postpartum haemorrhage and beta₂-adrenoceptor agonists used to relax the uterus and prevent premature labour.

Postpartum Haemorrhage, Ergometrine and oxytocin differ in their actions on the uterus. In moderate doses oxytocin produces slow generalized contractions with full relaxation in between; ergometrine produces faster contractions superimposed on a tonic contraction. High doses of both substances produce sustained tonic contractions. Oxytocin is now recommended for routine use in postpartum and post - abortion haemorrhage since it is more stable than ergometrine. However, ergometrine may be used if oxytocin is not available or in emergency situations.

Premature labour. Salbutamol is a beta₂-adrenoceptor agonist which relaxes the uterus and can be used to prevent premature labour in uncomplicated cases between 23 and 24 weeks of gestation. Its main purpose is to permit a delay in delivery of at least 48 hours. The greatest benefit is obtained by using this delay to administer corticosteroid therapy or to implement other measures known to improve perinatal health. Prolonged therapy should be avoided since the risk to the mother increase after 48 hours and the response of the myometrium is reduced.

Treatment of vaginal and vulval conditions - Anti - infective drugs: Candidal vulvitis can be treated locally with cream but is almost invariably associated with vaginal infection which should also be treated. Vaginal candidiasis is treated primarily with antifungal pessaries or cream inserted high into the vagina (including during menstruation) local irritation may occur on application of vaginal antifungal products.

Imidazole drugs (clotrimazole, miconazole) are effective in short courses of 3 to 14 days according to the preparation used; single dose preparations after an advantage when compliance is a problem. Vaginal applications may be supplemented with antifungal cream for vulvitis and to treat other superficial sites of infection.

Nystatin is a well established treatment (but stain clothing yellow). One or two pessaries are inserted for 14 to 28 nights; they may be supplemented with cream for vulvitis and to treat other superficial sites of infection.

Trichomonal infections: Commonly involve the lower urinary tract as well as the genital system and need systemic treatment with metronidazole or tinidazole. Bacterial infections with Gram - negative organisms are particularly common in association with gynaecological operations and trauma. Metronidazole is effective against certain Gram - negative organisms, especially *Bacteroides spp.* and may be used prophylactically in gynaecological surgery. Metronidazole is also indicated for bacterial vaginosis.

Aminocaproic Acid

Injection, 100 mg/ml in 1 ml ampoule.

Indications: treatment of excessive bleeding from fibrinolysis.

Cautions: cardiac, renal or hepatic disease.

Drug interactions: oral contraceptives, estrogens.

Contraindications: hypersensitivity to aminocaproic acid; disseminated intravascular coagulation (without heparin); evidence of an intravascular clotting process.

Side effects: arrhythmia, bradycardia, hypotension, peripheral ischemia, syncope, confusion, thrombosis, fatigue, hallucinations, headache, rash, pruritus, abdominal pain, anorexia, cramps, GI irritation, nausea, dry ejaculation, agranulocytosis, bleeding time increased, watery eyes, vision decreased, tinnitus, failure, myoglobinuria, dyspnea, nasal congestion, pulmonary embolism.

Dose and Administration:

Adult: *IV:* 4 - 5 g during the first hour, followed by 1 g/hour for 8 hours or until bleeding controlled (maximum daily dose: 30 g).

Storage: store at room temperature.

Bromocriptine Mesylate

Tablet, 2.5 mg

Indications: galactorrhea, amenorrhea and infertility associated with hyperprolactinaemia, and certain cases of acromegaly (adjunctive therapy). It is used to suppress lactation after stillbirth or abortion, or when breast - feeding is contraindicated.

Cautions: psychotic disorders, parkinsonism with dementia, compromised cerebral circulation, ischaemic heart disease, liver disease, peptic ulcers.

Drug interactions: metoclopramide, domperidone, antipsychotic agents, tricyclic antidepressants, methyl dopa, reserpine, antihypertensive agents, alcohol.

Contraindications: hypersensitivity to ergot alkaloids, toxemia of pregnancy, uncontrolled hypertension or severe cardiovascular disease.

Side effects: nausea, postural hypotension, drowsiness and dizziness, especially early in therapy. Hypertension, myocardial infarction, seizures and stroke, dyskinesia, hallucinations, confusion and behavioral disturbances, urticaria, skin rashes, peptic ulceration, nasal stuffiness, visual disturbance, impotence and urinary retention, retroperitoneal fibrosis, pleural thickening and effusions, and digital vasospasm.

Dose and Administration: *Oral: Adult:*

Suppression of lactation: 2.5 mg twice daily for 2 weeks, starting not before 4 hours after parturition, and provided that viral signs have established. If lactation recurs 2 - 3 days after treatment is stopped, it may be reinstituted and continued for another week.

Hypogonadism or amenorrhoeal, galactorrhea syndromes: initially 1.25 mg once daily at bedtime; gradually increases to an average of 2.5mg 2- 3 times daily.

Storage: store at a temperature less than 25°C.

Bupivacaine

Injection, 0.5% in 10ml vial

Indication: long-acting local anaesthetic agent. Particularly useful for producing prolonged analgesia during labour, where the interval between doses is usually 2-3 hours.

Cautions, Contraindications, Drug interactions, Side effects and Dose and Administration; see section 5.4 (local anaesthetic).

Clomiphene Citrate

Tablet, 50 mg

Indications: management of anovulatory or oligo - ovulatory infertility in women with an intact hypothalamic - pituitary - ovarian axis.

Cautions: ectopic pregnancy, breast-feeding.

Contraindications: hepatic dysfunction, ovarian cysts, undiagnosed abnormal uterine bleeding, pregnancy.

Side effects: reversible ovarian enlargement and cyst formation (withdraw therapy); hot flushes, abdominal discomfort and pain, nausea and vomiting, breast discomfort, abnormal uterine bleeding, headache, skin rashes, weight gain; CNS effects such as dizziness, nervousness, depression, fatigue, insomnia, visual disturbances (blurring of vision, diplopia and photophobia), reversible hair loss, hepatotoxicity.

Dose and Administration: *Oral:*

Adult: initially 50 mg daily for 5 days, starting on day 3 - 5 of the menstrual cycle or after an induced bleed. If ovulation is confirmed but conception fails, the same dose may be repeated during the next cycle. If ovulation fails, the dose may be increased to 100 mg daily (as a single dose) for 5 days.

Storage: store at room temperature.

Clotrimazole

Tablet (vaginal), 100mg, 500mg

Cream (vaginal), 1%

Indications: in the local treatment of vulvovaginal candidiasis caused by *Candida albicans* and other species of candida in pregnant (second and third trimester only) and non-pregnant women.

Note: - It is not effective in the treatment of vulvovaginitis caused by other common pathogens such as *Trichomonas vaginitis*.

Cautions: pregnancy and labour and in those patients who are allergic to clotrimazole and its family. Use hygienic measures to cure infection and prevent reinfection by wearing cotton panties instead of synthetic underclothes and wearing only freshly washed under clothes. Sex partners should be advised to use condom.

Contraindications: hypersensitivity to clotrimazole

Side effects: vaginal burning, itching, discharge, or other irritation not present before therapy, abdominal or stomach cramps or pain, burning or irritation of penis of sexual partner; headache.

Dose and Administration:

Clotrimazole cream: Intravaginal, 50mg (1 applicatorful of 1% vaginal cream), once a day, preferably at bed time, for six to fourteen consecutive day.

Clotrimazole tablets: Non-pregnant patients - Intravaginal, 500mg as a single dose, preferably at bedtime or 100mg once a day preferably at bedtime, for six or seven consecutive days.

Pregnant patients - Intravaginal (100mg once a day), preferably at bedtime, for seven consecutive days.

Storage: vaginal cream - store between 2 and 30°C in a collapsible tube or in a tight container. Vaginal tablet - at room temperature in a well-closed container

Dinoprostone (prostaglandin E₂)

Tablet (vaginal), 3 mg

Suppository (vaginal), 20mg

Indications:

Suppositories: Terminate pregnancy from 12th through 28th week of gestation; evacuate uterus in cases of missed abortion or intrauterine fetal death.

Vaginal insert: Initiation and/or cervical ripening in patients at or near term in whom there is a medical or obstetrical indication for the induction of labor.

Cautions: cervicitis, infected endocervical lesions, acute vaginitis, compromised (scarred) uterus or history of asthma, hypertension or hypotension, epilepsy, diabetes mellitus, anemia, jaundice, cardiovascular, renal, or hepatic disease.

Drug interactions: oxytocin.

Contraindications: hypersensitivity to prostaglandins, fetal distress, unexplained vaginal bleeding during this pregnancy, acute pelvic inflammatory disease, uterine fibroids, and cervical stenosis.

Side effects: headache, vomiting, diarrhea, nausea, bradycardia, fever, back pain, bronchospasm, cardiac arrhythmia, chills, cough, dizziness, dyspnea, flushing, hot flushes, hypotension, pain, shivering, syncope, tightness of the chest, vasomotor and vasovagal reactions, wheezing.

Dose and Administration:

Abortifacient: Insert 1 suppository high in vagina, repeat at 3- 5 hour intervals until abortion occurs up to 240 mg (maximum dose); continued administration for longer than 2 days is not advisable.

Cervical ripening:

Suppositories: *Intracervical:* 2 - 3 mg.

Storage: store suppositories at a temperature not exceeding 20 °C.

Ergometrine maleate

Tablet, 0.25mg, 0.5mg

Injection, 0.25 mg/ml, 0.5mg/ml in 1ml ampoule

Indications: prevention and treatment of postpartum and postabortion hemorrhage in emergency situations and where oxytocin not available.

Cautions: cardiovascular diseases, hypertension, renal and hepatic function impairment, multiple pregnancy, sepsis, or hypersensitivity.

Drug interactions: adrenaline. Smoking tobacco should also be avoided.

Contraindications: induction of labour, first and second stages of labour, coronary artery disease, eclampsia or preeclampsia, or pregnancy.

Side effects: dizziness, mild and transient headache, ringing in the ears, and hypertension may occur rarely. Abdominal pain, nausea, vomiting and uterine cramping may also occur, especially after intravenous injection.

Dose and Administration: Adult:

Prevention and treatment of postpartum haemorrhage, when oxytocin is not available: IM injection: 200 mcg when the anterior shoulder is delivered or immediately after birth

Excessive uterine bleeding: Slow IV injection: 250-500 mcg when the anterior shoulder is delivered or immediately after birth.

Secondary postpartum haemorrhage: Oral: 0.2-0.4 mg 2-4 times daily, usually for 48 hours.

Storage: Injection: 2-8°C, or as specified by manufacturer. Protect from light and freezing.

Note: Discoloured solution or solutions containing visible particles should not be used.

Tablets – at room temperature, in tight container. Protect from light.

Isoconazole

Vaginal tablet, 300mg, 600mg

Indications: treatment of vaginal mycoses, particularly due to *Candida spp.*

Cautions: pregnancy.

Side effects: local reactions including burning or itching may occur following the application of isoconazole.

Dose and Administration: *Pessaries:* 600mg or 300mg daily for 3 days.

Storage: protect from light.

Magnesium Sulfate

Injection, 10 %, 20 %, 50 % in 20 ml

Indications: prevention of recurrent seizures in eclampsia.

Cautions: hepatic impairment, renal failure.

Drug interactions: alcuronium, nifedipine, suxamethonium, vecuronium.

Contraindications: hypersensitivity to magnesium sulfate.

Side effects: generally associated with hypermagnesaemia, nausea, vomiting, thirst, flushing of skin, hypotension, arrhythmias, coma, respiratory depression, drowsiness, confusion, loss of tendon reflexes, muscle weakness.

Dose and Administration: Adult: *IV injection:* initially 4 g over 5 - 10 minutes followed by IV infusion at a rate of 1 g every hour for at least 24 hours after the last seizure; recurrence of seizures may require additional IV bolus of 2 g.

Storage: store at room temperature.

Methylergometrine Maleate

Tablet, 0.12mg

Injection, 0.2mg/ml

Indications: prevention and treatment of postpartum or postabortal uterine bleeding due to uterine atony or subinvolution. Its use is not recommended prior to delivery of the placenta since placental entrapment may occur. It is also used to lessen expulsion of uterine contents in cases of incomplete abortion.

It is not indicated for induction or augmentation of labor, to induce abortion, or in cases of threatened spontaneous abortion because of its propensity to produce non-physiologic, tetanic contractions and its long duration of action.

Cautions: hepatic and renal function impairment, hypocalcaemia, mitral valve stenosis, venoatrial shunts and in those patients allergic to methylergometrine or ergot alkaloids.

Drug interactions: general anaesthetic especially halothane, bromocriptine, other ergot alkaloids, nicotine, smoking tobacco, nitroglycerine, vasoconstrictors and vasopressors.

Contraindications: pregnancy, labour and delivery, unstable anginal pectoris, recent myocardial infarction, history of cerebrovascular accident, history of transient ischemic attack, cardiovascular disease, coronary artery disease, eclampsia or preeclampsia, (history of) severe hypertension, occlusive peripheral vascular disease, severe raynaud's phenomenon.

Side effects: nausea, vomiting, abdominal pain, diarrhoea, uterine cramping dizziness, sweating, tinnitus (ringing in the ears)

Dose and Administration:

Adult: uterine stimulant: *Oral:* 0.2 to 0.4mg two or four times a day until the danger of uterine atony and hemorrhage has passed.

IV, or IM : 0.2mg repeated in two or four hours if necessary, up to five doses.

Storage: at room temperature in a tight container (tablets), protect from light and from freezing.

Metronidazole

Tablet, 250mg

Tablet (vaginal), 500mg

Intravenous infusion, 5mg/ml in 100ml

Syrup, 4% w/v, 250mg/5ml

Indications: used for the treatment of bacterial vaginosis (formerly called, *Haemophilus vaginitis*, *Gardnerella vaginitis*, non-specific vaginitis, *Carynebacterium vaginitis*, or anaerobic vaginosis) which is a non-inflammatory vaginal syndrome characterized by replacement of the normal vaginal flora (predominantly hydrogen producing lactobacillus) with a mixed flora including *Gardnerella vaginalis*.

It is also used in the treatment of female pelvic infections, including endometritis, endomyometritis, tube-ovarian abscess, and liver abscess, caused by bacteriodes species, including the *B. fragilis* group, clostridium species, petrococcus species, and peptostreptococcus species. See also section 7.1.2 & 7.4.2 for other uses.

Cautions: abnormal neurologic symptoms, history of blood dyscrasias. Caution and reduce dosage in patients with such hepatic impairment. Use of the drug

during pregnancy with caution when it is clearly needed. Breastfeeding should be interrupted in nursing mothers.

Drug interactions: alcohol, anticoagulants (cumarin - or indandione - derivatives), cimetidine, disulfiram, phenobarbital, phenytoin.

Contraindications: history of hypersensitivity to the drug or other nitroimidazole derivative.

Side effects: nausea, vomiting, diarrhoea, loss of appetite, dry mouth, sharp unpleasant metallic taste, constipation, abdominal discomfort, numbness, tingling, pain, or weakness in hands or feet, seizures, leucopenia, thrombocytopenia, vaginal candidiasis (any vaginal irritation, discharge, or dryness not present before therapy).

Dose and Administration:

Adult:

Vaginosis (bacteria): Oral: 2 g as a single dose or 400 – 500 mg twice daily for 5-7 days. *Intravaginal:* 500mg placed high into the vagina every night for ten or twenty consecutive days. *IV-infusion,* 15mg (base) per kg of body weight initially, then 7.5mg per kg of body weight up to a maximum of 1gm, every six hours for seven days or longer

Pelvic inflammatory disease: Oral: 500mg of metronidazole twice daily with ofloxacin given orally in a dosage of 400mg twice daily. Therapy should be continued for 14 days.

Note: - Metronidazole may cause dizziness patients should be advised to avoid alcoholic beverage and to comply with full time of treatment.

Storage: at room temperature in a well-closed, light-resistant container.

Miconazole Nitrate

Tablet (vaginal), 200mg, 400mg

Cream (vaginal), 2%

Indications: treatment of Vulvovaginal candidiasis caused by *Candida albicans* and other species of candida in pregnant (second and third trimesters only), non-pregnant women.

Cautions, Contraindications, Side effects: Same as clotrimazole

Dose and Administration: Adult:

Vaginal cream - Intravaginal, one applicatorful once a day at bed time for seven or fourteen days. May be repeated if needed.

Vaginal tablets - Intravaginal, 100mg once a day at bed time for seven days. May be repeated for seven days if needed or 200mg or 400mg once a day at bedtime for three days. May be repeated if needed.

Storage: at room temperature in a tight container

Mifepristone

Tablet, 200 mg

Indications: medical termination of intrauterine pregnancy, through day 49 of pregnancy. Patients may need treatment with misoprostol and possibly surgery to complete therapy.

Cautions: severe anemia.

Drug interactions: substrate of CYP3A4, progestin.

Contraindications: hypersensitivity to mifepristone, misoprostol, other prostaglandins; chronic adrenal failure; porphyrias; hemorrhagic disorder or concurrent anticoagulant therapy; pregnancy termination > 49 days; intrauterine device (IUD) in place; ectopic pregnancy or undiagnosed adnexal mass; concurrent long term corticosteroid therapy; inadequate or lack of access to emergency medical services; inability to understand effects and/or comply with treatment.

Side effects: vaginal bleeding and uterine cramping; bleeding or spotting occurs in most women for a period of 9-16 days; headache; dizziness; abdominal pain; nausea; vomiting; diarrhea; uterine cramping.

Dose and Administration: *Oral: Adult:*

Termination of pregnancy: treatment consists of three visits by the patient; the patient must read medication guide and sign patient agreement prior to treatment:

Day 1: 600 mg (three 200 mg tablets) taken as a single dose under physician supervision.

Day 3: patient must return to the healthcare provider 2 days following administration of mifepristone; if termination of pregnancy cannot be confirmed using ultrasound or clinical examination: 400 mcg (two 200 mcg tablets) of misoprostol; patient may need treatment for cramps or gastrointestinal symptoms at this time

Day 14: patient must return to the healthcare provider ~14 days after administration of mifepristone; confirm complete termination of pregnancy by ultrasound or clinical exam. Surgical termination is recommended to manage treatment failures.

Storage: store at room temperature.

Nystatin

Cream (vaginal), 100,000 units in 4g

Pessary (ovules), 100,000 units

Indications: local treatment of vulvovaginal candidiasis caused by *Candida (monilia) albicans* and other candida species.

Note: - It is not effective against *Trichomonas Vaginalis* or *Gardnerella vaginalis* (*Haemophilus Vaginalis*).

Cautions: discontinue treatment with nystatin therapy if irritation or sensitization occurs. They are also advised against interrupting or discontinuing, vaginal nystatin therapy during a prescribed regimen, even during menstruation or if symptomatic relief occurs after only a few days of therapy, unless otherwise instructed by their physician.

Contraindications: sensitivity to nystatin

Side effects: vaginal irritation not present before therapy

Dose and Administration: Adult:

Nystatin vaginal cream - Intravaginal, insert 1-2 applicatorfuls at night for at least 14 nights.

Nystatin vaginal pessary - Intravaginally, insert 1-2 pessaries at night for at least 14 nights.

Storage: at room temperature in a tight, light-resistant container.

Oxytocin

Injection, 10units/ml in 0.5 and 1ml ampoules, 1unit/ml, 5units/ml in 1ml

Indications: for nonselective induction of labour for medical reasons and for stimulation or reinforcement of labour in patients with dysfunctional inertia. Parenteral oxytocin is also indicated for management of incomplete or therapeutic abortion, as well as to produce uterine contractions during the third stage of labour. Oxytocin is also indicated to control postpartum bleeding or hemorrhage.

Cautions: particular caution needed when given for induction or enhancement of labour in presence of borderline cephalopelvic disproportion (avoid if significant), mild or moderate pregnancy-induced hypertension or cardiac disease, women over 35 years or with history of lower-uterine segment caesarean section; if fetal death in utero or meconium-stained amniotic fluid avoid tumultuous labour (may cause amniotic fluid embolism); water intoxication and hyponatraemia-avoid large infusion volumes and restrict fluid intake by mouth; effects enhanced by concomitant prostaglandins (very careful monitoring) caudal block anaesthesia (may enhance hypersensitive effects of sympathomimetic vasopressors), see also interaction.

Drug interactions: hydrocarbon, inhalation anesthetic such as enflurane, halothane, isoflurane, and with vasopressors, other oxytocins.

Contraindications: significant cephalopelvic disproportion, cold presentation, total placenta previa, vasa previa, where vaginal delivery is contraindicated, fetal distress, hypertonic uterine patterns, obstetrical emergencies requiring surgical intervention, uterine inertia or severe toxemia on prolonged use.

Side effects: fast or irregular heartbeat, nausea or vomiting

Dose and Administration: Adult:

Induction or stimulation of labour: IV infusion: initially at an initial rate 0.5 to 4 milli units (0.0005 to 0.004 unit) per minute, and then increased gradually at intervals every 20-60 minutes in increments of 1 to 2 milliunits (0.001-0.002 unit) per minute until a contraction pattern similar to that of normal labour is obtained. The rate of up to 6 milli units per minute is reported to produce plasma oxytocin concentrations comparable to those in natural labour but doses of up to 20 milliunits (0.02 unit) or more per minute may be required. The rate may be reduced gradually once labour is induced.

Incomplete or therapeutic abortion: IV infusion: 10 units at a rate of 20 to 40 milliunits (0.02 to 0.04 unit) per minute.

Control of postpartum uterine bleeding: IV infusion: 10 units at a rate of 20 to 40 milliunits per minute following delivery of the infant(s) and preferably placenta(s). A rate of 20-100 milliunits per minute may be used following abortion.

Storage: store oxytocin at 2 to 8°C, protect from freezing. 10units/mL (1mL) may also be stored at 15 to 25°C for up to 30 days.

Oxytocin + Ergometrine Maleate*Injection, 5 units + 500mcg in each ml*

See notes under ergometrine maleate

Dose: *IM injection:* 1ml; *IV injection,* no longer recommended**Ritodrine Hydrochloride***Injection, 10mg/ml in 5ml ampoule***Indications:** prevention of premature labour and abortion.**Cautions:** mild-to-moderate preeclampsia, hypertension, or diabetes.**Drug interactions:** atropine, beta-adrenergic blockers, corticosteroids, magnesium sulfate, diazoxide, meperidine, general anesthetics, sympathomimetics.**Contraindications:** before 20th week of pregnancy and when continuation of pregnancy is hazardous to mother or fetus; hypersensitivity; pre-existing maternal conditions that would be seriously affected by pharmacologic properties of beta-mimetic agent.**Side effects:** palpitations; chest pain or tightness; heart murmur; angina pectoris; myocardial ischemia; alterations in BP; pulmonary edema; sinus bradycardia upon drug withdrawal; arrhythmias; drowsiness; weakness; mild tachycardia, tremor, headache (including migraines); nervousness; restlessness; emotional upset; anxiety; malaise; hyperventilation, erythema; rash, nausea; constipation; diarrhea; vomiting; epigastric distress; ileus; bloating, leukopenia; agranulocytosis, hemolytic icterus; impaired liver function, lactic acidosis, glycosuria, dyspnea, sweating; chills; hypokalemia; hyperglycemia.**Dose and Administration:** *IM:* 10 mg every 3 to 8 hours and continued for 12 to 48 hours after the contractions have stopped.**Storage:** store at room temperature and protect from excessive heat.**Salbutamol***Injection, 0.5mg/ml in 1ml ampoule***Indications:** arrest uncomplicated premature labour between 24-33 weeks gestation; see also sec. 2.2.**Cautions:** suspected cardiac disease, hypertension, hyperthyroidism, hypokalaemia, diabetes mellitus, mild to moderate pre-eclampsia. The patient's state of hydration and heart rate should be monitored carefully**Drug interactions:** corticosteroids, diuretics, theophylline.**Side effects:** nausea, vomiting, flushing, sweating, tremor, hypokalemia, tachycardia, muscle cramps, palpitation, and hypotension, increased tendency to uterine bleeding, pulmonary oedema, chest pain or tightness, arrhythmias, headache.**Contraindications:** cardiac disease, eclampsia and severe pre-eclampsia, intra-uterine infection, antepartum haemorrhage (requires immediate delivery), placenta praevia, cord compression, not for use in first or second trimesters.**Dose and Administration:** *Premature labour: Adult: intravenous infusion:* 10 micrograms/minute gradually increased to maximum of 45 micrograms/minute until contractions have ceased, then gradually reduced; or *by intravenous or*

intramuscular injection, 100 – 250 micrograms repeated according to patient's response; Subsequently *by mouth* 4 mg every 6 – 8 hours:

Storage: Store at room temperature. Protect from light.

Tetracycline + Amphotericin B

Tablet (vaginal), 100mg + 50mg

10. ANTINEOPLASTIC AND RELATED AGENTS

The treatment of cancer with drugs, radiotherapy and surgery is complex and should only be undertaken by an oncologist. For this reason the following information is provided merely as a guide. Chemotherapy may be curative or used to alleviate symptoms or to prolong life. Where the condition can no longer be managed with cytotoxic therapy, alternative palliative treatment should be considered.

For some tumours, single - drug chemotherapy may be adequate, but for many malignancies a combination of drugs provides the best response. Examples of combination therapy include:

- 'CHOP' (cyclophosphamide, doxorubicin, vincristine, prednisolone) for non-Hodgkin disease;
- 'ABVD' (doxorubicin, bleomycin, vinblastine, dacarbazine) for hodgkin disease;
- 'MOPP' (chlormethine, vincristine, procarbazine, prednisolone) for hodgkin disease.

Cytotoxic drugs are often combined with other classes of drugs in the treatment of malignant conditions. Such drugs include hormone agonists and antagonists, corticosteroids and immunostimulant drugs. Combinations are, however, more toxic than single drugs.

The following information covers drugs that have specific anti-tumor activity. However, they are toxic drugs which should be used with great care and monitoring. .

Precautions and Contraindications: treatment with cytotoxic drugs should be initiated only after baseline tests of liver and kidney function have been performed and baseline blood counts established. It may be necessary to modify or delay treatment in certain circumstances. The patient should also be monitored regularly during chemotherapy and cytotoxic drugs withheld if there is significant deterioration in bone marrow, liver or kidney function.

Many cytotoxic drugs are teratogenic and should not be administered during pregnancy especially in the first trimester. Contraceptive measures are required during therapy and possibly for a period after therapy has ended.

Cytotoxic drugs should be administered with care to avoid undue toxicity to the patient or exposure during handling by the health care provider.

General adverse effects: Antineoplastic agents exert their effect on rapidly dividing cells (malignant cells, bone marrow, mucous membranes, hair follicles) and therefore have common toxicities, despite different modes of action. Toxicities depend on dose, schedule and route of administration as well as predisposing factors in the patient. Potential benefit of particular regimen needs to be weighed against toxicity for each individual patient.

The acute effects of antineoplastic medication frequently include nausea and vomiting, which may be severe.

Bone Marrow suppression: Malignant tumours may develop as a long term complication of cytotoxic therapy. These include acute myeloid leukaemia, solid tumours, Hodgkin's disease, ovarian cancer and gastric cancer.

Reproductive toxicity: Most cytotoxic drugs are teratogenic effective contraception should be ensured before initiating therapy. In most men receiving chemotherapy the sperm count will return to normal within 2 years of of subsequent recovery of spermatogenesis.

Hyperuricaemia. Hyperuricaemia may complicate treatment of conditions such as non-Hodgkin lymphomas and leukaemia. Renal damage may result from the formation of uric acid crystals. Patients should be adequately hydrated and hyperuricaemia may be managed with allopurinol initiated 24 hours before cytotoxic treatment and continued for 7 to 10 days afterwards.

Alopecia is common.

Alkylating Agents

Alkylating drugs are among the most widely used drugs in cancer chemotherapy. They act by damaging DNA and therefore interfering with cell replication. However, there are two complications. Firstly, they affect gametogenesis and may cause permanent male sterility; in women, the reproductive span may be shortened by the onset of a premature menopause. Secondly, they are associated with a marked increase in the incidence of acute non-lymphocytic leukaemia, in particular when combined with extensive radiation therapy. Alkylating agents include; busulfan, chlorambucil, cyclophosphamide, mechlorethamine hydrochloride, melphalan and thiopeta.

Busulfan

Tablets, 0.5 mg, 2 mg

Indications: chronic myeloid leukaemia, conditioning regimens for bone marrow transplantation.

Cautions: seizures, patients recently given other myelosuppressive drugs or radiation treatment.

Drug interactions: azole antifungals, ciprofloxacin, clarithromycin, diclofenac, doxycycline, erythromycin, isoniazide, nifedipine, propofol, protease inhibitors, quinidine, verapamil, aminoglutethimide, carbamazepine, nafcillin, nevirapine, phenobarbital, phenytoin, rifamycins.

Contraindications: pregnancy, hypersensitivity to busulfan.

Side effects: sterility, ovarian suppression, amenorrhea, testicular atrophy, malignant tumors, leukopenia, thrombocytopenia, anemia, nausea, vomiting, diarrhea, alopecia, amenorrhea, hyperpigmentation, bone marrow suppression.

Dose and Administration: (refer to individual protocols) *Oral:*

For remission induction of CML:

Adult: 4 - 8 mg/day (may be as high as 12 mg/day).

Child: 0.06 - 0.12 mg/kg/day or 1.8 - 4.6 mg/m²/day;

BMT marrow –ablative conditioning regimen:

Adult and Child: 1mg/kg/dose every 6 hours for 16 doses.

Storage: store in a well-closed container at room temperature.

Chlorambucil

Tablet, 2 mg, 5 mg

Indications: chronic lymphocytic leukaemia; Hodgkin and non-Hodgkin lymphomas; breast, ovarian and testicular carcinoma, thrombocythemia.

Cautions: seizure and bonemarrow suppression.

Drug interactions: live vaccine, ethanol.

Contraindications: pregnancy.

Side effects: myelosuppressive, leukopenia, thrombocytopenia, anemia, skin rash, hyperuricemia, menstrual changes, nausea, vomiting, diarrhea, oral ulceration, agitation, ataxia, confusion, fever.

Dose and Administration: (refer to individual protocols): *Oral:*

Adult: 0.1- 0.2 mg/kg/day **or** 3 - 6 mg/m²/day for 3-6 weeks, then adjust dose on basis of blood counts **or** 0.4 mg/kg and increased by 0.1mg/kg biweekly or monthly **or** 14 mg/m²/day for 5 days, repeated every 21-28 days.

Child: general short courses: 0.1- 0.2 mg/kg/day or 4.5 mg/m²/day for 3 - 6 weeks for remission induction (usual: 4-10mg/day); maintenance therapy: 0.03 - 0.1mg/kg/day.

Chronic lymphocytic leukaemia (CLL):

Biweekly regimen: Initial: 0.4 mg/kg/dose every 2 weeks; increase dose by 0.1mg/kg every 2 weeks until a response occurs and/or myelosuppression occurs.

Monthly regimen: Initial: 0.4 mg/kg, increase dose by 0.2 mg/kg every 4 weeks until a response occurs and /or myelosuppression occurs.

Malignant lymphomas: Non-Hodgkin's lymphoma: 0.1mg/kg/day.

Hodgkin's lymphoma: 0.2mg/kg/day.

Storage: store in refrigerator at 2-8°C; protect from light.

Cyclophosphamide

Tablet, 50 mg

Powder for injection, 200 mg, 500 mg, in vial

Indications: malignant lymphomas including non-Hodgkin lymphoma, lymphocytic lymphoma; multiple myeloma; leukaemias, mycosis, fungoides; neuroblastoma; adenocarcinoma of the ovary, retinoblastoma; breast cancer; severe rheumatoid arthritis.

Cautions: hepatic, renal, or bone marrow damage.

Drug interactions: allopurinol, succinyl choline, halothane, chloramphenicol, carbamazepine, nevirapine, phenytoin, suxamethonium, phenobarbitol, thiazide, digoxine,azole antifungals, ciprofloxacin, clarithromycin, diclofenac, doxycycline, erythromycin, isoniazide, protease inhibitors, quinidine, verapamil, aminoglutethimide, phenobarbitol.

Contraindications: pregnancy and breast feeding.

Side effects: sterility, amenorrhea, leukopenia, thrombocytopenia, anemia, nausea, vomiting, anoxia, mucositis, acute hemorrhagic cystitis, renal tubular necrosis, headache, skin rash, nasal congestion, diarrhea, alopecia, amenorrhea.

Dose and Administration: (refer to individual protocols):

Adult and Child:

Oral: 50-100 mg/m²/day as continuous therapy or 400-1000 mg/m² in divided doses over 4-5 days as intermittent therapy.

IV: single doses: 400-1800 mg/m² (30-50 mg/kg) per treatment course (1-5 days) which can be repeated at 2-4 week intervals.

Continuous daily doses: 60-120 mg/m² (1-2.5mg/kg) per day.

Storage: store at a temperature not exceeding 25°C.

Mechlorethamine Hydrochloride (Nitrogen Mustard)

Powder for injection, 10 mg in vial

Indications: Hodgkin's disease, non-hodgkin's lymphoma, malignant effusions.

Cautions: patients with lymphoma.

Drug interactions: vaccines, ethanol.

Contraindications: pre-existing profound myelosuppression or infection, pregnancy.

Side effects: delayed menses, oligomenorrhea, amenorrhea, impaired spermatogenesis, nausea, vomiting, myelosuppressive, fever, vertigo, alopecia, hyperuricemia, diarrhea, anorexia, metallic taste, ototoxicity, precipitation of herpes zoster.

Dose and Administration: (refer to individual protocols):

Adult: *IV:* 0.4 mg/kg or 12-16 mg/m² for one dose or divided into 0.1 mg/kg/day for 4 days, repeated at 4-6 week intervals.

Adult and Child: *IV:* 6 mg/m² on days 1 and 8 of a 28 day cycle (MOPP regimen)

Storage: store intact vials at room temperature.

Melphalan

Tablet, 2 mg, 5 mg

Indications: treatment of multiple myeloma, ovarian carcinomas and malignant melanoma.

Cautions: impaired renal function, elderly.

Drug interactions: cimetidine, cyclosporine, ethanol.

Contraindications: pregnancy, severe bone marrow suppression.

Side effects: leukopenia, thrombocytopenia, anemia, rash, nausea, vomiting, diarrhea, vasculites, alopecia, pruritus, sterility, amenorrhea, bladder irritation, hemorrhagic cystitis, agranulocytosis, hemolytic anemia, hepatitis, jaundice, pulmonary fibrosis.

Dose and Administration: (refer to individual protocols) *Oral:*

Adult: *Multiple myeloma:* 6 mg/day initially adjusted as indicated **or** 0.15 mg/kg/day for 7 days **or** 0.25 mg/kg/day for 4 days; repeat at 4-6 week intervals.

Ovarian carcinoma: 0.2 mg/kg/day for 5 days, repeat every 4-5 weeks.

Storage: store in refrigerator at 2-8°C; protect from light.

Thiotepa

Powder for injection, 15 mg/vial

Indications: treatment of superficial tumors of the bladder; palliative treatment of breast and ovarian carcinomas and malignant lymphomas.

Cautions: hepatic, renal, or bone marrow damage.

Drug interactions: other alkylating agents, succinylcholine and other neuromuscular agents.

Contraindications: pregnancy, severe myelosuppression.

Side effects: myelosuppression, anaemia, pancytopenia, dizziness, fever, rash, pruritus, headache, hyperpigmentation, hyperuricemia, anorexia, nausea, vomiting, hemorrhagic cystitis, pain at injection site, hematuria.

Dose and Administration: (refer to individual protocols):

Adult: *I.M., I.V., SC:* 30-60mg/m² once weekly.

I.V.: 0.3-0.4 mg/kg by rapid IV administration every 1-4 weeks **or**

0.2 mg/kg or 6-8 mg/m²/day for 4-5 days every 2-4 weeks.

Child: *Sarcomas:* *I.V.:* 25-65 mg/m² as a single dose every 21 days.

Storage: store intact vials under refrigeration (2-8°C) and protect from light.

Cytotoxic antibiotic

Drugs used in this group are widely used. Many cytotoxic antibiotics act as radiomimetics and simultaneous use of radiotherapy should be avoided as it may result in markedly enhanced toxicity.

Daunorubicin Hydrochloride, Doxorubicin hydrochloride (Adriamycin), Epirubicin are anthracycline antibiotics.

The anthracyclines can cause acute cardiotoxicity (arrhythmias) and long-term dose-related cardiomyopathy, which is often irreversible. Assessment of adequate left ventricular function and careful monitoring for cardiac symptoms and signs is required during the following treatment. The anthracyclines are contraindicated in patients with pre-existing cardiac disease or severe hepatic or renal impairment. The elderly are at special risk of developing cardiac complications with this group of drugs.

Other cytotoxic antibiotics include actinomycin-D and bleomycin.

Actinomycin-D (Dactinomycin)

Powder for injection, 0.5 mg in vial

Indications: trophoblastic tumours, wilm tumour, Ewing sarcoma, rhabdomyosarcoma.

Cautions: hepatobiliary dysfunction.

Drug interactions: vaccine (live), radiation therapy.

Contraindications: infants <6 months of age, herpeszoster.

Side effects: fatigue, malaise, fever, lethargy, alopecia, skin eruptions, acne, increased pigmentation, hypocalcemia, severe nausea, vomiting, anorexia, myelosuppression, anemia, mucositis, stomatitis, diarrhea, abdominal pain, hepatitis.

Dose and Administration: (refer to individual protocols): *I.V.*:

Adult: 2.5 mg/m² in divided doses over 1 week, repeated every 2 weeks or 0.75-2 mg/m² every 1-4 weeks or 400-600 mcg/m²/day for 5 days, repeated every 3-6 weeks.

Child > 6 months: 15 mcg/kg/day or 400-600 mcg/m²/day for 5 days every 3-6 weeks.

Storage: protect from light and humidity and store at room temperature.

Bleomycin

Powder for injection (lyophilised), 15 mg in vial.

Indications: adjunct to surgery and radiotherapy in palliative treatment of Hodgkin and non-Hodgkin lymphomas; reticulum cell sarcoma and lymphoma; carcinomas of the head, neck, larynx, cervix, penis, skin, vulva, testicles and including embryonal cell carcinoma, choriocarcinoma and teratoma; malignant effusions.

Cautions: pulmonary disease.

Drug interactions: lomustine, cisplatin, digoxin, phenytoin, oxygen, vaccine (live).

Contraindications: pregnancy.

Side effects: Raynaud's phenomenon, pain at the tumor site, phlebitis, peeling of the skin, hyperkeratosis, hyperpigmentation, alopecia, stomatitis, mucositis, anorexia, weight loss, tachypnea, pulmonary fibrosis, hypoxia, rash, anaphylactoid reactions.

Dose and Administration: (refer to individual protocols):

1 unit = 1 mg

Adult and Child: *Single agent therapy: I.M, I.V, SC:*

Squamous cell carcinoma, lymphoma, testicular carcinoma: 0.25-0.5 units/kg (10-20 units/m²) 1-2 times/week.

Combination agent therapy: I.M, I.V: 3-4 units/m²

I.V: ABVD: 10 units/m² on days 1 and 15

Pleural sclerosing: 60-240 units as a single infusion

Storage: store at 2 - 8°C.

Daunorubicin Hydrochloride

Powder for injection, 20 mg in vial

Indications: acute leukaemias.

Cautions: impaired hepatic, renal, or biliary function.

Drug interactions: vaccine, Live.

Contraindications: congestive heart failure or arrhythmias; bone marrow suppression, pregnancy.

Side effects: alopecia, mild nausea or vomiting, discolouration of urine, darkening or redness of skin, hyperuricemia, diarrhea, GI ulceration, myelosuppressive.

Dose and Administration: (refer to individual protocols) *I.V:*

Adult: 30-60 mg/m²/day for 3-5 days, repeat dose in 3-4 weeks.

Storage: store at room temperature.

Doxorubicin hydrochloride (Adriamycin)

Powder for injection, 10 mg, 50 mg in vial.

Indications: acute leukaemias; carcinomas of the breast, bladder, ovary and thyroid; neuroblastoma; wilm tumour, non-Hodgkin and Hodgkin lymphomas; soft tissue sarcomas, osteosarcoma.

Cautions: hepatic impairment.

Drug interactions: ciclosporin, phenytoin, stavudine, vaccine (live), allopurinol, cyclophosphamide, mercaptopurine, verapamil, promethazine, azole antifungals, chlorpromazine, erythromycin, ciprofloxacin.

Contraindications: pregnancy and breast feeding; bone marrow suppression.

Side effects: cardiovascular disease, alopecia, nausea, vomiting, mucositis, ulceration, anorexia, diarrhea, esophagitis, discolouration of urine (red), myelosuppression, leukopenia, arrhythmias, heart block, facial flushing, hyperpigmentation of nail beds, hyperuricemia.

Dose and Administration: (refer to individual protocols) *I.V:*

Adult: 60-75 mg/m² as a single dose, repeat every 21 days or other dosage regimens like 20-30 mg/m²/days for 2-3 days, repeat in 4 weeks or 20 mg/m² once weekly.

Child: 35-75 mg/m² as a single dose, repeat every 21 days or 20-30 mg/m² once weekly or 60-90 mg/m² given as a continuous infusion over 96 hours every 3-4 weeks.

Storage: store at room temperature.

Epirubicin

Powder for injection, 20 mg in vial.

Indications: adjuvant therapy for primary breast cancer.

Cautions: hepatic impairment, renal dysfunction, cardiac disease.

Drug interactions: cimetidine, ethanol.

Contraindications: severe myocardial insufficiency, severe arrhythmias, pregnancy.

Side effects: lethargy, alopecia, amenorrhea, nausea, vomiting, mucositis, diarrhea, leucopenia, hot flashes, anemia, thrombocytopenia, conjunctivitis, infection, fever, rash, skin changes, anorexia.

Dose and Administration: (refer to individual protocols) *I.V.*:

Adult: 100-120 mg/m² once weekly every 3-4 weeks or 50-60 mg/m² days 1 and 8 every 3-4 weeks

Storage: store in refrigerator (2-8°C).

Antimetabolites

Antimetabolites are incorporated into new nuclear material or combine irreversibly with vital cellular enzymes, preventing normal cellular division.

Antimetabolites include calcium folinate, capecitabine, cytarabine, fluorouracil, mercaptopurine and methotrexate.

Calcium Folate

Powder for injection, Folinic Acid (as Calcium salt), 15mg

Tablet, 50mg

Indications: high-dose methotrexate therapy (folate rescue), inadvertent overdose of methotrexate; with fluorouracil in the palliative treatment of advanced colorectal cancer.

Cautions: pernicious anemia or other megaloblastic anemias due to vitamin B₁₂ deficiency; pregnancy; breastfeeding.

Drug interactions: phenobarbital, phenytoin, and co-trimoxazole.

Contraindications: hypersensitivity to leucovorin.

Side effects: allergic reactions; pyrexia after parenteral administration.

Dose and Administration: (refer to individual protocols):

Adult and Child: *IM or IV injection or infusion:*

Antidote to methotrexate (usually started 24 hour after methotrexate), up to 120 mg in divided doses over 12 - 24 hours, then 12 - 15 mg by IM

every 6 hours for 48 - 72 hours.or 15mg by mouth every 6 hours for 48-72 hours

Methotrexate overdosage (started as soon as possible, preferably within 1 hour of methotrexate), by IV injection or infusion, Adult and Child, dose equal to or higher than that of methotrexate, at rate not exceeding 160mg/minute.

With fluorouracil in colorectal cancer, consult specialist literature.

Storage: store at room temperature and protect from light.

Capecitabine

Tablet, 150mg, 500mg

Indications: treatment of metastatic colorectal cancer, metastatic breast cancer.

Cautions: bone marrow suppression, poor nutritional status, on warfarin therapy, ≥ 80 years of age, or renal or hepatic dysfunction.

Drug interactions: warfarin.

Side effects: edema, fatigue, fever, dermatitis, diarrhea, mild to moderate nausea, vomiting, stomatitis, decreased appetite, anorexia, abdominal pain, constipation, anemia, lymphopenia, thrombocytopenia, dyspnea.

Dose and Administration: (refer to individual protocols): *Oral:*

Adult: 2500 mg/m²/day in 2 divided doses (~ 12 hours apart) at the end of a meal for 2 weeks followed by a 1 or 2 week rest period.

Storage: store at room temperature.

Cytarabine

Powder for injection, 20 mg in vial

Indications: acute lymphoblastic leukaemia; chronic myeloid leukaemia; meningeal leukaemia; erythroleukemia; non-Hodgkin lymphoma.

Cautions: hepatic impairment.

Drug interactions: alkylating agents, methotrexate, gentamicin, flucytosin, digoxin.

Contraindications: hypersensitivity to cytarabine.

Side effects: cerebral toxicity, conjunctivitis, corneal keratitis, pulmonary edema, pericarditis, seizures, oral/anal ulceration, rash, nausea, vomiting, anorexia, stomatitis, bleeding, leukopenia, thrombocytopenia, hepatic dysfunction, mild jaundice, dizziness, headache, confusion, itching, hyperuricemia, diarrhea, urinary retention, hepatotoxicity, megaloblastic anemia, thrombophlebitis, myalgia, peripheral neuropathy.

Dose and Administration: (refer to individual protocols):

Adult and Child:

Remission induction: IV: 100-200 mg/m²/day for 5-10 days; a second course, beginning 2-4 weeks after the initial therapy.

Remission maintenance: IV: 70-200 mg/m²/day for 2-5 days at monthly intervals.

IM, SC: 1-2.5 mg/kg single dose for maintenance at 1-4 week intervals.

Storage: store at room temperature.

Fluorouracil

Injection, 50 mg/ml in 10ml ampoule

Indications: carcinomas of the colorectum, breast, stomach, pancreas, cervix, prostate, ovary and endometrium; liver tumours; head and neck tumours actinic keratoses.

Cautions: impaired kidney and liver function.

Drug interactions: cimetidine, warfarin, metronidazole, phenytoin, vaccine (live)

Contraindications: depressed bone marrow function, thrombocytopenia, potentially serious infections, dihydropyrimidine dehydrogenase (DPD) enzyme deficiency, pregnancy.

Side effects: rash, alopecia, nausea, vomiting, anorexia, diarrhea, stomatitis, esophagitis, leukopenia, dry skin, GI ulceration.

Dose and Administration: (refer to individual protocols): **Adult:**

IV bolus: 500-600 mg/m² every 3-4 weeks or 425 mg/m² on days 1-5 every 4 weeks

Continuous IV infusion: 1000 mg/m²/day for 4-5 days every 3-4 weeks or 2300-2600 mg/m² on day 1 every week or 300-400 mg/m²/day or 225 mg/m²/day for 5-8 weeks (with radiation therapy).

Storage: store at room temperature.

Mercaptopurine

Tablet, 50 mg

Indications: acute leukaemias.

Cautions: hepatic impairment, elderly.

Drug interactions: allopurinol, phenytoin, sulfamethoxazole + trimethoprim, vaccine (live), doxorubicin, warfarin, sulfasalazine.

Contraindications: severe bone marrow suppression, pregnancy.

Dose and Administration: (refer to individual protocols): *Oral*

Adult: Induction: 2.5 - 5 mg/kg/day (100-200mg)

Maintenance: 1.5 - 2.5 mg/kg/day or 80 - 100 mg/m²/day given once daily

Child: Induction: 2.5 - 5 mg/kg/day or 70 - 100 mg/m²/day given once daily

Maintenance: 1.5 - 2.5 mg/kg/day or 50 - 75 mg/m²/day given once daily

Storage: store at room temperature.

Methotrexate

Tablets, 2.5 mg, 10mg

Powder for injection, 5 mg, 50mg in vial

Indications: carcinoma of the breast, head and neck, and lung, trophoblastic tumours; acute lymphoblastic leukaemia, meningeal leukaemia, non-Hodgkin lymphomas; advanced cases of mycosis

fungoides; non-metastatic osteosarcoma; psoriasis, severe rheumatoid arthritis.

Cautions: renal and hepatic impairment.

Drug interactions: acetyl salicylic acid, amoxicillin, ampicillin, benzyl penicillin, ciclosporin, dexamethasone, fludrocortisone, hydrocortisone, ibuprofen, phenoxymethylpenicillin, phenytoin, prednisolone, pyrimethamine, sulfadiazine, sulfadoxine + pyrimethamine, sulfamethoxazole + trimethoprim.

Contraindications: pregnancy.

Side effects: headache, vomiting, fever, seizure, reddening of skin, hyperuricemia, defective oogenesis or spermatogenesis, ulcerative stomatitis, glossitis, nausea, vomiting, diarrhea, anorexia, mucositis, renal failure, nephropathy, pharyngitis, vasculitis, dizziness, malaise, encephalopathy, fever, chills, rash, diabetes, cystitis, hemorrhage, myelosuppressive, cirrhosis, blurred vision, renal dysfunction, pneumonitis.

Dose and Administration: (refer to individual protocols): **Adult:**

Trophoblastic tumours: Oral, I.M: 15-30 mg/day for 5 days; repeat in 7 days for 3-5 courses.

I.V: 11 mg/m² days 1 through 5 every 3 weeks.

Head and neck cancer: Oral, IM, IV: 25-50 mg/m² once weekly.

Mycosis fungoides: Oral, IM: initial (early stage): 5-50 mg once weekly or 5-37.5 mg twice weekly.

Bladder cancer: IV: 30 mg/m² day 1 and 8 every 3 weeks or 30 mg/m² day 1, 15, and 22 every 4 weeks.

Breast cancer: IV: 30-60mg/m² days 1 and 8 every 3-4 weeks.

Gastric cancer: IV: 1500mg/m² every 4 weeks.

Non-Hodgkin lymphomas: IV: 30mg/m² days 3 and 10 every 3 weeks or 120mg/m² day 8 and 15 every 3-4 weeks.

Sarcoma: IV: 8-12g/m² weekly for 2-4 weeks.

Rheumatoid arthritis: Oral: 7.5mg once weekly or 2.5 mg every 12 hours for 3 doses/week, not to exceed 20mg/week.

Psoriasis: Oral: 2.5-5mg/dose every 12 hours for 3 doses given weekly or Oral, IM: 10-25mg/dose given once weekly.

Storage: store in well-closed containers at 15 - 30°C.

Vinca Alkaloids and Etoposide

The vinca alkaloids vinblastine and vincristine are used to treat acute leukaemia, lymphomas, and breast and lung cancer. Reversible dose-limiting neurotoxicity is found: peripheral neuropathy with paraesthesiae, cranial nerve palsies, muscle weakness, loss of deep tendon reflexes, paralytic ileus, and grandmal seizures. Pre-existing neurological disease may predispose to severe neuropathy.

Etoposide is useful in small cell carcinoma of the bronchus, testicular cancer and lymphomas. It has been used in Kaposi's sarcoma.

Etoposide*Capsules, 50 mg, 100 mg**Concentrate for infusion, 20 mg/ml.**Powder for injection, 100 mg/vial***Indications:** refractory testicular tumours; lung cancer.**Cautions:** hepatic or renal impairment; elderly.**Drug interactions:** vaccine (live).**Contraindications:** intrathecal administration, pregnancy.**Side effects:** alopecia, diarrhea, nausea, vomiting, anorexia, anemia, leukopenia, mucositis, hypotension, unusual fatigue, stomatitis, hepatic dysfunction.**Dose and Administration:** (refer to individual protocols): **Adult:***Lung cancer: Oral:* Twice the IV dose rounded to the nearest 50 mg given once daily if total dose ≤ 400 mg or in divided doses if > 400 mg*IV:* 35 mg/m²/day for 4 days or 50 mg/m²/day for 5 days every 3-4 weeks total dose ≤ 400 mg/day*Testicular cancer: IV:* 100 mg/m² every other day for 3 doses repeated every 3-4 weeks**Storage:** store intact vials of injection at room temperature and oral capsules in refrigeration.**Vinblastine sulfate***Powder for injection, 10 mg in vial***Indications:** treatment of Hodgkin's and non-Hodgkin's lymphoma; advanced testicular carcinoma, breast carcinoma; palliative treatment of Kaposi's sarcoma, trophoblastic tumours.**Cautions:** hepatic impairment.**Drug interactions:** vaccine (live), azole antifungals, ciprofloxacin, clarithromycin, diclofenac, doxycycline, erythromycin, isoniazide, propofol, protease inhibitors, quinidine, and verapamil, aminoglutethimide, carbamazepine, nafcillin, nevirapine, phenobarbital, phenytoin and rifamycins.**Contraindications:** pregnancy and breastfeeding.**Side effects:** alopecia, diarrhea, stomatitis, anorexia, metallic taste, severe bone marrow suppression, granulocytopenia, thrombocytopenia, hypertension, Raynaud's phenomenon, depression, malaise, headache, seizure, rash, dermatitis, hyperuricemia, abdominal pain, nausea, vomiting, urinary retention, bronchospasm.**Dose and Administration:** (refer to individual protocols):**Adult and Child:** *IV:* 4-20 mg/m² (0.1-0.5mg/kg) every 7-10 days or 5 day continuous infusion of 1.5-2 mg/m²/day or 0.1-0.5 mg/kg/week.**Storage:** store at 2 - 8°C.**Vincristine Sulfate***Powder for injection, 1mg, 5mg in vial*

Indications: acute lymphoblastic leukaemia; neuroblastoma, wilm tumour, Hodgkin and non-Hodgkin lymphomas; rhabdomyosarcoma, Ewing sarcoma; mycosis fungoides.

Cautions: hepatic impairment.

Drug interactions: phenytoin, vaccine (live).

Contraindications: pregnancy and breastfeeding.

Side effects: alopecia, orthostatic hypotension or hypertension, seizure, headache, CNS depression, fever, rash, hyperuricemia, constipation, anorexia, nausea, vomiting, weightloss, diarrhea, bladder atony, photophobia

Dose and Administration: (refer to individual protocols):

Adult: 0.4-1.4 mg/m², may repeat every week **or** 0.4-0.5 mg/day continuous infusion for 4 days every 4 weeks **or** 0.25-0.5 mg/m²/day for 5 days every week.

Storage: store at 2 - 8°C.

Hormones and Antihormones

Anastrozole

Tablet, 1mg (film coated)

Indications: treatment of locally-advanced or metastatic breast cancer (ER-positive or hormone receptor unknown) in postmenopausal women; treatment of advanced breast cancer in postmenopausal women with disease progression following tamoxifen therapy; adjuvant treatment of early ER-positive breast cancer in postmenopausal women.

Caution: hyperlipidemias.

Drug interactions: estrogen, tamoxifen.

Contraindications: pregnancy (risk factor D), hypersensitivity reaction.

Side effects: vasodilation, headache, depression, hot flashes, arthritis, arthralgia, back pain, cough increased, pharyngitis, peripheral edema, hypertension, insomnia, dizziness, anxiety, rash, vomiting, constipation, diarrhea, anorexia, anemia, dyspnea.

Dose and Administration: *Breast cancer:* **Adult:** *Oral* (refer to individual protocols): 1 mg once daily.

Storage: store at room temperature.

Tamoxifen Citrate

Tablet, 10 mg

Indications: adjuvant treatment of estrogen - receptor-positive breast cancer; metastatic breast cancer; reduce the incidence of breast cancer in women at high risk.

Cautions: leukopenia, thrombocytopenia, or hyperlipidemias.

Drug interactions: warfarin, allopurinol, cyclosporine, delavirdine, fluconazole, gemfibrozil, ketoconazole, NSAIDs, sulfonamides, chlorpromazine, miconazole, fluoxetine, quinidine, quinine, ritonavir, erythromycin, ciprofloxacin, diclofenac, doxycycline, isoniazid,

verapamil, carbamazepine, phenobarbital, phenytoin, rifampin, nevirapine.

Contraindications: pregnancy; breast-feeding.

Side effects: hot flushes; endometrial changes (symptoms such as vaginal bleeding and other menstrual irregularities, vaginal discharge, pelvic pain); increased pain and hypercalcaemia with bony metastases; tumour flare; nausea and vomiting; liver enzyme changes; thromboembolic events; decreased platelet count; oedema; alopecia; rash; headache; visual disturbances; rarely hypersensitivity reactions.

Dose and Administration: Adult:

Breast cancer: Metastatic: 20-40 mg/day; daily doses > 20 mg should be given in 2 divided doses (morning and evening).

Prevention (high-risk females): 20mg/day for 5 years.

Storage: store in well closed containers at controlled room temperature.

Testosterone Propionate

Tablet (buccal), 10 mg

Monoclonal Antibodies

Bevacizumab

Injection, 25 mg /ml vial

Indications: treatment of metastatic colorectal cancer as a component of multidrug therapy.

Cautions: cardiovascular disease.

Drug interactions: it may potentiate the cardiotoxic effects of anthracyclines.

Contraindications: hypersensitivity reactions.

Side effects: hypertension, hypotension, thromboembolism, headache, dizziness, alopecia, weight loss, hypokalemia, abdominal pain, vomiting, diarrhea, anorexia, constipation, stomatitis, dyspepsia, flatulence, leukopenia, epistaxis, gastrointestinal hemorrhage, neutropenia, myalgia, dyspnea.

Dose and Administration: IV: Adult:

Colorectal cancer: 5-10 mg/kg every 2 weeks

Storage: store vials at 2 - 8 °C. Protect from light; do not freeze or shake.

Rituximab

Injection, 100 mg/10ml

Indications: treatment of relapsed or refractory CD20 positive, B-cell non-Hodgkin's lymphoma.

Cautions: cardiac or pulmonary disease and hypersensitivity reactions.

Side effects: abdominal pain, anemia, dyspnea, hypotension, and neutropenia are more common in patients with bulky disease. Central nervous system (fever, chills, headache, pain), rash, pruritus, angioedema, nausea, abdominal pain, lymphopenia, cough, rhinitis.

Dose and Administration: **Adult:** *I.V infusion* (refer to individual protocols):

Manufacturer's labeling: 375 mg/m² once weekly for 4 - 8 weeks. **or** 100 mg/m² IV day 1, then 375 mg/m² 3 times/week for 11 doses has also been reported (cycles may be repeated in patients with refractory or relapsed disease).

Retreatment following disease progression: 375 mg/m² once weekly for 4 doses.

Storage: store vials under refrigeration (2 - 8 °C).

Trastuzumab

Injection, 440 mg/vial

Indications: for treatment of metastatic breast cancer with overexpression of human epidermal growth factor receptor 2(HER): as monotherapy in patients who have received at least two chemotherapy regimens for their metastatic disease (including an anthracycline); or in combination with paclitaxel in patients who have received chemotherapy for metastatic disease and in whom an anthracycline is not suitable.

Cautions: congestive heart failure.

Drug interactions: anthracyclines, cyclophosphamide and myelosuppressive chemotherapy.

Contraindications: hypersensitivity reactions.

Side effects: fever, chills, headache, rash, nausea, diarrhea, vomiting, abdominal pain, anorexia, back pain, cough, dyspnea, rhinitis, pharyngitis.

Dose and Administration: *I.V infusion:* **Adult:**

Initial loading dose: 4 mg/kg intravenous infusion over 90 minutes

Maintenance dose: 2 mg/kg intravenous infusion over 90 minutes (can be administered over 30 minutes if prior infusions are well tolerated) weekly until disease progression.

Storage: store intact vials under refrigeration (2 - 8 °C).

Cytotoxic immunosuppressants

Azathioprine

Tablet, 50 mg

Indications: organ transplantation, in combination with steroids and/or other immunosuppressants; auto immune diseases such as

systemic lupus erythematosus, refractory rheumatoid arthritis, idiopathic thrombocytopenia purpura, autoimmune haemolytic anemia and chronic active hepatitis.

Cautions: liver and renal impairment, monitor hematologic function closely.

Drug interactions: allopurinol, sulfasalazine, warfarin.

Contraindications: pregnancy.

Side effects: myelosuppression with occasional thrombocytopenia and anaemia; severe red cell megaloblastosis, hepatotoxicity, hypersensitivity reactions, including anaphylaxis, may occur.

Dose and Administration: Adult and Child:

Renal transplantation: Oral: 2-5 mg/kg/day to start, then 1-3 mg / kg / day maintenance.

Adult: *Rheumatoid arthritis:* Oral: 1 mg/kg/day for 6-8 weeks; increase by 0.5 mg/kg every 4 weeks until response or up to 2.5 mg/kg/day.

Storage: store at room temperature.

Other Antineoplastics

Cisplatin

Powder for injection, 10 mg, 25mg, 50 mg vial

Indications: treatment of head and neck, breast, testicular and ovarian cancer; Hodgkin's and non-Hodgkin's lymphoma; neuroblastoma, sarcomas, bladder, gastric, lung, esophageal, cervical, and prostate cancer; myeloma, melanoma, mesothelioma, small cell lung cancer, and osteosarcoma.

Cautions: renal impairment, myelosuppression, hearing impairment.

Drug interactions: acetazolamide, amiloride, furosemide, gentamicin, hydrochlorothiazide, phenytoin, spironolactone, streptomycin, vancomycin, vaccine (live).

Contraindications: pregnancy.

Side effects: peripheral neuropathy, mild alopecia, nausea and vomiting, myelosuppressive, elevation of liver enzymes, nephrotoxicity, ototoxicity, arrhythmias, blurred vision, bradycardia, cerebral blindness, hemolytic anemia.

Dose and Administration: (refer to individual protocols) *I.V.*

Adult: *Advanced bladder cancer:* 50-70 mg/m² every 3-4 weeks.

Head and neck cancer: 100-120 mg/m² every 3-4 weeks.

Metastatic ovarian cancer: 75-100 mg/m² every 3 weeks.

Testicular cancer: 10-20 mg/m²/day for 5 days repeated every 3-4 weeks.

Storage: store at room temperature and protect from light.

Dacarbazine

Powder for injection, 100mg, 200mg, 500mg, 600mg, 1000mg/vial

Indications: treatment of malignant melanoma, hodgkin's disease, soft-tissue sarcomas, medullary carcinoma of the thyroid,

and neuroblastoma.

Dose and Administration: (refer to individual protocols) *I.V.*:

Hodgkin's disease, ABVD: 375mg/m² days 1 and 15 every 4

weeks or 100 mg/m²/day for 5 days

Metastatic melanoma (alone or in combination with other agents): 150-250mg/m² days 1-5 every 3-4 weeks

Metastatic melanoma: 850mg/m² every 3 weeks

Storage: store intact vials under refrigeration (2-8°C) and protect from light.

Hydroxycarbamide (hydroxyurea)

Capsule, 500 mg

Indications: treatment of metastatic disease, chronic myeloid leukaemia, haemoglobinopathies including sickle cell disease and tumours of the head and neck, an adjunct to nucleoside reverse transcriptase inhibitor in the treatment of HIV disease.

Cautions: renal impairment, bone marrow suppression, erythrocytic abnormalities, and elderly.

Drug interactions: zidovudine, zalcitabine, didanosine, fluorouracil, cytarabine, and stavudine.

Contraindications: severe anemia, pregnancy.

Side effects: edema, drowsiness, hallucinations, headache, dizziness, disorientation, seizure, fever, chills, erythema of hands and face, rash, pruritus, hyperpigmentation, dry skin, skin cancer, hyperuricemia, nausea, vomiting, stomatitis, anorexia, diarrhea, constipation, pancreatitis, dysuria, myelosuppression, hepatotoxicity, peripheral neuropathy, dyspnea, pulmonary fibrosis.

Dose and Administration: (refer to individual protocols):

Oral: Adult:

Solid tumors: Intermittent therapy: 80 mg/kg as a single dose every third day

Continuous therapy: 20-30 mg/kg/day given as a single dose/day

Concomitant therapy with irradiation: 80 mg/kg as a single dose every third day starting at least 7 days before initiation of irradiation.

Resistant chronic myelocytic leukemia: Continuous therapy: 20-30 mg/kg as a single daily dose

HIV (in combination with ARV agents): 1000-1500 mg daily in a single dose or divided doses.

Sickle cell anemia: initial: 15 mg/kg/day, increased by 5 mg/kg every 12 weeks if blood counts are in an acceptable range until the maximum tolerated dose of 35 mg/kg/day is achieved.

Storage: store at room temperature.

Procarbazine

Capsule, (as hydrochloride) 50 mg

Indications: treatment of Hodgkin's disease.

Cautions: renal and hepatic impairment.

Drug interactions: foods containing high amounts of tyramine, epinephrine, amphetamine, antidepressants, narcotics, phenothiazines, and other CNS depressants.

Contraindications: pre-existing bone marrow aplasia; ethanol ingestion; pregnancy.

Side effects: mental depression, manic reactions, hallucinations, dizziness, headache, nervousness, insomnia, nightmares, ataxia, confusion, CNS stimulation, amenorrhea, nausea, vomiting, anorexia, abdominal pain, stomatitis, dysphagia, diarrhea, constipation, thrombocytopenia, hemolytic anemia, myelosuppressive, paresthesia, neuropathies, nystagmus, pleural effusion, cough, hepatotoxicity, peripheral neuropathy, alopecia, hyperpigmentation.

Dose and Administration: (refer to individual protocols): *Oral:*

Adult: Initial: 2-4 mg/kg/day in single or divided doses for 7 days then increase dose to 4-6 mg/kg/day until response is obtained.

Child: *BMT aplastic anemia conditioning regimen:* 12.5 mg/kg/dose every other day for 4 doses.

Hodgkin's disease: MOPP/IC-MOPP regimens: 100 mg/m²/day for 14 days and repeated every 4 weeks

Neuroblastoma and medulloblastoma: dose as high as 100-200 mg/m²/day once daily have been used.

Storage: store in tight, light - resistant containers and at room temperature.

Miscellaneous

Filgrastim

Injection, 300 mcg/ml, 300 mcg/0.5ml syringe, 480 mcg/1.6ml, 480 mcg /0.8 ml syringe

Indications: stimulation of granulocyte production in patients with malignancies, including myeloid malignancies; receiving myelosuppressive therapy associated with a significant risk of neutropenia; severe chronic neutropenia (SCN); receiving bone marrow transplantation (BMT); undergoing peripheral blood progenitor cell (PBPC) collection.

Cautions: complete blood count and platelet count should be obtained prior to chemotherapy.

Drug interactions: drugs which may potentiate the release of neutrophils (e.g. lithium)

Contraindications: concurrent myelosuppressive chemotherapy or radiation therapy.

Side effects: neutropenic fever, alopecia, nausea, vomiting, diarrhea, mucositis, chest pain, fluid retention, headache, anorexia.

Dose and Administration: Refer to individual protocols: *IV or SC:*

Myelosuppressive therapy: 5 mcg/kg/day – doses may be increased by 5 mcg/kg according to the duration and severity of the neutropenia.

BMT: 5 – 10 mcg/kg/day – doses may be increased by 5 mcg/kg according to the duration and severity of neutropenia

PBPC: 10 mcg/kg/day or 5 – 8 mcg/kg twice daily in donors.

Severe chronic neutropenia: *Congenital*: 6 mcg/kg twice daily

Idiopathic/Cyclic: 5 mcg/kg/day

Storage: store in refrigerator at 2 – 8 °C.

Granisetron

Tablet, 2 mg

Indications: prophylaxis of chemotherapy - related emesis; prophylaxis of nausea and vomiting associated with radiation therapy, including total body irradiation and fractionated abdominal radiation; prophylaxis of postoperative nausea and vomiting (PONV).

Cautions: chemotherapy -related emesis; liver disease or in pregnancy.

Drug interactions: substrate of CYP3A4.

Contraindications: hypersensitivity reactions.

Side effects: headache, constipation, hypertension, dizziness, insomnia, anxiety somnolence, fever, abdominal pain, diarrhea, dyspepsia, elevated liver enzymes.

Dose and Administration: *Oral: Adult*:

Prophylaxis of chemotherapy-related emesis: 2 mg once daily up to 1 hour before chemotherapy or 1 mg twice daily; the first 1 mg dose should be given up to 1 hour before chemotherapy.

Prophylaxis of radiation therapy-associated emesis: 2 mg once daily given 1 hour before radiation therapy.

Storage: store at room temperature and protect from light.

Interferon alfa-2a

Injection, solution, 3 million unit (11.1 mcg/0.5 ml syringe), 6 million unit (22.2 mcg/0.5 ml syringe), 9 million unit (33.3 mcg/0.5 ml syringe)

Indications:

Patients > 18 years of age: Hairy cell leukemia, AIDS-related Kaposi's sarcoma, chronic hepatitis C.

Child and Adult: Chronic myelogenous leukemia (CML), Philadelphia chromosome positive, within 1 year of diagnosis (limited experience in children).

Cautions: depression, seizure disorders, brain metastases, or compromised CNS function, autoimmune disease, pre-existing cardiac disease, arrhythmias, renal impairment, mild hepatic impairment or myelosuppression; diabetes or pre-existing thyroid disease.

Drug interactions: theophylline, ACE inhibitors, clozapine, warfarin, zidovudine.

Contraindications: hypersensitivity reactions, autoimmune hepatitis, visceral AIDS-related Kaposi's sarcoma associated with rapidly-progressing or life-threatening disease, hepatic decompensation.

Side effects: flu-like symptoms, chest pain, edema, hypertension, psychiatric disturbances, fatigue, headache, dizziness, irritability, insomnia, rash, anorexia, nausea, vomiting, diarrhea, and myelosuppression.

Dose and Administration: (Refer to individual protocols) **Adult:**

Hairy cell leukemia: SC, IM: 3 million units/day for 16-24 weeks, then 3 million units 3 times/week for up to 6 – 24 months.

Chronic myelogenous leukemia (CML): SC, IM: 9 million units/day, continue treatment until disease progression.

AIDS-related Kaposi's sarcoma: SC, IM: 36 million units/day for 10-12 weeks, then 36 million units 3 times/week; to minimize adverse reactions, can use escalating dose (3-9, then 18 million units each day for 3 days, then 36 million units daily thereafter)

Hepatitis C: SC, IM: 3 million units 3 times/week for 12 months.

Storage: store in refrigerator (2 – 8 °C). Do not freeze.

Ondansetron

Tablet, 4mg, 8mg

Syrup, 4mg/5ml

Injection, 2mg/ml, 4mg/ml

Suppository, 16mg

Indications: management of nausea and vomiting induced by chemotherapeutic agents and radiotherapy; prevention and treatment of post-operative nausea and vomiting.

Cautions: previous hypersensitivity to other selective 5HT₃-receptor antagonists; hepatic impairment; subacute intestinal obstruction; porphyria; pregnancy; lactation.

Contraindications: known hypersensitivity to the product.

Side effects: headache, flushing, hiccups, constipation, transient, asymptomatic increase in aminotransferases. Hypersensitivity reactions (anaphylaxis, bronchospasm, hypotension, shock, angioedema, urticaria).transient visual disturbances and dizziness with rapid IV administration; pain, redness at injection site.

Dose and Administration: Adult: *Highly emetogenic chemotherapy (e.g. cisplatin):* Slow IV or IM, 8mg immediately before treatment, followed by 2 further IV or IM doses of 8mg 2-4 hours apart (or by a continuous IV infusion of 1mg/hour for up to 24 hours). Alternatively , a single dose of 32mg diluted in 50-100ml 0.9% sodium chloride solution and infused over not less than 15 minutes immediately before chemotherapy. To protect against delayed or prolonged emesis after the first 24hours, continue with oral, 8mg 12hourly for up to 5 days.

Less emetogenic chemotherapy: Oral: 8mg 1-2 hours before treatment (or slow IV or IM, 8mg immediately before treatment), followed by oral, 8mg 12 hourly for up to 5 days.

Post-operative nausea and vomiting: immediately before induction of anaesthesia or postoperatively, 4mg IM or IV over 2-5 minutes.

Alternatively, 16mg orally 1 hour before induction. Repeat dosing has not been studied.

Moderate to severe hepatic impairment : total daily dose of 8mg should not be exceeded.

Child: Emetogenic chemotherapy: >4 years, IV, 5mg/m² given over 15 minutes, immediately before treatment, followed by oral, 4mg 12 hourly for up to 5 days

Post-operative nausea and vomiting: ≥ 2 years, slow IV, 0.1mg/kg up to a maximum of 4 mg, prior to, at, or after, induction of anaesthesia.

11. BLOOD PRODUCTS AND DRUGS AFFECTING THE BLOOD

11.1. Anticoagulants

Anticoagulants are used to prevent thrombus formation or extension of an existing thrombus in the slower-moving venous side of the circulation, where the thrombus consists of a fibrin web enmeshed with platelets and red cells. They are therefore used widely in the prevention and treatment of deep-vein thrombosis in the legs, prophylaxis of embolization in rheumatic heart disease and atrial fibrillation and to prevent thrombi forming on prosthetic heart valves.

Dalteparin

Injection, Antifactor Xa 10,000u, 25,000u

Prefilled syringe, Antifactor Xa 5000u, 75000u, 10,000u

Indications: see under enoxaparine.

Cautions and Side effects; see under heparin.

Dose and Administration: Adult: SC:

Abdominal surgery: 2500u or 5000u 1-2 hours prior to surgery, then once daily for 5-10 days postoperatively.

Storage: store at a temperatures 20 to 25°C.

Enoxaparine

Injection, 20mg/0.2ml, 40mg/0.4ml, 60mg/0.6ml, 80mg/0.8ml, 100mg/ml

Indications: prevention of postoperative venous thrombosis and embolism in high-risk patients; treatment of deep venous thrombosis.

Cautions and Side effects, see under heparin.

Dose and Administration: Adult:

Prevention of venous thrombosis after orthopaedic surgery: SC, 40mg once daily, initiated 12 hours pre-operatively and continued for as long as risk persists (generally for 7-10 days; hip replacement, 3 weeks).

Treatment of deep vein thrombosis: SC, 1 mg/kg 12 hourly lean body mass, usually for 5-10 days or until oral anticoagulation is established.

Unstable angina: SC, 1 mg/kg 12 hourly, given concurrently with aspirin; minimum duration of therapy, 2 days.

Heparin Sodium

Injection (solution for injection) 1000 units/ml, 5000 units/ml in 5 ml ampoule; 5000 units/ml, 12,500 units/ml in 1 ml ampoule; 24,000 USP_u/5ml.

Indications: treatment and prophylaxis of deep-vein thrombosis and pulmonary embolism.

Cautions: hepatic impairment and renal failure; spinal or epidural anaesthesia risk of spinal haematoma; pregnancy; diabetes mellitus, acidosis, concomitant potassium-sparing drugs increased risk of hyperkalaemia.

Drug interactions: acetylsalicylic acid, captopril and ibuprofen.

Contraindications: hypersensitivity to heparin; haemophilia and other haemorrhagic disorders, thrombocytopenia, peptic ulcer, recent cerebral hemorrhage, severe hypertension, after major trauma or recent surgery (especially to eye or nervous system).

Side effects: immune-mediated thrombocytopenia usually developing 6 to 10 days after commencement of therapy; haemorrhage, skin necrosis, hypersensitivity reactions including urticaria, angioedema and anaphylaxis, osteoporosis after prolonged use and rarely alopecia.

Dose and Administration:

Treatment of deep-vein thrombosis and pulmonary embolism:

Adult: *IV injection*, loading dose of 5000 units (10,000 units in severe cases) followed by continuous intravenous infusion of 15 - 25 units/kg/hour or by *SC injection* of 15000 units every 12 hours.

Child: lower loading dose, then by continuous *IV infusion*, 15 - 25 units/kg/hour or by *SC*, 250 units /kg every 12 hours.

Prophylaxis in general surgery: **Adult:** *SC*: 5000 units 2 hours before surgery, then every 8 - 12 hours for 7 days or until patient is ambulant.

Storage: store at room temperature.

Warfarin Sodium

Tablets, 2 mg, 5 mg, 10mg

Indications: prophylaxis of embolization in rheumatic heart disease and atrial fibrillation; prophylaxis after insertion of prosthetic heart valve; prophylaxis and treatment of venous thrombosis and pulmonary embolism; transient ischaemic attacks.

Cautions: hepatic or renal failure, recent surgery, breastfeeding.

Drug interactions: acetylsalicylic acid, alcohol, allopurinol, amoxicillin, ampicillin, azathioprine, carbamazepine, ceftazidime, ceftriaxone, chloramphenicol, cimetidine, ciprofloxacin, contraceptives, dexamethasone, doxycycline, erythromycin, fluconazole, fludrocortisone, glibenclamide, griseofulvin, hydrocortisone, ibuprofen, levonorgestrol, levothyroxine, medroxy progesterone, metronidazole, naldixic acid, norethisterone, ofloxacin, phenobarbital, phenytoin, phytomenadione, prednisolone, proguanil, quinidine, rifampicin, ritonavir, sulfadiazine, tamoxifen, testosterone.

Contraindications: pregnancy, bleeding disorders (haemophilia or leukaemia); open wounds, ulceration of the gastrointestinal tract or genitourinary tract; recent stroke, intracerebral bleeding; infective endocarditis, aneurysms and severe hypertension; recent or contemplated eye, brain or spinal cord surgery.

Side effects: haemorrhage, hypersensitivity, rash, alopecia, diarrhea, unexplained drop in haematocrit, 'purple toes', skin necrosis, jaundice, hepatic dysfunction, nausea, vomiting and pancreatitis.

Dose and Administration: *Oral:*

Adult: initially 5 - 10 mg daily for 2 - 5 days or until, the desired prothrombin activity is reached. Maintenance is determined by individual response and is usually 2 - 10 mg daily (taken at the same time each day).

Infants and Child: 0.05-0.34mg/kg/day; infants < 12 months of age may require doses at or near the high end of this range; consistent anticoagulation may be difficult to maintain in children < 5 years of age.

Storage: protect from light and store at room temperature.

11.2. Hemostatic Agents

Absorbable Gelatin Sponge

Indication: as a haemostatic agent by providing a physical meshwork within which clotting can occur.

Side effects: increase incidence of infection, compression of surrounding tissue due to fluid absorption, granuloma formation, and fibrosis. Generally, gelatin sponges cause little tissue reaction and can be applied to bone, dura, and pleural tissue.

Dose and Administrations: gelatin sponge can be applied dry or soaked in saline or thrombin solutions when applied to skin wounds the gelatin liquifies within 2 to 5 days; when implanted into tissues it is absorbed with in 4 to 6 weeks.

Aminocaproic Acid

Injection, 250 mg/ml in 20ml ampoule

For full profile; see section 9 under aminocaproic acid.

Clopidogrel

Tablet, 75mg

Indications: After coronary artery stenting to reduce stent thrombosis; added to aspirin, heparin and other conventional therapy, reduces the risk of death, myocardial infarction and stroke in patients with acute coronary syndromes; secondary prevention of thromboembolic stroke or TIA; patients with aspirin intolerance who require antiplatelet agents. Neutropenia and thrombotic thrombocytopenic purpura are rare adverse effects of clopidogrel.

Dose and Administration: *Oral:* 75mg daily. A loading dose of 300mg is conventionally prescribed for patients with acute coronary syndromes or those having a stent placed. Some authorities advise a loading dose of 600mg.

Fibrinogen

Powder, 1g in vial

Indications: for the control of bleeding and prophylactic treatment of patients deficient in fibrinogen.

Phytomenadione (vitamin K1)

Injection, 1mg/0.5ml in 0.5ml ampoule; 10mg/ml in 1 ml ampoule.

Indications: for the treatment of hemorrhage due to Vitamin k deficiency.

Cautions: severe liver diseases.

Drug interactions: antacids (aluminium hydroxide), wide spectrum antibiotics, quinidine, quinine, high doses of salicylates, antibacterials like sulfonamides, coumarin or indandione - derivative anticoagulants (such as dicumarol), and other hemolytics.

Side effects: flushing of face, redness, pain, or swelling at place of injection, unusual taste.

Dose and Administration: *Subcutaneously or intramuscularly.* It should not be given repeatedly to patient with severe liver diseases, once the response to the initial dose is unsatisfactory.

Adult: *I.M. or S.C.,* 2.5 – 10mg (up to 25mg), may be repeated after 6-8 hours if necessary. **Child: Infants** - *IM or SC,* 1-2 mg; **Child** - *IM or SC,* 5-10mg.

Storage: at room temperature. Protect from light and freezing.

11.3. Antianemic Agents

Iron - deficiency anaemia.

Anaemia is usually understood to mean a lowering of haemoglobin concentration, red cell count, or packed cell volume to below 'normal' values but the criteria for normality are somewhat arbitrary and difficult to establish. Before initiating treatment for anaemia it is essential to determine which type is present. Iron salt may be harmful and result in iron overload if given alone to patients with anemias other than those due to iron deficiency.

Treatment is only justified in the presence of a demonstrable iron - deficiency state. Before starting treatment, it is important to exclude any serious underlying cause of the anaemia (e.g gastric erosion, colonic carcinoma). Prophylaxis is justifiable in pregnancy only for women who have additional risk factors for iron deficiency (e.g poor diet), menorrhagia, after subtotal or total gastrectomy, and in the management of low birth - weight infants such as premature babies, twins, and in infants delivered by caesarean section.

Ferrous salt: many iron compounds have been used for this purpose, but do not offer any real advantage over the simple ferrous fumarate, gluconate, or sulphate salts.

The usual adult dose is sufficient of these salts to supply about 100 to 200mg of elemental iron daily. The approximate elemental iron content of various ferrous salts is ferrous fumarate 200mg (65mg iron), ferrous gluconate 300mg (35mg iron), ferrous succinate 100mg (35mg iron), ferrous sulfate 300mg (60mg iron), and dried ferrous sulfate 200mg (65mg iron)

Iron intake in the evening has been reported to improve its absorption. Iron intake with meals may reduce bioavailability but improve tolerability and adherence.

If adverse effects arise with one salt, dosage can be reduced or a change made to an alternative iron salt.

The hemoglobin concentration should rise by about 100 - 200mg/100ml per day. After the haemoglobin has risen to normal, treatment should be continued for a further three months in an attempt to replenish the iron stores. Gastrointestinal irritation may occur. Nausea and epigastric pain are dose related. Oral iron may exacerbate diarrhoea in patients with inflammatory bowel disease but care is also needed in patients with intestinal strictures and diverticulae. Iron as iron dextran or iron sorbitol should be given parenterally only if the patient has severe gastrointestinal adverse effects with oral preparations, continuing severe blood loss or malabsorption. Parenteral iron may cause more harm than benefit. Provided that the oral iron preparation is taken reliably and is absorbed then the haemoglobin response is not significantly faster with the parenteral route than the oral route.

Megaloblastic anaemias. These are due to lack of either vitamin B₁₂ (hydroxycobalamin) or folate or both. The clinical features of folate deficient megaloblastic anaemia are similar to those of vitamin B₁₂ deficiency except that the accompanying severe neuropathy does not occur; it is essential to determine which deficiency is present and the underlying cause is established in every case. Preparations containing ferrous salt and folic acid are used for the prevention of megaloblastic anaemia in pregnancy. The low doses of folic acid in these preparations are inadequate for the treatment of megaloblastic anaemias.

Calcium Folate (Leucovorin calcium)

Injection, 3 mg folinic acid in 1ml ampoule

Indications: treatment of megaloblastic anemias when folate is deficient as in infancy, sprue, pregnancy, and nutritional deficiency when oral folate therapy is not possible.

Cautions, Contraindications, Drug interactions, Side effects and Storage; see section 10. under calcium folinate.

Dose and Administration: Adult and Child: *Folate-deficient megaloblastic anemia:* IM: 1 mg/day

Megaloblastic anemia secondary to congenital deficiency of dihydrofolate reductase: IM: 3-6 mg/day.

Cyanocobalamin (Vitamin B₁₂)

Injection, 100 mcg/ml, 1000 mcg/ml in 1 ml ampoule.

Indications: treatment of pernicious anemia; vitamin B₁₂ deficiency; increased B₁₂ requirements due to pregnancy, thyrotoxicosis, hemorrhage, malignancy, liver or kidney disease.

Cautions: I.M - route used to treat pernicious anemia; Vitamin B₁₂ deficiency for > 3 months results in irreversible degenerative CNS lesions.

Drug interactions: ethanol, chloramphenicol, cholestyramine, cimetidine, colchicine, neomycin, potassium.

Contraindications: hypersensitivity to cyanocobalamin, hereditary optic nerve atrophy, Leber's disease.

Side effects: headache, anxiety, dizziness, pain, nervousness, hypoesthesia, itching, sore throat, nausea, vomiting, dyspepsia, diarrhea, weakness, back pain, arthritis, myalgia, paresthesia, abnormal gait, dyspnea, rhinitis.

Dose and Administration:

Anemias: IM or deep SC:

Pernicious anemia, congenital:

Adult: 100 mcg/day for 6 - 7 days; if improvement, administer same dose on alternate days for 7 doses; then every 3 - 4 days for 2 - 3 weeks; once hematologic values have returned to normal, maintenance dosage: 100 mcg/month.

Child: 30 - 50 mcg/day for 2 or more weeks (to a total dose of 1000 - 5000 mcg), Then follow with 100 mcg/month as maintenance dosage.

Vitamin B12 deficiency:

Adult: Initial: 30 mcg/day for 5 - 10 days; maintenance: 100 - 200 mcg/month.

Child:

Neurologic signs: 100 mcg/day for 10 - 15 days (total dose of 1-1.5 mg), then once or twice weekly for several months.

Hematologic signs: 10 - 50 mcg/day for 5 - 10 days, followed by 100 - 250 mcg/dose every 2 - 4 weeks.

Storage: store at room temperature, protect from light.

Epoetin alfa and beta

Injection, epoetin alfa, 2000 units/ml

Epoetin alfa prefilled syringe, 1000 units/ml, 2000 units/ml, 3000 units/ml, 4000 units/ml, 10,000 units/ml.

Epoetin beta powder for injection, 500 units/vial; 1000 units/vial; 2000 units/vial; 3000 units/vial; 4000 units/vial, 5000 units/vial; 6000 units/vial, 10,000 units/vial.

Epoetin beta powder for injection (multi dose injection), 50,000 units/vial, 100, 000 units/vial

Indications: treatment of anaemia of chronic renal failure; treatment of chemotherapy induced anaemia to reduce the need for transfusions. Not useful

in all cancer patients with anemia and should only be used in chemotherapy - induced anaemia.

Cautions: hypertension, ischaemic vascular disease, seizures, myeloid malignancy, untreated iron deficiency.

Contraindications: uncontrolled hypertension, known hypersensitivity to the product.

Side effects: clotting of vascular access and dialysers; hypertension, headache, seizures, flu-like symptoms and skin rash.

Dose and Administration: Ideally, erythropoietin should be assayed before commencing therapy. Dosage of individual product may vary, and the product literature should be consulted.

IV (given over 1 - 2 minutes) or *SC*, initially 40 - 50 IU/kg/dose given 2 - 3 times weekly. The response should be assessed at 2 - weekly intervals and, if necessary, the dose may be increased by 25 IU/kg.

Storage: store in refrigerator and should not be frozen.

Ferrous Salt[•]

Tablet

Capsule.

Drop

Indications: in the prevention and treatment of only iron deficiency anemia.

Cautions: hepatitis or hepatic function impairment, kidney diseases, intestinal tract inflammatory conditions (e.g. peptic ulcer, or colitis), or alcoholism. Caution patients about toxic effects of accidental overdose. Especially in children.

Drug interactions: acetohydroxamic acid, dimercaprol, etidronate (avoid using iron supplements with in two hours of etidronate), fluoroquinolones (it should be taken at least two hours before or two hours after iron supplements), tetracycline, chloramphenicol, antacids, calcium (carbonate or phosphate).

Side effects: abdominal discomfort, vomiting, diarrhoea or dark stools may occur commonly, large doses may have an irritant and corrosive effects of the gastrointestinal mucosa and necrosis and perforation may occur. Iron drops may temporarily stain the teeth.

Dose and Administration: *Orally.* Iron drops may be placed well back on the tongue followed with water. It is best given on an empty stomach but may be given with or after meals to lessen gastrointestinal irritation. Treatment may be continued for 3-6months, and not longer except in patients with continued bleeding, or repeated pregnancies.

Prophylactic –

[•] Any Ferrous salt containing elemental Iron of accepted therapeutic value

Adult: 300mg once daily.

Child: 5mg/kg of body weight once daily or, 150 – 300mg once daily.

Treatment –

Adult: 300mg every 12 hours, gradually increased up to 300mg every 6-8 hours daily as needed and tolerated.

Child: 10mg/kg of body weight every 8 hours daily. Or 6-12 years 300mg every 12 hours daily. 1-5 years -120mg every 8 hours daily. Under 1year – 60mg every 8 hours daily.

Storage: At room temperature, in a tight container. Protect from light and freezing.

Ferrous salt + Folic Acid[•]

Capsule

Tablet

Indications: Prevention of iron and folic acid deficiencies in pregnancy.

Cautions: low doses of folic acid in the combination preparations above are inadequate for treatment of megaloblastic anaemia;

Side effects: see ferrous salts

Dose and Administration:

Prevention of iron and folic acid deficiencies in pregnancy: Oral: **Adult** the equivalent of about 100mg elemental iron with 350 - 400 micrograms folic acid daily throughout pregnancy.

Fluxymesterone

Tablet, 2mg, 10mg

Indications: treatment of hypogonadism, delayed puberty in the male. In the palliation of inoperable neoplasms of the breast in postmenopausal women.

Caution: liver disease, heart disease, kidney disease, allergies, enlarged prostate.

Contraindications: known or suspected cancer of the prostate or (in men) breast. Pregnancy or breast-feeding.

Side effects: headache, indigestion, oily skin, acne, anxiety, and sleeplessness. Males may experience breast tenderness, change in sex drive, impotence or problems with erections. Females may experience deepening of the voice, change in sex drive, irregular menstruation or enlargement of the clitoris. Vomiting, swelling of the ankles or feet, unusual weight gains, yellowing of the eyes/skin.

Dose and Administration: Oral:

Hypogonadism: 5-20mg daily.

Delayed puberty: 2.5-10mg daily. Treatment was given only for 4 to 6 months.

Palliation of inoperable neoplasms of the breast: 40mg daily.

Storage: store at room temperature

Iron Complex

Injection, 50mg/ml in 2ml ampoule (Dextran, Sorbitol)

Iron dextran injection is a sterile colloidal solution of ferric hydroxide and dextrans of weight average molecular weight between 5000 and 7000.

Iron sorbitol injection is a sterile Colloidal solution of a complex of iron, Sorbitol and citric acid, stabilized with dextrin and Sorbitol.

Iron Dextran

• Any Ferrous salt containing elemental Iron of accepted therapeutic value

A complex of ferric hydroxide with dextrans containing 4% (50mg/ml) of iron.

Indications: iron deficiency anaemia, where oral therapy is ineffective or impracticable.

Cautions: facilities for cardiopulmonary resuscitation must be at hand; increased risk of allergic reaction in immune or inflammatory conditions; hepatic impairment, renal impairment; oral iron not to be given until 5 days after last injection; pregnancy.

Contraindications: history of allergic disorders including asthma and eczema; infection; active rheumatoid arthritis.

Side effects: nausea, dyspepsia, diarrhoea, chest pains, hypotension, dyspnoea, arthralgia, myalgia, pruritus, urticaria, rash, fever, shivering, flushing, headache; rarely anaphylactoid reactions; injection site reactions including phlebitis reported.

Dose and Administrations: Total dosage is calculated according to body-weight and the haemoglobin concentration of the blood, and tables are usually provided, consult product literature.

The total dose requirement may be administered as a series of IM injections daily or once or twice weekly. Iron dextran is also given intravenously. Child under 14 years, not recommended.

Iron Sorbitol

Colloidal solution of a complex of iron, Sorbitol and citric acid, stabilized with dextrin and Sorbitol, containing 5% (50mg/ml) of iron.

Indication: iron deficiency anaemia, where oral therapy is ineffective or impracticable.

Cautions: oral iron should be stopped at least 24 hours before; history of allergic disorders including asthma; elderly, underweight or debilitated; pregnancy.

Contraindications: liver disease, kidney disease, untreated urinary tract infections; preferably avoid in patients with pre-existing cardiac abnormalities (e.g angina or arrhythmias)

Side effects: nausea, vomiting, diarrhoea, haematuria, taste disturbances, dizziness, flushing myalgia; hypersensitivity reactions including urticaria and hypotension; occasionally severe arrhythmias; rarely anaphylactoid reactions; injection site reactions.

Dose and Administration: Total dosage is calculated according to body-weight and the haemoglobin concentration of the blood, and tables are usually provided, consult product literature.

IM: the recommended single dose is the equivalent of 1.5mg/kg of iron up to a maximum of 100mg daily; these doses are then given daily or every other day until the total dosage has been achieved. Not recommended in children under 3 kg in body-weight. Iron sorbitol should not be given intravenously.

Storage: at room temperature. Avoid freezing or low temperature.

Oxymetholone

Tablet, 2.5mg, 5mg, and 10mg

Indication: treatment of anaemias such as aplastic anemia.

Caution: liver impairment.

Side effects: liver disturbances and jaundice.

Dose and Administration: *Aplastic anaemia: Oral:* 1-5 mg/kg daily.

Treatment for 3 to 6 months has been suggested.

Storage: store at room temperature.

11.4. Blood Substitutes and Plasma Expanders

Dextran (Dextran 70 and Dextran 40) and polygeline are macromolecular substances which are metabolized slowly; they may be used at the outset to expand and maintain blood volume in shock arising from conditions such as burns or septicemia. Plasma substitutes may be used as an immediate short-term measure to treat haemorrhage until blood is available.

They are rarely needed when shock is due to sodium and water depletion because, in these circumstances, the shock responds to water and electrolyte repletion.

Plasma substitutes should not be used to maintain plasma volume in conditions such as burns or peritonitis where there is loss of plasma protein, water and electrolytes over periods of several days or weeks. In these situations, plasma or plasma protein fractions containing large amounts of albumin should be given.

Dextran 70 by intravenous infusion is used predominantly for volume expansion. Dextran 40 intravenous infusion is used in an attempt to improve peripheral blood flow in ischaemic disease of the limbs. Dextran 40 and 70 have also been used in the prophylaxis of thromboembolism but are now rarely used for this purpose.

Dextran may interfere with blood group cross-matching or biochemical measurements and these should be carried out before infusion is begun.

Cautions: plasma substitutes should be used with caution in patients with cardiac disease or renal impairment; urine output should be monitored. Care should be taken to avoid haematocrit concentration from falling below 25 - 30% and the patient should be monitored for hypersensitivity reactions.

Side effects: Hypersensitivity reactions may occur including, rarely, severe anaphylactoid reaction. Transient increase in bleeding time may occur.

Albumin

Solution, 20 % in 100 ml

Indications: plasma volume expansion and maintenance of cardiac output in the treatment of certain types of shock or impending shock; may be useful for burn patients.

Cautions: hepatic or renal failure.

Drug interactions: ACE inhibitors.

Contraindications: hypersensitivity to albumin, patients with severe anemia or cardiac failure.

Side effects: edema, hyper/hypotension, hypervolemia, tachycardia, chills, fever, headache, pruritus, rash, urticaria, nausea, vomiting, bronchospasm, pulmonary edema, anaphylaxis.

Dose and Administration: *IV:*

Adult: Usual dose: 25 g; initial dose may be repeated in 15 - 30 minutes if response is inadequate; no more than 250 g should be administered within 48 hours.

Hypoproteinemia: 0.5 - 1 g/kg dose; repeat every 1 - 2 days as calculated to replace ongoing losses.

Hypovolemia: 0.5 - 1 g/kg/dose; repeat as needed; maximum dose: 6 g/kg/day.

Child: *Hypovolemia:* 0.5 - 1 g/kg/dose (10-20ml/kg/dose of albumin 5 %); maximum dose: 6 g/kg/day.

Storage: store at a temperature $\leq 30^{\circ}\text{C}$; do not freeze.

Dextran (MW 40, 000)

Solution, 10% w/v in 5% Dextrose; 500ml

Indications: conditions associated with peripheral local slowing of the blood flow; prophylaxis of post surgical thromboembolic disease

Cautions: see notes above; can interfere with some laboratory tests (see also above); correct dehydration beforehand, give adequate fluids during therapy and, where possible, monitor central venous pressure; pregnancy.

Side effects: see notes above

Dose and Administrations:

IV infusion: initially 500 - 1000 ml; further doses are given according to the patient's condition (see notes above)

Dextran (MW 70,000)

Solution, 6% w/v in 5% dextrose; 500ml

Indications: short term blood volume expansion; prophylaxis of post surgical thromboembolic disease (but see notes above)

Cautions: see notes above; can interfere with some laboratory tests (see also above); where possible, monitor central venous pressure; pregnancy.

Side effects: see notes above

Dose and Administrations

IV infusion: after moderate to severe haemorrhage or in the shock phase of burn injury (initially 48 hours), 500 - 1000ml rapidly initially followed by 500ml later if necessary (see also notes above); total dosage should not exceed 20ml/kg during initial 24 hours: C total dosage should be not exceed 20ml/kg.

Isoplasma

Solution, 500 ml.

Plasma Antihaemophilic (Human)

Solution, 50 ml, 100 ml, 250 ml

Indications: management of hemophilia A for patients in whom a deficiency in factor VIII has been demonstrated; treatment of spontaneous bleeding in patients with severe von Willebrand disease and in mild and moderate von Willebrand disease where desmopressin is known or suspected to be inadequate.

Cautions: hypersensitivity to any component of the formulation.

Side effects: acute hemolytic anemia, allergic reactions, blurred vision, chest tightness, chills, edema, fever, headache, hyperfibrinogenemia, increased bleeding tendency, itching, lethargy, nausea, tachycardia.

Dose and Administration: Adult and Child:

I.V: individualize dosage based on coagulation studies performed prior to treatment and at regular intervals during treatment: 1AHF unit is the activity present in 1 ml of normal pooled human plasma; dosage should be adjusted to actual vial size currently stocked in the pharmacy.

Storage: store under refrigeration, and avoid freezing

Polygeline + Na⁺ + K⁺ + Ca⁺⁺ + Cl⁻

Solution, 35g + 145 mmol + 5.1 mmol + 6.25 mmol + 145mmol/1000ml

Indications: correction of low blood volume

Cautions: blood samples for cross-matching should be taken before infusion; haemorrhagic diathesis; congestive heart failure, renal impairment, hypertension, oesophageal varices.

Contraindications: severe congestive heart failure; renal failure.

Side effects: urticarial and other hypersensitivity reactions - rarely severe anaphylactoid reactions.

Dose and Administrations:

Correction of low blood volume: IV infusion: initially 500 - 1000ml of a 3.5% solution.

12. DRUGS FOR CORRECTING WATER, ELECTROLYTE AND ACID-BASE DISTURBANCES

Electrolytes are used to correct disturbances in fluid and electrolyte homoeostasis or acid-base balance and to re-establish osmotic equilibrium of specific ions.

12.1. Oral Electrolytes

Ammonium Chloride

Tablet, 500mg

Indications: used to maintain the urine at an acidic pH in the treatment of some urinary- tract disorders; for treatment of metabolic alkalosis; as a diuretic (example in premenstrual water retention).

Cautions: hepatic or renal impairment.

Side effects: ammonium salts are irritant to the gastric mucosa and may produce nausea and vomiting.

Dose and Administration: *Oral:* 1 to 2 g every four to six hours;

As a diuretic: 650 mg three times daily for up to 6 days.

Storage: store in airtight containers.

Calcium

Tablet (ionizable), 500 mg, 1g (eff.).

Indications: used as calcium supplementation in pregnant and lactating women and in growing children, latent tetany, rickets and osteomalacia (additional to specific therapy). Prevention of pre-and postmenopausal bone demineralisation, osteoporosis, as supportive treatment in allergic conditions

Cautions: calcium salts should be used cautiously if at all, in patients with sarcoidosis, renal or cardiac disease, and in patients receiving cardiac glycosides. Check urinary calcium excretion in patients with mild hypercalciuria impaired renal function or a history of urinary concrements; reduce dosage or discontinue therapy if necessary. Avoid high doses of Vitamin D.

Drug interactions: oral tetracycline or fluoride (avoid concomitant use within 3 hours); cardiac glycosides; calcium channel blockers; phenytoin; gallium nitrate; Etidronate, cellulose sodium phosphate, thiazide.

Contraindications: hypersensitivity to the drug, hypercalcaemia, severe hypercalcium, severe renal failure, sarcoidosis, and renal calculi.

Side effects: hypotension (dizziness), flushing and /or sensation of warmth or heat, irregular heart beat. Nausea or vomiting, gastrointestinal irritation & constipations, skin redness, rash, pain, or burning at injection site, sweating.

Dose and Administration:

Hypocalcaemia (prophylaxis):

Oral: amount based on normal daily-recommended intakes:

Persons

Adolescent and adult males/females

Milligram

800 - 1200

Pregnant females and Breast-feeding females	1200
Birth to 3 years of age	400 – 800
4 to 10 years of age	800

Hypocalcaemia (treatment):

Treatment dose is individualized by prescriber based on severity of deficiency.

Storage: store at room temperature in a tight container or original foil packaging.

Calcium Glubionate + Calcium Galacto gluconate

Syrup, 28.75 g+ 5.9 g/100ml

Indications, Cautions, Drug interactions, Contraindications; see under calcium gluconate.

Calcium Gluconate

Syrup, 4gm/15ml

Tablet, 500mg

Indications: as a source of calcium ion for treating calcium depletion occurring in conditions such as chronic hypoparathyroidism, pseudohypoparathyroidism, osteomalacia, rickets, chronic renal failure, and hypocalcaemia secondary to the administration of anticonvulsant medications.

It is also used as a dietary supplemental therapy for persons who may not get enough calcium in their regular diet.

Cautions: dehydration or electrolyte imbalance, diarrhoea, chronic gastrointestinal malabsorption, history of renal calculi, chronic renal function impairment.

Drug interactions: calcitonin, calcium channel blocking agents such as verapamil, calcium or magnesium containing medications, estrogens, milk and milk products phenytoin, oral tetracyclines, vitamin D.

Contraindications: Primary or secondary hypercalcemia, hypercalciuria or calcium renal calculi, sarcoidosis.

Side effects: acute hypercalcemic syndrome (drowsiness, continuing nausea, and vomiting, weakness), calcific renal calculi.

Dose and Administration:

Adult: *Antihypocalcemic or Nutritional supplement:* Oral: 8.8 - 16.5gm (800 - 1500 mg of calcium ion) a day, in divided doses.

Child: *Antihypocalcemic:* Oral: 500-720mg (45-65mg of calcium ion) per kg of body weight a day, in divided doses.

Storage: at room temperature in a well-closed container.

Calcium Lactate

Tablet, 300mg

Indications: as a source of calcium ion for treating calcium depletion.

Cautions, Contraindication, Drug Interaction, Side effects; see under calcium gluconate.

Dose and Administration:

Adult: *Antihypocalcemic:* *Oral:* 7.7 gms (1gms of calcium ion) a day, in divided doses

Child: *Antihypocalcemic:* *Oral:* 345mg - 500mg (45 to 65mg of calcium ion) per kg of body weight a day, in divided doses.

Note: Drink a full glass of water.

Storage: at room temperature in a tight container.

Oral Rehydration Salts (ORS)

Powder –

Sodium Chloride-----3.5g/litre

Trisodium Citrate Dihydrate-----2.9g/litre

Potassium Chloride-----1.5g/litre

Glucose-----20.0g/litre

Indications: For the prevention and treatment of mild to moderate dehydration, particularly dehydration from acute diarrhoea of any cause, in all age group.

Note: Severe dehydration should be treated with intravenous fluids (Lactated ringer's injection).

Cautions and Side effects: See notes on section 1.6.

Dose and Administration: *Orally (by cup and spoon in young children):* Dissolve one sachet of ORS in 1 liter of water. Do not boil the prepared solution. Discard any remaining solution after 24 hours.

Prevention of dehydration:

In diarrhoea without signs of dehydration, after each loose stool give –

Less than 2 years, 50 - 100ml (1 - 2 small coffee cups); 2 - 10 year, 100 - 200ml (2 - 4 small coffee cups).

Treatment of diarrhea:

In diarrhoea with moderate dehydration:

75ml of ORS solution per Kg of body weight in 4—6 hours. Repeat if dehydration persists.

See table on next page.

Note: The Table shows the approximate amount of ORS solution to be given. Use the patients age only when the weight is not known. During rehydration therapy, continue breast-feeding the infants. In Infants under 6 months of age who are not breastfeed, also give 100 – 200ml of clean water. In dehydrated children with pneumonia, without concurrent diarrhoea, give half the amounts of ORS shown in the Table below.

Oral Rehydration Salt dose by Age and weight --

Age	Less than 4 months	4 -11 Month	12-23 month	2 - 4 year	5–14 year	15 year or older
Weight (Kg.)	<5	5-7.9	8 -10.9	11–15.9	16-29.9	30+

Amount (ml.)	200-400	400-600	600-800	800-1200	1200-2200	2200-4000
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Note: puffy eyelids indicate excess. It should be discontinued until it disappears.

Storage: at room temperature. In a dry place out of direct sunlight. In high humidity, the ORS may lump or become hard. If the powder is white, even if it is hard, the ORS has deteriorated and it should not be used.

Potassium chloride

Tablet, 300mg, 500mg, 600mg, 750mg, and 1gm

Indications: for treatment of potassium depletion

Cautions: in elderly, mild to moderate renal impairment (close monitoring required), intestinal stricture, and history of peptic ulcer; see also interactions.

Drug interactions: special hazard if given with drugs liable to raise plasma potassium concentration such as potassium-sparing diuretics, angiotension converting enzyme inhibitors, or cyclosporins.

Contraindications: severe renal impairment, plasma potassium concentrations above 5 m mol/liter.

Side effects: nausea, vomiting (severe symptoms may indicate obstruction), oesophageal or small bowel ulceration.

Dose and Administration: Adult: *for prevention of hypokalaemia: Oral:* 2-4gm daily by mouth in patients taking normal diet. Smaller doses must be used if there is renal insufficiency (common in the elderly) otherwise there is danger of hyperkalaemia.

Storage: at room temperature.

Sodium Bicarbonate

Tablet, 500 mg

Indications: used for the treatment of metabolic acidosis. It is also used as an antacid. Relief of discomfort in mild urinary tract infections.

Cautions: the drug should be administered with extreme caution to patients with heart failure, oedema, renal impairment, hypertension, or aldosteronism and elderly, avoid prolonged use. Sodium bicarbonate should be used during pregnancy only when clearly needed.

Contraindications: metabolic or respiratory alkalosis, in patients with hypocalcemia in whom alkalosis may induce tetany, in patients with excessive chloride loss from vomiting or continuous GI suctioning, and in patients at risk of developing diuretic – induced hypochloremic alkalosis. The drug should not be used orally as an antidote in the treatment of acute ingestion of strong mineral acids.

Side effects: stomach cramps, belching, and flatulence, alkalosis on prolonged use.

Dose and Administration: 3 g in water every 2 hours until urinary PH exceeds 7; maintenance of alkaline urine 5-10 g daily.

Storage: in tightly closed containers at room temperature.

Sodium Chloride*Tablet, 650 mg, 1 g*

Indications: used for the treatment of extracellular volume depletion and in the prevention or treatment of deficiencies of sodium and chloride ions and in the prevention of muscle cramps and heat prostration resulting from excessive perspiration during exposure to high temperature.

Cautions: hypertension, heart failure, peripheral or pulmonary oedema, impaired renal function or pre-eclampsia; in patients receiving corticosteroids or corticotropin, particular caution is necessary in geriatric or post operative patients.

Contraindications: in patients with conditions in which administration of sodium and chloride is detrimental.

Side effects: administration of large doses may give rise to sodium accumulation and oedema, nausea, vomiting, diarrhoea, abdominal cramps, thirst, reduced salivation and lachrymation, sweating, fever, tachycardia, hypertension, renal failure.

Dose and Administration:

A suggested oral replacement dose of sodium chloride is about 1 to 2 g (approximately 17 to 34 mmol of sodium) three times daily depending on individual needs either with food or as a solution; doses of up to 12 g daily may be necessary in severe cases.

12.2. Parenteral Electrolyte

Solutions of electrolytes are given intravenously, to meet normal fluid and electrolyte requirements or to replenish substantial deficits or continuing losses, when the patient is nauseated or vomiting and is unable to take adequate amounts by mouth.

Sodium, potassium, chloride, magnesium, phosphate, and water depletion can occur singly and in combination with or without disturbances of acid - base balance.

Calcium gluconate or levulinate*Injection, 10% in 10ml ampoule*

Indications: in the treatment of hypocalcaemia in conditions that require a rapid increase in serum calcium - ion concentration, such as neonatal hypocalcaemia tetany; tetany due to parathyroid deficiency.

It is also indicated to decrease or reverse the cardiac depressant effect of hyperkalemia on electrocardiographic (ECG) function, and as an aid in the treatment of CNS depression due to over dosage of magnesium sulfate.

Cautions: cardiac function impairment, ventricular fibrillation during cardiac resuscitation, renal function impairment, diarrhoea.

Drug interactions: calcitonin, verapamil, calcium and magnesium containing medications, digitalis glycoside, magnesium sulfate, milk and milk products, phenytoin, oral tetracyclines, vitamin D.

Contraindications: digitalis toxicity, primary or secondary hypercalcemia, hypercalciuria, calcium renal calculi, sarcoidosis.

Side effects: hypotension (dizziness), flushing and/or sensation of warmth or heat, irregular heartbeat; nausea or vomiting, skin redness, rash, pain, or burning at injection site, sweating, tingling sensation.

Dose and Administration:

Adult:

Antihypocalcemic or Electrolyte replenisher. IV: 970mg (94.7mg of calcium ion), administered slowly at a rate not to exceed 5ml (47.5mg of calcium ion) a minute. The dosage may be repeated, if necessary, until tetany is controlled.

Antihyperkalemic. IV: 1 to 2 grams (94.7 to 189 mg of calcium ion), administered slowly at a rate not to exceed 5ml a minute, the dosage being titrated and adjusted by constant monitoring of ECG changes during administration.

Antihypermagnesemic. IV: 1 to 2gms, administered at a rate not to exceed 5ml a minute.

Child: *Antihypocalcemic. IV:* 200-500mg (19.5-48.8mg of calcium ion) as a single dose, administered slowly at a rate not to exceed 5ml (47.5mg of calcium ion) a minute, repeated if necessary until tetany is controlled.

Storage: at room temperature, protect from freezing.

Dextrose

Injection, 5% in 500ml, 1000ml; 10% in 500ml, 1000ml; 40% in 20ml, 50%

Indications: for the treatment of hypoglycemia due to insulin excess or other causes.

Cautions: caution in patients with diabetes mellitus or with carbohydrate intolerance for any reason.

Contraindication: anuria.

Side effects: rapid administration may cause local pain; hyperglycemia and glycosuria, which if undetected and untreated can lead to dehydration, coma, and death.

Dose and Administration: The clear solution is given slowly *by intravenous* route.

For the treatment of hypoglycemia:

Adult and child: 20 – 40ml Dextrose 40%; may be repeated in severe cases.

Storage: at room temperature.

Dextrose in Normal Saline

Injection, 5% in 500ml, 1000ml; 10% in 500ml, 1000ml

Lactated potassic saline injection (Darrow's solution)

Injection solution, each 1000 ml contains K^+ 35mEq + Na^+ 121 mEq+Cl⁻ 103 mEq lactate 53 mEq in 500 ml, 1000 ml

Injection solution (half strength) – each 1000 ml contains; K^+ 17.5 meq+ Na^+ 60.5 mEq+Cl⁻ 51.5 meq + Lactate 26.5 meq in 500 ml, 1000 ml

Lactated Ringer's injection (Hartmann's solution)

Injectable solution, each 1000ml contains; K^+ 5.4meq + Na^+ 130.7meq + Ca^{++} 3.6meq + Cl^- 111.5meq + Lactate 28.2meq in 500ml, 1000ml

Indications: for replacement of electrolytes and water losses in severe dehydration.

Contraindications: severe liver and renal damage.

Dose and administration: *slow intravenous.*

Adult and Older Child: 100ml/kg of body weight within 4 hours, immediately until radial pulse is easily felt.

Infant: 30ml/kg of body weight within 1 hour followed by 40ml/kg of body weight within the next 2 hours; followed by Oral Rehydration Salts (ORS) 40ml/kg of body weight within the next 3 hours.

Note: If condition worsens, the rate of administration and the amount of fluid may need to be increased. After the first 6 hours, begin breast-feeding, or for nonbreastfeed infants give 100 – 200ml clean water before continuing ORS therapy. After rehydration is complete, feeding should start immediately.

Storage: at room temperature.

Peritoneal dialysis fluid no 1

Injectable solution, each 1000ml contains;

Na^+ 130.0-140mmol + Ca^{++} 1.5-2.0mmol + Mg^{++} 0.5-0.75mmol + HCO_3^- (as acetate/lactate) 35.0-45mmol + Cl^- 90.0-102mmol + Dextrose 15g in 1000ml, 2000ml

Peritoneal dialysis fluid No. 2

Injectable solution, each 1000ml contains;

Na^+ 130.0-140mmol + Ca^{++} 1.5-2.0mmol + Mg^{++} 0.5-0.75mmol + HCO_3^- (as acetate/lactate) 35.0 - 45mmol + Cl^- 90.0 - 102mmol + Dextrose 45g in 1000ml, 2000ml

Potassium chloride

Injection, 150mg/ml in 10ml ampoule

Indications: treatment of potassium depletion or hypokalaemia, with or without metabolic alkalosis, in chronic digitalis intoxication, and in patients with hypokalaemia familiar periodic paralysis; see also oral potassium supplements, section 11.1.

Cautions: for intravenous infusion the concentration of solution should not usually exceed 3.2g (43mmol)/litre; specialist advice and ECG monitoring in difficult cases.

Drug interactions: potassium sparing diuretics, angiotension converting enzyme inhibitors cyclosporins, digitalis glycoside, parenteral calcium salts, laxatives.

Contraindications: hyperkalemia.

Side effects: rapid infusion toxic to heart; see section 11.1

Dose and Administration: *IV infusion*

Note: - Injectable potassium chloride products, in strengths of 1.5mEq and 2mEq per ml must be diluted prior to IV administration. Direct patient injection of potassium concentrate may be instantaneously fatal. However, injectable potassium chloride products in strengths of 0.1 and 0.4mEq per ml are intended for use with a calibrated infusion device and do not require dilution.

Adult: *Antihypokalemic or electrolyte replenisher: IV infusion:* the dose and rate of infusion to be determined by the individual requirements of each patient, up to 400mEq of potassium a day (usually not more than 3mEq per kg of body weight). The response of the patient, as determined by the measurement of serum potassium concentration and the electrocardiogram following the initial 40 to 60mEq infusion, should indicate the subsequent infusion rate required.

Child: *Antihypokalemic or Electrolyte replenisher: IV infusion:* up to 3mEq of potassium per kg of body weight or 40mEq per square meter of body surface area a day. Volume of administered fluids must be adjusted to body size.

Storage: at room temperature, protect from freezing.

Ringer's injection

Injectable solution, each 100ml contains

Na^+ 147mEq + K^+ 4mEq + Ca^{++} 45mEq + Cl^- 155.5mEq in 300ml, 100ml

Sodium Bicarbonate

Injection (concentrated), 7.5 % (40 meq/50ml) in 50 ml ampoule

Indications: for the treatment of acute metabolic acidosis, and relief of discomfort in mild urinary tract infections.

Cautions: in acute metabolic acidosis – the manufacturers warn that avoid excessive IV administration or avoid rapid injection (10 ml /minute) of hypertonic sodium bicarbonate solutions in neonates and children younger than 2 years of age; and see also notes under sodium bicarbonate (oral).

Contraindications: see under sodium bicarbonate (oral).

Side effects: chemical cellulitis because of their alkalinity, subsequently resulting in tissue necrosis, ulceration, and/or sloughing at the site of injection; and see also notes under sodium bicarbonate (oral)

Note - The above side effect is caused due to inadvertent extravasation of hypertonic solutions of sodium bicarbonate and this can be treated by elevating the affected area, applying warm compresses to the site, and locally injecting lidocaine or hyaluronidase.

Dose and Administration:

By slow intravenous injection, a strong solution (up to 8.4 %), or *by continuous intravenous infusion*, a weaker solution (usually 1.26 %), an amount appropriate to the body base deficit

Storage: at room temperature & freezing should be avoided.

Sodium chloride

Injection, 235mg/ml in 20ml ampoule; 0.9% (Normal saline) in 10ml, 20ml, 500ml, 1000ml; 3% in 500ml

Indications: used for extracellular fluid replacement and in the management of metabolic alkalosis in the presence of fluid loss and mild sodium depletion. Hypertonic (3%, 5%) sodium chloride injection is used in the management of severe sodium chloride depletion when rapid electrolyte restoration is essential.

Cautions: see section 11.1

Contraindications: in patients with conditions in which administration of sodium and chloride is detrimental. Sodium chloride 3% and 5% injections are also contraindicated in the presence of increased, normal, or only slightly decreased serum electrolyte concentrations.

Side effects: venous thrombosis or phlebitis, extravasation, hypervolemia, hypernatremia (on excessive administration); see also section 11.1

Dose and Administration:

Adult: *IV infusion* - 1 liter of 0.9% sodium chloride injection daily or 1-2 L of 0.45% sodium chloride injection daily.

The usual initial IV dose of 3 or 5% sodium chloride injection is 100ml given over a 1-hour period, before additional amounts are administered. It should not exceed 100ml/hour.

Storage: at room temperature, protect from freezing.

Sodium lactate

Injection Na+ 16.7mEq + Lactate 16.7mEq in 100ml

Haemodialysis Fluid

12.3. Enteral Nutrition

Enteral nutrition includes feeding by mouth, by nasogastric or nasoenteric tube, or directly into a gastrostomy or other enterostomy. It may be supplemental, if normal food intake is possible but inadequate, or total. Individual patients vary in their requirements according to age, size, and metabolic state, but a diet supplying 2000 to 3000 kcal of energy and 10-15g of nitrogen (as 60 to 90 g of protein) in 2 to 3 litres of fluid is fairly typical; because absorption from the gastrointestinal tract is incomplete requirements are higher than by parenteral route. Preparations containing whole protein (often derived from milk or soya) are generally preferred. Although preferred to parenteral nutrition, enteral feeding is not without complications. Patients may be at risk of oesophagitis, aspiration, and regurgitation as a result of the tube insertion; other potential problems include diarrhea, nausea and vomiting, gastric retention, hyperglycaemia, fluid and electrolyte disturbances, and microbial contamination of the feed regimen.

1. **Calcium Caseinate**
 2. **Soya-based non-milk preparations**
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13. VITAMINS

Vitamins are used for the prevention and treatment of specific deficiency states or when the diet is known to be inadequate. Large doses of vitamins (megavitamin therapy) have been proposed for a variety of disorders, but adequate evidence of their value is lacking. Excessive intakes of most water-soluble vitamins have little effects due to their rapid excretion in urine, but excessive intakes of fat-soluble vitamins accumulate in the body and are potentially dangerous.

Vitamin A (Retinol) is a fat-soluble substance stored in body organs, principally the liver.

Deficiency of Vitamin A (Retinol) is associated with ocular defects (particularly xerophthalmia) and an increased susceptibility to infections particularly measles and diarrhoea. Despite initial epidemiological evidence suggesting that vitamin A or carotene may have a protective effect against some epithelial cancers, the claims have not been substantiated.

Massive overdose can cause rough skin, dry hair, an enlarged liver, and a raised erythrocyte sedimentation rate and raised serum calcium and serum alkaline phosphatase concentrations.

In view of evidence suggesting that high levels of vitamin A may cause birth defects women who are (or may become) pregnant are advised not to take vitamin A supplements (including tablets and fish liver oil drops), except on the advice of a doctor or an antenatal clinic; nor should they eat liver or products such as liver pate or liver sausage.

Vitamin B is composed of widely differing substances which are, for convenience, classed as 'vitamin B complex'. Thiamine (Vitamin B1) is used orally for deficiency due to inadequate dietary intake, severe deficiency may result in 'beri-beri'. Thiamine is given by intravenous injection in doses of up to 300mg daily (parenteral preparations may contain several B group vitamins) as initial treatment in severe deficiency states. Potentially severe allergic reactions may occur after parenteral administration; facilities for resuscitation should be immediately available. Pyridoxine (Vitamin B6) deficiency is rare as the vitamin is widely distributed in foods, but deficiency may occur during isoniazid therapy and is characterized by peripheral neuritis. High doses are given in some metabolic disorders, such as hyperoxaluria.

Nicotinic acid inhibits the synthesis of cholesterol and triglyceride and is used in some hyperlipidaemias.

Nicotinic acid and nicotinamide are used to prevent and treat nicotinic acid deficiency (pellagra). Nicotinamide is generally preferred as it does not cause vasodilation.

Folic acid is essential for the synthesis of DNA and certain proteins. Deficiency of folic acid or vitamin B₁₂ is associated with megaloblastic anaemia. Folic acid should not be used in undiagnosed megaloblastic anaemia unless Vitamin B₁₂ is administered concurrently, otherwise neuropathy may be precipitated.

Supplementation with folic acid 400 micrograms daily is recommended for women of child - bearing potential in order to reduce the risk of serious neural tube defects in their offspring.

Ascorbic acid (Vitamin c) is used for the prevention and treatment of scurvy. Claims that ascorbic acid is of value in the treatment of common colds are unsubstantiated.

The term Vitamin D covers a range of compounds including ergocalciferol (Vitamin D₂) and colecalciferol (Vitamin D₃). These two compounds are equipotent and either can be used to prevent and treat rickets.

Simple deficiency of Vitamin D occurs in those who have an inadequate dietary intake or who fail to produce enough colecalciferol (Vitamin D₃) in their skin from the precursor 7 - dehydrocholesterol in response to ultraviolet light.

Children with dark skin must continue vitamin D prophylaxis for up to 24 months because of their inability to produce enough vitamin D₃ in their skin. Dark skin with a high melanin content must be exposed to daylight longer than light skin in order to obtain the same synthesis of vitamin D₃. Vitamin D is also used in deficiency states caused by intestinal malabsorption or chronic liver disease and for the hypocalcaemia of hypoparathyroidism.

Vitamin K is necessary for the production of blood clotting factors (see sec. 10.1)

13.1. Vitamins, single

Ascorbic Acid (Vitamin C)

Tablet, 100mg, 500mg, 1gm

Drops, 200mg/ml

Injection, 50mg/ml in 2ml ampoule, 100mg/ml in 5ml ampoule, 200mg/ml

Indications: for prophylaxis and treatment of vitamin C (ascorbic acid) deficiency states which lead to scurvy.

Cautions: caution should be necessary not to take large amount during pregnancy. Importance of not taking more than the recommended dietary allowance (RDA) should also be considered. Caution is required in those with sensitivity to ascorbic acid.

Drug interactions: cellulose sodium phosphate, deferoxamine, disulfiram and vitamin B12 (with large doses of vitamin C).

Side effect: dizziness or faintness, kidney stones (oxalate)

Dose and Administration:

Adult:

Dietary supplement: Oral: 50 to 100mg a day

Treatment of deficiency: Oral, IV or IM: 100 to 250mg one or three times a day.

Child:

Dietary supplement: Infants and Children up to 4 years of age: *Oral:* 20 to 50mg a day.

Treatment of deficiency: *Oral, IV or IM:* 100 to 300mg a day in divided doses.

Storage: at room temperature in a tight, light resistant container.

Calciferol (Ergocalciferol/Vitamin D₂)

Tablet (strong), 1.25 mg (50,000units)

Oral solution, 20,000-units/ ml, 400,000 units/ml

Injection, 300,000-units/ml in 2 ml ampoule

Indications: used in the treatment of chronic hypocalcemia, hypophosphatemia, rickets and osteodystrophy associated with various medical conditions including chronic renal failure, familial hypophosphatemia, and hypoparathyroidism (post surgical or idiopathic or pseudohypoparathyroidism); for prevention and treatment of vitamin D deficiency states; and to treat anticonvulsant induced rickets & osteomalacia

Note: Ergocalciferol may not be the preferred agent in the treatment of familial hypophosphatemia or hypoparathyroidism because the large doses needed are associated with a risk of overdose and hypercalcemia, and ergocalciferol not usually preferred in patients with renal failure since these patients have impaired ability to synthesize calcitriol from colecalciferol and ergocalciferol.

Cautions: ergocalciferol should be administered with extreme caution, if at all, to patients with impaired renal function and with extreme caution in patients with heart disease, renal stones, or arteriosclerosis; large doses of Vitamin D analogs should not be administered to nursing women; take care to ensure correct dose in infants and pregnant

Drug interactions: antacids (magnesium containing), in high doses of calcium containing preparations and diuretics (thiazide), vitamin D analogs.

Contraindications: hypercalcemia, hypervitaminosis D, Renal Osteodystrophy with hyperphosphatemia, metastatic calcification, hypersensitivity to effects of Vitamin D.

Side effects: symptoms of over dosage include anorexia, lassitude, nausea and vomiting, diarrhoea, weight loss, polyuria, sweating, headache, thirst, vertigo, and raised concentrations of calcium and phosphate in plasma and urine.

Dose and Administrations:

Ergocalciferol injection

Adult:

Deficiency (prophylaxis or treatment):

Intravenous infusion, as part of total parenteral nutrition solutions, the specific amount determined by individual patient need.

Malabsorption: IM: 10,000 units per day

Child: see adult dose

Ergocalciferol oral solution

Adult:

Deficiency (prophylaxis):

Oral: amount based on normal daily-recommended intakes:

Person	Microgram	units
Adolescent and adult	5-10	200 – 400
Pregnant and breast feeding females	10	400

Deficiency (treatment):

Treatment dose is individualized by prescriber based on severity or deficiency

Vitamin D – resistant rickets: Oral: 12,000 to 500,000 units per day

Vitamin D – dependent rickets: Oral: 10,000 to 60,000 units per day (up to 500,000 units/day)

Osteomalacia due to prolonged use of anticonvulsants: Oral: 1000 to 4000 units per day

Familial hypo phosphatemia: Oral: 50,000 to 100,000 units per day

Hypoparathyroidism: Oral: 50,000 to 150,000 units per day

Child:

Deficiency (prophylaxis):

Oral amount based on normal daily-recommended intakes.

Persons	Microgram	Units
Birth to 3 years of age	7.5 - 10	300 - 400
4 to 10 years of age	10	400

Deficiency (treatment):

Treatment dose is individualized by prescriber based on severity of deficiency

Vitamin D-dependent rickets: Oral: 3000 to 10,000 units per day (up to 50,000 units/day).

Osteomalacia due to prolonged use of anticonvulsants: Oral: 1000 units per day

Hypoparathyroidism: Oral: 50,000 to 200,000 units per day.

Ergocalciferol tablets:

Adult: see Ergocalciferol oral solution

Child: see Ergocalciferol oral solution

Storage: in tight, light - resistant containers at a room temperature.

Cholecalciferol (Vitamin D₃)

Capsule, 250mcg

Injection (oily), 300,000 IU/ml

Indications, Cautions, Side effects, Drug interactions, Dose and Administration; see under ergocalciferol.

Folic Acid

Tablet, 200 mcg, 1 mg, 5 mg

Injection, 5 mg/ml in 1 ml ampoule

Indications: for prevention and treatment of folic acid deficiency states, including megaloblastic anemia and in anemias of nutritional origin, pregnancy,

infancy, or childhood; folic acid is being used in the diagnosis of folate deficiency

Cautions: women receiving antiepileptic therapy need counseling before starting folic acid.

Drug interactions: cyanocobalamin; agents causing folic acid deficiency with long term use (phenytoin, oral contraceptives, isoniazid, NSAIDs in high doses and glucocorticosteroids); antifolate agents (trimethoprim, pyrimethamine and methotrexate)

Contraindications: should never be given without vitamin B₁₂ in undiagnosed megaloblastic anaemia or other vitamin B₁₂ deficiency states because risk of precipitating subacute combined degeneration of the spinal cord; folate-dependent malignant disease.folic acid injection that contains benzyl alcohol as a preservative should not be used in new born and immature infants.

Side effects: allergic reaction, specifically; bronchospasm; erythema; fever; general malaise; skin rash; or itching.

Dose and Administrations:

Folic acid Injection: Adult:

Deficiency (prophylaxis): IV infusion, as part of total parenteral nutrition solutions, the specific amount determined by individual patients need.

Deficiency (treatment): IM, IV, or deep SC: 250 mcg (0.25 mg) to 1-mg a day until a hematologic response occurs.

Diagnostic aid (folate deficiency): IM: 100 to 200 mcg (0.1 to 0.2 mg) a day for ten days plus low dietary folic acid and Vitamin B₁₂.

Child: See usual adult dose.

Folic acid Tablets:

Deficiency (prophylaxis): Oral: amount based on normal daily-recommended intakes:

Persons	Microgram
Adult males	150 – 400
Adult females	150 – 400
Pregnant females	400 - 800
Breast feeding females	260 – 800
Birth to 3 years of age	25
4 to 6 years of age	75 – 400
7 to 10 years of age	100 – 400
<i>Diagnostic aid (folate deficiency): Oral:</i> 100 to 200 mcg (0.1 to 0.2 mg) a day for ten days plus low dietary folic acid and vitamin B ₁₂ .	
<i>Deficiency (treatment):</i> treatment dose is individualized by prescriber based on severity of deficiency.	

Storage: at room temperature in a well-closed container.

Menadiol Sodium Diphosphate

Tablet, 10 mg

Injection, 10mg /ml

Indications: in the prevention and treatment of hypoprothrombinemia secondary to factors limiting absorption or synthesis of Vitamin K.

Cautions: the drug should not be used in neonates; in patients with hepatic function impairment, G6PD deficiency and vitamin E deficiency.

Drug interactions: anticoagulants (coumarin or indandione – derivative), hemolytics

Contraindications: neonates and infants, late pregnancy

Side effects: anaphylaxis, cyanosis, dizziness, hypotension, profuse sweating, rapid and weak pulse, and in newborns, hemolytic anemia and liver toxicity, which may progress to kernicterus.

Dose and Administration:

Oral dosage forms

Adult:

Hypoprothrombinemia secondary to obstructive jaundice and biliary fistulas: Oral: 5 mg/day.

Hypoprothrombinemia anemia secondary to the administration of antibacterials or salicylate: Oral: 5 to 10 mg per day.

Child:

Vitamin (prothrombogenic); or Antidote (to drug- induced hypoprothrombinemia): Oral: 5 to 10 mg per day,

Parenteral dosage forms

Adult:

Nutritional supplement (Vitamin), prothrombogenic; or Antidote (to drug induced hypoprothrombinemia): IM or SC: 5 to 15 mg one or two times a day.

Storage: in a light resistant container at room temperature; especially menadiol sodium bicarbonate injection should be protected from freezing.

Nicotinamide

Tablet, 100 mg

Injection, 5 mg/ml, 100 mg/ml in 1 ml ampoule

Indications: nicotinamide and nicotinic acid (niacin) are used to prevent niacin deficiency and to treat pellagra. Niacin (but not nicotinamide) is also indicated in the treatment of hyperlipidemia.

Cautions: blood glucose concentration should be monitored periodically and also liver function should be determined periodically in patients receiving long-term niacin or nicotinamide therapy. Large doses of niacin or nicotinamide should be administered with caution to patients with gallbladder disease or a history of jaundice or liver disease, diabetes mellitus, gout, peptic ulcer, or allergy, in women who are or may become pregnant unless the possible benefits outweigh the potential risks to the fetus.

Drug interactions: niacin reportedly potentiates the hypotensive effect of ganglionic blocking drugs.

Contraindications: niacin and nicotinamide are contraindicated in patients with, active peptic ulcer, or hypersensitivity to the drugs. Niacin is also contraindicated in patients with arterial hemorrhaging or severe hypotension

Side effects: anaphylactic reaction with injection only, hepatotoxicity or cholestasis with high doses of extended – release niacin.

Dose and Administration:

Oral:

Deficiency (prophylaxis): Oral: amount based on normal daily-recommended intakes

Persons	Milligram
Adolescent and adult males	15 – 20
Adolescent and adult females	13 – 15
Pregnant females	17
Breast feeding females	20
Birth to 3 years of age	5-9
4 to 6 years of age	12
7 to 10 years of age	13

Deficiency (treatment): Treatment dose is individualized by prescriber based on severity of deficiency.

Parenteral:

Deficiency (prophylaxis): IV infusion: as part of total parenteral nutrition solutions, the specific amount determined by individual patient need.

Deficiency (treatment):

Adult: *IM:* 50 to 100 mg five to more times a day

IV (slow): 25 to 100 mg two to more times a day.

Child: *IV (slow):* up to 300 mg a day

Storage: at room temperature in a tight container.

Nicotinic Acid

Tablet, 50 mg

Injection, 50 mg/ml in 1 ml ampoule

Indications, Cautions, Side effects, Drug interactions, Contraindications, see notes under nicotinamide

Dose and Administrations:

Oral: Adult:

Antihyperlipidemic:

Initial: *Oral:* 1 gram three times a day, the dosage being increased in increments of 500 mg a day every two to four weeks as needed.

Maintenance: *Oral:* 1 to 2 grams three times a day.

Parental: see under nicotinamide

Storage: at room temperature in a well closed container. Protect from freezing.

Phytomenadione (Vitamin K₁)

Injection, 1mg/ml in 0.5ml ampoule, 10mg/ml in 1ml ampoule.

Indications: prothrombogenic nutritional supplement, it is also used for treatment and prevention of various coagulation disorders including

hypoprothrombinemia, or as an antidote to drug induced hypoprothrombinemia; see also section 10.1

Cautions, Drug interactions, Side effect; see section 10.1 under phytomenadione

Dose and Administration: *SC or IM*, it should not be given repeatedly to patients with severe liver disease, once the response to the initial dose is unsatisfactory.

Adult: *Nutritional supplement (Vitamins), prothrombogenic or Antidote (to drug-induced hypoprothrombinemia):* 2.5 to 10mg (up to 25mg), may be repeated after 6-8 hours if necessary.

Child: *Nutritional supplement (vitamin), prothrombogenic or Antidote (to drug-induced hypoprothrombinemia), Treatment of hypoprothrombinemia:*

Infants: *IM or Sc:* 1-2 mg.

Child: *IM or Sc:* 5-10mg.

Storage: at room temperature, protect from light and freezing.

Pyridoxine Hydrochloride (Vitamin B₆)

Tablet, 40mg, 100mg, 300mg.

Injection, 50mg/ml in 2ml ampoule, 150mg/ml

Indications: for prevention and treatment of pyridoxine deficiency states that may occur as a result of inadequate nutrition or intestinal malabsorption.

It is also used as antidote in cyclosporin poisoning and to terminate seizures and prevent neuropathy associated with isoniazid poisoning.

Cautions: sensitive to pyridoxine.

Drug interactions: levodopa, cycloserine, isoniazid, penicillamines, hydralazine.

Side effects: sensory neuropathy in prolonged use

Dose and Administration:

Adult:

Deficiency states: Oral: 20-50mg up to 3 times daily isoniazid neuropathy, prophylaxis 10mg daily, therapeutic - 50mg three times daily.

Idiopathic sideroblastic anaemia: Oral: 100-400mg daily in divided doses.

Nutritional supplement - Dietary supplement: Oral: 10-20mg per day for three weeks followed by 2 to 5mg per day (in a multivitamin preparation) for several weeks.

Drug Induced deficiency:

Prevention: Oral: 10-50mg per day for penicillamine or 100-300mg per day for cycloserine, hydralazine, or isoniazid.

Treatment: Oral: 50 to 100mg per day as needed to prevent relapse; *IM or IV*, 50 to 200mg per day for three weeks, followed by 25 to 100mg per day as needed.

Child:

Dietary supplement: Oral: 2.5 to 10mg per day for three weeks, followed by 2 to 5mg per day (in a multivitamin preparation) for several weeks.

Storage: at room temperature, protect from light and from freezing.

Thiamine Hydrochloride (Vitamin B₁)

Tablet, 5mg, 10mg, 100mg, 300mg

Injection, 50mg/ml in 2ml ampoule

Indications: for prevention and treatment of thiamine deficiency states that may occur as a result of inadequate nutrition or intestinal malabsorption.

It is used for temporary metabolic correction of genetic enzyme deficiency diseases such as subacute necrotizing encephalomyelopathy (SNE, Leigh's disease), maple syrup urine disease (branched-chain aminoacidopathy), and lactic acidosis associated with pyruvate carboxylase deficiency and hyperalaninemia.

Cautions: patients sensitive to thiamine and in those with Wernicke's encephalopathy.

Side effects: anaphylactic reaction (coughing, difficulty in swallowing; hives; itching of the skin, swelling of face, lips or eyelids, or wheezing or difficulty in breathing).

Dose and Administration:

Adult:

Nutritional supplement (Vitamin)

Beriberi (initial in mild or maintenance following severe): Oral: 5 to 10mg three times a day (in a multivitamin preparation).

Beriberi (critical illness): IM or slow IV, 5-100mg three times a day followed by maintenance oral administration.

Treatment of deficiency: Oral: 1-10mg three times a day until improvement occurs, followed by recommended dietary allowance.

Child:

Nutritional supplement (Vitamin)

Beriberi (mild): Infants: Oral: 10mg per day.

Beriberi (critical illness): IM or slow IV: 10-25mg per day.

Treatment of deficiency: Oral: 10 to 50mg per day in divided doses.

Dietary supplement:

Infants: *Oral: 300 to 500mcg (0.3-0.5mg) per day.*

Child: *Oral: 500mcg (0.5mg) to 1mg per day.*

Storage: at room temperature in a tight, light-resistant container. Protect from light and freezing.

Vitamin A

Tablet, 50,000 IU, 100,000 IU 200,000 IU

Capsule, 25,000 IU, 50,000 IU, 100,000 IU

Oral solution, 150,000 IU/ml (concentrated), 50,000 IU/ml

Injection, under 200,000 IU/ml

Indications: for prevention or treatment of vitamin A deficiency states, causing keratomalacia, xerophthalmia and nyctalopia (night blindness). This may occur as a result of inadequate nutrition or intestinal malabsorption.

Note: Vitamin A is not useful for treatment of dry or wrinkled skin, eye problems, or prevention or treatment of infections not related to vitamin A deficiency.

Cautions: high doses exceeding 6000 units are not recommended during pregnancy, caution is recommended in young children taking high doses of vitamin A; long-term vitamin A use in the elderly may increase the risk of vitamin A overload; in patients with chronic renal failure, chronic alcoholism, cirrhosis, hepatic disease and viral hepatitis.

Drug interactions: calcium supplements, isotretinoin, tetracycline, vitamin E, cholestyramine, colestipol, mineral oil, oral neomycin.

Contraindications: hypervitaminosis A

Side effects: symptoms of acute overdose - bleeding from gums or sore mouth; bulging soft spot on head in babies, confusion or unusual excitement; diarrhoea, dizziness, or drowsiness, double vision, severe headache, severe irritability, peeling of skin, especially on lips and palms; severe vomiting

Dose and Administration:

Adult:

Deficiency: Oral: 30,000 RE (100,000 units) a day for 3 days followed by 7500 to 15,000 RE (25,000 to 50,000 units) a day for 14 days.

With xerophthalmia: Oral: 7500 to 15,000 RE (25,000 to 50,000 units) a day.

Note: -RE=Retinol Equivalent; one RE = one mcg of Retinol = 3.33 units of vitamin A.

- *IM, Intravenous infusion*, as a part of total parenteral nutrition solution, the specific amount determined by individual patient need.

- *IM* 15,000 to 30,000 RE (50,000-100,000 units) a day for three days, followed by 15,000 RE (50,000 units) a day for two weeks.

Child:

Deficiency

Infants less than 1 year: *Oral:* 3000 RE (10,000 units) per kg per day for 5 days followed by 2250-4500 RE (7500 to 15,000 units) per day for 10 days; *IM*, 1500-3000 RE (5000-10,000 units) a day for ten days; in severe deficiency - *IM*, 2250 to 4500 RE (7500 to 15,000 units) a day for ten days.

Children 1-8 years of age: *Oral:* 3000 RE (10,000 units) per kg per day for 5 days followed by 5100 to 10,500 RE (17,000 to 35,000 units) a day for 10 days.

With xerophthalmia: *Oral:* 1500 RE (5000 units) per kg of body weight for five days, then in combination with intramuscular Vitamin A (7500 RE or 25,000 units per kg of body weight a day) until recovery occurs.

IM: 1500-4500 RE (5000-15,000 units) a day for ten days; in severe deficiency -

IM: 5250 to 10,500 RE (17,500-35,000 units) a day for ten days.

Storage: at room temperature in a tight, light-resistant container. Protect from light and freezing.

13.2. Vitamins, Combinations

Vitamin A + D

Capsule, 4,000 IU + 400 IU; see notes above

13.2.1. Vitamin B complex preparations[★]

The most important B group vitamins appear to be thiamine (vitamin B1), riboflavin (vitamin B2), pyridoxine (vitamin B6), Pantothenic acid (vitamin B5), nicotinic acid/nicotinamide (niacin, vitamin B3, niacinamide), cyanocobalamin (vitamin B12) and folic acid/folate.

Indications: supplement for use in the wasting syndrome in chronic renal failure, uremia, impaired metabolic functions of the kidney, dialysis; labeled for OTC use as a dietary supplement.

Dose and Administration: *Oral:* **Adult:**

Dietary supplement: One tablet daily

Renal patients: One tablet or capsule daily between meals; take after treatment if on dialysis.

13.2.2. Multivitamin preparations[★]**13.2.3. Multivitamin with minerals and/or extracts[★]**

[★] Any combination proven to be therapeutically effective can be used

14. ANTIHISTAMINES AND ANTIALLERGICS

14.1. Antihistamines

Antihistamines diminish or abolish the main actions of histamine in the body by competitive, reversible blockade of histamine receptor sites on tissues; they do not inactivate histamine or prevent its synthesis or release. Histamine H_1 receptors are responsible for vasodilatation, increased capillary permeability, flare and itch reactions in the skin, and to some extent for contractions of smooth muscle in the bronchi and gastro-intestinal tract.

Antihistamines are used for the symptomatic relief of hypersensitivity reactions including urticaria and angioedema, rhinitis, and conjunctivitis. Antihistamines are generally considered to be ineffective in asthma. They should not be used to control transfusion reactions caused by ABO incompatibility.

Antihistamines are widely used, often with a decongestant, in compound preparations for the symptomatic treatment of coughs and the common cold.

Antihistamines are also used to control the pruritus associated with skin disorders such as atopic eczema. Some antihistamines, including promethazine, are used for their sedative effects; antihistamines such as cyproheptadine may be of value in the prophylaxis of migraine, particularly in children.

Side effects: The most common side effects of the older antihistamines is sedation, varying from slight drowsiness to deep sleep, and including lassitude, dizziness, and in coordination, sedative effects, when they occur, may diminish after a few days of treatment.

Paradoxical CNS stimulation may occur especially in children, with insomnia, nervousness, euphoria, irritability, tremors and rarely nightmares, hallucinations, and convulsions. In high doses CNS stimulation may be attributed to antimuscarinic activity. Extrapyramidal symptoms may develop with phenothiazine derivatives and have been reported with some other antihistamines.

Older antihistamines possess antimuscarinic properties and may produce similar adverse effects to atropine. In addition headache, psychomotor impairment, gastro intestinal disturbances such as nausea, vomiting, diarrhoea, or epigastric pain have occurred with antihistamines.

Other side effects of antihistamines include palpitations and arrhythmias, hypotension, hypersensitivity reactions (including bronchospasm, angioedema, and anaphylaxis, rashes and photosensitivity reactions), extrapyramidal effects, dizziness, confusion, depression, sleep disturbances, tremor, convulsions, blood disorders, and liver dysfunction.

Caution and Contraindications.

Antihistamines should not be given to premature infants or neonates: this group of patients has an increased susceptibility to antimuscarinic effects. Phenothiazine antihistamines should be avoided in young children because of the potential risk of central and obstructive apnoea and reduced arousal. Recommendations range from avoidance in children under 1 year of age to

children under 2 years. Elderly patients are also more susceptible to many adverse effects of antihistamines, including antimuscarinic effects, sedation, and hypotension.

Many antihistamines may cause drowsiness; so patients should not drive or operate machinery. Because of their antimuscarinic properties antihistamines should be used with care in conditions such as closed angle glaucoma, urinary retention prostatic hyperplasia, or pyloroduodenal obstruction. Other adverse effects of antihistamines suggest caution in patients with epilepsy, severe cardiovascular disorders, or, for phenothiazines, in those with liver disorders.

Drug interactions: Antihistamines may enhance the sedative effects of central nervous system depressants including alcohol, barbiturates, hypnotics, opioid analgesics, anxiolytic sedatives, and neuroleptics. MAOIs may enhance the antimuscarinic effects of antihistamines, and antihistamines have an additive antimuscarinic action with other antimuscarinic drugs, such as atropine and tricyclic antidepressants. Antihistamines could mask the warning signs of damage caused by ototoxic drugs such as aminoglycoside antibiotics.

Cetirizine

Tablet, 5mg, 10mg

Oral solution, 1mg/ml

Indications: symptomatic relief of hypersensitivity reactions including rhinitis and chronic urticaria.

Cautions and Drug interactions; see notes above

Contraindications: see notes above; also pregnancy and breast-feeding

Side effects: see notes above, incidence of sedation and antimuscarinic effect is low

Dose and Administration: *Oral:*

Adult and Child over 6 years: 10mg daily or 5mg twice daily,

Child 2 - 6 years: *hay fever*, 5mg daily or 2.5mg twice daily.

Storage: store in a well - closed container at room temperature.

Chlorpheniramine Maleate

Tablet, 2mg, 4mg, 6mg

Syrup, 2mg/5ml

Indications: symptomatic relief of allergy such as hay fever, urticaria, emergency treatment of anaphylactic reactions.

Cautions: see notes above; also pregnancy and breast-feeding.

Drug interactions, Contraindications: see notes above.

Side effects: see notes above; also exfoliative dermatitis and tinnitus reported; injections may cause transient hypotension or CNS stimulation and may be irritant.

Dose and Administration: *Oral:*

Adult: 4 mg every 4-6 hours, max. 24 mg daily;

Child: under 1 year not recommended. 1-2 years 1mg twice daily; 2-5 years 1mg every 4-6 hours, max. 6 mg daily; 6-12 years 2 mg every 4-6 hours, max. 12 mg daily.

Storage: at room temperature in a tight, light-resistant container.

Chlorpheniramine + Paracetamol + Pseudoephedrin

Oral suspension, 1 mg + 325 mg + 15 mg

Indications: temporary relief of sinus symptoms.

Dose and Administrations: *Oral:*

Analgesic: Based on acetaminophen component:

Adult: 325–650 mg every 4–6 hours as needed; do not exceed 4 g/day

Child: 10–15 mg/kg/dose every 4–6 hours as needed; do not exceed 5 doses in 24 hours.

Antihistamine: Based on chlorpheniramine maleate component:

Child > 12 years and Adult: 4 mg every 4–6 hours (maximum: 24 mg/24 hours)

Child 2–6 years: 1 mg every 4–6 hours (maximum: 6 mg/24 hours)

6–12 years: 2 mg every 4–6 hours (maximum: 12 mg/24 hours)

Decongestant: Based on pseudoephedrine component:

Child > 12 years and Adult: 60 mg every 4 hours (maximum: 360 mg/24 hours)

Child: 2–6 years: 15 mg every 4 hours (maximum: 90 mg/24 hours)

6–12 years: 30 mg every 4 hours (maximum: 180 mg/24 hours)

Cyproheptadine Hydrochloride

Tablet, 4mg, 10mg

Syrup, 2mg/5ml

Indications: symptomatic relief of allergy such as hay fever, urticaria migraine.

Cautions, Drug interactions and Side effects; see notes above

Contraindications: see notes above; also breast-feeding

Dose and Administration: *Oral:*

Allergy: Adult: 4 mg 3–4 times daily; usual range 4–20 mg daily, max, 32 mg daily; **Child** under 2 years not recommended, 2–6 years, 2 mg 2–3 times daily, max. 16 mg daily.

Migraine: 4 mg with a further 4 mg after 30 minutes if necessary; maintenance, 4 mg every 4–6 hours.

Dexchlorpheniramine Maleate + Betamethasone

Tablet, 2mg + 0.25mg

Diphenhydramine Hydrochloride

Capsule, 25mg, 50mg

Elixir, 12.5mg/5ml

Injection, 50ml in 1ml ampoule

Indications: symptomatic relief of hypersensitivity reactions including urticaria and angioedema, rhinitis and conjunctivitis and in pruritic skin disorders; other indications also for motion sickness and in control of parkinsonism and drug induced extrapyramidal disorders; short term management of insomnia.

Cautions, Drug interaction, Contraindications, Side effects; see notes above.

Does and Administration:*Oral:***Adult:** 25 to 50 mg every four to six hours as needed**Child:** Up to 6 years of age, 6.25 to 12.5 mg every four to six hours; 6 to 12 years of age, 12.5 to 25 mg every four to six hours, not to exceed 150mg per day*Parenteral dosage forms***Adult:** *IM or IV:* 10 to 50 mg.**Child:** *IM:* 1.25 mg per kg of body weight or 37.5 mg per square meter of body surface four times a day not to exceed 300 mg per day.

Note: premature and full-term neonates – use is not recommended.

Storage: at room temperature, in tight and light-resistant containers. Protect from freezing.**Levocetirizine***Tablet, 5mg***Indications, Cautions, Drug interactions, Side effects and storage;** see under cetirizine.**Dose and Administration:****Adult:** *Allergic rhinitis and Urticaria:* *Oral:* 5mg once daily (at night)**Child:** over 12 years, as for adults. Safety and efficacy not established in children under 12 years.**Loratadine***Tablet, 10mg**Syrup, 5mg/5ml***Indications:** symptomatic relief of allergy such as hay fever, urticaria.**Cautions, Drug interactions:** see notes above**Contraindications:** see notes above, also pregnancy and breast-feeding**Side effects:** see notes above; incidence of sedation and antimuscarinic effect is low.**Dose and Administrations:***Oral:* **Adult and Child over 6 years:** 10mg daily;**Child 2 - 5 years:** 5mg daily.**Storage:** store in airtight containers, protect from light.**Pheniramine Aminosaliclate***Tablet, 50mg, 75mg***Indications:** symptomatic relief of hypersensitivity reactions including urticaria and angioedema, rhinitis and conjunctivitis, and in pruritic skin disorders; prevention and control of motion sickness.**Cautions, Drug interactions, Contraindications and Side effects;** see notes above.**Dose and Administration:***Oral:* 25 to 50 mg two or three times a day**Storage:** Protect from light.

Promethazine Hydrochloride*Tablet, 10 mg, 25 mg**Suppository, 25 mg, 50 mg**Elixir, 5 mg/5ml**Injection, 25 mg/ml in 1 ml and 2 ml ampoules*

Indications: symptomatic relief of allergy such as hay fever, urticaria, premedication; emergency treatment of anaphylactic reactions; sedation; motion sickness

Cautions: see notes above; also pregnancy and breast-feeding.

Contraindications, Drug interactions: see notes above

Side effects: see notes above; intramuscular injection may be painful.

Dose and Administration:

Adult:

Oral: 5-12.5 mg three times a day before meals and at bed time, or 25 mg at bed time as needed.

IM or IV: 25mg; may be repeated within two hour if necessary

Rectal: 25mg; may be repeated in two hours if necessary.

Child (Children 2 years of age and over):

Oral: 125mcg per kg of body weight every four to six hours, or 500 mcg (0.5mg) at bed time as needed, or 5 to 12.5mg three times a day or 25mg at bed time as needed.

IM: 125mcg (0.125mg) per kg of body weight every four to six hours or 500 mcg (0.5mg) per kg of body weight at bed time as needed, or 6.25-12.5mg three times a day or 25mg at bed time as needed.

Storage: Tablet and Injectables - store at room temperature in a tight and light resistant container. Suppository - store between 2°C and 8°C in a tight, light resistant container.

Terfenadine*Tablet, 60 mg**Syrup, 30 mg/5ml*

Indications: symptomatic relief of allergy such as allergic rhinitis, urticaria

Cautions: see notes above; also pregnancy and breast-feeding

Contraindications: see notes above; avoid grapefruit juice (may inhibit metabolism of terfenadine)

Drug interactions: see notes above

Side effects: see notes above; incidence of sedation and antimuscarinic effects low; erythema multiform and galactorrhoea reported; ventricular arrhythmias (including torsades de pointes) have followed excessive dosage.

Dose and Administration:

Allergic rhinitis and conjunctivitis: **Adult** and **child** over 50 kg: *Oral:* 60 mg daily increased if necessary to 120 mg daily in single or 2 divided doses.

Allergic skin disorders: **Adult** and **Child** over 50 kg: *Oral:* 120 mg daily in single or 2 divided doses.

Triprolidine Hydrochlorides

Tablet, 2.5 mg, 10 mg

Elixir, 2mg/5ml

Indications: symptomatic relief of hypersensitivity reactions including urticaria, rhinitis and conjunctivitis and in pruritic skin disorders

Cautions, Drug interactions, Contraindications, Side effects; see notes above

Dose and Administration:

Adult: 2.5 to 5 mg three times daily

Storage: in airtight containers, protect from light.

14.2. Drugs used in Allergic Emergencies

Anaphylactic shock and conditions such as angioedema are medical emergencies that can result in cardiovascular collapse and/or death. They require prompt treatment of possible laryngeal edema, bronchospasm or hypertension. Atopic individuals are particularly susceptible. Insect bites and certain foods including eggs, fish, peanuts and nuts are also a risk for sensitized persons. Therapeutic substances particularly associated with anaphylaxis include blood products, vaccines, hyposensitizing (allergen) preparations, antibiotics (especially penicillins), iron injections, heparin, and neuromuscular blocking drugs. Acetyl salicylic acid and other non-steroidal anti-inflammatory drugs (NSAIDs) may cause bronchoconstriction in leukotriene-sensitive patients. In the case of drug allergy, anaphylaxis is more likely to occur after parenteral administration. Resuscitation facilities should always be available when injecting a drug associated with a risk of anaphylactic reactions.

First line treatment of a severe allergic reaction includes administering epinephrine (adrenaline), keeping the airway open (with assisted respiration if necessary) and restoring blood pressure. Epinephrine (adrenaline) should immediately be given by intramuscular injection to produce vasoconstriction and bronchodilation and injections should be repeated every 10 minutes until blood pressure and pulse have stabilized. If there is cardiovascular shock with inadequate circulation, epinephrine (adrenaline) must be given cautiously by slow intravenous injection of a dilute solution. An intravenous corticosteroid e.g. hydrocortisone (as sodium succinate) in a dose of 100 - 300 mg is of secondary value in the initial management of anaphylactic shock because the onset of action is delayed for several hours, but should be given to prevent further deterioration in severely affected patients.

Adrenaline (Epinephrine)

Injection, 0.1 % in 1 ml ampoule

Indications: emergency treatment of acute anaphylaxis; angioedema; cardiopulmonary resuscitation; see also section 2.5 and 3.2 for other uses of Adrenaline

Cautions: hyperthyroidism, diabetes mellitus, heart disease, hypertension, arrhythmias, cerebro-vascular disease, angle-closure glaucoma, second stage of labor, elderly patients.

Side effects: anxiety, tremor, tachycardia, arrhythmias, headache, cold extremities; also hypertension (risk of cerebral hemorrhage) and pulmonary edema (on excessive dosage or extreme sensitivity) nausea, vomiting, sweating, weakness, dizziness, and hyperglycemia also reported

Dose and Administrations:

Caution: Different dilutions of epinephrine injection are used for different routes of administration

IM or SC injection use 1:1000 epinephrine injection.

Slow IV injection use 1:10 000 epinephrine injection.

This route should be reserved for severely ill patients when there is doubt about the adequacy of circulation and absorption from the intramuscular site.

Hydrocortisone

Injection (sodium succinate), 50 mg/ml in 2 ml ampoule

Indications: used for life-threatening shock only after less toxic therapies have proven ineffective.

Cautions: pregnancy and in children; in patients with hypothyroidism or cirrhosis, psychosis, hypertension, congestive heart failure, diverticulitis, HIV, herpes simplex, oral herpetic lesions, renal function impairment or disease, tuberculosis, diabetes mellitus.

Drug interactions: alcohol, acetaminophen, non-steroidal anti-inflammatory drugs, parenteral amphotericin B, atropine, oral antidiabetic agents or insulin, digitalis glycoside, diuretics, isoniazid.

Contraindications: known hypersensitivity to any of corticosteroids, recent surgery, osteoporosis, scleroderma, Cushing's syndrome.

Side effects: immunosuppression, muscle pain or weakness, delayed wound healing, edema, hypertension, cataract, diabetes mellitus, nausea, vomiting, anorexia, headache, vertigo, insomnia, restlessness, acne, impaired wound healing, increased sweating, hirsutism.

Dose and Administration:

Adult: *for life threatening shock:* IV-massive dose 50 mg/kg initially and repeated in 4 hours and/or every 24 hours if needed, or 0.5-2g IV initially and repeated at 2 to 6 hours intervals as required.

Storage: at room temperature.

15. OPHTHALMIC AGENTS

15.1. Antiglaucoma

Agents used in the management of glaucoma include:

- Topical preparations - eye drops containing a beta-adrenergic blocking agent (e.g. timolol), miotic (e.g. pilocarpine), adrenergic/ α_2 - adrenergic agonist (e.g. brimonidine), carbonic anhydrase inhibitor (e.g. dorzolamide), or prostaglandin receptor agonist (e.g. latanoprost).
- Systemic preparations - ocular hypotensives (e.g. acetazolamide, a carbonic anhydrase inhibitor), and osmotic agents (e.g. mannitol and glycerol).

Beta Blocking Agents

Topical application of a beta-blocker to the eye reduces intra-ocular pressure effectively in chronic simple glaucoma, probably by reducing the rate of production of aqueous humour. Administration by mouth also reduces intra-ocular pressure but this route is not used since side-effects may be troublesome.

Betaxolol Maleate

Solution (eye drop), 0.25 %, 0.5 %

Indications: treatment of chronic open-angle glaucoma and ocular hypertension.

Cautions: concurrent use of beta-blockers.

Drug interactions: amiodarone, ciprofloxacin, ketoconazole, norfloxacin, chlorpromazine, fluoxetine, quinine, ritonavir, phenobarbital.

Contraindications: hypersensitivity to the drug, sinus bradycardia, overt cardiac failure, cardiogenic shock, pregnancy (2nd and 3rd trimester).

Side effects: bradycardia, breast abscess, cataracts, cystitis, diabetes melitus, gout, heart block, hypertension, hypothyroidism.

Dose and Administration: Adult: Instil one drop twice daily.

Storage: store at room temperature.

Levobunolol Hydrochloride

Solution (eye drop), 0.25%, 0.5%

Indications: treatment of chronic open-angle glaucoma or ocular hypertension.

Dose and Administration: Adult: Instil one drop in the affected eye(s) 1-2 times/day.

Storage: store at room temperature.

Timolol Maleate

Solution (eye drop), 0.25 %, 0.5 %

Indications: ocular hypertension; chronic open-angle glaucoma, aphakic glaucoma, some secondary glaucomas.

Cautions: older people; angle-closure glaucoma.

Drug interactions: acetazolamide, alcohol, epinephrine, lidocaine, nifedipine, prazosin, procainamide, quinidine, verapamil, thiopental, reserpine, metformin, hydralazine.

Contraindications: uncontrolled heart failure, bradycardia, heart block; asthma, obstructive airways disease.

Side effects: stinging, burning, pain, itching, erythema, transient dryness, allergic blepharitis, transient conjunctivitis, keratitis, decreased corneal sensitivity, diplopia, ptosis; systemic effects, particularly on the pulmonary, cardiovascular and central nervous systems, may follow absorption.

Dose and Administration: by *instillation* into the eye, 1 drop (0.25 % or 0.5 %) twice daily.

Storage: store at room temperature.

Parasympathomimetics (miotics)

They act by opening up the inefficient drainage channels in the trabecular meshwork resulting from contraction or spasm of the ciliary muscle.

Demecarium Bromide

Solution (eye drop), 0.25%, 0.5%, 1%

Indications: treatment of open-angle glaucoma, particularly in aphakic patients and when other drugs have proved inadequate.

Cautions, Contraindications, and Side effects: see pilocarpin.

Dose and Administration: Adult: 1 or 2 drops of 0.25% solution being instilled from twice weekly, preferably at bed time, to twice daily.

Storage: store in airtight containers and protect from light.

Isoflurophate

Eye ointment, 0.025 %

Indications: treatment of open-angle glaucoma, particularly in aphakic patients and when other drugs have proved inadequate.

Cautions, Contraindications, and Side effects: see under pilocarpin.

Dose and Administration: Adult: applied locally usually as a 0.025% ophthalmic ointment.

Storage: store at 8-15°C in sealed containers.

Physostigmine (salicylate/sulphate)

Solution (eye drop), 0.25%, 0.5%

Indications: used to decrease intra-ocular pressure in glaucoma.

Cautions, Contraindications, and Side effects; see under pilocarpin.

Dose and Administration: Adult and Child: One drop in each eye up to four times a day.

Storage: store at room temperature.

Pilocarpine

Pilocarpine hydrochloride, solution 2-10 %; eye ointment, 2-10%

Pilocarpine nitrate, solution, 2-10%

Indications: chronic open-angle glaucoma; ocular hypertension; emergency treatment of acute angle-closure glaucoma; to antagonize effects of mydriasis and cycloplegia following surgery or ophthalmoscopic examination.

Cautions: retinal disease, conjunctival or corneal damage; monitor intra-ocular pressure in chronic open-angle glaucoma and in long term treatment; cardiac disease, hypertension, asthma, peptic ulceration, urinary - tract obstruction, parkinson disease, stop treatment if symptoms of systemic toxicity develop.

Do not carry out skilled tasks, for example operating machinery or driving until vision is clear.

Drug interactions: beta-blockers, anticholinergic drugs (atropin).

Contraindications: acute iritis, acute uveitis, anterior uveitis, some forms of secondary glaucoma; acute inflammation of anterior segment; not advisable after angle closure surgery.

Side effects: eye pain, blurred vision, ciliary spasm, lacrimation, myopia, browache; conjunctival vascular congestion, superficial keratitis, vitreous hemorrhage and increased pupillary block have been reported; lens opacities have occurred following prolonged use; rarely systemic effects including hypertension, tachycardia, bronchial spasm, pulmonary oedema, salivation, sweating, nausea, vomiting, and diarrhea.

Dose and Administration: Adult:

Chronic open-angle glaucoma: by instillation into the eye, 1 drop (2% or 4%) up to 4 times daily.

Acute angle-closure glaucoma before surgery: by instillation into the eye, 1 drop (2%) every 10 minutes for 30-60 minutes, then 1 drop every 1-3 hours until intra-ocular pressure subsides.

Storage: store at room temperature.

Sympathomimetics

Adrenaline probably acts both by reducing the rate of production of aqueous humour and by increasing the outflow through the trabecular meshwork. It is contraindicated in angle-closure glaucoma because it is a mydriatic, unless an iridectomy has been carried out.

Dipivefrine is a pro-drug of adrenaline. It is claimed to pass more rapidly through the cornea and is then converted to the active form.

Brimonidine is a relatively selective α_2 -adrenoceptor agonist. The effect of 0.2% brimonidine is comparable to many of the beta blockers and it is used as adjunctive therapy to these agents.

Apraclonidine is a potent α_2 -adrenergic receptor agonist, but with some affinity for α_1 receptors. It acts by decreasing the formation and flow of aqueous humour.

Apraclonidine

Eye drop, 0.5%, 1%

Indications: the 0.5% drops are used as adjunctive treatment for a short period to delay laser treatment or surgery in patients not adequately controlled by another agent.

the 1 % drops are used for pre-operative prevention of intraocular pressure induced by anterior segment laser surgery.

Dose and Administration:

1% solution: Control or prevention of post-surgical elevation in intraocular pressure after anterior segment laser surgery: 1 drop 1 hour before surgery, and a second drop on completion of the procedure.

0.5 % solution: short-term adjunctive use in lowering intraocular pressure: 1 drop 3 times daily, with an interval of at least 5 minutes between administering different medications.

Brimonidine

Eye drop, 0.2%

Indications: lowering of intraocular pressure in chronic open-angle glaucoma or ocular hypertension.

Cautions: cardiovascular disease, cerebral or coronary insufficiency, Raynaud's phenomenon, orthostatic hypotension, hepatic or renal impairment.

Drug interactions: MAOIs, tricyclic and related antidepressants and systemic sympathomimetics, antihypertensive agents.

Contraindications: concomitant monoamine oxidase inhibitor

Side effects: Local effects include hyperaemia, burning and stinging, pruritus, corneal staining and erosion, photophobia, allergy, eyelid oedema, and conjunctivitis. Fatigue, drowsiness, headache, hypersensitivity reactions, mouth and nasal dryness, taste disturbances, dizziness and, rarely, depression and palpitations have also been reported.

Dose and Administration: Instil 1 drop 12 hourly.

Dipivefrine

Solution (eye drop); 0.1 % in 15 ml

Indications: open - angle glaucoma or ocular hypertension.

Cautions: asthma, aphakic patients, vascular hypertension or cardiac disorders.

Drug interactions: with ocular hypotensive agents.

Contraindication: hypersensitivity to the drug.

Side effects: blepharoconjunctivitis, bulbar conjunctival follicles, conjunctival hyperemia, keratomegaly of the conjunctival epithelial cells.

Dose and Administration: Adult: 1 drop of a 0.1 % solution every 12 hours.

Storage: store at room temperature.

Carbonic Anhydrase Inhibitors

The carbonic anhydrase inhibitors, acetazolamide and dorzolamide, reduce intra-ocular pressure by reducing aqueous humour production. Systemic use also produces weak diuresis.

Acetazolamide is given by mouth or by intravenous injection (intramuscular injection are painful because of the alkaline pH of the solution). It is used as an adjunct to other treatment for reducing intra-ocular pressure.

Dorzolamide is licensed for use in patients resistant to beta-blockers or those in whom beta-blockers are contra-indicated. It is used alone or as an adjunct to a topical beta-blocker.

Acetazolamide

Capsule (s/r), 500 mg

Tablet, 250 mg

Powder for injection, (sodium), 250 mg, 500 mg in vial

Indications: reduction of intra-ocular pressure in open-angle glaucoma, secondary glaucoma, and peri-operatively in angle-closure glaucoma; *diuresis; epilepsy* (see section 2.6).

Cautions: elderly; pregnancy; breastfeeding; diabetes; pulmonary obstruction; monitor blood count and electrolytes if used for long periods.

May impair ability to perform skilled tasks, for example operating machinery, driving.

Drug interactions: quinidine, procainamide, mexiletine and TCAs, lithium, diuretics and potassium-depleting agents.

Contraindications: hypersensitivity to sulfonamides; chronic angle-closure glaucoma, hypokalaemia, hyponatraemia, hyperchloraemic acidosis; renal and hepatic impairment.

Side effects: nausea, vomiting, diarrhea, taste disturbance; loss of appetite, paraesthesia, flushing, headache, dizziness, fatigue, irritability, depression; thirst, polyuria; reduced libido; metabolic acidosis and electrolyte disturbances on long-term therapy; occasionally drowsiness, confusion, hearing disturbances, urticaria, melaena, glycosuria, haematuria, abnormal liver function, renal calculi, blood disorders including agranulocytosis and thrombocytopenia, rashes including Stevens-Johnson syndrome and toxic epidermal necrolysis; transient myopia reported.

Dose and Administration:

Adult: Glaucoma:

Chronic simple (open-angle): Oral: 250 mg 1 - 4 times daily or 500 mg sustained release capsule twice daily.

Secondary, acute (closed angle): IV: initially 250 - 500 mg repeated if necessary in 2 - 4 hours to a maximum of 1g/day.

Child: Glaucoma:

Oral: 8 - 30 mg/kg/day in 3 - 4 divided doses

IV: 20-40 mg/kg/24 hours divided every 6 hours, not to exceed 1g/day.

Storage: store at room temperature.

Dorzolamide

Drops, 2 % (as dorzolamide hydrochloride)

Drops, dorzolamide 2% and timolol 0.5%

Indications: topical treatment of ocular hypertension and open angle glaucoma.

Cautions and Side effects: see acetazolamide

In dorzolamide, local effects include bitter taste, burning, stinging or itching of the eye, blurred vision, tearing, conjunctivitis, eye lid inflammation.

Dose and Administration: Adult:

Monotherapy: Instil 1 drop 3 times daily

Adjunctive therapy with a topical beta-blocker: Instil 1 drop twice daily

Storage: store in light- resistant containers at room temperature.

Methazolamide

Tablet, 25mg, 50mg, 100mg

Indications: adjunctive treatment of open-angle or secondary glaucoma; short-term therapy of narrow-angle glaucoma when delay of surgery is desired.

Cautions, Drug interactions, Contraindications and Side effects; see under acetazolamide.

Dose and Administration: Adult: *Oral:* 50-100 mg 2-3 times / day

Prostaglandine analogue

Latanoprost and travoprost are prostaglandin analogues which increase uveoscleral outflow; bimatoprost is a related drug. they are used to reduce intra-ocular pressure in ocular hypertension or in open-angle glaucoma. Patients receiving prostaglandin analogues should be monitored for any changes to eye coloration since an increase in the brown pigment in the iris may occur; particular care is required in those with mixed coloured irides and those receiving treatment to one eye only.

Bimatoprost

Eye drop, 0.003%

Indications: raised intra-ocular pressure in open-angle glaucoma and ocular hypertension.

Cautions: see under latanoprost and notes above

Side effects: see under latanoprost; also ocular pruritus, allergic conjunctivitis, cataract, conjunctival oedema, eye discharge, photophobia, superficial punctuate keratitis, headache; hypertension

Dose and Administration: apply once daily, preferably in the evening; **Child and Adolescent under 18 years, not recommended.**

Latanoprost

Eye drops, 0.005%

Indications: raised intra-ocular pressure in open-angle glaucoma and ocular hypertension

cautions: before initiating treatment, advise patients of possible change in eye colour; aphakia, or pseudo

Dose and Administration: Adult: Instill 1 drop once daily.

Storage: store at room temperature.

Travoprost

Eye drop, 0.004%

Indications: raised intra-ocular pressure in open-angle glaucoma and ocular hypertension

Cautions: see under latanoprost and notes above

Side effects: see under latanoprost; also headache, ocular pruritus, photophobia, and keratitis reported; rarely, hypotension, bradycardia, conjunctivitis, browache.

Dose and Administration: see under latanoprost;

Osmotic agents

Glycerol and Mannitol are useful short - term ocular hypotensive drugs, used in the pre-operative treatment of acute closed - angle glaucoma.

Glycerol

Oral solution, 50%, 75% v/v

Indications: used for short-term reduction of vitreous volume and intraocular pressure before and after ophthalmic surgery, and as an adjunct in the management of acute glaucoma.

Cautions: caution in applying glycerol to the cornea.

Side effects: headache, nausea, vomiting, diarrhoea, thirst, dizziness, and mental confusion may occur less frequently. Cardiac arrhythmias have been reported.

Dose and Administration: **Adult and Child:** *Oral:* 1 to 1.8 g/kg given as a 50 % solution.

Storage: store in airtight container.

Mannitol

Injection, 20% in 250 ml, 25% in 50ml

Indications: reduction of increased intraocular pressure.

Cautions; see section 2.6.

Dose and Administration: **Adult:** *IV:* 1.5-2 g/kg administered as a 20 %, or 25% solution over a period of 30-60 minutes.

15.2. Mydriatics/Cycloplegics

Both dilation of the pupil (mydriasis) and paralysis of accommodation (cycloplegia) are produced by anticholinergic agents applied topically. These agents are not only used as aids in the examination of the eye and other ophthalmic procedures but also in the management of inflammatory conditions of the eye to treat or prevent the formation of adhesions between the lens and the iris.

Mydriasis can be achieved by two mechanisms: paralysis of the pupillary constrictor muscles (which is how antimuscarinic agents act) or stimulation of the dilator muscles. Cycloplegia results from paralysis of the ciliary muscles.

Atropin is useful in inflammatory conditions involving the iris and uveal tract, and for refraction in children up to about 6 years of age.

Cyclopentolate has a more rapid onset and shorter duration of action than atropine. Systemic toxicity is possible, especially in infants.

Homatropine has weaker effects than atropine; action is more rapid and less prolonged. It may be preferred to atropine for diagnostic purposes but is considered an inadequate cycloplegic in children.

Tropicamide displays action similar to atropine but with more rapid onset and shorter duration. It is considered an inadequate cycloplegic in children.

Hyoscine onset of action is more rapid, duration shorter and it is more toxic than atropine.

Phenylephrine is mainly a direct acting alpha-adrenoceptor stimulant. 2.5-10% solutions produce mydriasis with insignificant effect on accommodation. 10% solutions may have profound effects on the cardiovascular system and should be used with caution. It is mainly indicated for dilatation of the pupil for funduscopy, sometimes in combination with cyclopentolate or tropicamide.

Atropine Sulphate

Solution (eye drops), 0.5 %, 1 %

Eye ointment, 1%

Indications: iritis, uveitis; cycloplegic refraction procedures.

Cautions: may precipitate acute attack of angle-closure glaucoma, particularly in the elderly or long-sighted; risk of systemic effects with eye drops in infants under 3 months - eye ointment preferred. May cause sensitivity to light and blurred vision. Do not carry out skilled tasks, for example operating machinery or driving, until vision is clear.

Contraindication: angle - closure glaucoma.

Side effects: transient stinging and raised intra-ocular pressure; on prolonged administration, local irritation, hyperaemia, edema, conjunctivitis, contact dermatitis; systemic toxicity may occur in the very young and the elderly.

Dose and Administration: *by instillation into the eye:*

Cycloplegic refraction:

Adult: 1 drop (1%) twice daily for 1-2 days before procedure or a single application of 1 drop (1%) 1 hour before procedure.

Child: under 3 months (see cautions), 3 months-1 year (0.1%), 1-5 years (0.1-0.5%), over 5 years (0.5-1%), 1 drop twice daily for 1-3 days before procedure with a further dose given 1 hour before procedure.

Iritis, Uveitis: **Adult:** instill 1 drop (0.5 or 1%) up to 4 times daily.

Child: instill 1 drop (0.5 or 1%) up to 3 times daily.

Storage: store at room temperature.

Cyclopentolate Hydrochloride

Solution (eye drops), 0.5 %, 1 %, 2 %

Indications: diagnostic procedures requiring mydriasis and cycloplegia.

Cautions, Contraindications and Side effects; see under atropine sulphate.

Dose and Administration:

Adult: Instill 1 drop of 1 % followed by another drop in 5 minutes; 2 % solution in heavily pigmented iris.

Child: Instill 1 drop of 0.5 %, 1 %, or 2 % in eye followed by 1 drop of 0.5 % or 1 % in 5 minutes, if necessary

Storage: store at a temperature not exceeding 8 °C in airtight containers.

Homatropine Hydrobromide

Solutions (eye drop), 1%, 2%

Indications: mydriasis and cycloplegia; uveitis.

Cautions: see notes above.

Contraindications: angle closure glaucoma.

Side effects: transient stinging and raised intraocular pressure, on prolonged administration, local irritation, hyperaemia, oedema and conjunctivitis may occur: contact dermatitis; systemic toxicity may occur in the very young and the elderly.

Dose and Administration:

For the determination of refraction: one or two drops may be instilled, repeated if necessary 5 or 10 minutes later.

Uveitis (treatment): one or two drops may be installed up to every 3 to 4 hours.

Storage: store in airtight containers. Protect from light.

Hyoscine (scopolamine) Hydrobromide

Solution (eye drop), 0.25 %

Indications: produce cycloplegia and mydriasis; treatment of iridocyclitis.

Cautions, Drug interactions, Contraindications, Side effects and Storage, see section 1.3.

Dose and Administration:

Refraction: **Adult:** Instill 1- 2 drops of 0.25 % to eye(s) 1 hour before procedure.

Child: Instill 1 drop of 0.25 % to eye(s) twice daily for 2 days before procedure.

Iridocyclitis: **Adult:** Instill 1 - 2 drops of 0.25 % to eye(s) up to 4 times /day.

Child: Instill 1 drop of 0.25 % to eye(s) up to 3 times/day.

Storage: store at room temperature.

Phenylephrine

Solution (eye drop), 1 %, 2 %, 2.5 %, 5 %, 10 %.

Indications: mydriasis, diagnostic aid and ophthalmic decongestion.

Cautions: The 10% solution should be used with caution in patients with diabetes, hypertension, cardiac disease, severe arteriosclerotic changes or thyrotoxicosis. (A dramatic increase in blood pressure may be produced). It should be avoided in the elderly and neonates.

Drug interactions: beta-blockers and other antihypertensives (reserpine), TCA, MAO inhibitors.

Contraindications: hypersensitivity, hypertension, and ventricular tachycardia.

Side effects: systemic effects include hypertension, subarachnoid haemorrhage, ventricular arrhythmias and myocardial infarction; also trembling, headache, agitation and sweating. Blood pressure changes are most pronounced in the

elderly, neonates and patients with orthostatic hypotension. Hypersensitivity reactions such as allergic conjunctivitis or dermatitis may occur. Pigment granules may be released from the iris into the aqueous; they disappear within 12-24 hours. Rebound miosis the day after administration and subsequent decreased sensitivity to the mydriatic effect may occur in the elderly.

Dose and Administration: Adult: 1 drop of a 10 % solution as required.

Storage: store at controlled room temperature; protect from light and excessive heat.

Tropicamide

Solution (eye drop), 0.5 %, 1 %

Indications: dilatation of the pupil to examine the fundus.

Cautions: patients aged over 60 years and hypermetropic (long-sighted) – may precipitate acute angle-closure glaucoma; darkly pigmented iris, more resistant to papillary dilatation – exercise caution to avoid overdosage.

Avoid operating machinery or driving for 1 – 2 hours after mydriasis

Side effects: transient stinging and raised intraocular pressure; on prolonged administration - local irritation, hyperaemia, oedema and conjunctivitis.

Dose and Administration: Adult and Child: *Ocular instillation:* 1 or 2 drops of 0.5%; 15 - 20 minutes before examination of eye.

Storage: store at room temperature.

15.3. Anti-infectives, Ophthalmic

15.3.1. Antibacterials

Acute bacterial infection of the external eye, including acute bacterial conjunctivitis, corneal ulceration, blepharitis, dacryocystitis, and discharging sockets are caused by the pathogens *Staphylococcus aureus*, *Streptococcus pneumoniae*, and *Haemophilus influenza*.

Bacterial infections are generally treated topically with eye drops and eye ointments. Systemic administration is sometimes appropriate in blepharitis.

Intra-ocular infection, a variety of routes (intra corneal, intra vitreal and systemic) may be used. Chloramphenicol has a broad spectrum of activity and is the drug of choice for superficial eye infections. Chloramphenicol eye drops are well tolerated and the recommendation that chloramphenicol eye drops should be avoided because of an increased risk of aplastic anaemia is not well founded.

Gentamicin is a broad-spectrum bactericidal aminoglycoside antibiotic with particular activity against *Pseudomonas aeruginosa*, *Neisseria gonorrhoea* and other bacteria that may be implicated in blepharitis or conjunctivitis.

Tetracycline is a broad spectrum antibiotic with activity against many Gram-positive and Gram-negative bacteria including *N. gonorrhoea*. Ophthalmic tetracycline is used in blepharitis, conjunctivitis, and keratitis produced by susceptible bacteria.

Amikacin

Eye drop, 0.3%**Chloramphenicol***Eye ointment, 1 %, 5 %**Solution (eye drop), 0.4 %, 0.5 %, 1 %, 5 %***Indications:** topical treatment of superficial ocular infections involving the conjunctiva and/or cornea caused by susceptible organisms.**Contraindications:** previous allergy or toxic reaction to chloramphenicol**Side effects:** hypersensitivity (burning, itching, redness, skin rash, swelling or other signs of irritation not present before therapy)**Dose and Administration:****Adult and Child:** *Ointment topical:* to the conjunctiva, a thin strip (approximately 1cm) of ointment every three hours or more frequently;*Solution (eye drops), topical:* to the conjunctiva, 1 drop every one to four hours.**Storage:** at room temperature in a tight container, protect from freezing.**Ciprofloxacin****Eye drop, 0.3%****Indications:** treatment of corneal ulcer and conjunctivitis caused by susceptible organisms.**Dose and Administration:****Corneal ulcers:** Day 1, instil 1 drop every 15 minutes for 6 hours, then 1 drop every 30 minutes for the rest of the day; day 2, 1 drop every hour; day 3-14, 1 drop 4 hourly. Drops are instilled while awake, but extra doses may be required during the night for the first 24-48 hours.**Bacterial conjunctivitis:** Instil 1 drop 2 hourly for 2 days, then 1 drop 4 hourly for 5 days, while awake.**Erythromycin***Eye ointment, 0.5 %**Eye drop, 1%***Indications:** topical prophylaxis of neonatal conjunctivitis caused by *Chlamydia trachomatis*. It is also used in the topical treatment of superficial ocular infections of the conjunctiva and/or cornea caused by susceptible organisms.**Cautions:** intolerance to erythromycin.**Side effects:** eye irritation not present before therapy.**Dose and Administration:****Adult and Child:** *ocular infection topical:* to the conjunctiva, a thin strip (approximately 1cm) of ointment up to six times a day, depending on the severity of the infection.*Neonatal conjunctivitis/Ophthalmia neonatorum: topical:* to each conjunctiva, a thin strip (approximately 0.5 to 1 cm) of ointment as a single dose following cesarean or vaginal delivery.**Storage:** at room temperature. Protect from freezing.**Gatifloxacin**

Eye drop, 0.3%**Indications:** bacterial conjunctivitis**Side effects:** conjunctival irritation, keratitis, lacrimation increased, papillary conjunctivitis.**Dose and Administration:** Adult and Child ≥ 1 year: Ophthalmic:**Day 1 and 2:** Instill 1 drop into affected eye(s) every 2 hours while awake (maximum: 8 times/day)**Day 3-7:** Instill 1 drop into affected eye(s) up to 4 times/day while awake**Storage:** at room temperature.**Gentamicin***Solution (eye drop), 0.3 %***Indications:** blepharitis; bacterial conjunctivitis; systemic infections.**Cautions:** prolonged use may lead to skin sensitization and emergence of resistant organisms including fungi; discontinue if purulent discharge; inflammation or exacerbation of pain.**Contraindications:** hypersensitivity to aminoglycoside group of antibiotics.**Side effects:** burning, stinging, itching, dermatitis.**Dose and Administration:***Mild to moderate infection: by instillation into the eye:* **Adult and Child:** 1 drop every 2 hours, reducing frequency as infection is controlled, then continue for 48 hours after healing is complete.*Severe infection: by installation in to the eye:* **Adult and Child:** 1 drop every hour, reducing frequency as infection is controlled, then continue for 48 hours after healing is complete.**Moxifloxacin****Eye drop, 0.3%****Indications:** bacterial conjunctivitis**Cautions:** eye drops should not be injected subconjunctivally or introduced directly into the anterior chamber of the eye. Contact lenses should not be worn during therapy.**Side effects:** conjunctivitis, dry eye, ocular discomfort, ocular hyperemia, ocular pain, ocular pruritus, subconjunctival hemorrhage, tearing, visual acuity decreased.**Dose and Administration:** Adult and Children ≥ 1 year: Instill 1 drop into affected eye (s) 3 times/day for 7 days**Neomycin Sulphate***Eye ointment 0.5 %, 2 %***Indications:** treatment of superficial ocular infections, involving the conjunctiva and, or cornea, caused by susceptible organisms. It is also used in the treatment of bacterial blepharitis, blepharoconjunctivitis, bacterial conjunctivitis, bacterial keratitis and bacterial keratoconjunctivitis.**Cautions:** sensitive to neomycin.

Side effects: hypersensitivity (itching, rash, redness, swelling, or other sign of irritation not present before therapy, burning or stinging, blurred vision).

Dose and Administration:

Adult and Child: *topical to the conjunctiva:* a thin strip (approximately 1cm) of ointment every eight to twenty-four hours.

Storage: at room temperature, protect from freezing

Norfloxacin

Eye drop, 0.3%

Ofloxacin

Eye drop, 0.3%

Dose and Administration: Conjunctivitis: 1 drop 2-4 hourly for 2 days, then 1 drop 4 times daily. Treatment should not exceed 10 days.

Corneal ulcer: First 2 days, 1 drop every 30 minutes while awake and 4-6 hours after retiring; next 7-9 days, 1 drop hourly while awake; then 4 times daily until treatment is complete.

Oxytetracycline Hydrochloride

Eye ointment, 0.5

Indications: oxytetracycline (in combination with polymyxin B sulphate) is used topically in the treatment of superficial infections of the eye caused by susceptible bacteria.

Cautions: sensitive to tetracyclines.

Side effect: burning, stinging, increased lachrymation, foreign body sensation.

Dose and Administration:

Adult: *topical, in the lower conjunctival sac of the infected eye:* a thin amount of ophthalmic ointment every 2-12 hours daily.

Storage: at room temperature in a collapsible ophthalmic ointment tube, protect from freezing.

Polymyxin B and Bacitracin

Eye ointment, polymyxin B 100, 000 units and Bacitracin 500,000 units

Indications: treatment of superficial infections caused by susceptible organisms.

Dose and Administration: Adult and Child:

Instil ½ ribbon in the affected eye(s) every 3 - 4 hours for acute infections or 2 -3 times/day for mild to moderate infections for 7 - 10 days.

Rifamycin

Solution (eye drop), 1%

Rifamycin is an antibacterial that has been used in the treatment of infections caused by susceptible organisms such as staphylococci. It is given by local instillation and topical application.

Silver Nitrate

Solution (eye drop), 1 %

Indications: prophylaxis of neonatal conjunctivitis (*Ophthalmia neonatorum*) due to *Neisseria gonorrhoea*, if tetracycline not available.

Cautions: avoid use of old, concentrated drugs; wipe excess drops from skin near the eye to prevent staining.

Side effects: skin and mucous membrane irritation, mild conjunctivitis; repeated use may cause skin discoloration, corneal cauterization and blindness.

Dose and Administration:

Prophylaxis of neonatal conjunctivitis: by instillation into the eye, Newborn at birth after cleansing eyes with sterile gauze, 2 drops into each eye.

Tetracycline

Eye ointment, 1 %

Solution (eye drop), 1 %

Indications: for the treatment of superficial bacterial infections of the eye (*Purulent conjunctivitis*), trachoma, and for the prophylaxis of gonococcal and nongonococcal ophthalmia neonatorum.

Dose and Administration: *Topical*, to the conjunctiva.

Purulent Conjunctivitis: Adult and Child: Apply a thin strip (approximately 1cm) of ointment onto the infected eye every 6 hours daily for 5 days.

Trachoma: Adult and Child: Apply a thin strip of ointment onto each eye twice daily for a minimum of 6 weeks.

Prophylaxis of gonococcal and nongonococcal ophthalmia neonatorum: Apply a thin strip of ointment onto each of neonates shortly (no later than 1 hour) after delivery.

Storage: at room temperature.

Tobramycin

Solution (eye drop), 0.3 %

Indications: topically used to treat superficial ophthalmic infections caused by susceptible bacteria.

Cautions, Contraindications and Drug interactions; see under section 7.1.2.

Side effects: conjunctival erythema, lid itching, lid swelling.

Dose and Administration: Adult and Child ≥ 2 months: Instill 1 - 2 drops of solution every 4 hours; for severe infections instill 2 drops every 30 - 60 minutes initially, then reduce to less frequent intervals.

Storage: store at 2-30 °C.

15.3.2. Antivirals

Herpes simplex virus may cause serious sight-threatening eye infections – vesicular lesions of the eyelids, conjunctivitis, punctate keratitis or epithelial keratitis (e.g. in the form of dendritic ulceration), stromal keratitis and uveitis. These conditions should be treated by specialist ophthalmologists.

Acyclovir is the drug of choice for all herpes simplex eye infections. It is highly active in vitro against herpes simplex (HSV) types I and II. Penetration through the cornea is sufficient to provide antiviral concentrations in the aqueous

humour. It is converted to the active compound inside herpes infected cells and does not act (nor exert toxic effects) on non-infected cells. With usual doses, clinically significant amounts are not absorbed systemically.

Acyclovir

Eye ointment, 3 %

Indications: used for herpes simplex keratitis.

Side effects: transient stinging which occasionally may follow immediately after application. Aciclovir has caused superficial punctate keratopathy, but this has healed without apparent sequelae.

Dose and Administration:

The ointment should be placed inside the lower conjunctival sac 5 times a day, at about 4 hourly intervals. Treatment should be continued for 14 days, or at least 3 days after healing is complete, whichever is shorter.

Storage: store at room temperature.

Idoxuridine

Solution (eye drop), 0.1 %

Eye ointment, 0.5 %

Indications: keratitis or keratoconjunctivitis caused by herpes simplex.

Cautions: existing deep ulceration of cornea; prolonged or excessive use may damage the cornea; do not exceed frequency or duration of treatment, discontinue if no relief within 7 days; concurrent use of a corticosteroid.

Contraindications: pregnancy; concurrent use of an eye preparation containing boric acid.

Side effects: burning, itching, irritation, pain, conjunctivitis, oedema, inflammation, photophobia, pruritus, and rarely allergic reactions.

Dose and Administration:

Herpes simplex keratitis: by *instillation* into the eye, 1 drop every hour during daytime and every 2 hours at night-time, reducing frequency as infection is controlled to 1 drop every 2 hours during daytime and every 4 hours at night-time, then continue for 3 - 5 days after healing is complete; maximum length of treatment 21 days; alternatively, by application to the eye, 1 application of ointment every 4 hours during daytime and once at night time (5 applications), then continue for 3 - 5 days after healing is complete; maximum length of treatment 21 days.

Storage: store at room temperature.

Trifluridine

Solution (eye drop), 1 %

Indications: treatment of herpetic keratitis and infections with stromal involvement.

Cautions: hypersensitivity to trifluridine.

Side effects: transient irritation, itching and oedema; allergic reactions.

Dose and Administration: Instil 1 drop 2 hourly upto a maximum of 9 times daily, until complete reepithelialisation has occurred; then reduce to 4 hourly, continued for a few days.

Storage: store between 2 °C and 8 °C.

Vidarabine

Eye ointment, 3%

Indications: treatment of herpes simplex keratitis and keratoconjunctivitis.

Side effects: irritation and pain of the eye; superficial punctate keratitis, photophobia, lachrymation, and occlusion of the lachrymal duct.

Dose and Administration: applied 5 times daily every 3 hours until corneal re-epithelialisation has occurred, then twice daily for a further 7 days to prevent recurrence.

Storage: store in airtight containers.

15.3.3. Antifungal

Fungal infections of the cornea can cause serious sight-threatening disease. Fungal ulcers are often associated with excessive and prolonged topical corticosteroid use or eye injuries involving vegetative material. The ulcers are indolent and require specialist management.

Topical preparations may need to be made by a pharmacist, e.g. miconazole, amphotericin B.

Natamycin is topical ophthalmic preparation. Effective concentrations are produced within the corneal stroma, but not in intraocular fluid. Systemic absorption is not expected.

Amphotericin B

Eye ointment, 0.3%, 2%

Econazole

Eye drop, 1%

Natamycin

Solution (eye drop), 5 %

Indications: conjunctivitis and fungal blepharitis, fungal keratitis.

Cautions: concurrent application of natamycin and a topical corticosteroid.

Contraindications: hypersensitivity to the drug.

Side effects: eye irritation, redness, or swelling.

Dose and Administration: Adult:

Fungal keratitis: Instill 1 drop 1 - 2 hourly, reduced to 6 - 8 times daily after 3 - 4 days, and generally continued for 14 - 21 days.

Fungal blepharitis and Conjunctivitis: Instillation 4 - 6 times daily may be sufficient.

Shake well before use.

Storage: store at room temperature.

Nystatin*Eye ointment, 1%*

15.4. Anti-inflammatories**Corticosteroids**

Although corticosteroids play an important role in the management of some ocular disorders, the widespread use of corticosteroid-containing eye drops for minor inflammatory eye conditions has led to serious complications. It is therefore recommended that they should be reserved for the treatment of uveitis, severe allergies and for post-operative use, and then when regular slit lamp examinations and tonometry can be performed to monitor the effect of treatment and identify complications.

Several preparations are available for topical application, including betamethasone, dexamethasone, fluorometholone and prednisolone; they may also be administered sub-conjunctivally. For conditions involving the posterior eye segment, addition of systemic corticosteroids may be required.

Indications: corticosteroid-responsive allergic and inflammatory conditions of the palpebral and bulbar conjunctiva, cornea, and anterior segment of the globe.

Contraindications: ocular fungal diseases; herpes simplex keratitis, tuberculosis, viral disease, cataracts, diabetes mellitus, open angle glaucoma, conjunctiva.

Drug interactions: antiglaucoma agents, anticholinergics, especially atropine and related compounds.

Side effects: decreased vision, watering of the eyes, burning, stinging, redness; glaucoma, ocular hypertension, optic nerve damage, nausea, eye pain, vomiting.

Preparations include:**Dexamethasone***Solution (eye drop), 0.1 %*

Dose and Administration: 1 or 2 drops of a 0.1 % solution upto six times a day.

Storage: store at room temperature.

Fluorometholone*Eye Ointment, 0.1 %**Eye drop, 1%*

Dose and Administration: *Topical, to the conjunctiva:* a thin strip of a 0.1 % ointment one to three time a day.

Storage: store at room temperature.

Loteprednol*Eye drop, 0.1%, 0.2%, 0.5%*

Methylprednisolone Acetate

Injection, 40 mg/ml in 1ml ampoule

Prednisolone Acetate

Suspension (eye drop), 0.25 %, 1 %

Dose and Administration: *Topical, to the conjunctiva:* 1 or 2 drops of a 0.12 to 1% suspension two to four times a day.

Non steroidal anti-inflammatory drugs

Non-steroidal anti-inflammatory agents (NSAIDs) inhibit prostaglandin synthesis, thereby reducing prostaglandin-mediated intraocular inflammation initiated by surgical trauma. Pre-operative treatment with NSAIDs prevents intra-operative miosis and reduces the disruption of the blood-aqueous barrier which results in postoperative inflammation. They are also used in the treatment of cystoid and other types of macular oedema, pain relief after excimer laser photorefractive surgery, and in mild superficial inflammatory conditions such as episcleritis. Agents currently available include diclofenac, flurbiprofen.

Bromfenac

Eye drop, 0.1%

Diclofenac sodium

Eye ointment, 0.1%

Flurbiprofen

Solution (eye drop), 0.03 %

Indications: inflammation, miosis (during ophthalmic surgery), cystoid macular edema, photophobia.

Cautions: epithelial herpes simplex keratitis, hemophilia or other bleeding problems.

Drug interactions: acetylcholine chloride; anticoagulant, coumarin or heparin; epinephrine (ophthalmic).

Contraindications: allergic reaction to aspirin or other systemic or ophthalmic NSAIDs.

Side effects: keratitis, elevated intraocular pressure, corneal edema, chemosis, bleeding in eye; redness in eye.

Dose and Administration:

Miosis inhibitor, in ophthalmic surgery: Topical, to the conjunctiva: 1 drop every thirty minutes, beginning two hours prior to surgery, for a total of 4 drops.

Treatment of inflammation following ophthalmic surgery: Topical, to the conjunctiva: 1 drop every four hours for one to three weeks.

Storage: store at room temperature.

Indomethacin

Eye drop, 0.5%, 1%

Ketrolac

Eye drop, 0.4%, 0.5%

Suprofen

Eye drop, 1%

15.5. Anti-infective/Anti-inflammatory combination.

Many antibacterial preparations also incorporate a corticosteroid but such mixtures should not be used unless a patient is under close specialist supervision. In particular they should not be prescribed for undiagnosed 'red eye' which is sometimes caused by the herpes simplex virus and may be difficult to diagnose.

Chloramphenicol + Dexamethasone

Eye drop, 0.5% + 0.1%

Gentamicin + Dexamethasone

Eye drop, 0.3% + 0.1%

Neomycin + Dexamethasone phosphate

Solution (eye drop), 0.5% + 0.05%; 0.5% + 0.1%

Indications: treatment of steroid responsive inflammatory conditions of the palpebral and bulbar conjunctiva, lid, cornea, and anterior segment of the globe.

Dose and Administration: instill 1-2 drops in eye(s) every 3-4 hours.

Neomycin + Hydrocortisone + Polymixin B Sulphate

Suspension (eye drop), 3.5mg (base) + 10mg + 10,000 units (base) in each ml

Indications: steroid-responsive inflammatory condition for which a corticosteroid is indicated and where bacterial infection or a risk of bacterial infection exists.

Dose and Administration: Duration of use should be limited to 10 days unless otherwise directed by the physician.

Adult and Child: Instill 1-2 drops 2-4 times/day, or more frequently as required for severe infections; in acute infections; instill 1-2 drops every 15-30 minutes gradually reducing the frequency of administration as the infection is controlled.

Flucocortolone pivalate + Chloramphenicol

Solution (eye drop), 0.5%+0.2%

Gentamycin+ Betamethasone

Solution (eye drop), 3mg+1mg in each ml

Oxytetracycline Hydrochloride+ Hydrocortisone Acetate + Polymixin B sulphate*Solution (eye drop), 5 mg + 15 mg + 10,000 units in each ml.***Indications:** inflammation of the eye; and see notes above (tetracycline).**Dose and Administration:**

Apply 1 drop at least every 2 hours then reduce frequency as infection is controlled and continue for 48 hours after healing.

Tobramycin + Dexamethasone*Eye drop, 0.3% + 0.1%***15.6. Anesthetics, Local**

Topical local anesthetics are employed for simple ophthalmological procedures and for short operative procedures involving the cornea and conjunctiva. Local anesthetics are generally administered as acidic solutions of the water - soluble hydrochloride salts; alkalisation of these solutions may increase the speed of onset and reduce the pain associated with injection.

As with any other drugs local anesthetics are contraindicated in patients with known hypersensitivity. Prolonged use of topical anesthetics in the eye can lead to severe contact keratitis and cornea damage. Patients should be warned not to rub or touch the eye while anesthesia persists and the anaesthetized eye should be protected from dust and bacterial contamination.

Benoxinate hydrochloride*Solution (eye drop), 0.4 %***Indication:** local anesthetic**Bupivacaine Hydrochloride***Injection, 0.5 %, 0.75 % in 10 ml ampoule***Indication:** local anesthetic**Procaine Hydrochloride***Injection 2 % in 2 ml ampoule***Indication:** local anesthetic**Propanocaine Hydrochloride***Solution (eye drop), 0.5 %**Injection, 2 %***Indications:** local anesthetic**Tetracaine Hydrochloride***Solution (eye drop), 0.5 %***Indications:** short-acting local anaesthesia of cornea and conjunctiva.

Cautions: patients should be warned not to touch or rub the eye(s) until the anesthesia has worn off. If signs or symptoms of allergy or sensitivity occur during treatment with ophthalmic tetracaine hydrochloride preparations, the drug should be discontinued. Avoid prolonged use (cause of severe keratitis, permanent corneal opacification, scarring, delayed corneal healing).

Contraindications: hypersensitivity to tetracaine hydrochloride or other local anesthetics of the ester type, or to p-aminobenzoic acid or its derivatives, or to any ingredient in the formulation.

Side effects: stinging and rarely, local idiosyncratic reactions including lachrymation, photophobia and chemosis,

Dose and Administration:

Local anaesthesia, by instillation into the eye: **Adult** and **Child:** 1 drop.

Storage: in tight, light-resistant containers at room temperature: freezing should be avoided.

15.7. Antiallergics, Diagnostics and Miscellaneous Agents

Acetylcholine Chloride

Powder for injection (intra-ocular), 100 mg

Indications: produces complete miosis in cataract surgery, keratoplasty, iridectomy and other anterior segment surgery where rapid miosis is required.

Cautions: acute cardiac failure, bronchial asthma, peptic ulcer, hyperthyroidism, GI spasm, urinary tract obstruction, and Parkinson's disease.

Drug interactions: tacrine, flubiprofen and suprofen.

Contraindications: hypersensitivity to acetylcholine chloride, acute iritis and acute inflammatory disease of the anterior chamber.

Side effects: bradycardia, hypotension, altered vision, transient ventricular opacities, dyspnea.

Dose and Administration: **Adult:** *Intraocular:* 0.5 - 2 ml of 1 % injection (5 - 220 mg) instilled into anterior chamber before or after securing one or more sutures.

Storage: store at room temperature.

Acetylcysteine + Hypermellose

Eye drop, 5% + 0.35%

Alphachymotrypsin

Powder for injection, 300 units

Chymotrypsin is a proteolytic enzyme that has been used in ophthalmology for the dissection of the zonule of the lens, thus facilitating intracapsular cataract extraction and reducing trauma of the eye. For this purpose a solution of chymotrypsin in a sterile diluent such as sodium chloride 0.9% has been injected to irrigate the posterior chamber.

Azelastin

Eye drop, 0.05%

Balanced salt solution

Solution (eye drop), 15 ml, 30 ml, 500 ml

Fluorescein sodium

Eye paper (sterile strip)

Injection (IV), 5 % in 10 ml ampoule

Indications: demonstrates defects of corneal epithelium, diagnostic aid in ophthalmic angiography.

Cautions: transient blurring of vision - advise patient not to operate machinery or drive until vision is clear.

Contraindications: avoid use with soft contact lenses.

Dose and Administration:

Strips: moisten strip with sterile water. Place moistened strip at the fornix into the lower cul-de-sac close to the punctum. For best results, patient should close lid tightly over strip until desired amount of staining is obtained. Patient should blink several times after application.

Injection: prior to use, perform intradermal skin test; have epinephrine 1:1000, an antihistamine, and oxygen available.

Adult: 500 - 750 mg injected rapidly into antecubital vein.

Child: 3.5 mg/lb (7.5 mg/kg) injected rapidly into antecubital vein.

Glycerin

Eye drop

Hydroxypropyl Methyl Cellulose (Hypromellose)

Solution (eye drop), 0.3%, 0.5%, 1%, 2.5%

Indications: as a vehicle for eye drops and as artificial tears and contact lens solution.

Levocabastine

Eye drop, 0.05%

Lissamine green

Eye drop, 1%

Nedocromil

Eye drop, 2%

Oxymetazoline Hydrochloride

Solution (eye drop), 0.025%, 0.05%

Oxymetazoline Hydrochloride is a direct-acting sympathomimetic agent which has a vasoconstrictor effect on mucosal blood vessels when applied topically. Oxymetazoline may occasionally cause local stinging or burning, sneezing, and dryness of the mouth and throat. Prolonged or excessive use may cause rebound congestion and drug-induced rhinitis.

A 0.025% or 0.05% solution of oxymetazoline hydrochloride may be instilled in to the eye as a conjunctival decongestant.

Rose benegal

Solution (eye drops), 1%

It is used to detect epithelial defects of the cornea and conjunctiva, especially in dry eyes. Unlike fluorescein, which stains epithelial defects, rose bengal will stain damaged cells and give a clearer indication of the extent of damage. It is irritating to the eyes.

Sodium Cromoglycate

Eye ointment, 4%

Solution (eye drop), 2%

Indications: allergic conjunctivitis, vernal keratoconjunctivitis.

Side effects: transient burning and stinging

Dose and Administration: apply eye drops 4 times daily, eye ointment 2-3 times daily.

Tetrahydrozoline Hydrochloride

Solution (eye drop), 0.05 %

Tetrahydrozoline is a sympathomimetic agent with alpha-adrenergic activity. It acts as a local vasoconstrictor and when applied topically to mucous membranes it reduces swelling and congestion. Prolonged or excessive use may cause rebound congestion. Solution of tetrahydrozoline hydrochloride containing 0.05 % is used as a conjunctival decongestant.

Trypan blue

Injection, 0.5%

Zinc sulphate

Eye drop, 0.25%

16. EAR, NOSE, AND THROAT PREPARATIONS

16.1. Nasal and Oropharyngeal, Preparations

Symptoms of nasal congestion associated with vasomotor rhinitis and the common cold can be relieved by the short-term use (usually not longer than 7 days) of decongestant nasal drops and sprays. These all contain sympathomimetic drugs which exert their effect by vasoconstriction of the mucosal blood vessels which in turn reduces oedema of the nasal mucosa. They are of limited value because they can give rise to a rebound congestion (rhinitis medicamentosa) on withdrawal, due to a secondary vasodilatation with a subsequent temporary increase in nasal congestion. Ephedrine nasal drop is the safest sympathomimetic preparation and can give relief for several hours. The more potent sympathomimetic drugs xylometazoline, and oxymetazoline are more likely to cause a rebound effect. All of these preparations may cause a hypertensive crisis if used during treatment with a monoamine oxidase inhibitor. Mild cases of allergic rhinitis are controlled by topical nasal corticosteroids or oral antihistamines; systemic nasal decongestants are of doubtful value. Antazoline are often used with a vasoconstrictor such as naphazoline for the treatment of rhinitis.

Non-allergic watery rhinorrhoea often responds well to treatment with ipratropium bromide. Inhalations of warm moist air are useful in the treatment of symptoms of acute infective conditions, and the use of compounds containing volatile substances such as menthol and eucalyptus may encourage their use.

Mouthwashes have a mechanical cleansing action and freshen the mouth. Providone - Iodine mouthwash is useful for mucosal infections but does not inhibit plaque accumulation. It should not be used for periods longer than 14 days because a significant amount of iodine is absorbed.

There is no convincing evidence that antiseptic lozenges and sprays have a beneficial action and they sometimes irritate and cause sore tongue and sore lips. Some of these preparations also contain local anesthetics which relieve pain but may cause sensitization. The throat lozenges are Amyl-metacresol + Dichlorobenzyl Alcohol and Dequalinium Chloride.

The most common cause of a sore throat is a viral infection which does not benefit from anti-infective treatment. Fungal mouth infections such as candida albicans which are sometimes associated with the use of broad - spectrum antibiotics or of cytotoxics; withdrawing the causative drug may lead to rapid resolution. Otherwise, an antifungal drug may be effective. Of the antifungal drugs used for mouth infections, miconazole and nystatin is not absorbed from the gastro-intestinal tract and is used by local application in the mouth. Miconazole occupies an intermediate position since it is used by local application in the mouth but is also absorbed to the extent that potential interactions need to be considered.

Amyl Meta-cresol + Dichlorobenzyl Alcohol

Lozenges, 0.6 mg + 1.2 mg

See notes above

Antazoline + Naphazoline*Solution (nose drop), 0.5 % + 0.025 %***Indication:** allergic rhinitis

See notes above

Beclomethasone Dipropionate*Nasal spray (aerosol), 50 mcg/dose***Indications:** prophylaxis and treatment of seasonal (intermittent) and non-seasonal (persistent) allergic rhinitis. Sometimes useful in non-allergic (vasomotor) rhinitis.**Cautions:** systemic infections or ocular herpes simplex.**Drug interactions:** salmeterol.**Contraindications:** status asthmaticus.**Side effects:** agitation, depression, dizziness, angioedema, rash, urticaria, burning, sneezing, nasal stuffiness, nose bleedings, cough, wheezing.**Dose and Administration: Adult:** 100 mcg (2 sprays) into each nostril twice daily, or 50 mcg into each nostril 3-4 times daily.**Storage:** store at room temperature. Do not store near heat or open flame.**Dequalinium chloride***Lozenge, 0.25 ml*

See notes above

Ephedrine Sulphate*Solution (Nose drop), 1 %***Indication:** nasal congestion**Cautions:** avoid excessive or prolonged use, caution in infants under 3 months (no good evidence of value - if irritation occurs might narrow nasal passage)**Drug interactions:** anesthetics, antibacterial, antidepressants, antihypertensives, Beta-blockers, dopaminergics.**Side effects:** local irritation, nausea, headache; after excessive use tolerance with diminished effect; rebound congestion; cardiovascular effects also reported.**Dose and Administration:**

Instill 1 - 2 drops into each nostril up to 3 or 4 times daily when required.

Gentian Violet*Solution, 1 %***Indications:** candidal infections of the mouth and throat (thrush).**Cautions:** avoid swallowing of the solution. Infants should be turned face downward after application to minimize the amount of drug ingested.**Side effects:** irritation or sensitivity reactions, or ulceration of mucosal membranes may occur. Esophagitis, laryngitis, or trachitis may result from swallowing the solution.**Dose and Administration:** *Topical*, to the oral mucous membranes.

It should be painted only on individual lesions with cotton.

Adult and Child: every 8 – 12 hours daily for 3 years.

Storage: at room temperature, in tight containers.

Hexetidine [☞]

Solution, 0.1 %

Indications: used as a 0.1% mouthwash for local infection and/or hygiene.

Side effects: allergic contact dermatitis and alterations in taste and smell.

Dose and Administration: Rinse with 15-30ml, undiluted, for 30 seconds twice daily.

Hydrogen peroxide

Solution, 3 %

Indications: hydrogen peroxide 1.5% solution is used as an antiseptic and deodorant mouthwash. By its effervescence, it may liberate debris from inaccessible cavities and aid in proper cleansing of the buccal cavity.

Dose and Administration: dilute to 1.5% before use as a mouthwash.

Menthol + Eucalyptus oil + Light Magnesium carbonate

Inhalation, 2 % + 10 % + 7 %

Indications: for relief of nasal obstruction in acute rhinitis or sinusitis and to promote warm moist air inspiration in bronchitis.

Cautions: boiling water should not be used for the preparation.

Dose and Administration: add one teaspoonful to a pint of hot, not boiling, water and inhale the vapour.

Miconazole

Oral Gel, 25 mg/ml

Indications: oral fungal infections

Cautions: pregnancy, avoid in porphyria

Drug interactions: anticoagulants, antidiabetics (sulphonylureas), phenytoin, cisapride, and cyclosporin.

Side effects: mild gastrointestinal disturbances reported

Dose and Administration:

Place 5 – 10 ml in the mouth after food and retain near lesions 4 times daily; child under 2 years 2.5 ml twice daily, 2 – 6 years 5 ml twice daily, over 6 years 5 ml 4 times daily

* Localized lesions smear small amounts of gel on affected area with clean finger

Storage: Store at room temperature protected from light

[☞] Any mouth wash and antiseptic preparations are also acceptable

Mometasone furoate*Intranasal spray, 0.05%*

Indications: treatment of nasal symptoms of seasonal and perennial allergic rhinitis in adults and children ≥ 2 years of age; prevention of nasal symptoms associated with seasonal allergic rhinitis ≥ 12 years of age and adults; treatment of nasal polyps in adults.

Cautions: use caution if replacing systemic corticosteroid; patients with systemic infections, active or quiescent tuberculosis infection, or ocular herpes simplex.

Side effects: headache, pharyngitis, cough, epistaxis, viral infection, chest pain, dysmenorrhea, vomiting, myalgia, conjunctivitis, otitis media, upper respiratory tract infection, sinusitis, asthma, bronchitis, nasal irritation, rhinitis, wheezing.

Dose and Administration: *Nasal spray:*

Allergic rhinitis:

Adult and Child ≥ 12 years: 2 sprays in each nostril daily; when used for the prevention of allergic rhinitis, treatment should begin 2-4 weeks prior to pollen season.

Child 2-11 years: 1 spray in each nostril daily.

Nasal polyps: **Adult:** 2 sprays in each nostril twice daily; 2 sprays once daily may be effective in some patients.

Storage: store at room temperature and protect from light.

Nystatin*Pastilles, 100,000 units**Suspension, 100,000 units/ml*

Indications: oral and perioral fungal infections

Contraindications: hypersensitivity to the drug or any ingredient in the respective formulation.

Side effects: nausea, vomiting, and diarrhoea, oral irritation and sensitization reported

Dose and Administration:

100,000 units 4 times daily after food. Usually for 7 days (continued for 48 hours after lesions have resolved). Nystatin 100,000 units up to four times daily may be given to neonates.

Note: Immuno suppressed patients may require higher doses (e.g 500,000 units 4 times daily). The formulation should be kept in contact with the affected area for as long as possible and patients should avoid taking food or drink earlier than one hour after a dose.

Storage: nystatin deteriorates on exposure to heat, light, moisture, or air. Nystatin oral suspension should be stored in tight, light resistant containers at room temperature; freezing of the oral suspension should be avoided.

Oxymetazoline Hydrochloride*Nasal solution, 0.05%*

Indications: short-term symptomatic relief of nasal congestion.

Cautions: hyperthyroidism, ischaemic heart disease, hypertension or diabetes mellitus.

Drug interactions: MAO inhibitors, psycho stimulants, TCA, propranolol, digoxin, quinidine, and halothane.

Side effects: transient blurring or dryness of the mucosa; rebound congestion, and rhinitis medicamentosa with prolonged use, may develop.

Dose and Administration: Adult: Instill into each nostril 1 - 3 times daily (8-12 hourly).

Storage: store at 2-30 °C. Freezing should be avoided.

Phenylephrine

Nose drops, 0.25%, 1%

Indications: symptomatic relief of nasal and eustachian tube congestion.

Cautions: breast-feeding women and children.

Side effects: prolonged use will cause increase in running nose with chronic nasal mucosa swelling. Burning, dryness, or stinging of nasal mucosa may occur rarely.

Dose and Administration: *Intranasal.* Avoid prolonged use, and avoid using more medications than the amount recommended. Rinse dropper with hot water and dry with clean tissue after using.

Adult and Child over 12 year: 2 or 3 drops of the 1% solution into each nostril every 3-4 hours as necessary.

Child 6-12 years: 2-3 drops or 0.25% solution into each nostril every 3-4 hours as necessary.

Storage: at room temperature. In a tight and light-resistant container.

Povidone - Iodine*Solution, 1 %***Indications:** for oral hygiene.**Cautions:** caution should be taken during pregnancy and breast feeding.**Contraindications:** avoid regular use in patients with thyroid disorders and receiving lithium therapy.**Side effects:** idiosyncratic mucosal irritation and hypersensitivity reactions, may interfere with thyroid function tests and with tests for occult blood.**Dose and Administration:** *Mouth wash or gargle.***Adult and Child** over 6 years, up to 10ml undiluted or diluted with an equal quantity of warm water for 30 seconds up to 4 times daily for 14 days.**Pseudoephedrine Hydrochloride***Syrup, 30 mg/ml***Indications:** symptomatic relief or nasal congestion.**Cautions, Side effects, Drug interactions;** see under ephedrine sulphate**Dose and Administrations:***Orally:* **Adult:** 60mg, 3 - 4 times daily, **child,** 2 to 5 years, 15 mg 3 times daily; 6 to 12 years, 30 mg 3 times daily.**Pseudoephedrine + Loratadine***Tablet, 120 mg + 5 mg***Indications:** temporary relief of symptoms of seasonal allergic rhinitis, other upper respiratory allergies, or the common cold.**Dose and Administration:** 1 tablet every 12 hours.**Triamcinolone Acetonide***Oral paste, 0.1 %***Indications:** adjunctive treatment and temporary relief of symptoms associated with oral inflammatory lesions and ulcerative lesions resulting from trauma.**Cautions:** hypothyroidism, cirrhosis, nonspecific ulcerative colitis and patients at increased risk for peptic ulcer disease, hepatic impairment, diabetes, hypertension, osteoporosis, glaucoma, cataracts or tuberculosis.**Drug interactions:** NSAIDs, barbiturates and phenytoin, rifampin, vaccine.**Contraindications:** fungal, viral, or bacterial infections of the mouth or throat.**Side effects:** hypertension, convulsions, fever, atrophy of oral mucosa, burning, and irritation.**Dose and Administration:** *Oral topical:* press a small dab (about ¼ inch) to the lesion until a thin film develops. A larger quantity may be required for coverage of some lesions. For optimal results use only enough to coat the lesion with a thin film; do not rub in.**Storage:** store at room temperature.**Xylometazoline Hydrochloride***Solution (Nasal drop), 0.05 %, 0.1 %***Indications:** nasal congestion

Cautions, Side effects: see under ephedrine sulfate

Dose and Administration:

Adult: *instil* 2 - 3 drops of 0.1 % solution into each nostril 2 - 3 times daily when required; maximum duration 7 days; not recommended for children under 12 years.

Child: over 3 months *instil* 1 - 2 drops of 0.05 % solution into each nostril 1 - 2 times daily when required (not recommended for infants under 3 months of age, doctor's advice only under 2 years); maximum duration 7 days.

16.2. Otic Agents

Otitis externa. Otitis externa or inflammation of the skin of the external auditory canal may be due to infections with bacteria, viruses, or fungi or secondary to skin disorders such as eczema, although more than one factor is often responsible for chronic otitis externa. The treatment includes thorough cleansing and the use of appropriate antibiotic eardrops, often containing a corticosteroid as well, even though some have doubted the value of topical antibiotics. Eardrops containing aminoglycosides, such as gentamicin, neomycin, or polymixins should not be used when the eardrum is perforated because of the risk of ototoxicity.

A solution of acetic acid 2 % acts as an antifungal and antibacterial in the external ear canal. It may be used to treat mild otitis externa but in severe cases an anti-inflammatory preparation with or without an anti-infective drug is required. Solutions containing an anti-infective and a corticosteroid are used for treating cases where infection is present with inflammation and eczema.

Otitis media. Otitis media or inflammation of the middle ear can be acute or chronic, serous (with effusion; secretory) or supportive local treatment of acute otitis media is ineffective and there is no place for drops containing a local anaesthetic. Many attacks are viral in origin and need only treatment with a simple analgesic such as paracetamol for pain. Severe bacterial infection should be treated with systemic antibiotics. The organisms recovered from patients with chronic otitis media are often opportunists living in the debris, keratin, and necrotic bone present in the middle ear and mastoid. Thorough cleansing with an aural suction tube may completely resolve infection of many years duration.

Acute exacerbations of chronic infection may require systemic antibiotics.

Acetic Acid

Solution (ear drop), 2 %

See notes above

Betamethasone

Solution (ear drop), 0.1 %

Indications: management of non-infected inflammatory conditions of the external ear.

Cautions: it should be avoided in the presence of infection, and excessive use also avoided.

Dose and Administration: Instill 2 or 3 drops into the ear every 2 - 3 hours until inflammation is controlled, after which the frequency may be reduced.

Chloramphenicol

Solution (ear drop), 1 %, 2 %, 5 %

Indications: used in the treatment of bacterial infection in otitis externa.

Cautions: over growth with non-susceptible organisms. Avoid prolonged use

Side effects: high incidence of sensitivity reactions to vehicle, optic and peripheral neuritis.

Drug interactions: alfentanil, chlorpropamide, phenytoin, tolbutamide, rifampicin, warfarin, vitamin B₁₂, folic acid

Contraindications: hypersensitive to the drug or any ingredients in the formulations; perforated tympanic membrane. Mothers receiving otic chloramphenicol should not breast-feed their infants.

Dose and Administration:

Chloramphenicol 5 % in propylene glycol; apply 2 – 3 drops into the ear 2 – 3 times daily

Storage: Store below 30°C in a tight container protected from freezing

Clotrimazole

Solution (ear drop), 1 %

Indications: fungal infection in otitis externa.

Side effects: occasional local irritation or sensitivity

Dose and Administration:

Ear, apply 2 - 3 times daily continuing for at least 14 days after disappearance of infection.

Dichlorobenzene + Chlorobutol + Turpentine oil

Solution (ear drop), Dichlorobenzene 2 %, Chlorobutol 5 %, Turpentine oil 10 %

Dose and Administration: *Instill:* 5 drops into the ear 10 - 30 minutes before syringing.

Flumetasone + Clioquinol

Ear drops, Flumetasone pivalate 0.02% + Clioquinol 1%

Indications: treatment of external ear infections caused by bacterial and fungal organisms.

Dose and Administration: Instill 2 - 3 drops into the ear twice daily.

Gentamicin

Solution (ear drop), 0.3 %

Indications: bacterial infection in otitis externa

Cautions: avoid prolong use.

Contraindications: perforated tympanic membrane (see also notes above)

Side effects: local sensitivity

Dose and Administration:

Ear, apply 3 - 4 drops 3 - 4 times daily; reduce frequency when relief obtained.

Hydrogen peroxide

Solution, 3 %

Hydrogen peroxide have antimicrobial properties, which are reduced in the presence of organic matter. Their frothing action makes them useful to loosen and aid removal of debris in the ear canal.

Storage: at room temperature in airtight container. Solutions should not be stored for long periods. Those not containing a stabilizer should be stored at a temperature not exceeding 15 °C. Protect from light.

Neomycin Sulphate + Hydrocortisone + Polymixin B Sulphate

Suspension (ear drop), 3.5 mg + 10 mg + 10,000 units in each ml.

Indications: see section 15.5.

Dose and Administration:

Adult: instill 4 drops 3-4 times/day

Child: instill 3 drops into affected ear 3-4 times/day.

Oxytetracycline

Solution ear drop, 0.5%

Oxytetracycline Hydrochloride + Hydrocortisone Acetate + Polymyxin B sulphate

Suspension (ear drop), 4 mg +15 mg + 10,000 units in each ml.

Indications: bacterial infection with eczematous inflammation in otitis external (see also notes above).

Caution: avoid prolonged use

Contraindications: perforated tympanic membrane.

Side effects: local sensitivity reactions.

17. DERMATOLOGIC AGENTS

17.1. Anti-infective, Topical

Antifungals

Ringworm. Ringworm infection can affect the scalp (tinea capitis), body (tinea corporis), groin (tinea cruris), hand (tinea manuum), foot (tinea pedis, athlete's foot) or nail (tinea unguium). Scalp and nail infection requires systemic treatment; additional topical application of antifungal may reduce the risk of transmission.

Most other local ringworm infections can be treated adequately with topical antifungal preparations. **Benzoic acid** and **Gentian violet** solution are inexpensive and effective fungistatic compounds for the treatment of ringworm infections. Minor skin lesions due to ringworm can be cleared with repeated applications of compound benzoic acid ointment (Whitfield ointment), which combines the fungistatic action of benzoic acid with the keratolytic action of salicylic acid. However, the most effective topical treatment for dermatophyte infections is a cream containing an imidazole such as **clotrimazole**, **ketoconazole** and **miconazole**, which are effective for long established lesions but is more expensive than compound benzoic acid ointment.

Candidiasis. Candida can infect the oral cavity, the vagina or the skin. The most severe infections of candida are now seen in patients with HIV infection. Candidal skin infections may be treated with topical imidazole antifungals, **clotrimazole**, **ketoconazole**, **miconazole**. Topical application of **nystatin** is also effective for candidiasis but it is ineffective against dermatophytosis. Refractory candidiasis requires systemic treatment.

Pityriasis versicolor. Pityriasis (tinea) versicolor is caused by a commensal yeast. It may be treated topically with a course of **selenium sulphide** repeated after one month. Topical imidazole antifungals and topical terbinafine are alternatives but large quantities may be required. If topical therapy fails or if the infection is widespread, pityriasis versicolor is treated systemically with an azole antifungal. Relapse is common, especially in immunocompromised.

Choice of Antifungal formulation.

Lotions or sprays are suitable for application to large and hairy areas. Ointments are generally used on dry areas; they are best avoided on moist skin. Creams are cosmetically more acceptable than ointments and they are best suitable for moist areas.

Paints and solutions for application to the nail are occasionally effective for early dystrophy in onychomycosis. Dusting powders are of little therapeutic value in the treatment of fungal skin infections and may cause skin irritation; they may have some role in preventing re-infection.

Cautions. Contact with eyes and mucous membranes should be avoided.

Side effects. Occasional local irritation and hypersensitivity reactions include mild burning sensation, erythema, and itching. Treatment should be discontinued if these are severe.

Benzoic Acid + Salicylic Acid (White field's Ointment)

Ointment, 6 % + 3 %, 12 % + 6 %

Indications: fungal infections of the skin.

Cautions: it should not be applied to broken or inflamed skin.

Side effects: skin irritation and dryness may occur.

Dose and Administration: *Topical*, to the skin for several weeks until the infected stratum is shed. Prolonged use should be avoided and irritation of the skin occurs.

Apply sparingly to the affected area every 8-12 hours daily.

Storage: at room temperature, in a tight container.

Castellani's paint (Magenta + Boric Acid + Phenol + Resorcinol + Alcohol 90 % + Acetone)

Solution each 100 ml contains: 400 mg + 800mg + 4g + 8g + 8.5 ml + 4 ml (water q.s. 100 ml).

Indications: castellani's paint is applied topically in the treatment of superficial fungal infections of the skin including tinea pedis and ringworm infections.

Cautions: the drug is poisonous when ingested. The drug should not be applied to eroded skin or over extensive areas.

Dose and Administration:

Castellani's paint is applied topically by means of an applicator or swab. The skin should be cleansed with soap and water and thoroughly dried prior to application.

It is usually applied once or twice daily, however, application of the drug 3 times daily may be necessary in chronic or stubborn infections. The solution should be applied no more often than once daily in infantile eczema. In dry, scaling dermatophytoses, application of the solution may be alternated with ointments containing other antifungal agents or keratolytics.

Storage: the solution should be stored in a tight, light resistant container at room temperature; freezing should be avoided.

Clotrimazole

Cream 1 %

Solution 1 %

Topical powder, 1%

Mouth paint, 1%

Indications: topical clotrimazole is indicated in the treatment of cutaneous candidiasis (moniliasis) caused by *Candida albicans*.

It is also indicated for treatment of *tinea corporis* (ring worm of the body), *tinea cruris* (ringworm of the groin, jock itch), and *tinea pedis* (ringworm of the foot; athlete's foot).

It is also used in the treatment of *tinea versicolor* (*pityriasis versicolor*, 'sun fungus'), and in the treatment of paronychia, *tinea barbae*, and *tinea capitis*.

Cautions: sensitive to clotrimazole

Side effects: hypersensitivity (skin rash, hives, blistering, burning, itching peeling, redness, stinging, swelling and other sign of skin irritation not present before therapy).

Dose and Administration: **Adult** and **Child:** *topical*, to the skin and surrounding area, two times a day, morning and evening.

Storage: at room temperature in a tight container, protect from freezing.

Gentian Violet

Solution, 0.5 %, 1 %

Indications: for the treatment of skin infections caused by candida and bacteria, and genital candidiasis.

Cautions: It should not be applied on ulcerative lesions of the face.

Side effects: skin or genital irritation may occur. It also stains skin and clothing.

Dose and Administration: *Topical*, to the skin. Do not cover the affected area with dressings after application.

Apply every 8 – 12 hours daily for about 3 days.

Storage: at room temperature, in tight containers.

Isoconazole

Cream, 1%, 2%

Indications: cutaneous mycotic infections.

Cautions, Side effects: see notes above

Dose and Administration: apply twice daily.

Ketoconazole

Cream, 2 %

Ointment

Shampoo, 2 %

Indications: fungal skin infections.

Cautions: patients should be advised to avoid contact of ketoconazole shampoo with the eyes since irritation may occur. Ketoconazole 2 % cream or shampoo should be used with caution in nursing women, during pregnancy and pediatrics.

Side effects: itching, stinging, or irritation not present before therapy for cream and shampoo; contact dermatitis for cream.

Note – Ketoconazole 2 % cream is intended for topical application to the skin only and should not be applied to the eye nor administered intravaginally.

Dose and Administration:

Ketoconazole cream

Adult: *Topical* to the affected skin and surrounding area.

Tinea corporis or *Tinea cruris*, *Tinea pedis* or *Pityriasis versicolor*: once a day.

Candidiasis, cutaneous: once a day. More resistant cases may require twice a day treatment.

Seborrheic dermatitis: two times a day.

Paronychia or *Tinea barbae* or *Tinea capitis*: two or three times a day.

Safety and efficacy have not been established for pediatric use.

Ketoconazole shampoo

Adult:

Dermatitis, seborrheic: *Topical*, twice a week for 2 to 4 weeks. Leave in place for 3 to 5 minutes before rinsing. Prophylaxis: once a week every 1 or 2 weeks

Pityriasis versicolor: *Topical*, to the affected skin and surrounding area(s), as a single application. Leave in place for 5 minutes before rinsing.

Child: safety and efficacy have not been established.

Storage: at room temperature. Protect from freezing.

Miconazole Nitrate

Cream, 2 %

Lotion, 2 %

Tincture, 2 %

Indications: fungal skin infections

Cautions, Side effects: see notes above

Dose and Administration:

Apply twice daily continuing for 10 days after lesions have healed; nail infections, apply 1 – 2 times daily.

Storage: at room temperature in a tight container

Nystatin

Cream, 100,000 IU/g

Ointment, 100,000 IU/g

Powder 100,000 IU/g

Indications: skin infections due to *Candida Spp.* (see also notes above)

Cautions: see notes above

Dose and Administration: Apply 2 – 4 times daily

Storage: in airtight containers at a temperature between 2 and 8°C and protect from light.

Salicylic Acid

Ointment, 2 %, 5 %, 10 %

Indications: treatment of acne vulgaris, seborrheic dermatitis, psoriasis, and common wart (excluding on the face).

Cautions: avoid contact with eyes, mouth, and mucous membranes; avoid application to large areas.

Contraindications: broken or inflamed skin; children under 2 years.

Side effects: stinging, local irritation, and salicylism may occur when large areas are treated particularly in children.

Dose and Administration: *Topical to the skin:*

Apply to affected area every 12-24 hours daily starting with the 2% progressively increasing the concentration up to 5% for *acne vulgaris* and up to 10% for *seborrheic dermatitis*, *psoriasis* and *common wart*. Apply until it gets better.

Storage: at room temperature, in tight containers.

Selenium Sulphide

Suspension, 2.5 %

Indications: seborrheic dermatitis; treatment of tinea versicolor.

Cautions: do not apply to damaged skin (risk of systemic toxicity); avoid contact with eyes; do not use with in 48 hours of applying any type of hair coloring or permanent waving preparation.

Contraindications: children under 5 years.

Side effects: local irritation, hair discoloration or loss; absorption may result in systemic toxicity including tremors, weakness, lethargy, pain in lower abdomen, occasional vomiting (symptoms usually resolve with in 10 days).

Dose and Administration:

Seborrheic dermatitis: massage 5 – 10 mg of suspension in to wet hair and leave for 2 – 3 minutes before rinsing thoroughly; repeat twice weekly for 2 weeks, then once weekly for 2 weeks, and then only when needed.

Note: To minimize absorption, rinse hair thoroughly after use and remove all traces from skin (including nails)

Tinea versicolor: apply the 2.5% lotion to affected area and lather with small amount of water; leave on skin for 10 minutes, then rinse thoroughly; apply every day for 7 days.

Storage: at room temperature. Freezing should be avoided.

Terbinafine

Cream, 1%

Indications: indicated for dermatophyte and yeast infections of the skin and appendages, including tinea versicolor.

Dose and Administration: clean and dry affected area before application. Apply 1-2 times daily until infection is clear (usually 1-2 weeks).

Tolnaftate

Solution, 1%

Indications: tolnaftate is an antifungal agent used topically in the treatment or prophylaxis of various forms of tinea and of pityriasis versicolor.

Note –Tolnaftate is not considered suitable for deep infections in nail beds or hair follicles but it may be used concomitantly with a systemic agent

Cautions: if irritation or hypersensitivity occurs, or if the patient's skin disease does not improve with in 10 days or becomes worse during self medication with tolnaftate, treatment should be discontinued and the patient should consult a physician or pediatricist. Tolnaftate preparations should not come in contact with the eyes.

Side effects: irritation, contact dermatitis.

Dose and Administration: Tolnaftate is applied twice daily for 2 to 6 weeks. Repeat treatment may be required.

Storage: It should be stored in tight container at room temperature. Freezing of the solution should be avoided.

Zinc undecenoate + Undecenoic Acid

Ointment, 20 % + 5 %

Powder, 20 % + 2 %

Powder (aerosol), 20 % + 2 %

Indications: for the treatment of athlete's foot (tinea pedis), jock itch (tinea cruris), and other skin infections caused by dermatophytic fungi (ring worm)

Dose and Administration:

Athlete's foot ringworm: topically: twice daily after cleansing the affected area, for 4 weeks.

Jock itch: topically, twice daily after cleansing the affected area, for two weeks.

Note: - The ointment or cream should be used at night and the powder may be used during the day.

Antibacterial preparations

Staphylococcal infections of the skin such as impetigo, folliculitis, and furunculi and streptococcal infections such as cellulitis and erysipelas are very common where the climate is hot and humid, where standards of hygiene are compromised, and in immunodeficient patients.

Skin infections such as erysipelas and cellulitis systemic antibacterial treatment is more appropriate because the infection is too deeply seated for adequate penetration of topical preparations.

An ointment containing 2% **mupirocin**, which is active against Gram-positive bacteria, is of value, particularly in impetigo.

Mupirocin is not related to any other antibacterial in use; it is effective for skin infections, particularly those due Gram-positive organisms but it is not indicated for pseudomonal infection. Although *Staphylococcus aureus* strains with low-level resistance to mupirocin are emerging, it is generally useful in infections resistant to other antibacterials. To avoid the development of resistance mupirocin should not be used for longer than 10 days and its use in hospital should be avoided if possible.

Infected burns should be treated with **silver sulfadiazine** which is bactericidal against both Gram-positive and Gram-negative organisms. Topical preparations containing **neomycin and bacitracin** are also widely used but these carry a risk of sensitization particularly with continued or repeated use.

Topical use of preparations containing antimicrobials which are widely used systemically should be avoided. These include penicillins, sulfonamides, streptomycin and gentamicin which should be reserved for the systemic treatment of infections because of the possibility of including sensitivity and favouring the emergence of resistant organisms.

Clindamycin Phosphate

Solution 1%

Indications: treatment of severe acne.

Dose and Administration: apply a thin film twice daily.

Clioquinol

Cream, 3%

Ointment, 3%

Indications: topically for treating primary skin infections such as impetigo, or skin conditions complicated by infection.

Side effects: allergic or irritant reactions of the skin occur occasionally; staining of fomites and hair can occur.

Dose and Administration: Apply 2- 3 times daily to affected areas.

Storage: store at a temperature less than 30°C; freezing should be avoided.

Erythromycin

Cream, 2%

Ointment, 1%

Solution, 2%

Indications: treatment of acne vulgaris.

Dose and Administration: Apply over the affected area twice daily after the skin has been thoroughly washed and patted dry.

Storage: store solution at 15-30 °C, and ointment at a temperature less than 27 °C.

Fusidic Acid

Cream, 2%

Indications: for staphylococcal infections.

Cautions: should be used for acute skin infections (5 days) and not for prolonged periods.

Side effects: local hypersensitivity reactions.

Dose and Administration: Apply 3 - 4 times daily.

Gentamicin

Cream, 0.1%

Ointment, 0.3%

Indications: treatment of superficial infections of the skin. Caused by susceptible bacteria.

Cautions: hypersensitivity to the drug.

Dose and Administration: Apply 3 - 4 times/day to affected area.

Storage: store at 2-30 °C.

Metronidazole

Cream, 0.75%, 1%

Gel, 1%

Lotion, 1%

Indications: treatment of inflammatory lesions and erythema of rosacea.

Cautions and Contraindications: A history of hypersensitivity reactions to any of the components. Use with caution in those with blood dyscrasias. Avoid contact with the eyes.

Side effects: tearing of the eyes, transient erythema, dryness, burning and skin irritation.

Dose and Administration: *Acne rosacea: Topical:*

0.75%: Apply and rub thin film twice daily, morning and evening, to entire affected areas after washing. Significant therapeutic results should be noticed within 3 weeks.

1%: Apply thin film to affected area once daily.

Mupirocin

Ointment, 2%

Indications: bacterial skin infection (see also notes above)

Cautions: renal impairment; may sting

Dose and Administration

Skin infection: apply up to 3 times daily for up to 10 days

Note: contains macrogol and manufacturer advises caution in renal impairment

Storage: at room temperature

Neomycin + Bacitracin

Ointment, 4 mg + 500,000 IU

Powder, 0.25 % + 9.5 %

Indications: superficial bacterial infections of the skin due to staphylococci and streptococci

Cautions: avoid application to substantial areas of skin or to broken skin (risk of significant systemic absorption), over growth of resistant organisms on prolonged use.

Side effects: sensitization, especially to neomycin, causing reddening and scaling, anaphylaxis reported rarely; systemic absorption leading to irreversible ototoxicity, particularly in renal impairment.

Dose Administration: Apply thin layer 3 times daily.

Storage: at room temperature.

Nitrofurazone Gauze Dressing

Indications: as an adjunctive therapy for second and third degree burns when resistance to other agents is a real or potential problem.

It is also indicated in skin grafting when bacterial contamination may cause graft rejection or donor site infection, especially in hospitals with a history of resistant bacteria.

Cautions: if over growth of nonsusceptible organisms occur, or if irritation, sensitization, or superinfection develops, treatment should be discontinued. Caution should be taken in patient with renal function impairment.

Side effects: contact dermatitis

Dose and Administration:

Adult:

Burns or Skin infections: Topical directly to lesion or place on gauze depending on the usual dressing technique

Child: safety and efficacy have not been established

Storage: at room temperature in a well-closed container. Protect from freezing.

Silver Sulphadiazine

Cream, 1 %

Indications: prophylaxis and treatment of infection in burns.

Cautions: renal or hepatic impairment; G6PD deficiency; breastfeeding.

Contraindications: hypersensitivity to sulfonamides; pregnancy; neonates.

Side effects: allergic reactions include rashes, burning and itching; argyria and sulfonamide – induced systemic toxicity, including blood disorders following application to large areas or prolonged use; transient leucopenia reported.

Dose and Administration:

Apply using aseptic technique daily (more frequently if volume of exudate is large) whilst there is a possibility of infection, or until healing is complete.

Storage: At room temperature. Discard, if the cream changes its colour (dark) up on storage.

Sodium Fusidate

Ointment, 2 %

Indications: staphylococcal skin infections

Cautions: avoid contact with eyes

Contraindications: hypersensitive to fusidates

Side effects: rarely hypersensitivity reactions

Dose and Administrations: Apply 3 – 4 times daily,

Storage: store in airtight containers at a temperature of 2 °C to 8°C. Protect from light.

Tetracycline

Ointment, 3 %

Indications: bacterial skin infections

Cautions: sensitivity to tetracyclines; over growth with non-susceptible organisms; stains clothing

Side effects: rarely local hypersensitivity reaction

Dose and Administration:

Adult: *Antibacterial (topical): Topical*, to the skin, one or two times a day.

Child: see adult dose.

Storage: store at room temperature in a well-closed container. Protect from freezing.

Scabies and Pediculicides

Permethrine are used for Scabies (*Sarcoptes scabiei*). Aqueous preparations are preferable to alcoholic lotion, which are not recommended owing to irritation of excoriated skin and the genitalia. Older preparations include **benzyl benzoate**, which is an irritant and should be avoided in children; it is less effective than Permethrine.

The itch of scabies persists for some weeks after the infestation has been eliminated and antipruritic treatment may be required. Application of **crotamiton** can be used to control itching after treatment with more effective acaricides, but caution is necessary if the skin is excoriated.

Head and body lice are readily treated with **permethrin**; **malathion** is effective against public lice. **Benzyl benzoate** may be used for all lice infections.

Benzyl Benzoate

Lotion, 25 %,

Indications: scabies; head, body and pubic lice.

Cautions: avoid contact with face, eyes, mucous membranes and urethral meatus. Do not apply to inflamed skin or weeping surfaces; not recommended for children; breastfeeding (withhold during treatment).

Side effects: slight local irritation, transient burning sensation, occasionally rashes. Frequent use causes contact dermatitis.

Dose and Administration:

Scabies: Adult: apply from neck down at night for 2 nights; on each occasion wash off after at least 24 hours.

A single treatment is usually effective but, if necessary, may be repeated after 1 week.

Dilute with an equal amount of water for children (12.5%), and 1 part with 3 parts of water for infants (6%).

Pediculosis: Adult: apply to affected area and wash off 24 hours later; further applications possibly needed after 7 and 14 days.

Storage: At room temperature, in airtight, light resistant containers. Protect from heat.

Crotamiton

Cream, 10 %

Lotion, 10 %

Indications: topical treatment of scabies and pruritus.

Cautions: crotamiton should not be applied to acutely inflamed skin or raw, weeping surfaces. If primary irritation or hypersensitivity occurs, treatment should be discontinued and the drug should be removed with soap and water. Crotamiton should be used during pregnancy only when clearly needed. Contact with the face, eyes, mucous membranes and urethral meatus should be avoided.

Contraindications: a history of sensitivity or allergy to the drug and in those who exhibit a primary irritation response to topically applied medications. Acute exudative dermatoses

Side effects: slight local irritation, allergic skin sensitivity may occur with prolonged use

Dose and Administration:

Crotamiton, in the form of a 10 % cream or lotion is applied topically. The drug should not be administered orally.

A thin layer of the 10 % cream or lotion should be applied uniformly and massaged gently into all skin surfaces from the neck to the toes. A second coat of the cream should be applied after 24 hours.

In adults, 30 g of the cream for one application; a proportionately smaller amount is used in children. Treatment may be repeated after 7 – 10 days if mites appear or new lesions develop. The patient should bath 48 hours after the last application to remove the drug.

Note – Before applying crotamiton, advice the patient to bath with soap and water, taking cares to scrub and remove scaling or crusted detritus, then towel dry.

Storage: It should be stored in tight, light resistant containers at a room temperature.

Gamabenzene Hexachloride (Lindane)

Cream, 1 %

Indications: for treatment of pediculosis (lice) infestation caused by *Pediculus humanus var. capitis* (head louse) and *phthirus pubis* (pubic or crab louse) and their ova.

It is also indicated for the treatment of scabies infestation caused by *Sarcoptes scabies*.

Cautions: caution is required in children and infants. It is not recommended for use in premature neonates. Caution should be taken in patients with convulsive disorders, in those who are sensitive to lindane and in patients with skin rash or raw or broken skin.

Side effects: skin irritation not present before therapy (if it is applied in correctly and repeatedly), itching of skin, CNS toxicity (if absorbed systemically) - convulsions, dizziness, clumsiness, or unsteadiness, fast heartbeat, muscle cramp, nervousness, restlessness, or irritability, vomiting.

Dose and Administration: pediculicide, scabicide - *Topical*, to the skin, as a 1% cream for one application.

Storage: at room temperature in a tight container.

Permethrine

Cream, 5 %

Lotion, 1%, 5%

Indication: scabies, head and body lice

Cautions: do not use on inflamed or broken skin: avoid contact with eyes; breast feeding (with hold during treatment)

Side effects: local irritation; rarely rashes and oedema

Dose and Administration:

Scabies and body lice: apply cream over whole body and wash off after 8 – 12 hours.

Storage: store between 15 and 25°C. Protect from freezing

Note: for external use only.

Sulphur

Ointment, 5 %, 10 %

Indications: for the treatment of seborrheic dermatitis, scabies especially infants under 2 months of age and in pregnant and nursing women. It is also indicated as an aid in the treatment of acne vulgaris.

Cautions: sensitivity to sulfur.

Drug interactions: medicated soaps, acne preparations or preparations containing a peeling agent, such as benzoyl peroxide, resorcinol, salicylic acid, tretinoin, after shave lotions, astringents, perfumed toiletries, shaving creams or

lotions, cosmetics, isotretinoin, medicated cosmetics or “cover-ups”, topical mercury compounds.

Side effect: skin irritation not present before therapy, redness and peeling of skin.

Dose and Administration:

Adult and Child (>2 years)

Antiacne agent: topical, to the skin, as a 0.5% ointment as needed.

Antiseborrheic or keratolytic: topical, to the skin, as to 10% ointment once or two times a day.

Scabicides: Topical, to the entire body from the neck down, as 6% sulfur in petrolatum at bedtime for 3 nights, patients may bath before each application and should bath after 24 hours following the last application to remove the drug.

Storage: at room temperature, protect from freezing

Antiviral

Acyclovir

Ointment, 5%

Indications: treatment of mucocutaneous herpes simplex infections, herpes labialis, for serious skin and mucosal (including genital) herpetic infections.

Cautions: indiscriminate use of topical aciclovir may result in the emergence of resistance. It has no role in the treatment of herpes zoster.

Side effects: mild pain, burning or stinging often occurs when applied to ulcerated lesions. Erythema, itch, mild dryness and skin hypersensitivity rashes occur.

Dose and Administration: *topical:* **Adult:** ½ inch ribbon of ointment for a 4 inch square surface area every 3 hours (6 times/day) for 7 days.

Storage: store at room temperature.

Others

Fluorouracil

Cream, 2%, 4%

Indications: management of actinic or solar keratoses and superficial basal cell carcinomas.

Dose and Administration: apply 10 minutes after washing, rinsing, and drying the affected area. Apply using fingertip (wash hands immediately after application) or nonmetal application. Avoid eyes, nostrils, and mouth. Do not cover area with an occlusive dressing.

Storage: store at controlled room temperature.

17.2. Anti-Inflammatories, Topical

Topical corticosteroids often produces dramatic suppression of skin diseases, such as eczema, infantile eczema, atopic dermatitis, dermatitis herpetiformis,

contact dermatitis, seborrhoeic dermatitis, neurodermatitis, some forms of psoriasis, and intertrigo, in which inflammation is a prominent feature. However, the disease may return or be exacerbated when corticosteroids are withdrawn.

Application of the corticosteroids to the skin has lead to loss of skin collagen, subcutaneous atrophy local hypopigmentation of deeply pigmented skins. Topical corticosteroids should not be applied with an occlusive dressing to large areas of the body because of the risk of systemic absorption. Also they should not be used for the treatment of rosacea and should not be used indiscriminately for pruritus. Corticosteroids should not be applied to ulcers of the leg and long term topical use is best avoided, especially in children. Patients should be advised that topical corticosteroids should be applied sparingly in thin layers, by smoothing gently into the skin preferably after a bath and that no benefit is gained from more frequent than twice daily application or by vigorous rubbing. Treatment should be discontinued as soon as a positive result is obtained.

Betamethasone

Betamethasone Dipropionate, Cream, 0.025%, 0.05%

Betamethasone Valerate, Cream, 0.1%; Ointment, 0.1%; Scalp application, 0.1%

Indications: inflammatory dermatoses such as seborrheic or atopic dermatitis, neurodermatitis, anogenital pruritus, psoriasis, inflammatory phase of xerosis.

Cautions; Side effects, Contrindications: see under hydrocortisone and notes above.

Dose and Administration: apply thin film 2-4 times/day. Therapy should be discontinued when control is achieved; if no improvement is seen, reassessment of diagnosis may be necessary.

Clobetasol Propionate

Cream, 0.05% w/w

Ointment, 0.05% w/w

Scalp Application, 0.1%

Indications: short term relief of inflammation of moderate to severe corticosteroid-responsive dermatoses (very high-potency topical corticosteroid).

Cautions; Side effects, Contrindications: see under hydrocortisone and notes above.

Dose and Administration: discontinue when control is achieved; if improvement not seen within 2 weeks, reassessment of diagnosis may be necessary.

Adult and Child ≥ 12 years: Steroid responsive dermatoses: apply twice daily for up to 2 weeks (maximum dose: 50 g/week).

Desoximethasone

Cream, 0.05% 0.25%

Gel, 0.05%

Lotion, 0.25%

Ointment, 0.25%

Indications: relieves inflammation and pruritic symptoms of corticosteroid-responsive dermatoses (intermediate-to high-potency topical corticosteroid).

Cautions; Side effects, Contraindications: see under hydrocortisone and notes above.

Dose and Administration: apply a thin film to affected area twice daily.

Ointment: **Child** ≥ 10 years and **Adult:** apply a thin film to affected area twice daily.

Dexamethasone sodium Phosphate

Cream, 0.1%

Indications: systemically and locally for chronic swelling; allergic diseases.

Cautions; Side effects, Contraindications: see under hydrocortisone and notes above.

Dose and Administration: apply 1-4 times/day.

Flucinolone Acetonide

Cream, 0.025%

Ointment, 0.025%

Flucortolone and Flucortolone Hexanoate (caproate)

Ointment 0.25% + 0.25%

Hydrocortisone Acetate

Cream 1%

Ointment 1%

Indications: contact dermatitis, atopic dermatitis (eczema), lichen planus; intractable pruritus and phototoxic reactions, including polymorphic light eruptions and actinic prurigo; short-term treatment of psoriasis of the face and flexures.

Cautions: children (avoid prolonged use); occlusive dressings increase penetration into keratinized lesions (use occlusive dressing only at night and for no longer than 2 days; avoid use on weeping lesions); secondary infection requires treatment with an appropriate antimicrobial.

Contraindications: untreated skin infections or broken skin; rosacea, acne, perioral dermatitis.

Side effect: exacerbation of local infection; atrophic changes less likely with mild corticosteroids, but infants and children particularly susceptible. Contact dermatitis (burning and itching of skin, apparent chronic therapeutic failure), folliculitis, furunculosis, pustules, pyoderma, or vesiculation (painful, red or itchy, pus containing blisters in hair follicles), hyperaesthesia (increased skin sensitivity). Burning, dryness, irritation, itching, or redness of skin, mild and transient increased redness or scaling of skin lesions, minor and transient skin rash.

Dose and Administration:

Adult: *topical*, to the skin, as a 0.1 - 1% cream or 0.5 - 2.5% ointment one to four times a day.

Child 2 years of age and older: *topical*, to the skin, as 0.5% cream one to four times a day or as a 1% ointment one or two times a day.

Note:- Advise patient not to use it in or around the eye.

Storage: at room temperature in a well closed container, protect from freezing.

Methyl Prednisolone Aceponate

Ointment, Cream 0.1%

Mometasone furoate

Cream, Lotion, Ointment 0.1 %

Indications: see under hydrocortisone and notes above

Cautions; Side effects, **Contraindications:** see under hydrocortisone and notes above.

Dose and Administration

Adult: *Topical*, to the site, once a day.

Child: dosage has not been established.

Storage: Store between 2 °C to 30°C in a well-closed container

Note: For external use only. Do not use in or around the eye

Pimecrolimus

Cream, 1%

Indications: short-term and intermittent long-term treatment of mild to moderate atopic dermatitis in patients not responsive to conventional therapy or when conventional therapy is not appropriate.

Cautions: do not apply to areas of active cutaneous viral infection. Minimize or avoid natural/artificial sunlight exposure. Not recommended in children < 2 years of age.

Drug interactions: CYP3A inhibitors.

Contraindications: hypersensitivity reactions.

Side effects: headache, pyrexia, burning at application site, nasopharyngitis, cough, bronchitis.

Dose and Administration: Adult and Child ≥ 2 years: *Topical:* Apply thin layer to affected area twice daily; rub in gently and completely.

Note: Continue as long as signs and symptoms persist; discontinue if resolution occurs; re-evaluate if symptoms persist > 6 weeks.

Storage: store at room temperature. Do not freeze.

Triamcinolone

Ointment, 0.1%

Indications: inflammatory dermatoses responsive to steroids.

Cautions; Side effects, **Contraindications:** see under hydrocortisone and notes above.

Dose and Administration: apply thin film to affected areas 2-4 times/day.

17.3. Anti-infective/Anti-inflammatory Combinations

Combination of an imidazole and a mild corticosteroid (such as hydrocortisone 1%) may be of value in the treatment of eczematous intertrigo and in the first few days only of a severely inflamed patch of ringworm.

Such combinations should only be used under supervision because of the risk that signs of resistant infection may be suppressed.

Clioquinol+ Hydrocortisone

Cream, 3 % + 0.5 or 1 %

Ointment, 3% + 0.5% or 1%

Indications: see notes above, and under hydrocortisone

Cautions: see notes above and under section. 16.2

Dose and Administration: *Topical*, Apply thinly 1 – 2 times daily

Clotrimazole + Hydrocortisone

Cream, Ointment, 1% + 1%

Indications: athlete's foot and fungal infection of skin folds with associated inflammation; see notes above and under hydrocortisone

Cautions, Side effects, Contraindications; see notes above and under section 16.2 and clotrimazole (sec. 16.1)

Dose and Administration: *Topical*, apply thinly 1 – 2 times daily

Storage: protect from light.

Isoconazole + Diflucortolone valerate

Cream, Ointment, 1% + 0.1%

17.4. Keratolytics/Caustics and Antiacne Agents

Benzoyl peroxide is a keratolytic drug with bacteriostatic activity against *propionibacterium acnes* and *staphylococcus epidermidis*. It is used mainly in the treatment of acne usually in topical preparations containing 2.5 to 10 %. Adverse effects include initial stinging effect & contact sensitization. Caution is required when applying it near the eyes, the mouth and other mucous membranes, and to sensitive areas of the neck.

Salicylic acid may be used in all hyperkeratotic and scaling conditions to enhance the rate of loss of surface scale. Coal tar is more active than salicylic acid and has anti-inflammatory and antiscaling properties. Some preparations contain both preparations of **Glutaraldehyde**, and combination of **salicylic acid**, **lactic acid** and **polidocanol** are available. They are suitable for the removal of warts on hands and feet. The topical retinoids, which include tretinoin and isotretinoin, are effective in treating acne vulgaris in which comedones, papules and pustules predominate, but are usually inadequate in eradicating severe pustular or deep nodular cystic lesions. They act by normalizing keratinisation, but their exact mechanism of action remains to be fully elucidated. Comedone formation is inhibited and they thus provide prophylactic treatment for acne.

The antimicrobial effect on *Propionibacterium acnes* and its influence on follicular hyperkeratosis make azelaic acid a suitable topical agent for moderate acne vulgaris.

Podophyllum resin is a mixture of resins, strongly irritant to normal skin and mucous membranes. It has an antimitotic action and is used as a paint in the topical treatment of soft venereal warts, or as an ointment (with salicylic acid) for plantar and non mucosal warts. The main active component of podophyllin is podophyllotoxin. Purified podophyllotoxin is being used in newer preparations at low concentration with good effect. It is also useful for the treatment of molluscum contagiosum.

Azelaic Acid

Cream, 20%

Indications: topical treatment of mild to moderate inflammatory acne vulgaris and rosacea.

Cautions: about 2% of applied azelaic acid is systemically absorbed and excreted unchanged in urine; a daily application of 10 g cream (2 g azelaic acid) should not be exceeded; avoid contact with the eyes; safety and efficacy have not been proven for use for more than 6 months.

Contraindications: hypersensitivity to propylene glycol or azelaic acid.

Side effects: local skin irritation (redness, itching, scaling, burning) may occur initially, but usually regresses. If persistent, reduce frequency of application.

Hypersensitivity and photosensitivity reactions have been reported.

Dose and Administration: apply to clean skin twice daily; maximum 10 g/day (2 g azelaic acid).

Sensitive skin: start with daily applications and gradually increase to twice daily. Improvement occurs after 4 weeks.

Storage: store at room temperature.

Benzoyl peroxide

Gel, 2.5 %, 5 %, 10 %

Solutions, 2.5 %, 5 %, 10 %

Indications: mild to moderate acne and as an adjunct to oral therapy in more severe cases.

Cautions: avoid contact with eyes, mouth, and mucous membranes; avoid use of occlusive dressings; avoid excessive exposure to sunlight.

Side effects: initial irritation common but subsides with continued use; rarely, contact sensitivity occurs, occasionally even 1 application can cause severe irritation; may bleach fabrics, hair and skin.

Dose and Administration:

Apply 1 – 2 times daily preferably after washing with soap and water, start treatment with lower – strength preparations

Storage: at 2 to 8°C in a container that has been treated to reduce static charges and that has a device for the release of excess pressure.

Note: -caution, Benzoyl percussion on heat.

Coal Tar + Salicylic Acid*Ointment, 2 % + 5 % or 2 % + 10 %***Indications:** hyperkeratotic skin disorders associated with psoriasis and occasionally chronic atopic eczema.**Cautions:** avoid eyes, mucous, genital or rectal areas and broken or inflamed skin. Use suitable chemical protection gloves for extemporaneous preparation. Salicylate toxicity. If large areas of skin are treated; salicylate toxicity may be a hazard.**Side effects:** skin irritation and acne-like eruptions, photosensitivity: stains skin, hair and fabric, excessive drying.**Dose and Administration:** Apply 1 – 2 times daily.**Glutaraldehyde***Solution. 10 %***Indications:** warts, particularly planar warts (see also notes above)**Cautions:** protect surrounding skin, not for application to face, mucosa, or anogenital areas.**Side effects:** rashes, skin irritation (discontinue if severe), stains skin brown.**Dose and Administrations:** Apply twice daily.**Storage:** store at a temperature not exceeding 15°C.**Liquid Nitrogen**

It is used as a cryotherapeutic agent for the removal of warts.

Salicylic Acid + Lactic Acid + Polidocanol*Tincture, 2 g + 0.5 g + 0.2g in each 10 g*

See notes above.

Podophyllin Paint*Solution, 25%***Indications:** topical treatment of benign growths including external genital and perianal warts, papillomas, fibroids.**Cautions:** avoid application to healthy tissues; do not use for treating facial or oral mucosal warts; use of large amounts of drug should be avoided; should not be applied to or near mucous membranes.**Contraindications:** pregnancy, diabetic patient.**Side effects:** pruritus, nausea, vomiting, abdominal pain, and diarrhea.**Dose and Administration:** 10% to 25% solution in compound benzoin tincture; apply drug to dry surface, use 1 drop at a time allowing drying between drops until area is covered; total volume should be limited to < 0.5 ml per treatment session.**Storage:** store at room temperature.**Retinoic Acid (Tretinoin)**

Cream, 0.025%

Gel, 0.01%, 0.025%

Lotion, 0.025%, 0.05%

Ointment, 0.05%

Indications: treatment of acne vulgaris, photodamaged skin; palliation of fine wrinkles, mottled hyperpigmentation, and tactile roughness of facial skin as part of a comprehensive skin care and sun avoidance program.

Caution: eczema.

Drug interactions: topical application of sulphur, benzoyl peroxide, salicylic acid, resorcinol, photosensitizing medications (thiazides, tetracyclines, fluoroquinolones, phenothiazines, sulfonamides).

Contraindications: hypersensitivity to retinoic acid.

Side effects: most likely to occur with incorrect use. Transient burning, excessive redness, dryness, oedema or blistering, heightened susceptibility to sunlight and temporary hyper and hypopigmentation, apparent exacerbation of inflammatory lesions.

Dose and Administration: apply to dry skin, after thorough cleansing, before bedtime. Frequency of application should be individualized.

Storage: store at 25 °C; gel is flammable, keep away from heat and flame.

Silver Nitrate + Potassium Nitrate

Toughened, 95% + 5%

Indications: cauterization of wounds and sluggish ulcers, removal of granulation tissue and warts; aseptic prophylaxis of burns.

Cautions: do not use application sticks on the eyes; prolonged use may result in skin discoloration.

Contraindications: not for use on broken skin, cuts, or wounds

Side effects: burning and skin irritation, staining of the skin, hyponatremia, methemoglobinemia.

Dose and Administration: *Sticks:* Apply to mucous membranes and other moist skin surfaces only on area to be treated 2 - 3 times/ week for 2- 3 weeks.

Storage: store in a tight, light- resistant container and in dry place.

17.5. Drugs for Psoriasis and Eczema

Zinc oxide is mildly astringent and is used topically as a soothing and protective application in eczema and slight excoriations and for hemorrhoids. It is usually mixed with purified talc, which is used in massage to allay irritation and prevent chafing. Zinc oxide reflects UV radiation and is used as sunscreens.

Ichthammol is usually used in chronic lichenified forms of eczema or to control pruritus.

Dithranol is an effective, but difficult-to-administer, topical treatment for psoriasis. When used optimally, responsive plaques should clear with approximately 3 weeks of treatment. Dithranol needs to be incorporated into a

suitable base to minimize side-effects. The presence of salicylic acid is necessary to prevent its inactivation. It is most commonly used in a stiff paste.

Vitamine D has both keratinocyte differentiation and inflammatory modifying effects. The synthetic analogue of 1, 25-dihydroxyvitamin D₃, calcipotriol, is less calcaemic than the parent compound. It has been shown to be effective in plaque psoriasis.

Calcipotriol

Cream, Ointment, Scalp application, 0.005%

Indication: treatment of moderate plaque psoriasis.

Cautions: hypercalcaemia.

Contraindication: hypersensitivity to calcipotriol.

Side effects: skin irritation and allergic rashes, facial dermatitis with applications to the face; indiscriminate use of calcipotriol can cause hypercalcaemia.

Dose and Administration: Apply twice daily to affected areas to a maximum of 100 g/week. Wash off immediately if face becomes contaminated.

Dithranol

Paste, 1%

Scalp application, 0.25%, 0.5%

Indications: treatment of psoriasis

Cautions and Contraindications: dithranol is an irritant; avoid contact with the eyes and tender parts of the body. Its use on the face should be limited to carefully supervised inpatient management only. It should not be used on acute eruptions or excessively inflamed areas.

Side effects: irritation of normal and psoriatic skin. Fever, rigors, flu-like symptoms and lymphadenopathy. It stains skin, hair, nails, fabrics and fomites a reddish brown color.

Dose and Administration:

Skin application: Apply sparingly only to psoriatic lesions and rub gently and carefully into the skin until absorbed. Avoid applying an excessive quantity, which may cause unnecessary soiling and staining of the clothing or bed linen.

Scalp application: comb hair to remove scalar debris, wet hair and after suitably parting, rub cream well into the lesions, taking care to prevent the cream from spreading on to the forehead.

Remove by washing or showering; optimal period of contact will vary according to the strength used and the patient's response to treatment. Continue treatment until the skin is entirely clear (i.e. when there is nothing to feel with the fingers and the texture is normal).

Storage: store at a temperature of 8-15 °C in airtight containers.

Ichthammol

Ointment, 10 %

Indications: for treatment of chronic lichenified eczema.

Side effect: skin irritation.

Dose and Administration: topically, apply to the skin 1-3 times daily.

Zinc Oxide

Ointment 15 %

Lotion. 15 %

Zinc oxide + Talc

Paste, 15 % + 25 %

17.6. Antipruritics

Pruritus (itching) is a common symptom of many skin disorders as well as of several systemic diseases and may be extremely distressing. However, contact with certain substances, conditions that dry the skin, stress, and extremes of temperature may also be a cause. Thus, an important part of treatment is to eliminate or minimize the reason for the irritation.

Preparations containing crotamiton are used as an antipruritic agent. One application may be effective for 6 to 10 hour.

Preparations containing calamine are often ineffective.

Calamine

Lotion (oily), 5 %

Indications: mild pruritus

Dose and Administrations: *Topically:* Apply liberally 3 – 4 time daily

Calamine + Zinc Oxide*Cream, 4 % + 3 %**Lotion, 15 % + 5 %***Indications:** mild pruritus**Dose and Administrations:** *Topically:* Apply liberally 3 – 4 times daily**Crotamiton***Lotion, 10 %*

See under sec. 16.1

17.7. Pigmenting Agents

Psoralens (furocoumarins) occur in nature and are found primarily in plants. They are photosensitisers. Photochemotherapy using 8-methoxypsoralen, 5-methoxypsoralen or 4,5,8-trimethoxypsoralen with ultraviolet light (usually UVA) is an effective method of treating several dermatological conditions including psoriasis, vitiligo, mycosis fungoides and atopic eczema. Because specialized facilities and expertise are required, it is recommended that this therapy be limited to hospitals and specialist practices.

Psoralens applied topically (lotion, cream) are useful for localized disease or when oral administration is contraindicated or not tolerated.

Methoxsalen (8-Methoxypsoralen)*Solution, 1 %**Capsule, 10 mg, 20 mg**Tablet, 10 mg, 20 mg*

Indications: symptomatic control of severe, recalcitrant disabling psoriasis; repigmentation of idiopathic vitiligo; palliative treatment of cutaneous T-cell lymphoma (CTCL).

Cautions: albinism, erythropoietic protoporphyria, lupus erythematosus, porphyria cutanea tarda, xeroderma pigmentosum, aphakia, cataracts.

Drug interactions: anthracin, certain organic dyes (methylene blue, methylene orange), coal tar or coal tar derivatives, diuretics, griseofulvin, bacteriostatic soaps, naldixic acid, phnothiazines, sulfonamides, tetracyclines.

Contraindications: cataract, melanoma, and pregnancy.

Side effects: Immediate- nausea, vomiting, headache, pruritus, oedema and CNS disturbances (dizziness, nervousness, insomnia, depression and excitation). Delayed- actinic damage (accelerated ageing, carcinomas, cataracts, pigmented naevi); immunosuppression; precipitation of lupus erythematosus and herpes simplex.

Dose and Administration:

Adult:

Psoriasis: Oral: 10-70mg 1.5-2 hours before exposure to UVA light; dose may be repeated 2-3 times per week, based on UVA exposure; doses must be given at least 48 hours apart; dosage is based upon patient's body weight and skin type:

<30kg: 10mg; 30-50kg: 20mg; 51-65kg: 30mg; 66-80kg: 40mg; 81-90 kg: 50mg; 91-115kg: 60mg; >115kg: 70mg.

Vitiligo: Oral: 20mg 2-4 hours before exposure to UVA light; dose may be repeated based on erythema and tenderness of skin; do not give on 2 consecutive days.

Adult and Child >12 years:

Vitiligo: Topical Apply up to 1% solution 2 hours before exposure to UVA light, treatment is repeated usually once weekly.

Psoriasis: apply approximately 0.15% solution 15 minutes before UVA exposure.

Storage: store at room temperature and protect from light.

Methoxsalen (Ammoidin) + Pentosalen (Ammidin)

Solution, 0.75% + 0.25%

17.8. Depigmenting Agents

Hydroquinone

Solution, 2%, 4%

Indications: gradual bleaching of hyperpigmented skin conditions.

Cautions: limit application to area no larger than face and neck or hands and arms.

Contraindications: hypersensitivity to hydroquinone, sunburn, depilatory usage.

Side effects: dermatitis, dryness, erythema, stinging, inflammatory reaction, sensitization, irritation.

Dose and Administration: **Adult and Child** ≥ 12 years: *topical:* apply and rub twice daily.

17.9. Dermatological, systemic

Acitretin

Capsule, 10 mg, 25 mg, 50 mg

Indications: severe psoriasis not responsive to make conventional therapy; pustular psoriasis; severe extensive disorders of keratinisation resistant to conventional treatments, such as congenital ichthyosis, Darrier's disease and pityriasis rubra pilaris.

Cautions: hepatic and renal impairment; hypervitaminosis A; hyperlipidaemias; known hypersensitivity.

Drug interactions: agents causing intracranial pressure (e.g. tetracyclines), hepatotoxic agents (e.g. methotrexate), protein bound drugs (e.g. phenytoin), vitamin A.

Contraindications: pregnancy or breast-feeding, patients under 18 years of age.

Side effects: hypervitaminosis A, e.g. dryness of mucosae (dry mouth, nose and eyes, cheilitis, keratitis, stomatitis, epistaxis); reversible hair loss; nail dystrophies and paronychia; thin fragile skin, exfoliation especially of palms and soles.

Skin rashes; reversible impairment of dark adaptation; raised intracranial pressure; musculoskeletal pains with hyperostosis and extra skeletal soft-tissue calcification, osteoporosis; premature epiphyseal closure; gastrointestinal irritation; hepatitis and transient reversible elevations of liver enzymes; elevation of serum lipids; disturbance in glucose metabolism, malaise; sweating; drowsiness.

Dose and Administration: Adult: Individually adjusted to limit side effects and to maximize therapeutic response.

Oral: Initially, 25 - 30 mg once daily with a meal for 2 - 4 weeks, increasing to 50 mg/day for a further 6-8 weeks; maximum 75 mg/day.

Maintenance: 50 mg/day or less, based on therapeutic results and tolerability.

Storage: store at room temperature.

Cyproterone acetate and Ethinyl estradiol

Tablet, 2mg + 35mcg

Indications: indicated for resistant and severe acne, severe signs of androgenisation in women (e.g. hirsutism), male sexual deviation, and inoperable prostatic carcinoma.

Cautions: cyproterone should be administered only after full endocrine assessment.

Contraindications: pregnancy, cardiac disease, diabetes mellitus, liver disease.

Side effects: abnormal vision, allergic reaction, anemia, cerebrovascular accident, liver failure, depression, in women weight gain, decreased libido and dry vagina.

Dose and Administration: Cyproterone acetate 2mg and ethinylestradiol 0.035 mg daily from day 1 of cycle.

Storage: store at room temperature.

Etretinate

Capsule, 10mg, 25mg

Indications: treatment of severe, extensive psoriasis that has not responded to other treatment, especially generalized and palmo-plantar pustular psoriasis.

Cautions, Contraindications, Drug interactions and Side effects see isotretinoin.

Dose and Administration: *Oral:* 0.75 to 1mg/kg daily in divided doses. A maximum dose of 1.5 mg/kg daily.

Erythrodermic psoriasis: 250 mcg/kg daily, increased at weekly intervals by 250 mcg/kg daily until optimal response occurs.

Following the initial response, generally after 8-16 weeks of therapy, maintenance doses of 500 to 750 mcg/kg daily have been given.

Isotretinoin

Capsules, 10 mg, 20 mg

Indications: mainly for the management of intractable acne, but may also be effective in controlling keratinisation disorders such as the ichthyoses and keratosis follicularis.

Cautions: history of depression.

Drug interactions: tetracyclines, acitretin, tretinoion, vitamin A.

Contraindications: pregnancy, hypervitaminosis A; hepatic and renal insufficiency; hyperlipidaemia's; known hypersensitivity.

Side effects: dryness of mucosa; reversible hair loss, nail dystrophies and paronychia, thin fragile skin, exfoliation especially of palms and soles.

Skin rashes; reversible impairment of dark adaptation; raised intracranial pressure; musculoskeletal pains with hyperostosis and extraskeletal soft-tissue calcification, osteoporosis; premature epiphyseal closure; gastrointestinal irritation; hepatitis and transient reversible elevations of liver enzymes; elevation of serum lipids; disturbance in glucose metabolism; malaise; sweating; drowsiness, haematological abnormalities. Depression, psychosis, behavioral disorders, and seizures have been reported.

Dose and Administration: Adult: Oral:

Initially: 0.5 mg/kg/day in a single or 2 divided doses with food. Adjust after 2 - 4 weeks, if necessary, according to response and adverse effects. If the response is slight, increase up to a maximum of 1 mg/kg/day, if well tolerated.

Maintenance: 0.5 - 1 mg/kg/day for a further 12 weeks. In the event of intolerance of the initial dose, reduce to 0.1 - 0.2 mg/kg/day with longer duration of therapy. Total dose 120 mg/kg. Usual treatment period, 16 - 24 weeks.

Repeat treatment: allow an interval of 3 - 4 months (at least 8 weeks) as improvement may continue despite stopping therapy.

Storage: store at room temperature.

Methoxsalen (8-Methoxypsoralen)*Capsule, 10mg, 20mg**Tablet, 10mg, 20mg*

See section 17.7.

Methoxasalen + Pentosalen*Tablet, 10mg + 5mg***Prednisolone***Tablets, 1mg, 2mg, 5mg***Indications:** short-term suppression of inflammation in allergic disorders.**Cautions:** tuberculosis, amebiasis, strongyloidiasis, risk of severe chicken pox in non-immune patient, avoid exposure to measles, diabetes mellitus; peptic ulcer; hypertension.**Contraindications:** untreated systemic infection; administration of live virus vaccines.**Side effects:** nausea, dyspepsia, malaise, hiccups, hypersensitivity reactions including anaphylaxis.**Dose and Administration: Adult and Child:***Oral:* initially up to 10 - 20 mg daily as a single dose in the morning (in severe allergy up to 60 mg daily as a short course of 5 - 10 days).**Storage:** store at room temperature.**17.10. Skin Disinfecting Agents**

The choice of disinfectant is an important factor in treating skin conditions. For example, scaling disorders are best treated with emulsifying ointment or other disinfectants that do not irritate the skin. Some of the useful disinfectants for skin cleansing available at district hospital level include Chlorhexidine; Potassium permanganate and Povidone - iodine. Povidone- iodine is preferred to chlorinated solutions (such as dilute sodium hypochlorite solution; not described here) which are too irritant and are no longer recommended. Astringent preparations, such as potassium permanganate solution are useful for oozing eczematous reactions.

Chlorhexidine Gluconate + Cetrimide*Solution 1.5 % + 15 %, 0.3% + 3%w/v***Indications:** for skin disinfection and wound cleansing, and also for the cleansing and disinfection of equipments.**Side effects:** skin sensitivity may occur rarely. Strong solutions may cause irritation of the conjunctiva and other sensitive tissues.**Dose and Administration:** *Topically**For skin disinfection and wound cleansing:*

Apply to the affected area the diluted solution (1 in 100 (1%) with water).

For disinfection of equipment (e.g bowls, tables), spraying wards: Use 1 in 2000 dilution with water.

Storage: at room temperature protected from light.

Ethyl Alcohol

Solution, 70 %

Indications: for disinfection of the skin in preparation for injections.

Cautions: it should not be applied to fresh wounds.

Dose and Administration: Topical, to the skin.

Storage: in airtight containers, in a cool place.

Hydrogen peroxide

3 %, 6 %

Indications: skin disinfectant, particularly cleansing and deodorizing wounds and ulcers.

Cautions: in large and deep wounds, avoid use in normal skin.

Dose and Administration: topically, apply to the wound to cleanse.

Iodine

Solution, 2 %

Indications: for the disinfection of minor superficial skin wounds.

Cautions: do not apply to sensitive area such as the axillary, perianal, or genitalia.

Side effects: skin sensitivity, irritation, sloughing of soft tissues and staining of the skin may occur.

Dose and Administration: Topical to the affected areas as necessary. Do not cover with a tight bandage.

Storage: at room temperature. In yellowish brown coloured glass bottles, preferably glass stoppered.

Potassium permanganate

Tablet (for solution), 50 mg, 120 mg, 200 mg, 250 mg, 300 mg

Indications: as skin disinfectant for cleansing and deodorizing suppurating eczematous reactions and wounds.

Cautions: irritant to mucous membrane and it stains skin and clothing

Side effect: irritation to tissues, corrosive burns,

Dose and Administration: 1 tablet dissolved in suitable amount of water to provide a 0.01% solution. It is applied as wet dressings or baths, approximately of 0.01% solution.

Povidone - Iodine

Solution (aqueous), 4 %, 7.5 %, 10 %

Indications: as skin disinfectant and antiseptic mainly for the treatment of contaminated wounds and pre-operative preparation of the skin and mucous membranes.

Cautions: during pregnancy and breast-feeding, in patients with broken skin and renal impairment. The application of povidone - iodine to large wounds or severe burns may produce systemic adverse effects such as metabolic acidosis, hypernatremia and impairment of renal function.

Contraindications: avoid regular use in patients with thyroid disorders or those receiving lithium therapy, very low birth weight infants.

Side effects: rarely sensitivity, may interfere with thyroid function tests; see also caution.

Dose and Administration:

Alcoholic solution, povidone - iodine 10%:

Adult: to be applied undiluted in pre- and post-operative skin disinfection,

Child: not recommended for regular use in neonates (and contraindicated in very low birth weight infants)

Antiseptic solution, povidone - iodine, 10% in aqueous solution:

Adult: to be applied undiluted in pre-and postoperative skin disinfection

Child: not recommended for regular use in neonates (and contraindicated in very low birth weight infants)

Scalp and skin cleanser solution, povidone - iodine, 7.5%, in a surfactant basis:

Adult: use of seborrheic condition of scalp and acne vulgaris of face and neck 1-2 times daily child dose. **Child** under 2 years not recommended.

Skin cleanser solution, povidone - iodine, 4% in a surfactant basis:

Adult: for infective condition of the skin. Retain on skin for 3-5 minutes before rinsing, repeat twice daily. **Child** under 2 years not recommended

17.11. Dermatologicals, Others**Aluminum Chloride**

Solution (alcoholic), 20%, 25%

Indications: used for control of hyperhidrosis.

Dose and Administration: Applied to dry skin at night (and washed off in the morning); especially if occluded and the patient sedated.

Aminacrine (Aminoacridine) + Allantoin

Cream, 0.0695% + 2%

Methylsalicylate☞

Methyl salicylate is irritant to the skin and is used topically in rubefacient preparations in musculoskeletal, joint and soft-tissue disorders and for minor peripheral vascular disorders such as chilblains. It is absorbed through intact skin and can produce effects typical of systemic salicylates.

Paraffin Gauze Dressing

Paraffin Gauze Dressing - is Fabric of Leno weave, weft and warp threads of cotton and/or viscose yarn, impregnated with white or yellow soft paraffin.

Indications: treatment of abrasions, burns, and other injuries of skin, and ulcerative conditions; post-operatively as a penile and vaginal dressing and for sinus packing; heavier loading for skin graft transfer.

Talc Dusting powder

Indications: used in folds where a friction may occur between opposing skin surfaces.

Cautions: they should not be applied in areas that are very moist as they tend to take and abrade the skin.

☞ Any other rubefacient proven to be therapeutically effective can be used

18. ANTIDOTES AND OTHER SUBSTANCES USED IN POISONING

In the treatment of acute poisoning most patients require only supportive and symptomatic therapy. The active removal of poisons from the stomach by gastric lavage or emesis induction may be considered, as should the administration of substances like activated charcoal by mouth to reduce their absorption. However, the use of emetics and gastric lavage has been questioned and these measures, including the administration of charcoal are for instance inappropriate in corrosive poisoning, and aspiration should only be carried out with great care. Some poisons, in particular pesticides, may be absorbed through the skin and clothing should be removed and the skin thoroughly washed to avoid continued absorption.

Techniques such as forced diuresis, haemodialysis, or haemoperfusion are only of value for a limited number of poisons in a few severely poisoned patients.

The drugs included in this section act in a variety of ways. These are the antagonists, such as the opioid antagonist naloxone hydrochloride, that compete with the poison for the receptor sites. There are compounds that inhibit the poison by reacting with it to form less active or inactive complexes or by interfering with its metabolism; a typical examples of the first group.

Atropine sulphate is given in the case of organo-phosphorus poisoning which is characterized by intense muscarinic effects by inhibiting cholinesterase activity thereby prolonging and intensifying the effects of acetylcholine. Atropine will reverse the muscarinic effects of acetylcholine and is given in a dose of 2 mg as atropine sulphate (intramuscularly or intravenously according to the severity of poisoning) every 20 to 30 minutes until the skin becomes flushed and dry, the pupils dilate, and tachycardia develops.

Pralidoxime mesylate, a cholinesterase reactivator, is indicated, as an adjunct to atropine, in moderate or severe poisoning but is any effective if given within 24 hours.

Other specific antagonists include acetylcysteine used in paracetamol poisoning. Sodium nitrite is used in the treatment of cyanide poisoning in conjunction with sodium thiosulphate. And Flumazenil, a benzodiazepine antagonist, is used in anesthesia and intensive care to reverse benzodiazepine – induced sedation; it is also used to treat benzodiazepine over dosage.

Acetylcysteine

Injection, 200 mg/ml in 10 ml ampoule

Indications: antidote to acetaminophen overdose, to protect against hepatotoxicity.

Cautions: patients with history of asthma, conditions predisposing to gastrointestinal hemorrhage such as esophageal varices, peptic ulceration, and in patients sensitive to acetylcysteine.

Side effects: drowsiness, fever, nausea, or vomiting, bronchospastic allergic reaction (troubled breathing, tightness in chest, wheezing), skin rash or hives.

Dose and Administration:

Adult and Child: *Antidote: IV:* 300mg per kg of body weight administered over twenty hrs and fifteen minutes, divided as follows:

Initial loading dose - 150mg per kg of body weight in up to 200ml of 5% dextrose injection, administered over fifteen minutes.

Second infusion- 50mg per kg of body weight in 500ml of 5% dextrose injection, administered over four hours.

Third infusion - 100mg per kg of body weight in 1000ml of 5% dextrose injection, administered over the next sixteen hours.

Apomorphine Hydrochloride

Injection, 3 mg/ml in 1 ml ampoule

Indications: emetic in the treatment of acute poisoning; diagnosis and management of parkinsonism.

Cautions: if vomiting does not result from the first dose of apomorphine, then a second dose should not be given. Caution should be taken in children debilitated or elderly patients or those with cardiac decomposition.

Drug interactions: the effectiveness of apomorphine as an emetic is diminished by drugs that depress the vomiting center and they in turn may enhance its central depressant effects.

Contraindications: respiratory or central nervous system depression, in shock or seizure, or in patients suffering from the effects of corrosive poisons.

Side effects: protracted vomiting, shock, CNS stimulation, depression and respiratory depression.

Dose and Administrations:

Adult: *subcutaneous* 5 or 6 mg as a single dose; **Child:** *subcutaneous* 70 to 100 mcg per Kg body weight as a single dose:

Note: A glass of water being given before injection.

Storage: store in tight container. Protect from light.

Atropine Sulphate*Injection, 1 mg/ml in 1 ml ampoule***Indications:** for the treatment of poisoning from cholinesterase inhibitors such as neostigmine, pilocarpine, physostigmine, and methacholine, and in the treatment of the rapid type of mushroom (muscarine) poisoning.

It is also indicated in the treatment of poisoning caused by pesticides that are organophosphate cholinesterase inhibitors, chemical warfare, and 'nerve' gases.

Cautions: pregnancy and breastfeeding in children and in elderly, urinary retention, prostatic enlargement, tachycardia, cardiac insufficiency, paralytic ileus, ulcerative colitis, and pyloric stenosis.**Drug interactions:** antacids, antidiarrhoeals, other anticholinergics, cyclopropane, ketoconazole, haloperidol.**Contraindications:** closed angle glaucoma.**Side effect:** dryness of mouth, skin, blurred vision, loss of accommodation constipation, bradycardia followed by tachycardia, difficulty with micturation, flushing.**Dose and Administration:****Adult:** *Antidote to cholinesterase inhibitors: IV:* 2-4mg initially, then 2mg repeated every five to ten minutes until muscarinic symptoms disappear or signs of atropine toxicity appears.*Antidote to muscarine in mushroom poisoning: IM, or IV:* 1 to 2mg every hour until respiratory effects subside.*Antidote to organophosphate pesticides: IM or IV:* 1 to 2mg repeated in twenty or thirty minutes as soon as cyanosis has cleared. Continue dosage until definite improvement occurs and is maintained, sometimes for two days or more.**Child:** *Antidote to cholinesterase inhibitors: IV or IM:* 1mg initially, then 0.5 - 1mg every five to ten minutes until muscarinic symptoms disappear or signs of atropine toxicity appear.**Storage:** at room temperature, protect from freezing**Calcium Gluconate (Levulinate, or Chloride)***Injection, 10 % in 10 ml ampoule***Indications:** fluoride toxicity; hypocalcaemia and of calcium deficiency states (see sec.11.2)**Side effects, Drug interactions, Cautions, Contraindications:** see sec. 11.2**Dose and Administrations:**10 ml of Calcium gluconate 10 % *intravenously* repeated after one hour; 30 ml should be given if tetany is present. If the short term affected skin and tissue should be injected with a 10 % solution of calcium gluconate at a dose of 0.5 ml per cm².*Note: Inorganic fluoride is corrosive to skin and mucous membranes and acute intoxication disrupts many physiological systems and severe burns and profound hypocalcaemia may ensue. Absorption of the fluoride can be prevented by conversion to an insoluble form such as calcium fluoride and thus irrigation with limewater, milk, or a 1 % solution of calcium chloride or gluconate at the portable of entry (mouth, skin, stomach) is recommended*

Desferrioxamine Mesylate

Powder for injections, 0.5 g in vial

Indications: it is a chelating agent used in the treatment of acute iron poisoning, and chronic iron or aluminium overload.

Cautions: impaired renal function, if infection is suspected treatment with desferrioxamine should be stopped and appropriate antimicrobial treatment given.

Drug interactions: prochlorperazine

Contraindications: severe renal disease or anuria, pregnant women or women who may become pregnant.

Side effects: anaphylactic reactions, and hypotension when given too rapidly by intravenous injection

Dose and Administration:

Continuous IV infusion: up to 15 mg/kg /hour; maximum 80mg /kg in 24 hours.

IM: 1 - 2 g in 10 - 20 ml of water for injections every 3 - 12 hours; maximum 6g in 24 hours.

Storage: reconstituted solutions of desferrioxamine mesylate are stable for 1 week at room temperature when protected from light.

Note: - Inform the patient that the drug may colour the urine reddish brown

Digoxin Immune Fab (Ovine)/Digoxin-specific, Antibody fragments

Powder for injection, 40mg

Indications: treatment of life - threatening or potentially life threatening digoxin intoxication, associated with hyperkalaemia, life- threatening cardiac dysrhythmias or digoxin levels > 6ng/ml.

Cautions: renal or cardiac failure.

Drug interaction: digoxin.

Contraindications: hypersensitivity to sheep products or any component of the formulation.

Side effects: hypersensitivity reactions and hypokalaemia.

Dose and Administration: Each vial of 40mg will bind \approx 0.5 mg of digoxin or digitoxin.

Estimation of the dose is based on the body burden of digitalis. This may be calculated if the amount ingested is known or the post distribution serum drug level is known (round dose to the nearest whole vial). See the next table.

Digoxin Immune Fab

Tablet Ingested (0.25 mg)	Fab Dose (Vials)
5	2
10	4
25	10
50	20
75	30
100	40
150	60
200	80

Fab dose based on serum drug level post distribution:

Digoxin: No of vials = level (ng/ml) x body weight (kg) divided by 100.

Digitoxin: No of vials = digitoxin (ng/ml) x body weight (kg) divided by 1000.

If neither amount ingested nor drug level are known, dose empirically as follows:

For acute toxicity: 20 vials, administered in 2 divided doses to decrease the possibility of a febrile reaction, and to avoid fluid overload in small children.

For chronic toxicity: 6 vials, for infants and small children (≤ 20 kg), a single vial may be sufficient.

Storage: store in refrigerator (2 to 8°C).

Dimercaprol

Injection, 5% in 2ml ampoule.

Indications: antidote to gold, arsenic, mercury poisoning; adjunct to edetate calcium disodium in lead poisoning; possibly effective for antimony, bismuth, chromium, copper, nickel, tungsten, or zinc.

Cautions: oliguria; glucose 6-phosphate dehydrogenase deficiency.

Drug interactions: toxic complexes with iron, cadmium, selenium, or uranium.

Contraindications: hepatic insufficiency (unless due to arsenic poisoning); iron, cadmium, or selenium poisoning.

Side effects: hypertension, headache, nausea, vomiting.

Dose and Administration:

Adult and Children: Deep I.M.

Arsenic, mercury, and gold poisoning: 3mg /kg every 4 - 6 hours for 2 days, then every 12 hours for 7 - 10 days or until recovery (initial dose may be up to 5mg if severe poisoning).

Lead poisoning (in conjunction with calcium EDTA): For symptomatic acute encephalopathy or blood level > 100 mcg/dl: 4 - 5mg/kg every 4 hours for 3 - 5 days.

Storage: store at 2-8 °C; protect from light.

Flumazenil

Injection, 0.1 mg/ml in 5 ml ampoule

Indications: flumazenil is indicated for the management of benzodiazepine over dose.

Cautions: hypersensitivity to benzodiazepines; patients receiving benzodiazepines for prolonged periods; pediatrics, elderly; pregnant and breast-feeding women.

Drug interactions: cyclic (tricyclic or tetracyclic) antidepressants

Contraindications: cyclic (tricyclic or tetracyclic) antidepressant; status epilepticus severe head injury

Side effects: nausea, vomiting, flushing and very occasionally convulsions

Dose and Administration: Adult: IV: 0.2mg over 15 seconds; if a response is not achieved within 60 seconds; 0.1mg may be repeated at 60-second intervals as required to a total dose of 1mg (2mg in intensive care). Usual range 0.3-0.6 mg. If there is no response, aetiology should be questioned.

Storage: at room temperature.

Ipecac

Syrup, 7% powdered Ipecac

Indications: an emetic for emergency use in the treatment of drug overdose and in some cases of poisoning

Cautions: children under 1 year of age; heart disease active or impending seizures and in conditions of strychnine poisoning or ingestion of petroleum distillates, such as kerosene, gasoline, coal oil, fuel oil, paint thinner, or cleansing fluid.

Drug interactions: activated charcoal, milk or milk products, carbonated beverages, antiemetics.

Contraindications: impending coma, severe inebriation, corrosive poisoning with alkali and strong acids, depressed gag reflex, impending shock states.

Side effect: diarrhoea, fast or irregular heartbeat, nausea or vomiting, stomach cramps or pain, troubled breathing, unusual tiredness or weakness, aching, and stiffness of muscles, especially those of the neck, arms, and legs.

Dose and Administration: Oral:-

Adult: emetic: 15 to 30ml followed immediately by one glass (240ml) of water. Dose may be repeated in twenty minutes if emesis does not occur. The dosage should be reversed by gastric lavage if emesis does not occur after the second dose.

Child: Emetic:

Children up to 1 year of age: 5 to 10ml

Children 1-12 years of age: 15 ml, preceded or followed by ½-1 full glass (120-240ml) of water.

Storage: at a temperature below 25°C.

Methionine

Tablet, (DL – methionine), 250mg

Indications: management of paracetamol (acetaminophen) overdose. The efficacy and safety of late (> 15 hours post ingestion) or prolonged administration (> 16 hours) have not been sufficiently explored.

Dose and Administration: *Oral:* 2.5g 4 hourly for a total of 4 doses, started within 10 - 12 hours after paracetamol ingestion.

Storage: protect from light.

Methylene Blue

Injection, 1% in 10ml ampoule.

Indications: antidote for cyanide poisoning and drug-induced methemoglobinemia.

Cautions: G6PD deficiency, pregnancy and breastfeeding.

Contraindication: renal insufficiency.

Side effects: hypertension, precordial pain, dizziness, mental confusion, headache, fever, staining of skin, fecal discoloration, nausea, vomiting, abdominal pain, discoloration of urine, bladder irritation, anemia, diaphoresis.

Dose and Administration: Adult and Child: IV:

Methemoglobinemia: 1 - 2 mg/kg over several minutes; may be repeated in 1 hour if necessary.

Naloxone Hydrochloride

Injection, 0.02 mg/ml in 2 ml ampoule. 0.4 mg/ml in 1 ml and 10 ml ampoule

Indications: over dosage with opioids; postoperative respiratory depression

Cautions: physical dependence on opioids, cardiac problems or those patients receiving cardiotoxic drugs.

Dose and Administrations:

By IV, 0.8 - 2 mg repeated at intervals of 2 - 3 minutes to maximum of 10 mg if respiratory function does not improve (then question diagnosis); **Child** 10 microgram/kg; subsequent dose of 100 micrograms/kg if no response.

SC or IM: as intravenous injection but only if intravenous route not feasible (onset of action slower).

Continuous IV infusion: 2 mg diluted in 500 ml intravenous infusion solution at a rate adjusted according to the response

Storage: in airtight containers. Protect from light

Penicillamine

Capsule, 250mg

Indications: treatment of copper, mercury, arsenic, lead and zinc poisoning; Wilson's disease and cystinuria; adjunctive treatment of rheumatoid arthritis.

Caution: penicillin allergy.

Drug interactions: antacids, iron salts, digoxin.

Contraindications: renal insufficiency and pregnancy (in patients with rheumatoid arthritis); patients with previous penicillamine-related aplastic anemia or agranulocytosis; breast-feeding.

Side effects: vasculitis, anxiety, agitation, fever, psychiatric disturbances, alopecia, rash, urticaria, wrinkling, anorexia, diarrhea, hematuria, nephrotic syndrome and renal failure.

Dose and Administration: Oral:

Rheumatoid arthritis:

Adult: 125 - 250mg/day, may increase dose at 1- 3 month intervals up to 1 – 1.5g/day;

Wilson's disease:

Adult: 250 mg/4 times /day.

Child < 12 years: 20mg/kg/day in 2-3 divided doses, round off to the nearest 250 mg dose; maximum 1g/day.

Cystinuria:

Adult: 1-4g/day in divided doses every 6 hours; usual dose: 2g/day.

Child: 30mg/kg/day in 4 divided doses.

Chelation therapy:

Adult: 0.5 - 1.5 g daily in 4 divided doses.

Child: 20 - 40 mg/kg daily in 4 divided doses.

Storage: store in tight, well - closed containers.

Physostigmine salicylate

Injection, 1mg/ml in 1ml and 2ml ampoule

Indications: reverse toxic CNS effects caused by anticholinergic drugs.

Cautions: epilepsy, asthma, diabetes, gangrene, cardiovascular disease, brady cardia.

Drug interactions: bethanechol, methacholine, succinylcholine.

Contraindications: GI or GU obstruction.

Side effects: bradycardia, palpitations, restlessness, nervousness, hallucinations, seizure, nausea, salivation, diarrhea, stomach pain, frequent urge to urinate, muscle twitching, lacrimations, miosis, dyspnea, bronchospasm, respiratory paralysis, pulmonary edema, diaphoresis.

Dose and Administration:

Adult: *IM, IV, SC:* 0.5 - 2mg to start, repeat every 20 minutes until response occurs or adverse effect occurs. Repeat 1- 4mg every 30 - 60 min as life - threatening signs.

Child: *IV:* 0.01 - 0.03 mg/kg /dose (maximum: 0.5 mg/min); may repeat after 5 - 10 minutes to a maximum total dose of 2mg.

Storage: store at controlled room temperature.

Phytomenadione (Vitamin k₁)

Injection, 10mg/ml in 1ml ampoule

Indications: overdose of warfarin and related agents used in rodent poisons.

Cautions: G6PD deficiency.

Drug interactions: warfarine.

Contraindications: impaired hepatic function.

Side effects: shock- like reactions with bronchospasm, cyanosis, tachycardia and vascular collapse.

Dose and Administration:

Adult: *IM:* 10mg

Child: *IM:* 1-5mg. With severe toxicity, vitamin k₁ may be given *I.V.*

Storage: store in airtight containers.

Protamine Sulphate*Injection, 10mg/ml in 5ml ampoule***Indications:** treatment of heparin overdosage.**Cautions:** allergic to fish, vasectomised or infertile males, and prior exposure to protamine or protamine containing insulin; porphyria.**Side effects:** anaphylaxis, transient neutropenia, bradycardia, flushing, systemic hypotension and pulmonary hypertension.**Dose and Administration:**

Heparin route	Time elapsed since heparin given	Protamine Sulfate Per 100u heparin
IV	<15 minutes	1mg
IV	30 -60 minutes	0.5 - 0.75mg
IV	> 2 hours	0.25 - 0.375mg
SC	—	1mg

Protamine sulphate usually is administered by very slow IV injection over 10 minutes. No more than 50mg of the drug should be administered in any 10 minute period.

Storage: store at 2-8 °C.

Pralidoxime Chloride*Tablet, 500 mg**Powder for injection, 1 g in vial*

Indications: It is used as an adjunct to but not as a substitute for atropine in the treatment of poisoning by certain cholinesterase inhibitors. Its main indication is in poisoning due to organophosphorus pesticides or related compounds.

Cautions: It should be used cautiously in patients with impaired renal function (a reduction in dosage may be necessary); myasthenia gravis. It should not be used to treat poisoning by carbamate pesticides.

Drug interactions: succinylcholine, theophylline, aminophylline and respiratory depressants.

Side effects: drowsiness, dizziness, disturbances of vision, nausea, tachycardia, headache, hyperventilation, and muscle weakness; laryngospasm, muscle rigidity (due to rapid IV injection of pralidoxime)

Dose and Administration:

The usual initial parenteral dose of pralidoxime chloride is 1 – 2 g for adult, or 20-40 mg/kg for children; repeat the dose in about 1 hour if muscle weakness has not been relieved (*IV infusion* of 500 mg of the drug per hours)

For prophylactic use in workers exposed to organophosphate insecticides: 1-3g of pralidoxime chloride has been given orally just before exposure to the organophosphate and a second dose has been given after conclusion of exposure or 5 hours after the first dose whichever came first.

Sodium Calcium Edetate*Injection, 200 mg/ml in 5 ml ampoule.*

Indications: treatment of symptomatic acute and chronic lead poisoning.

Cautions: severe renal disease, anuria.

Drug interactions: zinc insulin preparation: do not mix in the same syringe with dimercaprol.

Side effects: arrhythmias, hypotension, chills, skin lesions, hypercalcemia, anorexia, anemia, renal tubular necrosis, sneezing, nasal congestion.

Dose and Administration:

Adult: *IV infusion* or *IM*: usually 1g twice daily or 50-75mg/kg/day for 5 days, followed by a 2-day interruption if a repeat dose is considered.

Child: *IV infusion* (over 8 - 12 hours) or *IM*: usually 1000 - 1500 mg/m² /day for 3- 5 days, followed by a 2-day interruption if a repeat course of therapy is necessary.

Storage: store at controlled room temperature.

Sodium Nitrite

Injection, 3 % (30 mg/ml)

Indications: sodium nitrite is used in the treatment of cyanide poisoning in conjunction with sodium thiosulphate.

Side effects: nausea and vomiting, abdominal pain, dizziness, headache, cyanosis, tachypnoea, and dyspnea; flushing and headache due to vasodilatation.

Dose and Administration:

10 ml *by intravenous injection* over 3 minutes, followed by 25 ml of sodium thiosulphate injection 50 % *by intravenous injection* over 10 minutes

The usual dosage regimen in children is 0.15 to 0.33 ml (approximately 4.5 to 10.0 mg per kg) followed by 1.65 ml per kg of a 25 % solution of sodium thiosulphate.

Storage: store in airtight container.

Sodium Polystyrene Sulphonate

Powder, 15g

Indications: treatment of hyperkalemia.

Cautions: severe CHF, hypertension, edema, or renal failure.

Drug interactions: antacids, laxatives (magnesium hydroxide, aluminum carbonate), digitalis.

Contraindications: hypernatremia, hypokalemia, obstructive bowel disease.

Side effects: hypernatremia, hypokalemia, hypocalcemia, hypomagnesemia, anorexia, constipation, fecal impaction, intestinal obstruction, nausea, vomiting.

Dose and Administration:

Adult: *Oral:* 15g (60ml) 1 - 4 times/day.

Rectal: 30 - 50g every 6 hours.

Child: *Oral:* 1g/kg/dose every 6 hours.

Rectal: 1g/kg /dose every 2 - 6 hours.

Storage: store prepared suspensions at 15-30 °C, store repackaged product in refrigerator and use within 14 days.

Sodium Thiosulphate

Injection, 10 % in 50 ml ampoule

Indications: poisoning with cyanides (used in conjunction with sodium nitrite)

Dose and Administration: See under sodium Nitrite

Universal Antidote (charcoal + tannic acid + magnesium oxide)

Powder, 2 parts + 1 part + 1 part

Indications: treatment of selected cases of acute poisoning to adsorb the toxic substance and thereby reduces its systemic absorption.

Note: The "Universal antidote" is inferior to activated charcoal alone. In addition, the tannic acid component is potentially hepatotoxic. Thus, there is no justification for the use of the "Universal antidote".

19. IMMUNOLOGICAL PREPARATIONS

Immunoglobulins

Immunoglobulins are preparations containing antibodies against infectious micro-organisms and are prepared usually from human plasma or serum. They are used for passive immunization, thus conferring immediate protection against some infectious diseases. They are preferred to antisera of animal origin as the incidence of adverse reactions is less.

Side effects: Local reactions with pain and tenderness at the site of intramuscular injection; hypersensitivity reactions, including rarely anaphylactic reactions, have also been reported; systemic reactions with fever, chills, facial flushing, headache, and nausea may occur following intravenous administration, particularly at high rates of infusion.

Cautions: If immunoglobulins are given after administration of a live vaccine at interval of at least 3 weeks should be allowed to elapse. An interval of 3 months should be allowed between the use of live vaccines and the prior administration of immunoglobulins.

Antisera

Antisera (immunoserum) are sterile preparations containing immunoglobulins obtained from the serum of immunised animals by purification. Antisera have the specific power of neutralising venoms or bacterial toxins, or combining with the bacterium, virus, or other antigen used for their preparation.

Side effects and cautions

Anaphylactic reaction may occur, with hypotension; dyspnoea, urticaria, and shock; serum sickness frequently 7 to 10 days after the injection of serum of animal origin.

Before injecting serum, information should be obtained whenever possible as to whether previous injections of serum have been received and whether the patient is subject to hypersensitivity disorders. Sensitivity testing should be performed before the administration of antisera.

Vaccines

Vaccines are preparations of antigenic materials which are administered with the object of inducing in the recipient active immunity to specific bacteria or viruses. They may contain living or killed microorganisms, bacterial toxoids, or antigenic material from particular parts of the bacterium, rickettsia or virus.

The term vaccination and immunization are often used synonymously and interchangeably. Vaccination is strictly only the administration of a vaccine whereas immunization results in the demonstrable presence of protective levels of antibodies confirmed usually by serological testing.

Side effects: Administration of a vaccine by injection may be followed by a local reaction, possibly with inflammation and lymphangitis. At the site of injected vaccine an induration or sterile abscess may develop. The administration of a

vaccine may be followed by fever, headache, and malaise starting a few hours after injection and lasting for 1 or 2 days.

Cautions: Vaccination should be postponed in patients suffering from any acute illness although minor infections without fever or systemic upset are not regarded as contra-indications. Immunization should not be carried out in individuals who have previously had a severe local or generalized reaction to the vaccine. Asthma, eczema, hay fever, or a history of allergy, should not be regarded as contraindications to vaccination. Before injection of a vaccine any alcohol or disinfectant used for cleansing the skin should be allowed to evaporate otherwise inactivation of live vaccines may occur.

Live vaccines should not be given to patients receiving high-dose systemic corticosteroid therapy; to patients receiving immunosuppressive therapy including general irradiation; to patients suffering from certain malignant conditions such as lymphoma, leukemia, Hodgkin's disease, or other tumors of the reticuloendothelial systems; or to patients with other types of impaired immunological responses, such as hypogammaglobulinaemia. Vaccination should also be postponed for at least 6 months after the cessation of antineoplastic chemotherapy and for at least 3 months after high-dose systemic corticosteroid therapy.

Because of a theoretical risk to the fetus, live vaccines should not be administered during pregnancy unless it is considered there is a significant risk of exposure to infection.

As with other causes of immunosuppression, the efficacy of vaccines may be reduced in HIV positive individuals.

Any agent which is active against the bacterial or viral strain present in the vaccine may interfere with development of a protective immune response but treatment with antibiotics should not be considered to be a contraindication to immunization.

Anti-Rho (D) Immune Globulin

Injection, 2ml in vial

Indications: to prevent a rhesus (Rh) negative mother actively forming antibodies to fetal rhesus positive (Rh+) red blood cells that may pass into the maternal circulation during child birth, abortion, or certain other sensitizing events causing disease of the new born (erythroblastosis fetalis).

Cautions: as for immunoglobuline in general; Rho (D) immune globulin should be used with caution in individuals with a history of prior allergic reactions to preparation containing human immune globulins. Caution also in those with thrombocytopenia or bleeding disorders.

Contraindications: Rho (D)- positive individuals, Rho (D) - negative individuals who have been previously sensitized to Rho (D) antigens, anaphylactic reaction to preparation containing human immune globulins.

Side effects: as for immunoglobulin in general; pain tenderness, and discomfort at site of injection, slight temperature elevations, fever, myalgia, lethargy.

Dose and Administration:

After full-time delivery: IM: 500 units (100ug). A higher dose may be required depending on the amount of transplacental bleeding.

Termination of pregnancy - Rh-negative women having spontaneous or induced up to 13 weeks of gestation or more: IM: 250 units (50ug) of anti (D) Immunoglobulin.

Occurrence of risk of sensitization during pregnancy from threatened abortion, amniocentesis or external version: IM: 250-500 units (50-100ug) of anti Rho (D) immunoglobulin.

Storage: at a temperature between 2°C and 8°C.

BCG Vaccine

Injection, 500,000 organisms /ml in 0.05ml and 0.1ml

Indications: active immunization against tuberculosis.

Cautions: pregnancy, eczema, scabies-vaccine site must be lesion-free; see also notes under general description above.

Drug interactions: asparaginase, azathioprine, bleomycin, ciclosporin, daunorubicin, dactinomycin, fluorouracil, vinblastin, vincristine.

Contraindications: generalized edema, antimycobacterial treatment see also notes under general description above.

Side effects: lymphadenitis and keloid formation; osteitis and localized necrotic ulceration, rarely, disseminated BCG infection in immunodeficient patients.

Dose and Administration: Intradermal injection:

Adult and Child > 3 month: 0.1 ml; **Infants** up to 3 months: 0.05ml.

Storage: store in refrigerator.

Botulism Antitoxin, polyvalent types A, B and E

Indications: treatment of botulism, caused by the injection of infected food.

Note: Treatment should be given as early as possible in the course of the disease. Botulism antitoxins are generally not effective for infant botulism.

Cautions, Contraindications, Side effects; see notes above, as for antisera in general.

Dose and Administrations

Prophylaxis: IM: 20 ml as soon as possible after exposure.

Treatment: 20 ml (diluted to 100 ml with sodium chloride 0.9%), slow IV infusion followed by 10 ml 2 - 4 hours later if necessary, and further doses at intervals of 12 - 24 hours.

Storage: store at 2° to 8° c in single use containers.

Cyclosporin A

Capsules, 10mg, 25mg, 50mg, 100mg

Oral solution, 100mg/ml

Concentrate for IV infusion (oily), 50mg/ml

Indications: prevention and treatment of graft rejection following organ and tissue transplantation; severe chronic plaque - type psoriasis, and severe atopic dermatitis.

Cautions: renal or hepatic disease; porphyria.

Contraindications: hypersensitivity to ciclosporin, malignancy, uncontrolled hypertension, or uncontrolled infections.

Drug interactions: amphotericin B, cimetidine, omeprazole, ketoconazole, itraconazole, fluconazole, erythromycin, doxycycline, diltiazem, verapamil, metoclopramide, colchicine, methyl prednisolone, oral contraceptives, danazol, norethisterone, androgens, allopurinol, amiodarone, and grapefruit juice, rifampicin, carbamazepine, phenytoin, phenobarbital, isoniazid, prubucol, ACE inhibitors, potassium-sparing diuretics, aminoglycosides, amphotericin B, ciprofloxacin, vancomycin, co-trimoxazole, NSAIDs, digoxin, colchicine, simvastatin, pravastatin, other immuno suppressants, fat rich meal.

Side effects: nephrotoxicity, hyperkalaemia, hyperuricaemia, hypomagnesaemia and hyperlipidaemia, microangiopathic haemolytic anaemia, hypertension, nausea, vomiting, headaches, hepatotoxicity, neurotoxicity includes tremor, seizures, dysarthria, confusion, drowsiness, hallucinations, visual disturbances and mental changes.

Dose and Administration:

Adult:

Organ transplantation (single therapy):

Oral: 10 - 15 mg/kg/day in 2 divided doses, reduced gradually according to blood levels; maintenance 2 - 6 mg/kg/day in 2 divided doses.

IV infusion: 2 - 6 mg/kg/day (diluted in 0.9% sodium chloride solution or 5% glucose and given as a continuous infusion over 24 hours) continued until patient can take oral therapy.

Severe psoriasis:

Oral: 2.5 mg/kg/day in 2 divided doses; may be increased gradually up to maximum of 5mg /kg/day if no improvement after 1 month. Discontinue if response still not adequate within 6 weeks on 5mg/kg /day.

Severe atopic dermatitis:

Oral: initially 2.5mg/kg/day in 2 divided doses; may be increased rapidly if response inadequate in 2 weeks, up to a maximum of 5mg/kg day. If very severe, initiate with 5 mg/kg/day and reduce gradually once response is satisfactory. Duration of treatment should not exceed 8 weeks.

Child: *organ transplantation:* As for adults. Higher or more frequent doses may be required.

Storage: store at room temperature.

Diphtheria Antitoxin

Injection, 200 units/ml

Indications: for passive immunization in suspected cases of diphtheria and should be given without waiting for bacteriological confirmation of the infection.

Note: - An antibacterial agent such as erythromycin or benzyl penicillin is usually given concomitantly. Diphtheria antitoxin is generally not used for the prophylaxis of diphtheria because of the risk of provoking a hypersensitivity reaction.

Contacts of a diphtheria case should be promptly investigated, given a prophylactic course of erythromycin and active immunization with a suitable diphtheria containing vaccine as appropriate and kept under observation.

Cautions, Contraindications, Side effects; as for antisera in general, see notes above.

Dose and Administration

Note: A test dose of diphtheria antitoxin should always be given to eliminate hypersensitivity 10,000 - 30,000 units increased to 40,000 - 100,000 units in severe cases: doses of up to 30,000 units should be given *intramuscularly* but for those over 40,000 units a portion is given *intramuscularly* followed by the bulk of the dose *intravenously* after an interval of $\frac{1}{2}$ - 2 hours.

Note: - children require the same dose as adults, depending on the severity of the awe.

Storage: store at 2° to 8°C.

Diphtherial and Tetanus Toxoid

Injection, 0.5 ml

Indications:

Infants and Children through 6 years of age: Active immunity against diphtheria and tetanus when pertussis vaccine is contraindicated.

Children ≥ 7 years of age and Adults: Active immunity against diphtheria and tetanus; tetanus prophylaxis in wound management.

Cautions: bleeding disorders or anticoagulant therapy.

Drug interactions: antimetabolites, alkylating agents, cytotoxic drugs, corticosteroids, irradiation.

Contraindications: hypersensitivity to diphtheria, tetanus toxoid.

Side effects: dizziness, seizure, rash, nausea, vomiting, local reactions, myalgia, arthralgia.

Dose and Administration: *I.M.*

Infants and Child ≤ 6 years (DT):

Primary immunization: 6 weeks to 1 year: three 0.5 ml doses at least 4 weeks apart; administer a reinforcing doses 6 - 12 months after the third injection.

1 - 6 years: two 0.5 ml doses at least 4 weeks apart, reinforcing dose 6 - 12 months after second injection;

Booster immunization: 4 - 6 years: 0.5 ml; not necessary if the fourth dose was given after fourth birthday; routinely administer booster doses at 10 -year intervals with the adult preparation.

Child ≥ 7 years and Adult:

Primary immunization: Patients previously not immunized should receive 2 primary doses of 0.5ml each, given at an interval of 4 - 6 weeks; third (reinforcing) doses of 0.5ml 6 - 12 months later.

Booster immunization: 0.5ml every 10 years; to be given to children 11 - 12 years of age if at least 5 years have elapsed since last dose of toxoid containing vaccine.

Storage: store at 2 - 8 °C. Do not freeze.

Diphtheria, Tetanus Toxoid and Pertussis Vaccine*Injection, 0.5ml***Indications:** active immunization against diphtheria, tetanus, and pertussis from age 6 weeks through seventh birthday.**Cautions:** children with coagulation disorders; seizure disorder.**Drug interactions:** anticoagulants, corticosteroids and immunosuppressant agents.**Contraindications:** children ≥ 7 years of age.**Side effects:** drowsiness, irritability, decreased appetite, redness, swelling, fever, vomiting, pain, redness, and tenderness.**Dose and Administration:****Child** 6 weeks to < 7 years: *I.M.* 0.5ml.*Primary series:* Three doses, usually given at 2, 4, and 6 months of age; may be given as early as 6 weeks of age and repeated every 4 - 8 weeks, use same product for all 3 doses.*Booster series:**Fourth dose:* given at ≈ 15 -20 months of age, but at least 6 months after third dose.*Fifth dose:* Given at 5 - 6 years of age, prior to starting school or kindergarten; If the fourth dose is given at ≥ 4 years of age, the fifth dose may be omitted.**Storage:** store in refrigerator at 2 - 8 °C; do not freeze.**Gas Gangrene Antitoxin, Mixed***Injection, 25,000 units in 20 ml***Indications:** treatment of gas gangrene and for prophylaxis in patients at risk following injury.

Note: They are now seldom used and have been superseded by antibacterials such as benzyl penicillin or metronidazole.

Cautions, Contraindication and Side effects; as for antisera in general,**Storage:** Store at 2° to 8°c, and not be allowed to freeze.**Haemophilus Influenza type B (Hib) vaccine***Injection, 0.5 ml***Indications:** for active immunization against Haemophilus influenzae type b infections, one of the major causes of meningitis and other severe systems illnesses in young children.**Cautions, Contraindications and Side effects;** As for vaccines in general, see notes above; and Erythema multiforme has been reported rarely in children.

Note: - Different proprietary vaccines may be conjugated to differing proteins and therefore the same vaccine should be used for an immunization course; if a different vaccine needs to be employed the entire primary course should be repeated.

Dose and Administrations*By deep SC or IM injection* in doses of 0.5 ml; doses are given at 2, 3 and 4 months of age.

Note: - The vaccine may be administered at the same time as combined diphtheria, tetanus, and pertussis vaccines of the primary immunization schedule children aged under 13 months who have already commenced or completed their primary immunization schedule should receive three doses of Hib at intervals of one month. Children aged 13 to 48 months should be given a single dose as they are at lower risk and the vaccine is effective after a single dose in this age group.

Hepatitis B Vaccine, inactivated

Injection, 16.5 % in 2 ml and 10 ml.

Indications: for active immunization against hepatitis B infections in persons at high risk of contracting the disease.

Cautions; Side effects; see notes above, as for vaccines in general.

Note: The high risk group include: health care personnel, laboratory workers, or any other personnel who have direct contact with patients or their body fluids; patients requiring haemodialysis; haemophiliacs and those receiving regular blood transfusions or blood products; contacts or sexual partners of cases or carriers of hepatitis B; individuals who frequently change sexual partners; parenteral drug abusers; and some travelers to areas where hepatitis B is endemic.

Dose and Administrations:

Note: National Immunization schedules may vary; WHO schedule is written below.

Immunization of Children against hepatitis B: IM: infant 0.5 ml either at birth and at 6 and 14 weeks of age, or at 6, 10 and 14 weeks of age.

Immunization of unimmunized high risk persons against hepatitis B: IM: Adult and child over 15 years of age 3 doses of 1 ml, with an interval of 1 month between the first and second dose and 5 months between the second and third doses; child under 15 years, 0.5 ml.

Note: Different products may contain different concentrations of antigen per ml. Consult manufacturer's literature.

The vaccine should be given in the deltoid region in adults; anterolateral thigh is the preferred site in infants and children; it should not be injected into the buttock (vaccine efficacy reduced); subcutaneous route used for patients with hemophilia.

Storage: store at 2° to 8° c, not be allowed to freeze.

Hepatitis B vaccine, Recombinant yeast DNA

Injection, 0.5ml

See under Hepatitis B Vaccine, Inactivated.

Dose and Administration

The basic immunization schedule consists of 3 doses of a hepatitis schedule consists of 3 doses of a hepatitis B vaccine, with the second and third doses 1 and 6 months, respectively, after the first. Typical doses for adults are 10 or 20mcg and for children 2.5 to 10mcg.

Storage: store at 2° to 8° c, not be allowed to freeze, and be protected from light. Under these conditions it may be expected to retain its potency for months.

Human Antirabies Immunoglobulin

Injection, 150 IU/ml, in 2 ml

Indications: Passive immunization either post-exposure or in suspected exposure to rabies in high-risk countries in unimagined individuals (in conjunction with rabies vaccine).

Cautions, Side effects: see notes above, as for immunoglobulin in general.

Contraindications: see notes above; avoid repeat doses after vaccine treatment initiated; intravenous administration.

Note: If schedule requires rabies vaccine and rabies immunoglobulin to be administered at the same time, they should be administered using separate syringes and separate sites.

Dose and Administration:

Immunization against rabies: Post-exposure (or suspected infiltration): **Adult and Child:** 20 units/kg (half by intramuscular injection and half by wound infiltration)

Storage: store at 2° to 8° c,

Immune Serum Globulin, Human (Gamma Globulin, Human)

Injection, 16.5% in 2ml, 5ml and 10ml

Indications: for replacement therapy in patients with immune deficiency states, e.g. agammaglobulinaemia or hypogammaglobulinaemia, and for the immediate protection of susceptible contacts against hepatitis A or measles.

Cautions: thrombocytopenia or coagulation disorders.

Drug interactions: Live virus, vaccines (measles, mumps, rubella).

Contraindications: IgA deficiency.

Side effects: flushing, angioedema, chills, lethargy, fever, urticaria, erythema, nausea, vomiting, local (myalgia, pain, tenderness, muscle stiffness at I.M site), hypersensitivity.

Dose and Administration: IM:

Hepatitis A prophylaxis: Contacts: 0.02 - 0.04 ml/kg within 1 week of exposure.

Pre-exposure prophylaxis for travellers:

- Period of stay < 3 months, 0.02 ml/kg

- Period of stay > 3 months (continued exposure), 0.06 ml/kg 4-6 monthly.

Measles prophylaxis: within 1 week of contact: 0.2 - 0.25 ml/kg (maximum 15 ml).

Immunocompromised patients: 0.5 ml/kg (maximum 15 ml). Follow after 3 months with active immunisation in patients ≥ 15 months of age, unless contraindicated.

Replacement therapy: congenital immunoglobulin deficiencies: 0.2 - 0.5 ml/kg, repeated 4 - 8 weekly.

Transient hypogammaglobulinaemia: 0.2 - 0.5 ml/kg, repeated when necessary.

Storage: store in refrigerator, do not freeze.

Influenza Virus Vaccine, Polyvalent

Injection, 0.5 ml

Indications: provide active immunity to influenza virus strains contained in the vaccine.

Cautions: thrombocytopenia or any coagulation disorder.

Drug interactions: DTP

Contraindications: hypersensitivity reaction.

Side effects: fever, malaise, angioedema, urticaria, local (tenderness, redness, or induration at the site of injection), myalgia, allergic or anaphylactoid reactions.

Dose and Administration: Adult: *I.M or deep SC*, 0.5 ml.

Storage: store between 2-8 °C.

Interferon Alpha

Injection, 3, 5, 10 million units.

Indications: treatment of malignant neoplasms such as non-Hodgkin's lymphoma, hairy-cell and chronic myeloid leukaemias, and renal cell carcinoma. Has some efficacy in chronic viral hepatitis B and C.

Cautions: depression, autoimmune disease, preexisting cardiac disease, renal and hepatic impairment, myelosuppression, diabetes, thyroid disease.

Drug interactions: theophylline, ACE inhibitors, melphalan, prednisolone, clozapine, warfarin and zidovudine.

Contraindications: hypersensitivity reaction, autoimmune hepatitis.

Side effects: fever, chills, myalgia, depression, unusual tiredness, hypo and hypertension, arrhythmias, transient confusion, somnolence, delirium, extrapyramidal symptoms, mania and neurasthenia with catatonic episodes. Clinical hypothyroidism preceded by appearance in the blood of thyroid autoantibodies reported with long-term interferon. Myelosuppression (granulocytopenia and thrombocytopenia); GI effects and elevation of liver enzymes reported.

Dose and Administration: Doses for individual products may differ; package insert should be consulted.

Hairy-cell leukaemia: SC, 2 million IU/M² administered (on alternate days) 3 times a week;

Chronic viral hepatitis:

Chronic Hepatitis B is usually treated with 5 - 10 million IU thrice weekly for 16 weeks.

Chronic hepatitis C is usually treated with 3 - 5 million IU thrice weekly for 24 weeks.

Storage: store in refrigerator at 2-8 °C; do not freeze.

Interferon Gamma

Injection, 3, 5, million units / 0.5ml

Indications: reduce frequency and severity of serious infections associated with chronic granulomatous disease; delay time to disease progression in patients with severe malignant osteopetrosis.

Cautions: cardiac disease, seizure disorders, CNS disturbances, or myelosuppression.

Contraindications: hypersensitivity reaction.

Side effects: fever, headache, chills, fatigue, rash, diarrhea, vomiting, injection site erythema or tenderness (local), depression, nausea, abdominal pain, myalgia, arthralgia, back pain.

Dose and Administration:

Chronic granulomatous disease: **Child** > 1 year and **Adult:** SC:

BSA $\leq 0.5 \text{ m}^2$: 1.5 mcg /kg/dose 3 times /week.

BSA > 0.5 m²: 50 mcg/m² (1 million int. units/m²) 3 times/week.

Severe, malignant osteopetrosis: **Child** > 1 year: SC:

BSA $\leq 0.5 \text{ m}^2$: 1.5mcg/kg/dose 3 times /week

BSA > 0.5m²: 50mcg/m² (1 million int. units/m²) 3 times/week.

Storage: store in refrigerator. Do not freeze.

Measles Virus Vaccine, Live Attenuated

Injection, 0.5 ml

Indications: active immunization against measles.

Side effects: as for vaccines in general, see notes above, and fever and skin rashes may occur following the administration of measles vaccines. The fever generally starts 5 to 10 days after the injection, lasts for about 1 or 2 days, and has sometimes been accompanied by convulsions. Conjunctivitis, coryza, pharyngitis, and cough may also occur. More serious effects reported rarely after the use of the vaccine include encephalitis and thrombocytopenic purpura.

Cautions: see notes above; pregnancy

Contraindications: see notes above; hypersensitivity to any antibiotic present in vaccine - consult manufacturer's literature; hypersensitivity to egg.

Dose and Administration:

Immunization of children against measles: IM or deep SC injection: infant at 9 months of age, 0.5 ml

Prophylaxis in susceptible children after exposure to measles: IM or deep SCneous injection within 72 hours of contact, child over 9 months of age 0.5 ml

Storage: store at 2° to 8° c and be protected from light.

Meningococcal polysaccharide vaccine

Injection, 0.5ml

Indications: for active immunization against *Neisseria meningitidis* infections which include meningitis and septicaemia.

Note: - Meningococcal vaccines are indicated in persons at risk, in epidemic or endemic areas, of meningococcal disease caused by the specific serotypes contained in the vaccine. It is given as an adjunct to chemoprophylaxis in close contacts of persons traveling to countries where the disease is endemic. Asplenic persons or those who have terminal complement component deficiencies are at higher than normal risk of acquiring meningococcal infection.

Cautions: as for vaccines in general; Immunity to some meningococcal vaccines may be insufficient to confer adequate protection against infection in infants under 2 years of age.

Contraindications and Side effects; as for vaccines in general.

Dose and Administration:

SC or IM: A single injection of 0.5ml

Storage: store both the freeze-dried and the reconstituted vaccine between 2 and 8°C. Protect from freezing.

Pneumococcal Polysaccharide Vaccine

Injection, 0.5ml

Indications: people at risk of developing serious pneumococcal infection, such as patients with chronic cardiac or pulmonary disease, and with illnesses or conditions known to predispose to pneumococcal infection (such as sickle cell disease, nephritic syndrome, previous splenectomy, multiple myeloma and Hodgkin's disease); also in immunocompromised patients, including those with HIV infection.

Contraindications: pregnancy, active infection and children under 2 years old.

Side effects: transient, local pain and erythematous at the injection site, fever may occur occasionally.

Dose and Administration: *SC or IM*, 0.5 ml.

Storage: store in refrigerator at 2- 8 °C.

Poliomyelitis Vaccines

Poliomyelitis is an acute viral infection spread by the faecal-oral route, which can cause paralysis of varying degree. There are two types of vaccine against poliomyelitis: oral and injectable. Oral poliomyelitis vaccine (OPV) is composed of three types of live attenuated poliomyelitis viruses.

Poliomyelitis vaccine, Trivalent

Types I, II, III

Oral suspension, 0.5 ml, 10ml and 20 ml.

Indications: active immunization against Poliomyelitis.

Cautions: pregnancy

Drug interactions: asparaginase, azathioprine, ciclosporin, immunoglobulin.

Contraindications: patients with diarrhea or vomiting; food which contains a preservative.

Side effects: rarely, vaccine-associated poliomyelitis in recipients of vaccine and contacts of recipients.

Dose and Administration: *Oral:*

Adult:

Primary immunization of unimmunized adults: 3 doses each of drops with an interval of at least 4 weeks between each dose.

Reinforcing immunization: 3 drop 10 years after completion of primary course.

Child:

Primary immunization: 3 drops at birth and at 6, 10 and at 14 weeks of age.

Reinforcing immunization: 3 drops at least 3 years after completion of primary course and a further 3 drops at 15 - 19 year of age.

Note: National immunization schedules may vary.

Storage: store between 2-8 °C or in the frozen state.

Rabies Antiserum, Equine

Injectio, 200 units in 5ml

Indications: rabies antiserum, equine is used to provide passive immunization to Rabis in patients who have received bites from rabid animals or animals suspected of being rabid.

Cautions: as for antisera in general; caution should be taken in allergic patients. The patient must be kept under observation after the administration of full doses of antisera and adrenaline injection kept in readiness for emergency use.

Side effects: as for antisera in general; nephritis, myocarditis, polyarthritis, neuritis and ureitis.

Dose and Administration: usual dose 40 units per kg of body weight given at the same time, but at different sites, as the first dose of a Rabis vaccine. It has been recommended that 50% of the dose should be administered by *local infiltration* at the site of the wound and the remainder given by *IM injection* unless the wound involves mucous membranes when the entire dose should be given *intramuscularly*.

Storage: between 2° and 8°c.

Rabies Vaccine

Injection, 100 ml in vial

Indications: for active immunization against rabies. They are given, with rabies immunoglobulin or antisera, for post exposure treatment to patient who have been bitten by rabid animals or animals suspected of being rabid. They are also used for pre-exposure prophylaxis against rabies in persons at high risk of exposure to rabies vaccine.

Cautions: as for vaccines in general; see notes above.

Note: studies have shown that when this vaccines is injected into the gluteal region, there is a poor response. Concomitant administration of chloroquine may also affect the antibody response. Because of the potential consequences of inadequately treated rabies exposure and because there is no indication that fetal abnormalities have been associated with rabies vaccination, pregnancy is not considered a contraindication to post exposure prophylaxis. If there is substantial risk of exposure to rabies, pre-exposure prophylaxis may also be indicated during pregnancy.

Side effects: as for vaccines in general, see notes above; and patients may experience pain, eurhythmic, and in duration at the injection site after the use of any type of rabies vaccine; nausea, headache, fever, malaise, or myalgia may also occur.

Neuroparalytic and hypersensitivity reactions have been associated with the vaccines derived from animal nerve tissues or duck embryos.

Dose and Administration

Prophylactic: deep SC or IM injection in the deltoid region, 1 ml on days 0, 7, and 28; also booster doses every 2 – 3 years to those at continued risk.

Storage: store at 2° to 8°c, not be allowed to freeze, and be protected from light. Under these conditions it may be expected to retain its potency for at least 2 years.

Rabies Vaccine, Duck Embryo

Injection; 100 ml in vial

See under Rabies vaccine

Dose Administration

Prophylactic, IM injection in the deltoid muscle or anterolateral thigh in small children, 1 ml on days 0,7 and 21 or 28; also booster doses every 2 - 5 years for those at continued risk.

Post exposure, IM injection in the deltoid muscle or anterolateral thigh in small children, 1ml.

Storage: store at 2° to 8° c.

Rabies (Human diploid cell) vaccine

Injection, 2.5IU/ml

Indications: rabies human diploid cell vaccine is used for active immunization against rabies. They are used as a part of post exposure treatment, for the prevention of rabies in patients who have been bitten by rabid animals or animals suspected of being rabid.

Cautions: as for vaccine in general; the vaccine should be administered with caution in patients with a history of allergic disorders or who have exhibited previous systemic allergic reaction to human diploid cell vaccine.

Drug interactions: rabies immunoglobulin, antimalarial agents, corticosteroids immuno suppressive agents.

Side effects: as for vaccine in general; pain, erythema and induration at injection site, pruritis, nausea, headache, fever.

Dose and Administration:

For post exposure therapy: deep *SC* or *IM*: 6 doses of human diploid cell vaccine, each of 1ml on days 0,3,7,14, 30 and 90

For pre-exposure prophylaxis against rabies: *IM* or *ID*: 2 doses of human diploid cell vaccine given 4 weeks apart with a third dose after 12 months, either 1ml may be given by deep *SC* or *IM injection* or 0.1ml *ID*. Booster doses should be given every 1 to 3 years depending upon the risk of exposure.

Storage: between 2° and 8°c.

Scorpion Venom Antisera (Scorpion Antivenom)

Injection

Indications: to neutralize the venom of one or more species of scorpion

Cautions: allergic to the antivenin, sensitivity testing should be preformed.

Side effect: as for antisera in general; urticaria, nephritis, myocarditis, polyarthritis, neuritis, ureitis.

Dose and Administration: The use of a scorpion antiserum suitable for the species of scorpion can prevent symptoms provided it is done with the least possible delay, other general supportive measures may also be needed. The volume stated on the label as the dose, should preferably be made directly into the site of the sting but if this cannot be done, as much as possible should be

injected into the site and the remainder *intramuscularly* into a convenient proximal position.

Snake Venom Antiserum Polyvalent

Injection, 10ml

Indications: antivenin (crotalidae) polyvalent neutralizes absorbed venom of crotalid snakes (pit vipers), including the rattlesnake, copperhead, water moccasin and tropical and asiatic crotalids, and is used to prevent or minimize the effects of poisoning by these snakes.

Cautions: in people who have been snake-bitten if they have a history of asthma hay fever, urticaria, or other allergic manifestation. Intradermally sensitivity testing should be performed before administration.

Side effect: as for antisera in general; itching, edema of the face, tongue and throat, cough, vomiting, cardiovascular collapse.

Dose and Administration: For *IV infusion*, a 1:1 to 1:10 dilution of reconstituted antivenin in 0.9% sodium chloride or 5% dextrose injection is prepared.

Usual dose - *IV infusion*, 5-10ml of diluted antivenin, infused over 3-5 minutes with careful observation of the patient.

Tetanus Antitoxin, Equine

Injection, 1500 units, 20,000 units

Indications: tetanus antitoxin, equine is indicated for temporary passive immunization against tetanus and also to prevent tetanus infection that arise from the toxins produced by *Clostridium tetani*.

Cautions: allergic to the antitoxin. For this sensitivity testing should be performed.

Side effects: Anaphylaxis (with hypotension, dyspnoea, urticaria, shock), serum sickness (fever, vomiting, diarrhoea, bronchospasm, urticaria).

Dose and Administration:

Adult: *prophylaxis after injury of non-immune or partially immune persons: SC, or IM:* 3000 - 5000 units of tetanus antitoxin.

Treatment of established tetanus: 50,000 - 100,000 units part of which is administered by *IV injection* with the remainder being given *intramuscularly*.

Tetanus Immune-Human Globulin

Injection, 3000 units

Indications: for passive immunization against tetanus.

Note: -The use of tetanus immunoglobulins is recommended as part of the management of tetanus-prone wounds in persons unimmunized or incompletely immunized against tetanus, in persons whose immunization history is unknown, and in persons who received the last dose of tetanus vaccine more than 10 years previously.

Cautions: - as for immunoglobulin in general; tetanus immunoglobulins should not be injected in to the same site or in the same syringe.

Contraindications and Side effects; see notes under general description above.

Dose and Administration: The usual dose of tetanus immunoglobulin is 250 units by *intramuscular injection* but if more than 24 hours have elapsed since the wound was sustained, if there is a risk of heavy contamination, or following burns 500 units should be given irrespective of the immunization history.

Tetanus immunoglobulin is also used in the treatment of tetanus, a recommended dose being 150 units per kg body-weight given *intramuscularly* in to different sites.

Note: The pediatric dose is the same as for adults. Alternatively, in children younger than 7 years of age, tetanus immunoglobulin can be given in doses of 4 units per kilogram of body weight.

Storage: store between 2 and 8°C. Do not freeze.

Tetanus Toxoid

Injection, 0.5 ml, 1ml

Indications: active immunization against tetanus and neonatal tetanus; wound management (tetanus - prone wounds and clean wounds).

Cautions: patients on anticoagulants.

Drug interactions: anticoagulants, corticosteroids.

Contraindications: hypersensitivity to tetanus toxoid.

Side effects: hypotension, fever, rash, urticaria, nausea, local (edema, redness, warmth), arthralgia.

Dose and Administration:

Unimmunized patients: IM, 2 doses of 0.5ml, 6 – 8 weeks apart. A third dose is recommended 6 -12 months after the second dose, and is essential when tetanus immunoglobulin was given at the time of the first injection. In these cases the interval between the first and second doses should be reduced to 4 weeks.

A booster should be given every 10 years, or following an injury.

Storage: store in refrigerator at 2-8 °C.

Yellow fever Vaccine

Injection, 500LD, 50 Doses (WHO specification)

Indications: active immunization against yellow fever.

Cautions: pregnancy.

Contraindications: infants under 6 months of age; hypersensitivity to any antibiotic present in vaccine and egg.

Side effects: rarely encephalitis, generally in infants under 9 months.

Dose and Administration: **Child** ≥ 9 months and **Adult:** SC: one dose (0.5ml).

Infant 6-9 months of age: 0.5ml, only if risk of yellow fever is unavoidable.

Booster: Every 10 years.

Storage: store at a temperature between 0- 5 °C. Do not freeze.

20. MISCELLANEOUS

Anticoagulant Citrate Dextrose solution (ACD Solution) Sodium Citrate + Citric Acid + Dextrose

Solution, 1.32g +0.44g +1.47g in each 100ml

Disulfiram

Tablet, 200 mg, 250 mg, 500 mg

Indications: adjunctive treatment of chronic alcoholism.

Cautions: epilepsy, diabetes mellitus, renal or hepatic disease.

Drug interactions: cumulative benzodiazepines such as diazepam and chlorthalidopoxide; isoniazid; metronidazole; phenytoin and warfarin; amitriptyline.

Contraindications: cardiac failure, coronary artery disease, psychosis and drug addiction.

Side effects: In the absence of alcohol - drowsiness, headache, an unpleasant taste, impotence, and mild gastrointestinal disturbances, allergic dermatitis.

❖ The alcohol - disulfiram reaction may be manifested by facial flushing, throbbing headache, tachycardia and nausea and vomiting. During severe reactions there may be respiratory depression, cardiovascular collapse, arrhythmias, seizures, coma and sudden death.

Dose and Administration: *Oral:* 200 - 400 mg daily, or 400 mg on alternate days.

Storage: store at room temperature.

Formaldehyde Solution

Solution, 3%, 8%

Indications: It is a disinfectant active against bacteria, fungi, and many viruses, with a slow action against bacterial spores. It is used for the disinfection of the blankets, bedding, and membranes in dialysis equipment.

Cautions and Side effects: Ingestion of formaldehyde solution causes intense pain, with inflammation, ulceration, and necrosis of mucous membranes. There may be vomiting, haematemesis, blood-stained diarrhoea, haematuria, and anuria; metabolic acidosis, vertigo, convulsions, loss of consciousness, and circulatory failure may occur. Death has occurred after the ingestion of the equivalent of about 30ml of formaldehyde solution. If the patient survives 48 hours, recovery is probable. Formaldehyde vapour is irritant to the eyes, nose, and upper respiratory tract, and may cause coughing, dysphagia, spasm and oedema of larynx, bronchitis, pneumonia, and rarely, pulmonary oedema. Asthma has been reported after repeated exposure.

Storage: at temperature between 15 and 25°C in airtight containers. Avoid contact with plastics.

Glutaraldehyde

Solution, 2%

Indications: It is a bactericidal disinfectant which is rapidly effective against Gram-positive and Gram-negative bacteria. It is also effective against *mycobacterium tuberculosis*, some fungi, and viruses, including hepatitis B virus and HIV, and is slowly effective against bacterial spores.

Side effects: as for Formaldehyde solution.

Glycine

Bladder irrigation solution, 1.5%

Indications: used as urogenital irrigation solutions during certain surgical procedures, particularly transurethral resection of the prostate.

Cautions: hepatic and renal impairment, cardiopulmonary.

Contraindications: anuric patients.

Side effects: systemic absorption of glycine irrigation solutions can lead to disturbances of fluid and electrolyte balance and cardiovascular and pulmonary disorders.

Halazone

Tablet, 4mg

Indications: -Halazone is a disinfectant with the general properties of chlorine in aqueous solution and is used for the disinfection of drinking water. One tablet containing 4mg of Halazone, stabilized with sodium carbonate and sodium chloride, is sufficient to treat about a litre of water in about 30 minutes to 1 hour, more being required for heavily contaminated water. The taste of residual chlorine may be moved by adding sodium thiosulphate.

Storage: -in airtight containers. Protect from light.

KY Jelly (Hydroxyethyl cellulose)

Indications: It is present in lubricant preparations, some of which are used as artificial tears in ocular disorder or dry eye.

Oxidized Cellulose

Indications: Oxidized cellulose is an absorbable haemostatic, when applied to bleeding surface, it swells to form a gelatinous mass that is gradually absorbed by the tissues, usually within 2 to 7 days. Complete absorption of large amounts of such material may take 6 weeks or more.

Cautions: Oxidized cellulose should not be used as a surface dressing, except for immediate control of bleeding, as it inhibits epithelialisation. It should not be used for packing or implantation in bone surgery

Drug interactions: silver nitrate or other escharotic chemicals should not be applied prior to use as cauterization might inhibit absorption of oxidized cellulose. It should not be impregnated with other haemostatic or antibiotics.

Contraindication: use should be avoided in infected wounds.

Side effects: foreign body reaction, headache, burning, stinging, sneezing.

Dose and Administration: the gauze, lint or knitted material should be laid on the bleeding surface or held firmly against the tissue until haemostasis is achieved. Removal of excess oxidized cellulose should then be considered.

Saccharin*Tablet*

Indications: Saccharin and its salts (sodium, calcium, potassium) are intense sweeteners being several hundred times sweeter than sucrose and are used as food additives and artificial sweetener for diabetes. The salts are more often used as they are considered to be the most palatable.

Side effects: allergic and photosensitivity reaction.

Dose and Administration: 5mg per kg of saccharine salt taken daily.

Sodium Chloride Free Salt

Indications: treatment of extracellular volume depletion and sodium depletion

Cautions: Sodium chloride should be used with extreme caution, if at all, in patients with hypertension, congestive heart failure, or other edematous or sodium-retaining conditions, in patients with liver cirrhosis and in patients receiving corticosteroids or corticotropin. Particular caution is necessary in geriatric and post-operative patients.

Contraindications: sodium chloride is contraindicated in patients with conditions in which administration of sodium and chloride is detrimental.

Side effects: nausea, vomiting, diarrhoea, abdominal cramps, thirst, reduce salivation and lachrymation, sweating, fever, tachycardia, hypertension, renal failure, peripheral and pulmonary oedema, respiratory arrest, headache.

Dose and Administration: *Oral:* 1-2 gm 3 times daily depending on individual needs either with food or as a solution; doses of up to 12g daily may be necessary in severe cases.

Sorbitol

Indications: Sorbitol is used in limited quantities either as a sweetening agent or as a source of carbohydrate in diabetic food products. It is also used as a sweetening agent instead of sucrose in many sugar-free oral liquid preparations and in sugar free-preparation of dental caries.

Cautions: impaired kidney function or severe liver damage.

Side effects: flatulence, abdominal pain, diarrhoea, and lactic acidosis hyperuricemia.

Storage: store in airtight container.

Supportive hepatic preparations that contain Essential Phospholipids and Vitamins**Water for injections**

In 2ml, 5ml, 10ml

Water for injection is distilled water free from pyrogens used to produce solutions for injections.

APPENDIXES

APPENDIX I. VITAL SIGNS

Normal Body Temperature

Thermometer held in Armpit (Axillary) = 36.5°c

Thermometer held under Tongue (Oral) = 37°c

Thermometer held in Anus (rectal) = 37.5°c

Normal Pulse Rate

In Babies = 100-140/minute

In Children = 80-100/minute

In Adults = 60-80/ minute

Normal Respiratory Rate

Infants (Birth-2 years) = About 50/minute

Babies (2-5 years) = About 40/minute

Adult = About 12-16/minute.

Normal Blood Pressure (measured after rest)

Adult = Systolic: 120 -140mmHg

Diastolic: 80 -90mmHg

APPENDIX II. ABBREVIATIONS

ACE	Angiotensin-converting enzyme
ADR	Adverse drug reaction
AIDS	Acquired immuno deficiency syndrome
APD	Action potential duration
ATP	Adenosine triphosphate
AV	atrioventricular
BPH	Benign prostatic hyperplasia
CAD	Coronary artery disease
CHF	Congestive heart failure
CNS	Central Nervous System
CNS	Central nervous system
COPD	Chronic obstructive pulmonary disease
CSF	Cerebrospinal fluid
DACA	Drug Administration and Control Authority
DOT	Direct observation of therapy
ECG	Electrocardiogram
EEG	Electro-encephalogram
FDA	Food and Drug Administration
GABA	Gamma –aminobutyric acid (GABA)
GERD	Gastroesophageal disease
GFR	Glomerular filtration rate

GI	Gastrointestinal
G6PD	Glucose 6-phosphate dehydrogenase
GPP	Good prescribing practice
HAART	Highly active antiretroviral therapy
HDL	High-density lipoproteins
HIV	Human immunodeficiency virus
HMG-CoA	3 hydroxy-3-methyl glutaryl Co enzyme A
HRT	Hormone replacement therapy
IU	International Units
LDL	Low-density lipoproteins
LIDE	List of drugs for Ethiopia
MAOI	Monoamine oxidase inhibitor
Mcg	Microgram
MDI	Metered dose inhaler
MTCT	Mother to child transmission
MU	Million Units
NNRTIs	Non nucleoside reverse transcriptase inhibitors
NRTIs	Nucleoside reverse transcriptase inhibitors
NSAID	Non steroidal anti inflammatory drug
OCD	Obsessive compulsive disorder
OTC	Over the counter
PEP	Post exposure prophylaxis
SA node	Sinoatrial node
Sec.	Section
SNRIs	Serotonin and Noradrenalin re-uptake inhibitors
spp.	Species
SSRI	Selective serotonin reuptake inhibitor
SNRIs	Serotonin and noradrenaline re-uptake inhibitors
TCAs	Tricyclic antidepressants
URTI	Upper respiratory tract infection
UTI	Urinary tract infection
USP	United state pharmacopeia
VLDL	Very low density lipid
WHO	World health organization

APPENDIX III. ROUTES OF ADMINISTRATION

- Oral = By Mouth
- I.M. = Intramuscular
- I.V. = Intravenously
- S.C = Subcutaneously
- I.D. = Intradermally

APPENDIX IV. AGE/BODY WEIGHT CHART

Age	Ideal Body Weight (Kg)
Newborn	3.4
1 Month	4.2
3 Months	5.6
6 Months	7.7
1 year	10.0
3 years	14.0
5 years	18.0
7 years	23.0
12 years	37.0
Adult	
Male	68.0
Female	56.0

Note: This is not a local data. It is intended as a guide only.

APPENDIX V. APPROXIMATE MEASURES

- 1 teaspoonful = 5ml
- 1 dessertspoonful = 10ml
- 1 tablespoonful = 15ml

APPENDIX VI. PREPARATION OF PROCAINE PENICILLIN 4 MU (DRY POWDER) FOR PARENTERAL USE

Add 8ml of water for injection to the Procaine Penicillin 4 MU vial to make it a 10ml solution. Each 1ml contains now 400,000IU (250mg) Procaine Penicillin. See Table below.

P.PEN ML	P.PEN IU	P.PEN Milligram
0.2	80,000	50
0.3	120,000	75
0.5	200,000	125
1.0	400,000	250
2.0	800,000	500
3.0	1,200,000	750
4.0	1,600,000	1000 (1gm)
5.0	2,000,000	1250 (1.25gm)
10.0	4,000,000	2500 (2.5gm)

APPENDIX VII. STORAGE CONDITION

- ".. in a dry place" - relative humidity less than 5%
- "..protect from heat" - not more than 30°C
- ".. at room temperature" - 15 to 25 °C
- "..in a cool/cold place" - 8 to 15°C
- "..in a refrigerator" - 0 to 8°C
- "..in a deep freezer" - -15 to 0°C

APPENDIX VIII. Pregnancy

During pregnancy the mother and the fetus form a non-separable functional unit. Maternal well-being is an absolute prerequisite for the optimal functioning and development of both parts of this unit. Consequently, it is important to treat the mother whenever needed while protecting the unborn to the greatest possible extent.

Drugs can have harmful effects on the fetus at any time during pregnancy. It is important to remember this when prescribing for a woman of childbearing age. However, irrational fear of using drugs during pregnancy can also result in harm. This includes untreated illness, impaired maternal compliance, suboptimal treatment and treatment failures.

Such approaches may impose risk to maternal well-being, and may also affect the unborn child. It is important to know the 'background risk' in the context of the prevalence of drug-induced adverse pregnancy outcomes. Major congenital malformations occur in 2–4% of all live births. Up to 15% of all diagnosed

pregnancies will result in fetal loss. The cause of these adverse pregnancy outcomes is understood in only a minority of the incidents.

During the *first trimester* drugs may produce congenital malformations (teratogenesis), and the greater risk is from third to the eleventh week of pregnancy. During the *second* and *third trimester* drugs may affect the growth and functional development of the fetus or have toxic effects on fetal tissues. Drugs given shortly before term or during labour may have adverse effects on labour or on the neonate after delivery. Few drugs have been shown conclusively to be teratogenic in man but no drug is safe beyond all doubt in early pregnancy. Screening procedures are available where there is a known risk of certain defects.

Prescribing in pregnancy

If possible counselling of women before a planned pregnancy should be carried out including discussion of risks associated with specific therapeutic agents, traditional medicines and abuse of substances such as smoking and alcohol. Folic acid supplements should be given during pregnancy planning because periconceptual use of folic acid reduces neural tube defects.

Drugs should be prescribed in pregnancy only if the expected benefits to the mother are thought to be greater than the risk to the fetus. All drugs should be avoided if possible during the first trimester. Drugs which have been used extensively in pregnancy and appear to be usually safe should be prescribed in preference to new or untried drugs and the smallest effective dose should be used. Well known single component drugs should usually be preferred to multi-component drugs.

The following list includes drugs which may have harmful effects in pregnancy and indicates the trimester of risk. It is based on human data but information on *animal* studies has been included for some newer drugs when its omission might be misleading.

Absence of a drug from the list does not imply safety

Table of drugs to be avoided or used with caution in pregnancy

Drug	Comment
Abacavir	Toxicity in <i>animal</i> studies; <i>see</i> section 7.3.1
Acetazolamide	Not used to treat hypertension in pregnancy First trimester: Avoid (toxicity in <i>animal</i> studies)
Acetylsalicylic acid	Third trimester: Impaired platelet function and risk of haemorrhage; delayed onset and increased

	duration of labour with increased blood loss; avoid analgesic doses if possible in last few weeks (low doses probably not harmful); with high doses, closure of fetal ductus arteriosus <i>in utero</i> and possibly persistent pulmonary hypertension of newborn; kernicterus in jaundiced neonates
Aciclovir	Not known to be harmful; limited absorption from topical preparations
Albendazole	Contraindicated in cestode infections; First trimester: avoid in nematode infections;
Alcohol	First, second trimesters: Regular daily drinking is teratogenic (fetal alcohol syndrome) and may cause growth retardation; occasional single drinks are probably safe Third trimester: Withdrawal may occur in babies of alcoholic mothers
Allopurinol	Toxicity not reported; use only if no safer alternative and disease carries risk for mother or child
Amiloride	Not used to treat hypertension in pregnancy
Aminophylline	Third trimester: Neonatal irritability and apnoea have been reported
Amitriptyline	Manufacturer advises avoid unless essential, particularly during first and third trimesters
Amoxicillin	Not known to be harmful
Amoxicillin + Clavulanic acid	Not known to be harmful
Amphotericin B	Not known to be harmful but use only if potential benefit outweighs risk
Ampicillin	Not known to be harmful
Artemether	First trimester: Avoid
Artemether + Lumefantrine	Avoid. Toxicity in <i>animal</i> studies with artemether
Artesunate	First trimester: Avoid
Atenolol	May cause intrauterine growth restriction, neonatal hypoglycaemia, and bradycardia; risk greater in severe hypertension
Atropine	Not known to be harmful
Azathioprine	Transplant patients should not discontinue azathioprine on becoming pregnant; use in pregnancy should be supervised in specialist units; there is no evidence that azathioprine is teratogenic
Azithromycin	Use only if potential benefit outweighs risk
Beclometasone	Benefit of treatment, for example in asthma, outweighs risk

Benzathine benzylpenicillin	Not known to be harmful
Benzylpenicillin	Not known to be harmful
Betamethasone	Benefit of treatment, for example in asthma, outweighs risk
Bleomycin	Avoid (teratogenic and carcinogenic in <i>animal</i> studies); <i>see also</i> section 10
Bupivacaine	Third trimester: With large doses, neonatal respiratory depression, hypotonia, and bradycardia after paracervical or epidural block
Calcium folinate	Manufacturer advises use only if potential benefit outweighs risk
Carbamazepine	First trimester: Risk of teratogenesis including increased risk of neural tube defects (counselling and screening and adequate folate supplements advised, for example 5 mg daily); risk of teratogenicity greater if more than one antiepileptic used; <i>see also</i> section 4.4 Third trimester: May possibly cause vitamin K deficiency and risk of neonatal bleeding; if vitamin K not given at birth, neonate should be monitored closely for signs of bleeding
Ceftazidime	Not known to be harmful
Ceftriaxone	Not known to be harmful
Chlorambucil	Avoid; use effective contraception during administration to men or women;
Chloramphenicol	Third trimester: Neonatal 'grey' syndrome
Chloroquine	First, third trimesters: Benefit of prophylaxis and treatment in malaria outweighs risk; important: <i>see also</i> section 7.4.1
Chlorphenamine	No evidence of teratogenicity
Chlorpromazine	Third trimester: Extrapyramidal effects in neonate occasionally reported
Ciclosporin	There is less experience of ciclosporin in pregnancy but it does not appear to be any more harmful than azathioprine; use in pregnancy should be supervised in specialist units
Ciprofloxacin	All trimesters: Avoid—arthropathy in <i>animal</i> studies; safer alternatives available
Cisplatin	Avoid (teratogenic and toxic in <i>animal</i> studies); <i>see also</i> section 10
Clindamycin	Not known to be harmful
Clomifene	Possible effects on fetal development
Clomipramine	Manufacturer advises avoid unless essential, particularly during first and third trimester

Clonazepam	Avoid regular use (risk of neonatal withdrawal symptoms); use only if clear indication such as seizure control (high doses during late pregnancy or labour may cause neonatal hypothermia, hypotonia and respiratory depression)
Cloxacillin	Not known to be harmful
Codeine	Third trimester: Depresses neonatal respiration; withdrawal effects in neonates of dependent mothers; gastric stasis and risk of inhalation pneumonia in mother during labour
Contraceptives, oral	Epidemiological evidence suggests no harmful effects on fetus
Cromoglicic acid	<i>see</i> Sodium cromoglicate
Cyclophosphamide	Avoid (use effective contraception during and for at least 3 months after administration to men or women)
Cytarabine	Avoid (teratogenic in <i>animal</i> studies); <i>see also</i> section 10
Dacarbazine	Avoid (carcinogenic and teratogenic in <i>animal</i> studies); ensure effective contraception during and for at least 6 months after administration to men or women; <i>see also</i> section 8.2
Dactinomycin	Avoid (teratogenic in <i>animal</i> studies); <i>see also</i> section 10
Dapsone	Third trimester: Neonatal haemolysis and methaemoglobinaemia; folic acid 5 mg daily should be given to mother
Daunorubicin	Avoid (teratogenic and carcinogenic in <i>animal</i> studies); <i>see also</i> section 10
Deferoxamine	Teratogenic in <i>animal</i> studies; manufacturer advises use only if potential benefit outweighs risk
Dexamethasone	Benefit of treatment, for example in asthma, outweighs risk; risk of intrauterine growth retardation on prolonged or repeated systemic treatment; corticosteroid cover required by mother during labour; monitor closely if fluid retention
Diazepam	Avoid regular use (risk of neonatal withdrawal symptoms); use only if clear indication such as seizure control (high doses during late pregnancy or labour may cause neonatal hypothermia, hypotonia and respiratory depression)
Didanosine	Avoid if possible in first trimester; increased risk of lactic acidosis and hepatic steatosis; <i>see</i> section 7.3.1
Diethylcarbamazine	Avoid: Delay treatment until after delivery

Digoxin	May need dosage adjustment
Diloxanide	Defer treatment until after first trimester
Doxorubicin	Avoid (teratogenic and toxic in <i>animal</i> studies); with liposomal product use effective contraception during and for at least 6 months after administration to men or women; <i>see also</i> section 10
Doxycycline	First trimester: Effects on skeletal development in <i>animal</i> studies Second, third trimesters: Dental discoloration; maternal hepatotoxicity with large doses
Efavirenz	Avoid (potential teratogenic effects); <i>see</i> section 7.3.1
Enalapril	All trimesters: Avoid; may adversely affect fetal and neonatal blood pressure control and renal function; also possible skull defects and oligohydramnios; toxicity in <i>animal</i> studies
Ephedrine	Increased fetal heart rate reported with parenteral ephedrine
Ergocalciferol	High doses teratogenic in <i>animals</i> but therapeutic doses unlikely to be harmful
Ergotamine	All trimesters: Oxytocic effects on the pregnant uterus
Erythromycin	Not known to be harmful
Ethambutol	Not known to be harmful
Ether, anaesthetic	Third trimester: Depresses neonatal respiration
Ethinylestradiol	Epidemiological evidence suggests no harmful effects on fetus
Ethosuximide	First trimester: May possibly be teratogenic; risk of teratogenicity greater if more than one antiepileptic used; <i>see also</i> section 5.1
Etoposide	Avoid (teratogenic in <i>animal</i> studies); <i>see also</i> section 10
Fluconazole	Avoid (multiple congenital abnormalities reported with long-term high doses)
Flucytosine	Teratogenic in <i>animal</i> studies; manufacturer advises use only if potential benefit outweighs risk
Fluorouracil	Avoid (teratogenic); <i>see also</i> section 10
Fluphenazine	Third trimester: Extrapyramidal effects in neonate occasionally reported
Furosemide	Not used to treat hypertension in pregnancy
Gentamicin	Second, third trimesters: Auditory or vestibular nerve damage, risk probably very small with gentamicin, but avoid unless essential (if given, serum-gentamicin concentration monitoring

	essential)
Glibenclamide	Third trimester: Neonatal hypoglycaemia; insulin is normally substituted in all diabetics; if oral drugs are used therapy should be stopped at least 2 days before delivery
Griseofulvin	Avoid (fetotoxicity and teratogenicity in <i>animals</i>); effective contraception required during and for at least 1 month after administration (important: effectiveness of oral contraceptives reduced); also men should avoid fathering a child during and for at least 6 months after administration
Haloperidol	Third trimester: Extrapyramidal effects in neonate occasionally reported
Halothane	Third trimester: Depresses neonatal respiration
Heparin	All trimesters: Osteoporosis has been reported after prolonged use; multidose vials may contain benzyl alcohol—some manufacturers advise avoid
Hydralazine	Avoid during first and second trimesters; no reports of serious harm following use in third trimester
Hydrochlorothiazide	Not used to treat hypertension in pregnancy Third trimester: May cause neonatal thrombocytopenia
Hydrocortisone	Benefit of treatment, for example in asthma, outweighs risk; risk of intrauterine growth retardation on prolonged or repeated systemic treatment; corticosteroid cover required by mother during labour; monitor closely if fluid retention
Ibuprofen	Avoid unless potential benefit outweighs risk Third trimester: With regular use closure of fetal ductus arteriosus <i>in utero</i> and possibly persistent pulmonary hypertension of the newborn. Delayed onset and increased duration of labour
Idoxuridine	Teratogenic in <i>animal</i> studies
Indinavir	Avoid if possible in first trimester; theoretical risk of hyperbilirubinaemia and renal stones in neonate if used at term; <i>see</i> section 7.3.1
Insulin	All trimesters: Insulin requirements should be assessed frequently by an experienced diabetic clinician
Iodine	Second, third trimesters: Neonatal goitre and hypothyroidism
Isoniazid	Not known to be harmful
Ivermectin	Delay treatment until after delivery; <i>see also</i> section 7.5.1

Ketamine	Third trimester: Depresses neonatal respiration
Lamivudine	Avoid if possible in first trimester; benefit of treatment considered to outweigh risk in second and third trimesters; <i>see</i> section 7.3.1
Levamisole	Third trimester: Avoid
Levodopa + Carbidopa	Toxicity in <i>animal</i> studies
Levonorgestrel	In oral contraceptives, epidemiological evidence suggests no harmful effects on fetus
Levothyroxine	Monitor maternal serum-thyrotrophin concentration—dosage adjustment may be necessary
Lidocaine	Third trimester: With large doses, neonatal respiratory depression, hypotonia, and bradycardia after paracervical or epidural block
Lithium	First trimester: Avoid if possible (risk of teratogenicity including cardiac abnormalities) Second and third trimesters: Dose requirements increased (but on delivery return to normal abruptly); close monitoring of serum-lithium concentration advised (risk of toxicity in neonate)
Magnesium sulfate	Third trimester: not known to be harmful for short-term intravenous administration in eclampsia but excessive doses may cause neonatal respiratory depression
Mebendazole	Toxicity in <i>animal</i> studies. Contraindicated in cestode infections; <i>see</i> section 7.5.3 First trimester: Avoid in nematode infections; <i>see</i> section 7.5.3
Medroxyprogesterone	Avoid (genital malformations and cardiac defects reported in male and female fetuses); inadvertent use of depot-medroxyprogesterone acetate contraceptive injection in pregnancy unlikely to harm fetus
Mefloquine	Use only if other antimalarials inappropriate, <i>see also</i> Prophylaxis and Treatment of Malaria, section 7.4.3
Melarsoprol	All trimesters: Avoid
Mercaptopurine	Avoid (teratogenic); <i>see also</i> section 10
Metformin	All trimesters: Avoid; insulin is normally substituted in all diabetics
Methotrexate	Avoid (teratogenic; fertility may be reduced during therapy but this may be reversible); use effective contraception during and for at least 6 months after

	administration to men or women; <i>see also</i> section 10
Methyldopa	Not known to be harmful
Metoclopramide	Not known to be harmful
Metronidazole	Avoid high-dose regimens
Morphine	Third trimester: Depresses neonatal respiration; withdrawal effects in neonates of dependent mothers; gastric stasis and risk of inhalation pneumonia in mother during labour
Nalidixic acid	All trimesters: Avoid—arthropathy in <i>animal</i> studies; safer alternatives available
Naloxone	Use only if potential benefit outweighs risk
Nelfinavir	Avoid if possible in first trimester; potential benefit of treatment considered to outweigh risk in second and third trimesters; <i>see</i> section 7.3.1
Neostigmine	Third trimester: Neonatal myasthenia with large doses
Nevirapine	Avoid if possible in first trimester; benefit of treatment considered to outweigh risk in second and third trimesters; <i>see</i> section 7.3.1
Niclosamide	<i>T. solium</i> infections in pregnancy should be treated immediately; <i>see</i> section 7.5.3
Nifedipine	May inhibit labour; some dihydropyridines are teratogenic in <i>animals</i> , but risk to fetus should be balanced against risk of uncontrolled maternal hypertension
Nitrofurantoin	Third trimester: May produce neonatal haemolysis if used at term
Nitrous oxide	Third trimester: Depresses neonatal respiration
Norethisterone	In oral contraceptives, epidemiological evidence suggests no harmful effects on fetus In higher doses masculinization of female fetuses and other defects reported
Nystatin	No information available, but absorption from gastrointestinal tract negligible
Ofloxacin	All trimesters: Avoid—arthropathy in <i>animal</i> studies; safer alternatives available
Oxamniquine	If immediate treatment not required schistosomiasis treatment should be delayed until after delivery; <i>see</i> section 7.5.2
Paracetamol	Not known to be harmful
Penicillamine	All trimesters: Fetal abnormalities reported rarely; avoid if possible
Pentamidine isetionate	Potentially fatal visceral leishmaniasis must be treated without delay.

	Should not be withheld in trypanosomiasis even if evidence of meningoencephalitic involvement. Potentially fatal <i>P. carinii</i> pneumonia must be treated without delay
Pentavalent antimony compounds	Potentially fatal visceral leishmaniasis must be treated without delay
Phenobarbital	First, third trimesters: Congenital malformations; risk of teratogenicity greater if more than one antiepileptic used. May possibly cause vitamin K deficiency and risk of neonatal bleeding; if vitamin K not given at birth, neonate should be monitored closely for signs of bleeding
Phenoxymethylpenicillin	Not known to be harmful
Phenytoin	First, third trimesters: Congenital malformations (screening advised); adequate folate supplements should be given to mother (for example folic acid 5 mg daily); risk of teratogenicity greater if more than one antiepileptic used. May possibly cause vitamin K deficiency and risk of neonatal bleeding; if vitamin K not given at birth, neonate should be monitored closely for signs of bleeding. Caution in interpreting plasma concentrations—bound may be reduced but free (or effective) unchanged
Phytomenadione	Use only if potential benefit outweighs risk—no specific information available
Podophyllum resin	All trimesters: Avoid—neonatal death and teratogenesis have been reported
Polyvidone–iodine	Second, third trimesters: Sufficient iodine may be absorbed to affect the fetal thyroid
Potassium iodide	Second, third trimesters: Neonatal goitre and hypothyroidism
Praziquantel	<i>T. solium</i> infections in pregnancy should be treated immediately; <i>see</i> section 7.5.2 Benefit of treatment in schistosomiasis outweighs risk If immediate treatment not considered essential for fluke infections, treatment should be delayed until after delivery
Prednisolone	Benefit of treatment, for example in asthma, outweighs risk; risk of intrauterine growth retardation on prolonged or repeated systemic treatment; corticosteroid cover required by mother during labour; monitor closely if fluid retention
Primaquine	Third trimester: Neonatal haemolysis and

	methaemoglobinaemia. Delay treatment until after delivery
Procarbazine	Avoid (teratogenic in <i>animal</i> studies and isolated reports in humans); <i>see also</i> section 10
Proguanil	Benefit of prophylaxis and of treatment outweighs risk. Adequate folate supplements should be given to mother
Promethazine	No evidence of teratogenicity
Propranolol	May cause intrauterine growth restriction, neonatal hypoglycaemia, and bradycardia; risk greater in severe hypertension; <i>see also</i> section 2.2
Propylthiouracil	Second, third trimesters: Neonatal goitre and hypothyroidism
Pyrazinamide	Use only if potential benefit outweighs risk
Pyridostigmine	Third trimester: Neonatal myasthenia with large doses
Pyrimethamine	First trimester: Theoretical teratogenic risk (folate antagonist); adequate folate supplements should be given to the mother. First trimester: avoid in Pneumocystosis and toxoplasmosis; <i>see also</i> Sulfadiazine
Quinine	First trimester: High doses are teratogenic; but in malaria benefit of treatment outweighs risk
Ranitidine	Not known to be harmful
Retinol	First trimester: Excessive doses may be teratogenic
Rifampicin	First trimester: Very high doses teratogenic in <i>animal</i> studies Third trimester: Risk of neonatal bleeding may be increased
Ritonavir	<i>See</i> Lopinavir with Ritonavir
Salbutamol	For use in asthma <i>see</i> section 2.2 [text] Third trimester: For use in premature labour <i>see</i> section 9
Saquinavir	Avoid if possible in first trimester; potential benefit of treatment considered to outweigh risk in second and third trimesters; <i>see</i> section 7.3.1
Silver sulfadiazine	Third trimester: Neonatal haemolysis and methaemoglobinaemia; fear of increased risk of kernicterus in neonates appears to be unfounded
Sodium cromoglicate	Not known to be harmful <i>see also</i> section 3.2 [text]
Sodium valproate	<i>see</i> Valproic acid
Spironolactone	Toxicity in <i>animal</i> studies
Stavudine	Avoid if possible in first trimester; increased risk of lactic acidosis and hepatic steatosis; <i>see</i> section 7.3.1

Streptomycin	Second, third trimesters: Auditory or vestibular nerve damage; avoid unless essential (if given, serum-streptomycin concentration monitoring essential)
Sulfadiazine	Third trimester: Neonatal haemolysis and methaemoglobinaemia; fear of increased risk of kernicterus in neonates appears to be unfounded In toxoplasmosis, avoid in first trimester, but may be given in second and third trimester if danger of congenital transmission
Sulfadoxine + Pyrimethamine	In malaria, benefit of prophylaxis and treatment outweigh risk. First trimester: Possible teratogenic risk (pyrimethamine a folate antagonist) Third trimester: Neonatal haemolysis and methaemoglobinaemia; fear of increased risk of kernicterus in neonates appears to be unfounded <i>See also</i> section 7.4.1
Sulfamethoxazole + Trimethoprim	First trimester: Teratogenic risk (trimethoprim a folate antagonist) Third trimester: Neonatal haemolysis and methaemoglobinaemia; fear of increased risk of kernicterus in neonates appears to be unfounded
Sulfasalazine	Third trimester: Theoretical risk of neonatal haemolysis; adequate folate supplements should be given to mother
Suramin sodium	In onchocerciasis, delay treatment until after delivery. In <i>T. b. rhodesiense</i> treatment should be given even if evidence of meningoencephalopathic involvement
Suxamethonium	Mildly prolonged maternal paralysis may occur
Tamoxifen	Avoid—possible effects on fetal development; effective contraception must be used during treatment and for 2 months after stopping
Testosterone	All trimesters: Masculinization of female fetus
Tetracycline	First trimester: Effects on skeletal development in <i>animal</i> studies Second, third trimesters: Dental discoloration; maternal hepatotoxicity with large doses
Theophylline	Third trimester: Neonatal irritability and apnoea have been reported
Thiopental	Third trimester: Depresses neonatal respiration
Trimethoprim	First trimester: Teratogenic risk (folate antagonist)
Vaccine, BCG	First trimester: Theoretical risk of congenital malformations, but need for vaccination may

	outweigh possible risk to fetus (<i>see also</i> section 19 [cautions])
Vaccine, Measles	First trimester: Theoretical risk of congenital malformations, but need for vaccination may outweigh possible risk to fetus (<i>see also</i> section 19 [cautions]); avoid MMR
Vaccine, MMR	Avoid; pregnancy should be avoided for 1 month after immunization
Vaccine, Poliomyelitis, live	First trimester: Theoretical risk of congenital malformations, but need for vaccination may outweigh possible risk to fetus (<i>see also</i> section 19 [cautions])
Vaccine, Rubella	Avoid; pregnancy should be avoided for 1 month after immunization
Vaccine, Yellow fever	First trimester: Theoretical risk of congenital malformations, but need for vaccination may outweigh possible risk to fetus (<i>see also</i> section 19 [cautions])
Valproic acid	First, third trimesters: Increased risk of neural tube defects (counselling and screening advised—folic acid supplement may reduce risk); risk of teratogenicity greater if more than one antiepileptic used; neonatal bleeding (related to hypofibrinaemia) and neonatal hepatotoxicity also reported; <i>see also</i> section 4.4 (sodium valproate)
Vancomycin	Use only if potential benefit outweighs risk—plasma-vancomycin concentration monitoring essential to reduce risk of fetal toxicity
Vecuronium	Use only if potential benefit outweighs risk—no information available
Verapamil	<i>Animal</i> studies have not shown teratogenic effect; possibility that verapamil can relax uterine muscles should be considered at term; risk to fetus should be balanced against risk of uncontrolled maternal hypertension
Vinblastine	Avoid (limited experience suggests fetal harm; teratogenic in <i>animal</i> studies); <i>see also</i> section 10
Vincristine	Avoid (teratogenicity and fetal loss in <i>animal</i> studies); <i>see also</i> section 10
Warfarin	All trimesters: Congenital malformations; fetal and neonatal haemorrhage <i>See also</i> section 11.1
Zidovudine	Avoid if possible in first trimester; benefit of treatment considered to outweigh risk in second and third trimesters; <i>see</i> section 7.3.1

APPENDIX IX. BREASTFEEDING

Administration of some drugs (for example, ergotamine) to nursing mothers may harm the infant, whereas administration of others (for example, digoxin) has little effect. Some drugs inhibit lactation (for example, estrogens).

Toxicity to the infant can occur if the drug enters the milk in pharmacologically significant quantities. The concentration in milk of some drugs (for example, iodides) may exceed that in the maternal plasma so that therapeutic doses in the mother may cause toxicity to the infant. Some drugs inhibit the infant’s sucking reflex (for example, phenobarbital). Drugs in breast milk may, at least theoretically, cause hypersensitivity in the infant even when the concentration is too low for a pharmacological effect.

The following table lists drugs:

which should be used with caution or which are contraindicated in breastfeeding for the reasons given above;

which, on present evidence, may be given to the mother during breastfeeding, because they appear in milk in amounts which are too small to be harmful to the infant;

which are not known to be harmful to the infant although they are present in milk in significant amounts.

For many drugs insufficient evidence is available to provide guidance and it is advisable to administer only drugs essential to a mother during breastfeeding. Because of the inadequacy of information on drugs in breast milk the following table should be used only as a guide; absence from the table does not imply safety.

Table of drugs present in breast milk

Drug	Comment
Abacavir	Breastfeeding recommended during first 6 months if no safe alternative to breast milk
Acetazolamide	Amount too small to be harmful
Acetylsalicylic acid	Short course safe in usual dosage; monitor infant; regular use of high doses could impair platelet function and produce hypoprothrombinaemia in infant if neonatal vitamin K stores low; possible risk of Reye syndrome
Aciclovir	Significant amount in milk after systemic administration, but considered safe to use
Acitretin	Avoid
Alcohol	Large amounts may affect infant and reduce milk consumption
Allopurinol	Present in milk – not known to be harmful
Amantadine	Avoid; present in milk ; toxicity in infant reported

Amiloride	Manufacturer advises avoid—no information available
Aminophylline	Present in milk—irritability in infant reported
Amiodarone	Avoid; present in milk in significant amounts; theoretical risk from release of iodine; see also Iodine
Amitriptyline	Detectable in breast milk; continue breastfeeding; adverse effects possible, monitor infant for drowsiness
Amlodipine	Manufacturer advises avoid - no information available
Amoxicillin	Trace amounts in milk; safe in usual dosage; monitor infant
Amoxicillin + Clavulanic acid	Trace amounts in milk
Amphetamines	Significant amount in milk. Avoid
Amphotericin B	No information available
Ampicillin	Trace amounts in milk; safe in usual dosage; monitor infant
Analgesics	See Aspirin, NSAIDs, Opioid Analgesics and Paracetamol
Anthraquinones	Avoid; large doses may cause increased gastric motility and diarrhea (particularly cascara)
Apomorphine	Manufacturer advises avoid – no information available
Artemether + Lumefantrine	Discontinue breastfeeding during and for 1 week after stopping treatment; present in milk in <i>animal</i> studies
Atenolol	Significant amounts in milk; safe in usual dosage; monitor infant
Atracurium	Breastfeeding unlikely to be harmful following recovery from neuromuscular block; some manufacturers advise avoiding breast-feeding for 24 hours after administration
Atropine	Small amount present in milk; monitor infant
Azathioprine	Breastfeeding contraindicated
Azithromycin	Present in milk; manufacturer advises use only if no suitable alternative
Baclofen	Amount too small to be harmful
Barbiturates	Avoid if possible (See also Phenobarbital); large doses may produce drowsiness
Beclometasone	Systemic effects in infant unlikely with maternal dose of <i>less than equivalent</i> of prednisolone 40 mg daily; monitor infant's adrenal function with

	higher doses
Benzodiazepines	Present in milk – avoid if possible
Benzathine	Trace amounts in milk; safe in usual dosage;
benzylpenicillin	monitor infant
Benzylpenicillin	Trace amounts in milk; safe in usual dosage;
	monitor infant
Beta - blockers	
Betamethasone	Systemic effects in infant unlikely with maternal dose of <i>less than equivalent</i> of prednisolone 40 mg daily; monitor infant's adrenal function with higher doses
Bethanechol	Manufacturer advises avoid
Bleomycin	Breastfeeding contraindicated
Bromocriptine	Suppresses lactation
Bupivacaine	Amount too small to be harmful
Busulfan	See Cytotoxic Drugs
Calciferol	See vitamin D
Calcipotriol	No information available
Calcium folinate	Manufacturer advises caution – no information available
Capecitabine	Discontinue breastfeeding
Capreomycin	Manufacturer advises caution – no information available
Captopril	Present in milk – manufacturers advise avoid
Carbamazepine	Continue breastfeeding; adverse effects possible (severe skin reaction reported in 1 infant); monitor infant for drowsiness
Carbimazole	Amount in milk may be sufficient to affect neonatal thyroid function therefore lowest effective dose should be used
Carvedilol	See Beta - blockers
Cascara	See Anthraquinones
Cefaclor	Presen in milk in low concentration
Cefadroxil	Presen in milk in low concentration
Cefalexin	Presen in milk in low concentration
Cefixime	Manufacturer advises avoid – no information available
Cefotaxime	Presen in milk in low concentration
Ceftazidime	Excreted in low concentrations; safe in usual dosage; monitor infant
Ceftriaxone	Excreted in low concentrations; safe in usual dosage; monitor infant
Cefradine	Presen in milk in low concentration

Cetirizine	See Antihistamines
Chloralhydrate	Sedation in infant – manufacturer advises avoid
Chlorambucil	Breastfeeding contraindicated
Chloramphenicol	Continue breastfeeding; use alternative drug if possible; may cause bone-marrow toxicity in infant; concentration in milk usually insufficient to cause ‘grey syndrome’
Chlordiazepoxide	See Benzodiazepines
Chloroquine	For malaria prophylaxis, amount probably too small to be harmful; inadequate for reliable protection against malaria, avoid breastfeeding when used for rheumatic disease
Chlorphenamine	Safe in usual dosage; monitor infant for drowsiness
Chlorpromazine	Continue breastfeeding; adverse effects possible; monitor infant for drowsiness
Chlorpropamide	See Sulphonylureas
Ciclosporin	Present in milk—manufacturer advises avoid
Ciprofloxacin	Continue breastfeeding; use alternative drug if possible; high concentrations in breast milk
Cisplatin	Breastfeeding contraindicated
Clarithromycin	Manufacturer advises avoid unless potential benefit out weighs risk – present in milk
Clindamycin	Amount probably too small to be harmful but bloody diarrhoea reported in 1 infant
Clomifene	May inhibit lactation
Clomipramine	Small amount present in milk; continue breastfeeding; adverse effects possible; monitor infant for drowsiness
Clonazepam	Continue breastfeeding; adverse effects possible; monitor infant for drowsiness
Clonidine	Present in milk – manufacturer advises avoid
Cloxacillin	Trace amounts in milk; safe in usual dosage; monitor infant
Clozapine	Manufacturer advises avoid
Codeine	Amount too small to be harmful
Colchicine	Present in milk but no adverse effects reported; caution because of risk of cytotoxicity
Contraceptives, oral	Combined oral contraceptives may inhibit lactation—use alternative method of contraception until weaning or for 6 months after birth; progestogen-only contraceptives do not affect lactation (start 3 weeks after birth or later)

Co-trimoxazole	Small risk of Kernicterus in jaundiced infants and of haemolysis in G6PD-deficient infants (due to Sulfamethoxazole)
Cyclophosphamide	Breastfeeding contraindicated during and for 36 hours after stopping treatment
Cycloserine	Amount too small to be harmful
Cyclosporine	See Ciclosporin
Cyproheptadine	See Antihistamines
Cyproterone	Caution ; possibly of anti-androgen effects in neonate
Cytarabine	Breastfeeding contraindicated
Dacarbazine	Breastfeeding contraindicated
Dactinomycin	Breastfeeding contraindicated
Danazol	No data available but avoid because of possible androgenic effects in infant
Dantrolene	Present in milk – manufacturer advises avoid
Dapsone	Although significant amount in milk risk to infant very small; continue breastfeeding; monitor infant for jaundice
Daunorubicin	Breastfeeding contraindicated
Deferoxamine	Manufacturer advises use only if potential benefit outweighs risk—no information available
Desmopressin	Not known to be harmful
Dexamethasone	Systemic effects in infant unlikely with maternal dose of <i>less than equivalent</i> of prednisolone 40 mg daily; monitor infant's adrenal function with higher doses
Diazepam	Continue breastfeeding; adverse effects possible; monitor infant for drowsiness; <i>see also</i> section 5.1
Diclofenac	Amount too small to be harmful
Didanosine	Breastfeeding recommended during first 6 months if no safe alternative to breast milk
Digoxin	Amount too small to be harmful
Diloxanide	Manufacturer advises avoid
Diltiazem	Significant amount present in milk – no evidence of harm but avoid unless no safer alternative
Diphenhydramine	See Antihistamines
Disulfiram	Manufacturer advises avoid – no information available
Docusate Sodium	Present in milk following oral administration -

	manufacturer advises caution; rectal administration not known to be harmful
Doxorubicin	Breastfeeding contraindicated
Doxycycline	Continue breastfeeding; use alternative drug if possible (absorption and therefore discoloration of teeth in infant probably usually prevented by chelation with calcium in milk)
Edrophonium	Amount probably too small to be harmful
Efavirenz	Breastfeeding recommended during first 6 months if no safe alternative to breast milk
Enalapril	Amount probably too small to be harmful
Enoxaparin	Manufacturer advises avoid – no information available
Ephedrine	Irritability and disturbed sleep reported
Epirubicin	See Cytotoxic Drugs
Epoetin	Manufacturer advises avoid – no information available
Ergocalciferol	Caution with high doses; may cause hypercalcaemia in infant
Ergotamine	Use alternative drug; ergotism may occur in infant; repeated doses may inhibit lactation
Erythromycin	Only small amounts in milk; safe in usual dosage; monitor infant
Esomeprazole	Manufacturer advises avoid – no information available
Ethambutol	Amount too small to be harmful
Ethinylestradiol	Use alternative method of contraception; may inhibit lactation; <i>see also</i> Contraceptives, Oral
Ethosuximide	Significant amount in milk; continue breastfeeding; adverse effects possible; monitor infant for drowsiness
Etomidate	Avoid breastfeeding for 24 hours after administration
Etoposide	Breastfeeding contraindicated
Ezetimibe	Present in milk in animal studies – manufacturer advises avoid
Famotidine	Present in milk – not known to be harmful but manufacturer advises avoid
Felodipine	Present in milk
Fentanyl	Manufacturer advises avoid
Flucloxacillin	See penicillins
Fluconazole	Present in milk; safe in usual dosage; monitor infant

Flucytosine	Manufacturer advises avoid
Fludarabine	See Cytotoxic drugs
Fluorouracil	Discontinue breastfeeding
Fluoxetine	Present in milk - manufacturer advises avoid
Fluphenazine	Amount excreted in milk probably too small to be harmful; continue breastfeeding; adverse effects possible; monitor infant for drowsiness
Flurazepam	See benzodiazepines
Flurbiprofen	Amount too small to be harmful
Fluvoxamine	Present in milk – manufacturer advises avoid
Fosinopril	Present in milk – manufacturer advises avoid
Furosemide	Amount too small to be harmful
Fusidic acid	See sodium Fusidate
Ganciclovir	Avoid
Gemfibrozil	Manufacturer advises avoid – no information available
Glibenclamide	Theoretical possibility of hypoglycaemia in infant
Glipizide	See Sulphonylureas
Glimepiride	See Sulphonylureas
Griseofulvin	Avoid – no information available
Haloperidol	Amount excreted in milk probably too small to be harmful; continue breastfeeding; adverse effects possible; monitor infant for drowsiness
Halothane	Excreted in milk
Hepatitis A vaccine	No information available
Hydralazine	Present in milk but not known to be harmful; monitor infant
Hydrochlorothiazide	Use alternative drug; may inhibit lactation
Hydrocortisone	Systemic effects in infant unlikely with maternal dose of <i>less than equivalent</i> of prednisolone 40 mg daily; monitor infant's adrenal function with higher doses
Hydroxyurea	See Cytotoxic Drugs
Hyoscine	Amount too small to be harmful
Ibuprofen	Amount too small to be harmful; short courses safe in usual doses
Idarubicin	See Cytotoxic drugs
Idoxuridine	May make milk taste unpleasant
Imipramine	See Antidepressants, Tricyclic (and related)
Indinavir	Breastfeeding recommended during first 6 months if no safe alternative to breast milk

Indomethacin	Amount probably too small to be harmful but convulsions reported in one infant – manufacturers advise avoid
Influenza Vaccine	Not known to be harmful
Insulin	Amount too small to be harmful
Interferons	Manufacturers advise avoid – no information available
Iodine	Stop breastfeeding; danger of neonatal hypothyroidism or goitre; appears to be concentrated in milk
Ipratropium	Amount probably too small to be harmful
Isoniazid	Monitor infant for possible toxicity; theoretical risk of convulsions and neuropathy; prophylactic pyridoxine advisable in mother and infant
Isotretinoin	Avoid
Isradipine	Manufacturer advises avoid – present in milk in animal studies
Itraconazole	Small amounts present in milk – may accumulate; manufacturer advises avoid unless potential benefit outweighs risk
Ivermectin	Avoid treating mother until infant is 1 week old
Ketoconazole	Manufacturer advises avoid
Lamivudine	Present in milk; breastfeeding recommended during first 6 months if no safe alternative to breast milk
Latanoprost	May be present in milk – manufacturer advises avoid
Levamisole	Breastfeeding contraindicated
Levodopa + Carbidopa	No information available
Levonorgestrel	Combined oral contraceptives may inhibit lactation—use alternative method of contraception until weaning or for 6 months after birth; progestogen-only contraceptives do not affect lactation (preferably start 6 weeks after birth or later)
Lidocaine	Amount too small to be harmful
Lisinopril	No information available – manufacturer advises caution
Lithium	Present in milk and risk of toxicity in infant; continue breastfeeding; monitor infant carefully, particularly if risk of dehydration
Loperamide	Amount probably too small to be harmful
Lopinavir + Ritonavir	Breastfeeding recommended during first 6

	months if no safe alternative to breast milk
Loratadine	See Antihistamines
Mebendazole	No information available
Medroxyprogesterone	Present in milk—no adverse effects reported (preferably start injectable contraceptive 6 weeks after birth or later)
Mefloquine	Present in milk but risk to infant minimal
Mercaptopurine	Breastfeeding contraindicated
Mestranol	See Contraceptives, oral
Metformin	Present in milk but safe in usual doses; monitor infant
Methadone	Withdrawal symptoms in infant; breastfeeding permissible during maintenance but dose should be as low as possible and infant monitored to avoid sedation
Methotrexate	Breastfeeding contraindicated
Methyldopa	Amount too small to be harmful
Methylphenidate	No information available – manufacturer advises avoid
Methylprednisolone	See corticosteroids
Metoclopramide	Present in milk; adverse effects possible; monitor infant for adverse effects
Metolazone	See Thiazides
Metoprolol	See Beta-blockers
Metronidazole	Significant amount in milk; continue breastfeeding; avoid large doses; use alternative drug if possible
Mexiletine	Amount too small to be harmful
Miconazole	Manufacturer advises caution – no information available
Mifepristone	No information available – manufacturer advises stop breastfeeding for 14 days after administration
Misoprostol	No information available – manufacturer advises avoid
Morphine	Short courses safe in usual doses; monitor infant
Nalidixic acid	Continue breastfeeding; use alternative drug if possible; one case of haemolytic anaemia reported
Naloxone	No information available
Nelfinavir	Breastfeeding recommended during first 6 months if no safe alternative to breast milk
Neostigmine	Amount probably too small to be harmful;

	monitor infant
Nevirapine	Present in milk; breastfeeding recommended during first 6 months if no safe alternative to breast milk
Nifedipine	Small amount in milk; continue breastfeeding; monitor infant
Nitrofurantoin	Only small amounts in milk but could be enough to produce haemolysis in G6PD-deficient infants
Norethisterone	Combined oral contraceptives may inhibit lactation—use alternative method of contraception until weaning or for 6 months after birth; progestogen-only contraceptives do not affect lactation (preferably start injectable contraceptive 6 weeks after birth or later)
Norfloxacin	No information available – manufacturer advises avoid
Nystatin	No information available, but absorption from gastrointestinal tract negligible
Oestrogens	Avoid; adverse effects on lactation; see also contraceptives, oral
Ofloxacin	Continue breastfeeding; use alternative drug if possible
Omeprazole	Manufacturer advises avoid – no information available
Orphenadrine	Present in milk – manufacturer advises avoid
Oxazepam	See Benzodiazepines
Oxytetracycline	See Tetracyclines
Pancuronium	Manufacturer advises avoid unless potential benefit outweighs possible risk – no information available
Paracetamol	Small amount present in milk: short courses safe in usual dosage; monitor infant
Paraldehyde	Manufacturer advises avoid unless essential – present in milk
Penicillins	Trace amounts in milk
Pentamidine isetionate	Manufacturer advises avoid unless essential
Pentazocin	Small amount present in milk – manufacturer advises caution
Phenobarbital	Continue breastfeeding; adverse effects possible; monitor infant for drowsiness
Phenoxymethylpenicillin	Trace amounts in milk; safe in usual dosage; monitor infant
Phentolamine	No information available

Phenylbutazone	Avoid – small amounts in milk
Phenytoin	Small amount present in milk; continue breastfeeding; adverse effects possible; monitor infant for drowsiness
Phytomenadione	Present in milk
Pilocarpine	Manufacturer advises avoid – no information available
Pimozide	See Antipsychotics
Piperacillin	Present in milk – manufacturer advises use only if potential benefit outweighs risk
Piperazine	Present in milk – manufacturer advises avoid breastfeeding for 8 hours after dose (express and discard milk during this time)
Piroxicam	Amount too small to be harmful
Polyvidone–iodine	Avoid; iodine absorbed from vaginal preparations is concentrated in milk
Praziquantel	Avoid breastfeeding during and for 72 hours after treatment; considered safe to continue breastfeeding in treatment of schistosomiasis
Prazosin	Amount probably too small to be harmful
Prednisolone	Systemic effects in infant unlikely with maternal dose of <i>less than</i> prednisolone 40 mg daily; monitor infant's adrenal function with higher doses
Primaquine	Avoid; risk of haemolysis in G6PD-deficient infants
Primidone	See Phenobarbital
Probenecid	No information available
Procainamide	Present in milk; continue breastfeeding; monitor infant
Procarbazine	Breastfeeding contraindicated
Proguanil	Amount probably too small to be harmful; inadequate for reliable protection against malaria
Promethazine	Safe in usual dosage; monitor infant for drowsiness
Propantheline	May suppress lactation
Propofol	Manufacturer advises avoid – no information available
Propranolol	Present in milk; safe in usual dosage; monitor infant
Propylthiouracil	Monitor infant's thyroid status but amounts in milk probably too small to affect infant; high doses might affect neonatal thyroid function

Pseudoephedrine	Amount too small to be harmful
Pyrazinamide	Amount too small to be harmful
Pyridostigmine	Amount probably too small to be harmful
Pyrimethamine	Significant amount—avoid administration of other folate antagonists to infant
Quinidine	Significant amount but not known to be harmful
Ranitidine	Significant amount present in milk, but not known to be harmful
Retinol	Theoretical risk of toxicity in infants of mothers taking large doses
Rifabutin	Manufacturer advises avoid – no information available
Rifampicin	Amount too small to be harmful
Risperidone	Present in milk – manufacturer advises avoid
Ritonavir	Breastfeeding not advised in HIV infection
Salbutamol	Safe in usual dosage; monitor infant
Saquinavir	Breastfeeding recommended during first 6 months if no safe alternative to breast milk
Senna	Avoid; large doses may cause increased gastric motility and diarrhoea
Sertraline	Present in milk but not known to be harmful in short-term use
Silver sulfadiazine	Continue breastfeeding; monitor infant for jaundice—small risk of kernicterus in jaundiced infants particularly with long-acting sulphonamides, and of haemolysis in G6PD-deficient infants
Simvastatin	Manufacturer advises avoid – no information available
Sodium cromoglicate	Unlikely to be present in milk
Sodium fusidate	Present in milk – manufacturer advises caution
Sodium valproate	<i>See</i> Valproic acid
Stavudine	Breastfeeding recommended during first 6 months if no safe alternative to breast milk
Sulfadiazine	Continue breastfeeding; monitor infant for jaundice—small risk of kernicterus in jaundiced infants particularly with long-acting sulphonamides, and of haemolysis in G6PD-deficient infants
Sulfadoxine + Pyrimethamine	Continue breastfeeding; monitor infant for jaundice—small risk of kernicterus in jaundiced infants and of haemolysis in G6PD-deficient infants (due to sulfadoxine)

Sulfamethoxazole + Trimethoprim	Continue breastfeeding; monitor infant for jaundice—small risk of kernicterus in jaundiced infants and of haemolysis in G6PD-deficient infants (due to sulfamethoxazole)
Sulfasalazine	Continue breastfeeding; monitor infant for jaundice—small amounts in milk (1 report of bloody diarrhoea and rashes); theoretical risk of neonatal haemolysis especially in G6PD-deficient infants
Sumatriptan	Present in milk – withhold breastfeeding for 24 hours
Suxamethonium	No information available
Tamoxifen	Suppresses lactation; avoid unless potential benefit outweighs risk
Temazepam	See Benzodiazepines
Tenoxicam	No information available
Terfenadine	See Antihistamines
Testosterone	Avoid; may cause masculinization in the female infant or precocious development in the male infant; high doses suppress lactation
Tetracaine	No information available
Tetracycline	Continue breastfeeding; use alternative drug if possible (absorption and therefore discoloration of teeth in infant probably usually prevented by chelation with calcium in milk)
Theophylline	Present in milk—irritability in infant reported; modified-release preparations preferable
Thiamine	Severely thiamine-deficient mothers should avoid breastfeeding as toxic methyl-glyoxal excreted in milk
Thiotepa	See Cytotoxic Drugs
Thyroxine	Amount too small to affect tests for neonatal hypothyroidism
Timolol	See Beta-blockers
Tinidazole	Present in milk – manufacturer advises avoid breastfeeding during and for 3 days after stopping treatment
Tramadol	Amount probably too small to be harmful, but manufacturer advises avoid
Tretinoin	Avoid
Triamcinolone	See corticosteroids
Trifluoperazine	See Antipsychotics
Trimethoprim	Present in milk; safe in usual dosage; monitor infant

Triprolidine	See Antihistamines
Valproic acid	Small amount present in milk; continue breastfeeding; adverse effects possible; monitor infant for drowsiness; (sodium valproate)
Vancomycin	Present in milk—significant absorption following oral administration unlikely
Vasopressin	Not known to be harmful
Vecuronium	No information available
Verapamil	Amount too small to be harmful
Vinblastine	Breastfeeding contraindicated
Vincristine	Breastfeeding contraindicated
Vitamin A	Theoretical risk of toxicity in infants of mothers taking large doses
Vitamine D	Caution with high systemic doses; may cause hypercalcaemia in infant; manufacturer of topical calcitriol advises avoid
Warfarin	Risk of haemorrhage; increased by vitamin-K deficiency; warfarin appears safe
Zalcitabine	Breastfeeding not advised in HIV infection
Zidovudine	Breastfeeding recommended during first 6 months if no safe alternative to breast milk

APPENDIX X. RENAL IMPAIRMENT

Reduced renal function may cause problems with drug therapy for the following reasons:

The failure to excrete a drug or its metabolites may produce toxicity.

The sensitivity to some drugs is increased even if the renal elimination is unimpaired.

The tolerance to adverse effects may be impaired.

The efficacy of some drugs may diminish.

The dosage of many drugs must be adjusted in patients with renal impairment to avoid adverse reactions and to ensure efficacy. The level of renal function below which the dose of a drug must be reduced depends on how toxic it is and whether it is eliminated entirely by renal excretion or is partly metabolized to inactive metabolites.

In general, all patients with renal impairment are given a *loading dose* which is the same as the usual dose for a patient with normal renal function. *Maintenance doses* are adjusted to the clinical situation. The maintenance dose of a drug can be reduced either by reducing the individual dose leaving the normal interval between doses unchanged or by increasing the interval between doses without changing the dose. The interval extension method may provide the benefits of convenience and decreased cost, while the dose reduction method provides more constant plasma concentration.

In the following table drugs are listed in alphabetical order. The table includes only drugs for which specific information is available. Many drugs should be used with caution in renal impairment but no specific advice on dose adjustment is available; it is therefore important to also refer to the individual drug entries. The recommendations are given for various levels of renal function as estimated by the glomerular filtration rate (GFR), usually measured by the creatinine clearance. The serum-creatinine concentration can be used instead as a measure of renal function but it is only a rough guide unless corrected for age, sex and weight by special nomograms.

Renal impairment is usually divided into three grades:

Mild —GFR 20–50 ml/minute *or* approximate serum creatinine 150–300 micromol/litre

Moderate —GFR 10–20 ml/minute *or* serum creatinine 300–700 micromol/litre

Severe —GFR < 10 ml/minute *or* serum creatinine >700 micromol/litre

When using the dosage guidelines the following must be considered:

Drug prescribing should be kept to a minimum.

Nephrotoxic drugs should, if possible, be avoided in all patients with renal disease because the nephrotoxicity is more likely to be serious.

It is advisable to determine renal function not only before but also during the period of treatment and adjust the maintenance dose as necessary.

Renal function (GFR, creatinine clearance) declines with age so that by the age of 80 it is half that in healthy young subjects. When prescribing for the elderly, assume at least a mild degree of renal impairment.

Uraemic patients should be observed carefully for unexpected drug toxicity. In these patients the complexity of clinical status as well as other variables for example altered absorption, protein binding or metabolism, or liver function, and other drug therapy precludes use of fixed drug dosage and an individualized approach is required.

Table of drugs to be avoided or used with caution in renal impairment

Drug	Degree of Impairment	Comment
Abacavir	Severe	Avoid
ACE Inhibitors	Mild to Moderate	Use with caution and monitor response. Hyperkalaemia and other side-effects more common. Initial doses: Captopril 12.5mg twice daily, enalapril 2.5 mg once daily
Acetazolamide	Mild	Avoid; metabolic acidosis
Acetylsalicylic acid	Severe	Avoid; sodium and water retention; deterioration in renal function; increased risk of gastrointestinal bleeding
Aciclovir	Mild	Reduce intravenous dose
	Moderate to severe	Reduce dose

Acitretin	Mild	Avoid; increased risk of toxicity
Allopurinol	Moderate	100–200 mg daily; increased toxicity; rashes
	Severe	100 mg on alternate days (maximum 100 mg daily)
Alprazolam		See Anxiolytics and Hypnotics
Aluminium hydroxide	Severe	Aluminium is absorbed and may accumulate NOTE. Absorption of aluminium from aluminium salts is increased by citrates which are contained in many effervescent preparations (such as effervescent analgesics)
Amantadine	Mild to Moderate	Reduce dose; avoid in elderly if creatinine clearance less than 60 ml/min
	Severe	Avoid
Amikacin		See Aminoglycosides
Amiloride	Mild	Monitor plasma potassium; high risk of hyperkalaemia in renal impairment; amiloride excreted by kidney unchanged
	Moderate	Avoid
Aminoglycosides	Mild	Reduce dose;
Amoxicillin	Severe	Reduce dose; rashes more common
Amoxicillin + Clavulanic acid	Moderate to severe	Reduce dose
Amphotericin B	Mild	Use only if no alternative; nephrotoxicity may be reduced with use of complexes
Ampicillin	Severe	Reduce dose; rashes more common
Anticoagulants, oral	Severe	Avoid
Antipsychotics	Severe	Start with small doses; increased cerebral sensitivity
Anxiolytics and Hypnotics	Severe	Start with small doses; increased cerebral sensitivity
Apomorphine	Severe	Use with caution; max. sublingual dose 2 mg
Artemether + Lumefantrine	Severe	Caution; monitor ECG and plasma potassium
Aspirin	Severe	Avoid; sodium and water retention; deterioration in renal function; increased risk of gastro-intestinal bleeding
Atenolol	Moderate	Reduce dose (excreted unchanged)
	Severe	Start with small dose; higher plasma concentrations after oral administration; may reduce renal blood flow and

		adversely affect renal function
Azathioprine	Severe	Reduce dose
Azithromycin	Moderate to severe	Use with caution —no information available
Baclofen	Mild	Use smaller doses (e.g. 5 mg daily); excreted by kidney
Benzathine benzylpenicillin	Severe	Neurotoxicity—high doses may cause convulsions
Benzylnicillin	Severe	Maximum 6 g daily; neurotoxicity—high doses may cause convulsions
Beta-blockers	Mild	Start with 2.5 mg of nebivolol;
	Moderate	Start with small dose of acebutolol (active metabolite accumulates); reduce dose of atenolo, nadolo, sotalol (all excreted unchanged)
	Severe	Start with small dose, higher plasma concentrations after oral administration; may reduce renal blood flow and adversely affect renal function in severe impairment;
Betaxolol		See Beta-blockers
Bismuth chelate	Severe	Avoid
Bleomycin	Moderate	Reduce dose
Capecitabine	Mild	Use three-quarters of starting dose if creatinine clearance 30-50 mL/minutes; avoid if creatinine clearance less than 30 mL/minute
Capreomycin	Mild	Reduce dose; nephrotoxic; ototoxic
Captopril		See ACE Inhibitors
Carbamazepine		Manufacturer advises caution
Cefaclor		No dose adjustment required manufacturer advises caution
Cefazolin	Mild	Reduce dose
Cefixime	Moderate	Reduce dose
Cefotaxime	Severe	Loading dose of 1g then use half normal dose
Cefradine	Moderate to Severe	Reduce dose
Ceftazidime	Mild	Reduce dose
Ceftriaxone	Severe	Maximum 2 g daily; also monitor plasma concentration if both severe renal impairment and hepatic impairment
Cefalexin	Severe	Max – 500 mg daily

Cefuroxime	Moderate to Severe	Reduce parenteral dose
Cetirizine	Moderate	Use half normal dose
Chloral Hydrate		See Anxiolytics and Hypnotics
Chlorambucil	Moderate	Use with caution and monitor response; increased risk of myelosuppression
Chloramphenicol	Severe	Avoid unless no alternative; dose-related depression of haematopoiesis
Chloroquine	Mild to moderate	Reduce dose in rheumatic disease
	Severe	Reduce dose for malaria prophylaxis; avoid in rheumatic disease
Chlorphenamine	Severe	Dose reduction may be required
Chlorpromazine	Severe	Start with small doses; increased cerebral sensitivity
Chlorpropamide		Avoid
Ciclosporin		Monitor kidney function—dose dependent increase in serum creatinine and urea during first few weeks may necessitate dose reduction (exclude rejection if kidney transplant)
Cimetidine	Mild to Moderate	600-800 mg daily; occasional risk of confusion
	Severe	400 mg daily
Ciprofloxacin	Moderate	Use half normal dose
Cisplatin	Mild	Avoid if possible; nephrotoxic and neurotoxic
Clarithromycin	Mild	Use half normal dose if creatinine clearance less than 30 mL/minute
Clindamycin		Plasma half-life prolonged—may need dose reduction
Clonazepam	Severe	Start with small doses; increased cerebral sensitivity
Cloxacillin	Severe	Reduce dose
Clozapine	Mild to Moderate	Initial dose 12.5 mg daily increased slowly
	Severe	Avoid
Codeine	Moderate to severe	Reduce dose or avoid; increased and prolonged effect; increased cerebral sensitivity
Colchicine	Moderate	Reduce dose
	Severe	Avoid or reduce dose if no alternative
Co-trimoxazole	Mild	Use half normal dose if creatinine clearance 15-30 mL/minute; avoid if

creatinine clearance less than 15mL/minute and if plasma – Sulphamethoxazole concentration cannot be monitored

Reduce dose

Reduce dose

Avoid

See ciclosporin

Dose reduction may be required

Avoid

Reduce dose

Metal complexes excreted by kidneys (in severe renal impairment dialysis increases rate of elimination)

Antidiuretic effect may be reduced

See Opioid Analgesics

Start with small doses; increased cerebral sensitivity

See NSAIDs

Reduce dose; consult manufacturer's literature

Reduce dose; plasma half life prolonged and urinary excretion considerably reduced

Reduce dose; toxicity increased by electrolyte disturbances

Start with smaller dose

Discontinue or use with extreme caution if impairment develops during treatment

See Opioid Analgesics

Monitor plasma K⁺; high risk of hyperkalaemia in renal impairment; amiloride excreted by kidney unchanged

Avoid

Use with caution; avoid excessive doses

No information available—caution advised

Use with caution and monitor response; initial dose 2.5 mg once daily. Hyperkalaemia and other adverse effects more common

Cyclophosphamide

Cycloserine

Mild to
Moderate
Severe

Cyclosporin

Dacarbazine

Mild to
moderate
Severe

Daunorubicin

Mild to
moderate

Deferoxamine

Desmopressin

Dextromethorphan

Diazepam

Severe

Diclofenac

Didanosine

Mild

Diethylcarbamazine

Moderate to
severe

Digoxin

Mild

Diltiazem

Dimercaprol

Diphenoxylate

Diuretics potassium-sparing

Mild

Moderate

Doxycycline

Mild

Efavirenz

Severe

Enalapril

Mild to
moderate

Enoxaparin		See Heparin
Ephedrine	Severe	Avoid; increased CNS toxicity
Ergometrine	Severe	Manufacturer advises avoid
Ergotamine	Moderate	Avoid; nausea and vomiting; risk of renal vasoconstriction
Erythromycin	Severe	Maximum 1.5 g daily (ototoxicity)
Esomeprazole	Severe	Manufacturer advises caution
Ethambutol	Mild	Reduce dose; if creatinine clearance less than 30 ml/minute monitor plasma-ethambutol concentration; optic nerve damage
Famotidine	Severe	Max. 20 mg at night
Fentanyl		See Opioid Analgesics
Flucloxacillin	Severe	Reduce dose
Fluconazole	Mild to moderate	Usual initial dose then halve subsequent doses
Flucytosine		Reduce dose and monitor plasma-flucytosine concentration—consult manufacturer's literature
Fluoxetine	Mild to Moderate	Reduce dose
Fluphenazine	Severe	Start with small doses; increased cerebral sensitivity
Flurazepam		See Anxiolytics and Hypnotics
Flurbiprofen		See NSAIDs
Fluvoxamine	Moderate	Start with smaller dose
Foscarnet	Mild	Reduce dose; consult product literature
Fosinopril		See ACE Inhibitors
Furosemide	Moderate	May need high doses; deafness may follow rapid i/v injection
Gallamine	Moderate	Avoid; prolonged paralysis
Ganciclovir	Mild	Reduce dose; consult product literature
Gemfibrozil	Severe	Start with 900 mg daily
Gentamicin	Mild	Reduce dose; monitor plasma concentrations
Glibenclamide	Severe	Avoid
Glipizide	Mild to Moderate	Increased risk of hypoglycemia; avoid if hepatic impairment also present
	Severe	Avoid
Haloperidol	Severe	Start with small doses; increased cerebral sensitivity
Heparin	Severe	Risk of bleeding increased
Hydralazine	Mild	Reduce dose if creatinine clearance less

		than 30 ml/minute
Hydrochlorothiazide	Moderate	Avoid; ineffective
Ibuprofen	Mild	Use lowest effective dose and monitor renal function; sodium and water retention; deterioration in renal function possibly leading to renal failure
	Moderate to severe	Avoid
Indomethacin		See NSAIDs
Insulin	Severe	May need dose reduction; insulin requirements fall; compensatory response to hypoglycaemia is impaired
Interferon alfa	Mild to moderate	Close monitoring required
	Severe	Avoid
Isoniazid	Severe	Maximum 200 mg daily; peripheral neuropathy
Isotretinoin	Mild	Avoid; increased risk of toxicity
Itraconazole		Bioavailability of oral formulations; avoid intravenous infusion if creatinine clearance less than 30 mL/minute
Lamivudine	Mild	Reduce dose; consult manufacturer's literature
Lithium	Mild	Avoid if possible or reduce dose and monitor plasma concentration carefully
	Moderate	Avoid
Lopinavir + Ritonavir		Avoid oral solution due to propylene glycol content; use capsules with caution in severe impairment
Magnesium hydroxide	Moderate	Avoid or reduce dose; increased risk of toxicity
Magnesium sulfate	Moderate	Avoid or reduce dose; increased risk of toxicity
Mannitol		Avoid unless test dose produces diuretic response
Melphalan		Reduce dose initially; avoid hIncreased risk of nephrotoxicity; avoid dehydration
Mercaptopurine	Moderate	Reduce dose
Metformin	Mild	Avoid; increased risk of lactic acidosis
Methadone		See Opioid Analgesics
Methocarbamol		Manufacturer advises caution
Methotrexate	Mild	Reduce dose; accumulates; nephrotoxic
	Moderate	Avoid

Methyldopa	Moderate	Start with small dose; increased sensitivity to hypotensive anigh doses in moderate to severe impairment
Metoclopramide	Severe	Avoid or use small dose; increased risk of extrapyramidal reactions
Metolazone		See Thiazides
Metoprolol		See Beta-blockers
Morphine	Moderate to severe	Reduce dose or avoid; increased and prolonged effect; increased cerebral sensitivity
Nalidixic acid	Moderate to severe	Use half normal dose; ineffective in renal failure because concentration in urine is inadequate
Nelfinavir		No information available—manufacturer advises caution
Neomycin	Mild	Avoid; ototoxic; nephrotoxic
Neostigmine	Moderate	May need dose reduction
Nitrofurantoin	Mild	Avoid; peripheral neuropathy; ineffective because of inadequate urine concentrations
Norfloxacin	Mild to Moderate	Use half normal dose if creatinine clearance less than 30 mL/minute
NSAIDs	Mild Moderate to Severe	Use lowest effective dose and monitor renal function; sodium and water retention; deterioration in renal function possibly leading to renal failure; deterioration also reported after topical use Avoid if possible
Opioid Analgesics	Moderate to Severe	Reduce dose or avoid; increased and prolonged effects; increased cerebral sensitivities
Oxazepam		See Anxiolytics and Hypnotics
Oxytetracycline		See Tetracyclines
Pancuronium	Severe	Prolonged duration of block
Penicillamine	Mild	Avoid if possible or reduce dose; nephrotoxic
Pentamidine isetionate	Mild	Reduce dose; consult manufacturer's literature
Pentazocine		See Opioid Analgesics
Pethidine		See Opioid Analgesics
Phenobarbital	Severe	Avoid large doses
Phenylbutazone		See NSAIDs
Pilocarpine		Manufacturer advises caution with tablets

Pimozide		See Antipsychotics
Piperazine	Severe	Reduce dose; neurotoxic
Piroxicam		See NSAIDs
Polyvidone–iodine	Severe	Avoid regular application to inflamed or broken mucosa
Potassium chloride	Moderate	Avoid routine use; high risk of hyperkalaemia
Prazosin	Moderate to Severe	Initially 500 micrograms daily; increase with caution
Primidone	Severe	Avoid large doses
Probenecid	Moderate	Avoid; ineffective and toxicity increased
Procainamide	Mild	Avoid or reduce dose
Procaine benzylpenicillin	Severe	Neurotoxicity—high doses may cause convulsions
Procarbazine	Severe	Avoid
Proguanil	Mild	100 mg once daily
	Moderate	50 mg on alternate days
	Severe	50 mg once weekly; increased risk of haematological toxicity
Propantheline		Manufacturer advises caution
Propranolol	Severe	Start with small dose; higher plasma concentrations after oral administration; may reduce renal blood flow and adversely affect renal function
Propylthiouracil	Mild to moderate	Use three-quarters normal dose
	Severe	Use half normal dose
Pseudoephedrine	Severe	Avoid; increased CNS toxicity
Pyridostigmine	Moderate	Reduce dose; excreted by kidney
Quinine		Reduce parenteral maintenance dose for malaria treatment
Ranitidine	Severe	Use half normal dose; occasional risk of confusion
Rifabutin	Mild	Use half normal dose if creatinine clearance less than 30 mL/minute
Ritonavir	See Lopinavir with Ritonavir	
Saquinavir	Severe	Dose adjustment possibly required
Sertraline		Manufacturer advises caution
Sildenafil	Mild	Initial dose 25 mg if creatinine less than 30 mL/minute
Simvastatin	Moderate to	Doses above 10 mg daily should be used

	Severe	with caution
Sodium Bicarbonate	Severe	Avoid; specialized role in some forms of renal disease
Sodium chloride	Severe	Avoid
Sodium nitroprusside	Moderate	Avoid prolonged use
Sodium valproate	<i>see</i> Valproic acid	
Spironolactone	Mild	Monitor plasma K^+ ; high risk of hyperkalaemia in renal impairment
	Moderate	Avoid
Stavudine	Mild	20 mg twice daily (15 mg if body weight less than 60 kg)
	Moderate to severe	20 mg once daily (15 mg if body weight less than 60 kg)
Streptomycin	Mild	Reduce dose; monitor plasma concentrations
Sucralfate	Severe	Avoid; aluminium is absorbed and may accumulate
Sulfadiazine	Severe	Avoid; high risk of crystalluria
Sulfamethoxazole + Trimethoprim	Mild	Use half normal dose if creatinine clearance 15–30 ml/minute; avoid if creatinine clearance less than 15 ml/minute and if plasma-sulfamethoxazole concentration cannot be monitored
Sulfasalazine	Moderate	Risk of toxicity including crystalluria—ensure high fluid intake
	Severe	Avoid
Temazepam		See Anxiolytics and Hypnotics
Tenofovir	Mild to moderate	Manufacturer advises caution
	Severe	Avoid
Tenoxicam		See NSAIDs
Terfenadine	Mild	Use half normal dose if creatinine clearance less than 40 mL/minute
Tetracyclines	Mild	Avoid tetracyclines except doxycycline or minocycline which may be used cautiously (avoid excessive doses)
Thiazides and Related Diuretics	Moderate	Avoid; ineffective (metolazone remains effective but risk of excessive diuresis)
Thioridazine		See Antipsychotics
Timolol		See Beta-blockers
Tobramycin		See Aminoglycosides

Tolbutamide	Mild to Moderate Severe	Reduce dose Avoid if possible; if no alternative reduce dose and monitor closely
Tramadol		See Opioid Analgesics
Tretinoin (oral)	Mild	Reduce dose
Trifluoperazine		See Antipsychotics
Trimethoprim	Mild Moderate to severe	Use half normal dose after 3 days if creatinine clearance 15–30 ml/minute Use half normal dose if creatinine clearance less than 15 ml/minute; avoid if creatinine clearance less than 10 ml/minute (unless plasma-trimethoprim concentration monitored)
Tripotassium Dicitrato bismuthate	Severe	Avoid
Valproic acid	Mild to moderate Severe	Reduce dose Alter dosage according to free serum valproic acid concentration
Vancomycin	Mild	Reduce dose—monitor plasma-vancomycin concentration and renal function regularly
Vecuronium	Severe	Reduce dose; duration of block possibly prolonged
Warfarin	Severe	Avoid
Zalcitabine	Mild to Moderate Severe	750 micrograms every 12 hours 750 micrograms daily
Zidovudine	Severe	Reduce dose; manufacturer advises oral dose of 300–400 mg daily in divided doses or intravenous dose of 1 mg/kg 3–4 times daily

APPENDIX XI. HEPATIC IMPAIRMENT

Liver disease may alter the response to drugs. However, the hepatic reserve appears to be large and liver disease has to be severe before important changes in drug metabolism take place. The ability to eliminate a specific drug may or may not correlate with liver's synthetic capacity for substances such as albumin or clotting factors, which tends to decrease as hepatic function declines. Unlike renal disease, where estimates of renal function based on creatinine clearance correlate with parameters of drug elimination such as clearance and half-life,

routine liver function tests do not reflect actual liver function but are rather markers of liver cellular damage.

The altered response to drugs in liver disease can include all or some of the following changes:

Impaired intrinsic hepatic eliminating (metabolizing) capacity due to lack of or impaired function of hepatocytes.

Impaired biliary elimination due to biliary obstruction or transport abnormalities (for example rifampicin is excreted in the bile unchanged and may accumulate in patients with intrahepatic or extrahepatic obstructive jaundice).

Impaired hepatic blood flow due to surgical shunting, collateral circulation or poor perfusion with cirrhosis and portal hypertension.

Altered volume of distribution of drugs due to increased extracellular fluid (ascites, oedema) and decreased muscle mass.

Decreased protein binding and increased toxicity of drugs highly bound to proteins (for example phenytoin) due to impaired albumin production.

Increased bioavailability through decreased first-pass metabolism.

Decreased bioavailability due to malabsorption of fats in cholestatic liver disease.

In severe liver disease increased sensitivity to the effects of some drugs can further impair cerebral function and may precipitate *hepatic encephalopathy* (for example morphine). *Oedema* and *ascites* in chronic liver disease may be exacerbated by drugs that cause fluid retention (for example acetylsalicylic acid, ibuprofen, prednisolone, dexamethasone).

Usually drugs are metabolized without injury to the liver. A few drugs cause dose-related hepatotoxicity. However, most hepatotoxic reactions to drugs occur only in rare persons and are unpredictable. In patients with impaired liver function the dose-related hepatotoxic reaction may occur at lower doses whereas unpredictable reactions seem to occur more frequently. Both should be avoided. Information to help prescribing in hepatic impairment is included in the following table. The table contains only those drugs that need dose adjustment. However, absence from the table does not automatically imply safety as for many drugs data about safety are absent; it is therefore important to also refer to the individual drug entries.

Table of drugs to be avoided or used with caution in liver disease

Drug	Comment
Abacavir	Avoid in moderate hepatic impairment unless essential; avoid in severe hepatic impairment
ACE inhibitors	Use of prodrugs such as enalapril, fosinopril requires close monitoring in patients with impaired liver function.
Acetylsalicylic acid	Avoid—increased risk of gastrointestinal bleeding
Acitretin	Avoid – further impairment of liver function may occur.
Allopurinol	Reduce dose

Alprazolam	See Anxiolytics and Hypnotics
Aluminium hydroxide	In patients with fluid retention, avoid antacids containing large amounts of sodium; also avoid those causing constipation (can precipitate coma)
Aminophylline	Reduce dose
Amitriptyline	Sedative effects increased (avoid in severe liver disease)
Amlodipine	Half-life prolonged – may need dose reduction
Amoxicillin + Clavulanic acid	Monitor liver function in liver disease. Cholestatic jaundice reported either during or shortly after treatment; more common in patients over the age of 65 years and in males; duration of treatment should not usually exceed 14 days
Anastrozole	
Antacids	In patients with fluid retention, avoid those containing large amounts of sodium, e.g. magnesium trisilicate mixture, Avoid those causing constipation- can precipitate coma.
Anticoagulants, oral	Avoid in severe liver disease, especially if prothrombin time already prolonged.
Antidepressants, SSRI	Reduce dose or avoid in severe liver disease
Antidepressants, Tricyclic (and related)	Tricyclics preferable to MAOIs but sedative effects increased (avoid in severe liver disease)
Antipsychotics	All can precipitate coma; phenothiazines are hepatotoxic; see also clozapine, Olanzapine and Risperidone.
Anxiolytics and Hypnotics	All can precipitate coma, avoid chloral hydrate; small dose of oxazepam probably safest
Apomorphine	Low sublingual doses may be used with caution
Artemether + Lumefantrine	Caution in severe impairment; monitor ECG and plasma potassium
Azathioprine	May need dose reduction
Azithromycin	Avoid; jaundice reported
Bupivacaine	Avoid (or reduce dose) in severe liver disease
Capecitabine	Manufacturer advises avoid in severe hepatic impairment
Carbamazepine	Metabolism impaired in advanced liver disease
Carvedilol	Avoid
Ceftriaxone	Reduce dose and monitor plasma concentration if both hepatic and severe renal impairment
Chloral Hydrate	See Anxiolytics and Hypnotics
Chloramphenicol	Avoid if possible—increased risk of bone-marrow depression; reduce dose and monitor plasma-

Chlordiazepoxide	See Anxiolytics and Hypnotics
Chlorphenamine	Sedation inappropriate in severe liver disease—avoid
Chlorpromazine	Can precipitate coma; hepatotoxic
Ciclosporin	May need dose adjustment
Cimetidine	Increased risk of confusion; reduce dose
Ciprofloxacin	Hepatic dysfunction reported
Clarithromycin	Hepatic dysfunction including jaundice reported
Clindamycin	Reduce dose
Clomifene	Avoid in severe liver disease
Clomipramine	Sedative effects increased (avoid in severe liver disease)
Clonazepam	Can precipitate coma
Cloxacillin	Cholestatic jaundice may occur up to several weeks after treatment has been stopped; administration for more than 2 weeks and increasing age are risk factors
Clozapine	Initial dose 12.5mg daily increased slowly with regular monitoring of liver function; avoid in symptomatic or progressive liver disease or hepatic failure.
Codeine	Avoid or reduce dose—may precipitate coma
Colestyramine	Interferes with absorption of fat-soluble vitamins and may aggravate malabsorption in primary biliary cirrhosis; likely to be ineffective in complete biliary obstruction
Contraceptives, oral	Avoid in active liver disease and if history of pruritus or cholestasis during pregnancy
Co-trimoxazole	Manufacturer advises avoid in severe liver disease
Cyclophosphamide	Reduce dose
Cyproheptadine	Sedation inappropriate in severe liver disease – avoid
Cyproterone Acetate	Dose-related toxicity
Cytarabine	Reduce dose
Dacarbazine	Dose reduction may be required in mild to moderate liver disease; avoid if severe
Daunorubicin	Reduce dose
Dextromethorphan	See opioid Analgesics
Diazepam	Can precipitate coma
Diclofenac	See NSAIDs
Didanosine	Insufficient information but consider dose reduction
Diltiazem	Reduce dose
Diphenhydramine	Caution in mild to moderate liver disease; avoid in severe disease if sedation is inappropriate
Diphenoxylate	See Opioid Analgesics

Doxorubicin	Reduce dose according to bilirubin concentration
Doxycycline	Avoid (or use with caution)
Efavirenz	In mild to moderate liver disease, monitor liver function; avoid in severe hepatic impairment
Enalapril	Closely monitor patients with impaired liver function
Enoxaparin	See Heparin
Epirubicin	Reduce dose according to bilirubin concentration
Epoetin	Manufacturers advise caution in chronic hepatic failure
Ergometrine	Avoid in severe liver disease
Ergotamine	Avoid in severe liver disease—risk of toxicity increased
Erythromycin	May cause idiosyncratic hepatotoxicity
Esomeprazole	In severe liver disease dose should not exceed 20 mg daily
Estradiol	See Oestrogens
Estriol	See Oestrogens
Ether, anaesthetic	Avoid
Ethinylestradiol	Avoid; <i>see also</i> Contraceptives, oral
Etoposide	Avoid in severe hepatic impairment
Felodipine	Reduce dose
Fentanyl	See Opioid Analgesics
Flucloxacillin	Cholestatic jaundice
Fluconazole	Toxicity with related drugs
Fluorouracil	Caution advised
Fluphenazine	Can precipitate coma; hepatotoxic
Flurazepam	See Anxiolytics and Hypnotics
Flurbiprofen	See NSAIDs
Fluvoxamine	See Antidepressants, SSRI
Fosinopril	See ACE Inhibitors
Furosemide	Hypokalaemia may precipitate coma (use potassium-sparing diuretic to prevent this); increased risk of hypomagnesaemia in alcoholic cirrhosis
Fusidic Acid	Impaired biliary excretion; possibly increased risk of hepatotoxicity; avoid or reduce dose.
Gemfibrozil	Avoid in liver disease
Glibenclamide	Increased risk of hypoglycaemia in severe liver disease; avoid or use small dose; can produce jaundice
Glipizide	See sulphonylureas
Griseofulvin	Avoid in severe liver disease
Haloperidol	Can precipitate coma
Halothane	Avoid if history of unexplained pyrexia or jaundice

	following previous exposure to halothane
Heparin	Reduce dose in severe liver disease
Hydralazine	Reduce dose
Hydrochlorothiazide	Avoid in severe liver disease; hypokalaemia may precipitate coma (potassium-sparing diuretic can prevent this); increased risk of hypomagnesaemia in alcoholic cirrhosis
Hydroxyprogesterone Caproate	See progestogens
Ibuprofen	Increased risk of gastrointestinal bleeding and can cause fluid retention; avoid in severe liver disease
Indinavir	Reduce dose to 600 mg every 8 hours in mild to moderate hepatic impairment; not studied in severe impairment
Indometacin	See NSAIDs
Interferon alfa	Close monitoring in mild to moderate hepatic impairment; avoid if severe.
Interferone beta	Avoid indecompensated liver disease
Iron dextran	Avoid in severe hepatic impairment
Iron sorbitol	Avoid
Isoniazid	Use with caution; monitor liver function regularly and particularly frequently in the first 2 months
Isotretinoin	Avoid – further impairment of liver function may occur
Isradipine	Reduce dose
Itraconazole	Half-lifeprolonged- dose reduction may be necessary
Ketoconazole	Avoid
Levonorgestrel	Avoid in active liver disease and if history of pruritus or cholestasis during pregnancy
Lidocaine	Avoid (or reduce dose) in severe liver disease
Loop Diuretics	Hypokalaemia may precipitate coma (use potassium-sparing diuretic to prevent this); increased risk of hypomagnesaemia in alcoholic cirrhosis
Lopinavir + Ritonavir	Avoid oral solution because of propylene glycol content; use capsules with caution in mild to moderate hepatic impairment and avoid in severe impairment
Magnesium hydroxide	Avoid in hepatic coma if risk of renal failure
Magnesium sulfate	Avoid in hepatic coma if risk of renal failure
MAOIs	May cause idiosyncratic hepatotoxicity
Medroxyprogesterone	Avoid in active liver disease and if history of pruritus or cholestasis during pregnancy
Mefloquine	Avoid for prophylaxis in severe liver disease
Mercaptopurine	May need dose reduction

Mesterolone	See Androgens
Metformin	Withdraw if tissue hypoxia likely
Methadone	See Opioid Analgesics
Methionine	May precipitate coma
Methocarbamol	Manufacture advises caution
Methotrexate	Dose-related toxicity—avoid in non-malignant conditions (for example, rheumatic disorders)
Methoxsalen	Avoid or reduce dose
Methyldopa	Manufacturer advises caution in history of liver disease; avoid in active liver disease
Metoclopramide	Reduce dose
Metolazone	See Thiazides
Metoprolol	Reduce oral dose
Metronidazole	In severe liver disease, reduce total daily dose to one-third and give once daily
Mexiletine	Avoid (or reduce dose) in severe liver disease
Miconazole	Avoid
Morphine	Avoid or reduce dose—may precipitate coma
Nalidixic acid	Hepatic dysfunction reported; partially conjugated in liver
Nelfinavir	No information available—manufacturer advises caution
Neomycin	Absorbed from gastro-intestinal tract in liver disease – increased risk of ototoxicity
Nevirapine	Caution in moderate hepatic impairment; avoid in severe hepatic impairment, <i>see also</i> section 6.5.2.2
Nifedipine	Reduce dose
Nitrofurantoin	Cholestatic jaundice and chronic active hepatitis reported
Norethisterone	Avoid in active liver disease and if history of pruritus or cholestasis during pregnancy
Norfloxacin	See Quinolones
NSAIDs	Increased risk of gastro-intestinal bleeding and can cause fluid retention; avoid in severe liver disease.
Oestrogens	Avoid; See also contraceptives, oral
Ofloxacin	Hepatic dysfunction reported; reduce dose in severe liver disease
Omeprazole	In liver disease not more than 20 mg daily should be needed
Opioid Analgesics	Avoid or reduce dose – may precipitate coma
Oxazepam	See Anxiolytics and Hypnotics
Oxytetracycline	See Tetracyclines

Pancuronium	Possibly slower onset; higher dose requirement and prolonged recovery time.
Paracetamol	Dose-related toxicity—avoid large doses
Pentavalent antimony compounds	Increased risk of liver damage and hepatic failure in pre-existing liver disease
Pentazocin	See opioid analgesics
Pethidine	See opioid analgesics
Phenobarbital	May precipitate coma
phenylbutazone	See NSAIDs
Phenytoin	Reduce dose to avoid toxicity
Pilocarpine	Reduce initial oral dose in moderate or severe cirrhosis
Pimozide	See Antipsychotics
Piperazine	Manufacturer advises avoid
Piroxicam	See NSAIDs
Prazosin	Initially 500 micrograms daily; increased with caution
Prednisolone	Adverse effects more common
Procainamide	Avoid or reduce dose
Procarbazine	Avoid in severe hepatic impairment
Promethazine	Avoid—may precipitate coma in severe liver disease; hepatotoxic
Propantheline	Manufacturer advises caution
Propranolol	Reduce oral dose
Propylthiouracil	Reduce dose
Pyrazinamide	Avoid—idiosyncratic hepatotoxicity more common
Ranitidine	Increased risk of confusion; reduce dose
Rifabutin	Reduce dose in severe hepatic impairment
Rifampicin	Impaired elimination; may be increased risk of hepatotoxicity; avoid or do not exceed 8 mg/kg daily
Risperidone	Manufacturer advises initial dose of 500 micrograms twice daily increased in steps of 500 micrograms twice daily to 1- 2 mg twice daily
Ritonavir	Avoid in severe hepatic impairment
Saquinavir	Plasma concentration possibly increased; manufacturer of gel-filled capsules advises caution in moderate hepatic impairment and avoid in severe impairment; manufacturer of capsules containing saquinavir mesilate advises caution in severe impairment
Sertraline	See Antidepressants, SSRI
Sildenafil	Initial dose 25 mg; manufacturer advises avoid in severe hepatic impairment
Simvastatin	See statins

Sodium Bicarbonate	See Antacids
Sodium Fusidate	See Fusidic Acid
Sodium nitroprusside	Avoid in severe liver disease
Sodium valproate	<i>see</i> Valproic acid
Sulfadiazine	Avoid if severe
Sulfamethoxazole + Trimethoprim	Manufacturer advises avoid in severe liver disease
Statins	Avoid in active liver disease or unexplained persistent elevations in serum transaminases
Sumatriptan	Manufacturer advises 50 mg oral dose
Suxamethonium	Prolonged apnoea may occur in severe liver disease due to reduced hepatic synthesis of plasma cholinesterase
Temazepam	See Anxiolytics and Hypnotics
Tenoxicam	See NSAIDs
Terfenadine	Avoid – risk of arrhythmias
Testosterone	Preferably avoid—possibility of dose-related toxicity and fluid retention
Tetracyclines	Avoid (or use with caution); tetracycline and demeclocycline max. 1g daily in divided doses
Theophylline	Reduce dose
Thiazides	Avoid in severe liver disease; hypokalaemia may precipitate coma (potassium-sparing diuretic can prevent); increased risk of hypomagnesaemia in alcoholic cirrhosis.
Thiopental	Reduce dose for induction in severe liver disease
Thioridazine	See Antipsychotics
Tolbutamide	Increased risk of hypoglycemia in severe liver disease; avoid or use small dose; can produce jaundice.
Tramadol	See Opioid Analgesics
Tretinoin (oral)	Reduce dose
Trifluoperazine	See Antipsychotics
Triprolidine	Sedation inappropriate in severe liver disease – avoid
Valproic acid	Avoid if possible—hepatotoxicity and hepatic failure may occasionally occur (usually in first 6 months)
Verapamil	Reduce oral dose
Vinblastine	Dose reduction may be necessary
Vincristine	Dose reduction may be necessary
Warfarin	Avoid in severe liver disease, especially if prothrombin time already prolonged
Zalcitabine	Further impairment of liver function may occur
Zidovudine	Accumulation may occur

GLOSSARY

Analgesics - drugs which relieve pain.

Antiflatulants - drugs which expel gases from the stomach or intestine.

Antipyretics- drugs which reduce elevated body temperature.

Central Nervous System (CNS) depressants - agents which reduce the activity of the brain (e.g. alcohol, phenobarbitone).

Contraindications - A sign or symptom suggesting that a certain line of treatment (usually used for that disease) should be discontinued or avoided.

Drug interactions- a condition of two or more drug interacting with one another when taken together to produce an undesirable effect such as nullifying the action of the drug or increasing the toxicity.

District Hospital- is the first referral level for health centers within the four tier health service system. It provides both out-patient and in-patient service with 50 bed capacities which renders service round the clock for a catchment population of 250,000.

Expectorants - drugs used to assist in the removal of mucus from the trachea, bronchi, or lungs.

Generic Name or Non-proprietary Name - the name by which a drug is scientifically and internationally recognized (often by reference to a pharmacological monograph).

Health Stations - the smallest health units in the conventional health service structure and are usually staffed with one to three health assistants.

A Standard Health center (HC) with its five satellite Community health Post (CHPs), is the first level health care unit which provides a package of public Health and essential curative services on ambulatory bases to a population of about 25,000. It has a capacity of ten beds provides emergency services through clock for 24 hours. Equipped with relevant diagnostic and therapeutic facilities.

Hematinic- an agent that improves the quality of blood by increasing the number of erythrocytes and the hemoglobin concentration

Hemostatic- an agent that arrests the escape of blood

Laxative- a drug that produces a soft formed stool over a prolonged period.

Side effects - any physiological change or undesirable drug reaction other than the desired one, which occurs when a drug is given or administered in therapeutic doses.

Cautions/Warnings- refers to careful attention to be taken when giving or administering drugs in the presence of conditions such as some other medical problems, pregnancy, breast-feeding or age of patient e.t.c.

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Adverse Drug Reaction Reporting Form

Patient's Name: (Initials only)_____Card N^o: _____Age:_____Sex:_____Habit:_____

Address: _____

Adverse Drug Reaction Description (Including Laboratory test results): _____Date of onset of Reaction: _____/_____/_____

Reaction necessitated: Discontinuation of drug/s/ ☐ Yes ☐ No
Prolonged Hospitalization☐ Yes ☐ No

Information on Suspected Drug						
Drug Name (use Brand Name . if generic name are use Please indicate manufacturer and batch no. if applicable.)	Route	Dose	Frequency	Date Drug		Therapeutic Indication
				Started	Stopped	
				Y D M Y	Y D M Y	

Other Drugs Taken Including self-medication

Reaction subside after D/C of Suspected Drug ☐ Y ☐ N ☐ NA
Reaction reappear after Restart of Suspected Drug ☐ Y ☐ N ☐ NA

Treatment of reaction :

Outcome: ☐ Died due to adverse reaction ☐ Died, drug may be contributory ☐ Died
 Unrelated to drug ☐ Not yet recovered ☐ Recovered with out sequelae
☐ Recovered with sequelae ☐ Unknown

Sequelae: _____

Additional information: (e.g. relevant history such as allergies, chronic disease, pregnancy etc.)

Reported by: Name _____ Profession: _____ Signature: _____
Date: _____ Name of health Institution: _____ Address: _____
Tele N^o: _____

Continued

For office use only

Received On: _____

RegistrationN

Key: D|M|Y Date |Month |Year; D/C Discontinue Treatment; Y Yes; N No; NA N
ailable

What to report
All suspected reactions to drugs
Unknown or unexpected ADRs
Serious adverse drug reactions
Unexpected therapeutic effects

All suspected drug interactions

Q2

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