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*FORMULARY OF NARCOTIC DRUGS  
AND PSYCHOTROPIC SUBSTANCES  
FOR  
ETHIOPIA*

*Drug Administration and Control Authority (DACA)  
of Ethiopia*

*Addis Ababa  
February 2004*

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## TABLE OF CONTENTS

	<u>Page</u>
BACKGROUND .....	i
PART I	
Narcotic Drugs .....	1
PART II	
Psychotropic Substances .....	17
A. Anxiolytics & Hypnotics .....	17
A1. Anxiolytics .....	17
A2. Hypnotics .....	21
A3. Treatment of Benzodiazepine dependence .....	28
B. Antidepressants .....	28
B1. Tricyclic & related antidepressants .....	29
B2. Monoamine Oxidase inhibitors (MOAI).....	33
C. Antipsychotics .....	38
C1. Extrapyramidal side effects .....	39
C2. Malignant Neuroleptic Syndrome .....	41
D. Antiepileptics .....	49
D1. Other Antiepileptics .....	55
E. Drugs used in Parkinsonism & related disorders .....	59
E1. Dopaminergic Drugs .....	60
E2. Anti-muscarinic Drugs .....	61
F. Central Nervous System stimulants .....	64
General Index.....	66

## Background

The history of human race has also been the history of drug use. Since earliest times, herbs, roots, bark leaves and plants have been used to relieve pain and help control disease. In and of itself, the use of drugs doesn't constitute an evil; drugs, properly administered have been a medical blessing. Unfortunately certain drugs also initially produce enticing side effects, such as feeling of euphoria; a sense of "feeling good", elation, seniority and power. What began as something of a recreational activity evolved in time into a problem of dependence and abuse.

The most ancient of the substance which were used for recreational activity are opium, from the poppy plant (*Papaver Somniferum* L); cocaine from the leaf of coca bush (*Erythroxyton coca*) and cannabis products from the hemp plant (*Cannabis Sativa* L.).

Until the end of the nineteenth century, it was possible to keep the use of these mood-altering substances within acceptable limits in most geographical areas and cultural settings. However, as chemical technology developed, it became possible to synthesize great quantities of morphine and its derivatives, as well as increasing number of other alkaloids. Drug development was made easier by the rapid expansion of communications, transport and international trade, which reduced geographical distances and eliminated many natural barriers between countries. A negative result of this development, however, was the drug abuse began to spread until it became a matter of increasing concern worldwide.

The evident relationship between drug abuse and health, economic, social and political problems have contributed to the growing conviction that international and governmental controls were needed. As a result of these, the international and governmental controls were needed. As a result of these, the international community has been urged to develop instruments of control at international level since the times of League of Nations until the late periods of this century.

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Among the many conventions and protocols issued and amended repeatedly, the whole matters of Narcotic Drugs and Psychotropic Substances is governed by the following international drug control treaties.

1. Single Convention on Narcotic Drugs, 1961; as amended by the 1972 protocol.
2. Convention on Psychotropic Substances, 1971;
3. United Nations Convention Against Illicit Traffic in Narcotic Drugs and Psychotropic Substances, 1988.

The main objective of the above conventions and protocol is to limit Narcotic Drugs and Psychotropic Substances; it has also covered the other narcotic and psychotropic substances, which are included in the List of Drugs for Ethiopia (but not controlled by the 1961 and 1971 Conventions respectively).

It is believed that the health professionals who use this formulary will have a substantial reference opportunity on both controlled and uncontrolled narcotic and psychotropic substances. This will especially be useful for those who are engaged in the treatment of psychiatric problems.

This formulary is designed to suite all categories of health workers those engaged in prescribing and dispensing Narcotic Drugs and Psychotropic Substances. In the course of preparation of the manual, international standard manuals and those of developing countries were utilized and assessed, and conditions, which suit the Ethiopian context, were consumed.

The formulary is divided in to two parts, part one is dealing with Narcotic Drugs and part two with Psychotropic Substances. Under each drug, information, which is deemed to be necessary, is incorporated as much as possible in concise and precise manner.

**Drug Administration and Control Authority  
February 2004**

## **PART I**

### **NARCOTIC DRUGS**

This Formulary will include information on the following: Codeine, Fentanyl, Methadone, Morphine, Pethidine, Pentazocine and Tramadol.

All of the opioid analgesics have similar pharmacological actions; however clinical uses among specific agents may vary because of actual pharmacokinetic differences, differences in potential for causing adverse effects, lack of specific testing and/or lack of clinical use data.

Opioid analgesics bind with stereo-specific receptors at many sites within the central nervous system to alter processes affecting both the perception of pain and the emotional response to pain. Although the precise sites and mechanisms of actions have not been fully determined, alterations in release of various neurotransmitters from afferent nerves sensitive to painful stimuli may be partially responsible for the analgesic effects.

When these medications are used as adjuncts to anesthesia, analgesic actions may provide dose-related protection against hemodynamic responses to surgical stress.

It has been proposed that there are multiple subtypes of opioid receptors, each mediating various therapeutic and/or side effects of opioid drugs. The actions of an opioid analgesic may therefore depend upon its binding affinity for each type of receptor and on whether it acts as a full agonist or a partial agonist or is inactive at each type of receptor.

At least two types of opioid receptors (Mu and Kappa) mediate analgesia. A third type of receptor (sigma) may not mediate analgesia; actions at this receptor may produce the subjective and psychomimetic effects characteristic of pentazocine.

Morphine and other opioid agonists exert their agonist activity primarily at Mu receptor, which is widely distributed through out the

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CNS. Pentazocine exerts its agonist activity from their receptor binding sites and competitively inhibits their actions.

Antidiarrheal – Act locally and possibly centrally to alter intestinal motility.

Antitussive - suppress the cough reflex by a direct central action, probably in the medulla or pons.

Substitute for other opioid drugs when administered orally and prevent or attenuate withdrawal symptoms that may occur when the substituted opioid is discontinued are usually greatly reduced in severity. With continued administration, methadone may produce cross-tolerance to the euphoric effects of other opioid drugs, thereby reducing the patient's desire for such drugs.

## **CODIENE PHOSPHATE**

### ***Indication:***

Codeine is indicated for relief of mild to moderate pain. It is indicated for the symptomatic treatment of diarrhea. In diarrhea caused by poisoning, it should not be used until the toxic material is eliminated from the gastrointestinal tract. It is also indicated for non-productive cough treatment – Although only codeine (oral dosage form) is indicated as antitussive all opioid analgesics depress the cough reflex.

### ***Dose***

#### Usual adult Dose

##### Analgesic -

Oral 30 to 60mg every 4 hours to a maximum of 240mg daily  
IM injection, 30 to 60mg every 4 hours when necessary

Anti-diarrheal –30 mg up to four times a day.

Antitussive- 15mg to 30mg three to four times a day

#### Usual Pediatric Dose

##### Analgesic –

Premature Infants: Use is not recommended

Newborn Infants: Dosage has not been established

Children aged 1 to 12 years: Oral 500 mcg (0.5 mg) per kg of body weight or 15 mg per square meter of body surface every four to six hours daily as needed.

##### Anti-diarrheal

Oral, 500 mcg (0.5mg) per kg of body weight up to 4 times a day.

### Antitussive –

Children up to 2 years of age: Use is not recommended  
Children 2 to 5 years of age: 1mg /kg of body weight per day.  
Administered in four equal divided doses, or for Children 2 years of age (average body weight 12 kg) – 3mg every 4 to 6 hours, not to exceed 14 mg per day.

Children 3 years of age (average body weight 14kg) 3.5mg every 4 to 6 hours, not to exceed 14 mg per day.

Children 4 years of age (average body weight 16 kg) 4mg every 4 to 6 hours not to exceed 16mg per day.

Children 5 years of age (average body weight 18kg) 4.5mg every 4 to 6 hours not to exceed 18mg per day.

Children 6 to 12 years of age: 5 to 10 mg every four to six hours not to exceed 60 mg per day.

### ***Precautions***

In pregnancy – Risk benefit must be considered because opioid analgesics cross the placenta. Regular use during pregnancy may cause physical dependence in the fetus, leading to withdrawal symptoms in the neonate. Codeine is known to be distributed in breast milk and should be avoided altogether in children under 1 year

Children up to 2 years of age may be more susceptible to the effects, especially likely to occur in pediatric patients receiving opioid analgesics, Renal and hepatic impairment, dependence.

### ***Drug Interaction***

Codeine should not be used with, alcohol, anticholinergics (which may result in the increased risk of severe constipation which may lead to paralytic ileus, and or urinary retention), antidiarrheals (may increase the risk of severe constipation as well as central nervous system depression) antihypertensives, or diuretics, hydroxyzine and methochlorpromide.

Guanidine can inhibit the analgesic effect of codeine, which impairs its metabolism.

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### ***Contraindications***

Except under special circumstances, this medication should not be used when the following medical problems exist: diarrhea caused by poisoning, until toxic material has been eliminated from gastrointestinal tract, acute respiratory depression: Risk benefit should be considered when the following medical problems exist: acute abdominal conditions, allergic reaction to opioid analgesic considered for use, history of asthma, acute attack or respiratory impairment, cardiac arrhythmias, history of drug dependence including alcoholism. Gallbladder disease, gastrointestinal tract surgery, head injury, hepatic function impairment, intracranial lesions (risk of respiratory depression and prolonged CNS depression is greatly increased).

### ***Side/Adverse Effects***

Codeine has lower dependence liability and potential for abuse than other agonists because of comparatively lower potency with usual doses.

***Less frequently:*** allergic reaction, respiratory depression, unusual excitement or restlessness, confusion, pounding heart beat, decreased urination, light headaches or dizziness, feeling faint.

***Rarely:*** Convulsions. Hallucinations, mental depression, muscle rigidity, especially in muscles or respiration – with large doses.

### ***Dosage Form***

30 mg tablets

30mg/ml in 1 ml amp. injection

## **FENTANYL**

### ***Indication:*** -

Fentanyl and its derivatives are indicated as opioid analgesic supplements to general anesthesia. During surgery they are often used in conjunction with other agents such as a combination of ultra-short-acting barbiturate, a neuromuscular blocking agent, and an inhalation anesthetic \*usually nitrous oxide), for the maintenance of “balanced” anaesthesia.

Fentanyl is indicated to supplement regional or local anaesthesia.

### ***Dose:*** -

Fentanyl derivatives should be administered only by personnel experienced in the use of intravenous anesthetics and in the management of the respiratory effects of opioid analgesics.

100 mcg of fentanyl produce analgesic effect equivalent to 10mg of morphine.

Dosage must be individualized on the basis of the age, weight, body size, and physical status of the patients; underlying pathology, other medications used concurrently, especially the type of anaesthesia to be used, type and anticipated duration of the surgical procedure involved; and patient response.

### ***Usual Adult Dose***

Anesthesia, general, adjunct

For minor surgery – 2mcg (0.002 mg) per kg of body weight.

For major surgery – Moderate dose-intravenous 2 to 20 mcg (0.002 to 0.02mg) (base) per kg body weight.

High dose (for open-heart surgery or complicated neurological or orthopedic procedures requiring prolonged anaesthesia and obliteration of stress response) intravenous, 20 to 50 mcg (0.02 to 0.05 mg) (base) per kg of body weight.

### ***Usual Pediatric Dose***

Anesthesia, as primary agent in major surgery.

Children up to 2 years of age: Dosage has not been established.

Children 2 to 12 years of age: intravenous, 2 to 3 mcg (0.002 to 0.003 mg) (base) per kg of body weight.

### ***Precautions***

Chronic respiratory disease, Myasthenia gravis; hypothyroidism; chronic liver disease are some of the precaution to be considered wherever fentanyl is used.

Neonates may be more susceptible to the effects especially the respiratory depressant effects, of opioid analgesics. Caution is recommended if fentanyl is used as pre-surgical or post surgical medication in these patients.

Geriatric patients may be more susceptible to the effects especially the respiratory depressant effects, of opioid analgesics. Also, elderly patients are more likely to have age related renal function impairment, which may require caution in patients receiving fentanyl (because excretion of fentanyl may be slowed).

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### ***Drug Interaction***

The following drug interactions and/or related problems have been selected on the basis of their potential significance. Anaesthetics, spinal, anti-hypertensives or diuretics, or hypo tension producing medication, benzo Diazepines, beta-adrenergic blocking agents, buprenorphine and other partial mu-receptor agonists. CNS depressants, hepatic enzyme inhibitors, monoamine oxidase inhibitors (MAOI), nalbuphine or pentazocine, naloxone, neuromuscular blocking agents, nitrous oxide, phenothiazine.

### ***Contra indication***

The medical problems/contraindications included here have been selected on the basis of their potential significance.

Allergic reaction to fentanyl or its derivative, history of cardiac bradyarrhythmias, cardiac conditions leading to compromised cardiac reserve, head injury, hepatic function impairment, pulmonary disease or respiratory impairment, caution is also advised in elderly, very ill, or debilitated patients who may be more sensitive to the effects, especially the respiratory depressant effects, of opioid analgesics.

### ***Side/Adverse Effects***

Fentanyl and its derivatives may cause rigidity in the muscles of respiration in the chest and pharynx. This effect is dose related and must be anticipated with anesthetic induction doses. Bradycardia, hypertension, cardiac arrhythmia, confusion, post-operative, bronchospasm, allergic, convulsions, skin rash, hives, itching, laryngospasm, mental depression, post operative, paradoxical CNS excitation, drowsiness, postoperative, biliary spasm, blurred vision, orthostatic (dizziness, light headedness, feeling faint, unusual tiredness or weakness) constipation, urethral spasm (decreased or difficult urination).

### ***Dosage Forum***

Injection 0.05 mg/ml in 2 ml ampoule.

## **METHADONE**

### ***Indication:***

Methadone may be dispensed for the treatment of opioid addiction only through treatment programs that have been approved. Thus methadone is indicated as narcotic abstinence syndrome suppressant, antitussive, it is not recommended for obstetrical analgesia.

### ***Dose:***

Methadone is used in detoxification and maintenance treatment programs for opioid addiction.

### **Usual Adult Dose**

#### **Analgesic**

Oral, 5 to 10 mg every six to eight hours; dosage may be increased or the interval between doses decreased if pain is very severe or if the patient becomes tolerant to the medication.

Parenteral, intramuscular or subcutaneous, 5 to 10 mg. every six to eight hours as needed, Dosage adjusted according to response; on prolonged use not to be given more frequently than every 12 hours

#### **Detoxification**

Oral, 15 to 40 mg once a day or as needed to control observed withdrawal symptoms; dosage to be reduced at one or two day intervals according to patient response.

Parenteral, intramuscular or subcutaneous, 15 to 40 mg once a day or as needed to control withdrawal symptoms.

**Maintenance:** Dosage must be individualized.

**Usual adult prescribing limits:** up to 120 mg per day.

Children – Not recommended.

### ***Preparation of dosage form***

Each dose must be diluted with water or another liquid before administration. For use in the treatment of chronic pain, each dose should be diluted to at least 30 ml. For use in methadone maintenance programmes, it is recommended that the medication be diluted to 90 ml or more and that it be given to the patient only after dilution, as a deterrent to misuse by injection.

### ***Precautions***

Hypotension, hypothyroidism, asthma, and decreased respiratory reserve; pregnancy and breast-feeding are some of the precautions to consider.

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### ***Drug Interaction***

Urinary acidifiers, such as: ammonium chloride, ascorbic acid, potassium or sodium phosphate (acidification of the urine by these medications increases methadone excretion, resulting in decreased methadone plasma concentration); alcohol, CNS depressants, anticholinergics, antidiarrheals, antiperistaltic such as difenoxin, kaolin, atropine, antihypertensives or diuretics, or hypotension producing medications, hydroxyzine and metoclopramide.

### ***Contraindication***

Methadone is not recommended for obstetrical analgesia because its long duration of action increases the risk of neonatal respiratory depression. Risk benefit should be considered when there is allergic reaction to the opioid analgesic, history of asthma, respiratory impairment, cardiac arrhythmias, history of convulsions, emotional instability, gallstones, recent gastrointestinal tract surgery, head injury, hepatic function impairment, hypothyroidism, renal function impairment.

### ***Side/Adverse Effects***

Less frequently: respiratory depression confusion, pounding heart beat, decreased urination, and blurred vision.

More frequently: Histamine release, \*decreased blood pressure fast heart dizziness, feeling faint or light-headedness.

Rarely: allergic reaction, CNS stimulation (unusual excitement or restlessness especially in children) hallucinations, mental depression, severe constipation, nausea, and cramps.

### ***Dosage Form:***

10 mg/ml – injections  
5 mg – tablets

## **MORPHINE SALTS**

### ***Indication:***

Drug of choice to relieve pain due to acute myocardial infarction. Also indicated as adjunctive therapy in the treatment of acute pulmonary edema secondary to left ventricular failure also used as antitussive in terminal care and in the management of uncomplicated acute diarrhea in adults but not in young children.

### ***Dose:***

#### ***Analgesic:***

*Adults:* Acute pain, by subcutaneous injection (not suitable for edematous patients) or by intramuscular injection, 10mg every 4 hours if necessary (15mg for heavier well-muscled patients);

*Children:* Up to 1-month 150mcg/kg,  
1-12 months 200 mcg/kg  
1-5 years 2.5-5mg;  
6-12 years 5-10mg

#### ***Preoperation:***

*Adults:* by subcutaneous or intramuscular injection, up to 10mg, 60-90 minutes before operation

*Children:* by intramuscular injection, 150mcg/kg

#### ***Post operation:***

*Adults:* by subcutaneous or intramuscular injection, 10mg every 2-4 hours if necessary (15 mg for heavier well muscled patients)

*Children:* up to 1 month, 150 mcg/kg  
1-12 months, 200 mcg/kg  
1-5 years, 2.5-5 mg  
6-12 years, 5-10 mg

***N.B.:*** - In the postoperative period, the patient should be closely monitored for pain relief as well as for side effects especially respiratory depression.

#### ***Myocardial infection:***

*Adults:* by slow intravenous injection (2 mg/minute), 10 mg followed by a further 5-10mg if necessary; elderly or frail patients reduce dose by half.

#### ***Acute Pulmonary edema:***

*Adults:* by slow intravenous injection (2mg/minute), 5-10mg

#### ***Chronic pain:***

*Adults:* by mouth or by subcutaneous injection (not suitable for edematous patients) or by intramuscular injection, 5-20 mg regularly every 4 hours, dose may be increased according to needs; oral dose should be approximately double corresponding intramuscular dose, by rectum, as suppositories, 15-30mg regularly every 4 hours.

**Precautions**

**Pregnancy:** - Risk benefit must be considered because opioid analgesics cross the placenta. Regular use during pregnancy may cause physical dependence in the fetus, leading to withdrawal symptoms in the neonate.

When used during labor it readily enters the fetal circulation and may cause respiratory depression in the neonate. This agent should be used with caution, if at all during the delivery of a premature infant. Morphine and possibly other opioids may prolong labor. Geriatric patients are more likely to be adversely affected by opioid – induced urinary retention.

Hypotension, hypothyroidism, asthma (avoid during attack) and decreased respiratory reserve, prostatic hypertrophy; pregnancy and breast feeding; may precipitate Coma in hepatic impairment (reduce dose or avoid but many such patients to relate morphine well); reduce dose or avoid in renal impairment, elderly and debilitated (reduce dose); convulsive disorders, dependence (sever withdrawal symptoms if withdrawn abruptly); use of cough suppressants containing opioid analgesics not generally recommended in children and should be avoided altogether in those under at least 1 year.

**Drug Interaction**

Alcohol or CNS depressants may result in increased CNS depression, respiratory depression, and hypotensive effects; caution is recommended and dosage of one or both agents should be reduced. When used with dependence producing CNS depressants the risk of dependence will increase. Anticholinergics will increase the risk of severe constipation.

Antidiarrheals such as difenoxin, atropine, kaolin, pectin, belladonna alkaloids, and opium may increase the risk of severe constipation as well as central nervous system depression.

Antihypertensives, diuretics or hypotension-producing medications. Concurrent use of hydroxyzine with morphine may result in increased analgesia as well as increased CNS depressant and hypotensive effects.

Morphine may antagonize the effects of metochlopramide on gastrointestinal motility.

**Contraindication:** avoid in acute respiratory depression, acute alcoholism and where risk of paralytic ileus; also avoid in raised intracranial pressure or head injury (in addition to interfering with respiration, affect pupillary responses vital for neurological assessment); avoid injection in phaeochromocytoma (risk of pressor response to histamine release).

**Side/Adverse Effects**

**Less frequently:** - Allergic reaction, respiratory depression, confusion, pounding heart beat, trembling, decreased urination, stomach cramps, blurred vision, dry mouth, false sense of well-being, gastrointestinal irritation, general feeling of discomfort, headache, loss of appetite, restlessness, burning at site of injection, difficult – urination.

**More frequently:-** Histamine release, constipation, dizziness, feeling faint, drowsiness, hypotension, nausea or vomiting, unusual tiredness or weakness.

**Rarely:-** CNS stimulation, hallucinations, mental depression, severe constipation, bloating, nausea, stomach cramps or pain, vomiting, trouble in sleeping.

**Dosage form:**

- 10mg/ml, 20 mg/ml injection as morphine hydrochloride
- 20mg, 50mg, 100mg, 200mg capsule (modified release)
- 20mg, 60mg, 100mg, 200mg per sachet granules for oral suspension
- 10mg/5ml, 100mg/5ml oral solution
- 10mg, 15mg, 20mg, 30mg suppository
- 5mg, 10mg, 15mg, 20mg, 30mg tablet

as  
Morphine  
sulphate

**PETHIDINE HYDROCHLORIDE**

**Indication:**

For relief of moderate to severe pain. Pethidine is indicated to supplement general, regional or local anesthesia. During surgery it is often used in conjunction with other agents, such as a combination of an ultra-short acting barbiturate, a neuromuscular blocking agent, and an inhalation anesthetic (usually nitrous oxide) for the maintenance of balanced anesthesia.

Pethidine has relatively less antitussive activity than other opioid analgesics, especially in low or moderate doses.



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**Dose:**

**Acute Pain:**

*Adults:* by mouth, 50-150 mg every 4 hours  
by subcutaneous or intramuscular injection, 25-100mg,  
repeated after 4 hours  
by slow IV injection, 25-50mg, repeated after 4 hours

*Children:* by mouth, 0.5-2mg/kg  
by IM injection, 0.5-2mg/kg

**Obstetric Analgesia:**

*Adults:* by S.C or IM, Injection 50-100mg, repeated 1-3 hours later if necessary, maximum 400mg in 24 hours.

**Pre operative pain:**

*Adults* – by IM, 25-100mg 1 hour before operation  
*Children* – by IM, 0.5 – 2mg/kg

**Post operative pain:**

*Adults:* by S.C. or IM injection, 25-100mg, every 2-3 hours if necessary.

*Children:* by IM, 0.5-2mg/kg

N.B. In the postoperative period, the patient should be closely monitored for pain relief as well as for side effects especially respiratory depression.

**Precautions**

Opioid analgesics readily enter the fetal circulation when used during labor and may cause respiratory depression in the neonate, especially the premature neonate.

Pethidine distribute into breast milk. Children up to 2 years of age may be more susceptible to the effects, especially the respiratory depressant effects, of this medication.

Not suitable for severe continuing pain.

**Drug Interaction**

Alcohol or CNS depressants, amphetamines, anticholinergics or other medication with anti cholinergic activity, anticoagulants, coumarin or indandione – derivative, antidiarrheals, antiperistaltic, antihypertensives, especially ganglionic blockers such as guanadrel, guanethidine and mecamlamine or diuretics or hypotension producing medications, buprenorphine, carbamazepine,

hydroxyzine, metoclopramide, monoamine oxidase (MAOI) inhibitors, naloxone, naltrexone, neuromuscular blocking agents and possibly other medications having some neuromuscular blocking activity, opioid agonist analgesics, including alfentanil, fentanyl, and sufentanil, avoid concomitant use of pethidine and Ritonavir because Ritonavir increase plasma concentration of pethidine which increases risk of toxicity.

**Contraindication**

As Morphine, Severe renal impairment.

**Side/Adverse Effects**

**Less Frequently:** - Atelectasis, bronchospastic allergic reaction, laryngeal edema, allergic, laryngospasm, or respiratory depression confusion, convulsions, fast, slow, or pounding heartbeat, trembling or uncontrolled muscle movement, antidiuretic effect (decreased urination), biliary spasm (stomach cramps or pain) blurred vision, dry mouth, false sense of well being, gastrointestinal irritation, general feeling of discomfort, loss of appetite, nervousness or restlessness, night mares, burning at site of injection.

**More Frequently:** -

Histamine release, constipation, dizziness, feeling faint, light-headedness, drowsiness, hypotension, nausea or vomiting, unusual tiredness or weakness.

**Rarely:** - Allergic reaction, CNS stimulation, paradoxical (unusual excitement or restlessness) hallucinations, mental depression, toxic megacolon (in patients with inflammatory bowel disease), trouble in sleeping and convulsions reported in over dosage.

**Dosage Form**

50 mg/ml in 1 and 2 ml ampoule

50mg tablet

**TRAMADOL HYDROCHLORIDE**

**Indication:** Moderate to severe pain.

**Dose:**

**Analgesic:**

*Adults:* by mouth, 50-100mg not more often than every 4 hours; total of more than 400mg daily by mouth not usually required.

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by intramuscular injection or by intravenous injection (over 2-3 minutes) or by intravenous infusion, 50-100mg every 4-6 hours.

*Children:* not recommended

**Post operative pain:**

*Adults:* 100mg initially then 50mg every 10-20 minutes if necessary during first hour to total maximum 250mg (including initial dose) in first hour, then 50-100mg every 4-6 hours; maximum 600mg daily;

*Children:* not recommended

**Precautions:** See under Morphine salts, history of epilepsy (convulsions reported, usually after rapid intravenous injection), avoid in pregnancy and breast feeding; not suitable as substitute in opioid dependent patients, Not recommended for analgesia during potentially very light planes of general anaesthesia.

**Interactions:**

- Alcohol or CNS depressants may result in increased CNS depression, respiratory depression, and hypotensive effects; caution is recommended and dosage of one or both agents should be reduced. When used with dependence producing CNS depressants the risk of dependence will increase. Anticholinergics will increase the risk of severe constipation.
- Effect of tramadol decreased by Antiepileptics (Carbamazepine)
- Antipsychotics enhance sedative and hypotensive effects and increased risk of convulsions with tramadol.
- Reports of digoxin toxicity with tramadol
- Tramadol may antagonize the gastro-intestinal effects

**Contraindications** - As morphine!

**Side Effects:** See under Morphine Salts, also hypotension & occasionally hypertension, anaphylaxis, hallucinations, and confusion.

**Dosage Form:**

Injection 50 mg/ml

Oral drops

Nasal spray 20mg/0.1ml

Tablet/capsule 50mg, 75mg, 100mg, 150mg, 200mg, 300mg

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**PENTAZOCINE**

**Indication:**

An opioid agonist/antagonist analgesic. It has agonist activity at the kappa and sigma receptors. It has antagonist activity at the Mu receptor, may precipitate withdrawal symptoms in patients who are physically dependent on Mu receptor agonists.

Pentazocine is less desirable than morphine or other opioid agonist analgesics for relief of pain due to myocardial infraction because of cardiovascular effects that tend to increase cardiac work & indicated in the management of moderate to severe pain.

**Dose:**

60 mg via intramuscular injection or 180 mg via oral administration therapeutically equivalent to 10 mg of intramuscular morphine.

If the product is misused by injection, the naloxone antagonizes the effects of pentazocine. Also injection of the medication will precipitate withdrawal symptoms if the patient is physically dependent on an opioid agonist.

For long-term administration, the oral form of the medication is preferred. If the parental form is used instead, dosage should be reduced gradually when the medication is to be discontinued to reduce the risk of withdrawal symptoms.

The extent to which pentazocine may produce withdrawal symptoms in patients who are physically dependent on opioid analgesics depends upon the dose of pentazocine, the specific opioid drug involved, and the degree to which physical dependence has developed.

Usual Adult Dose

Analgesic:

Oral, 50 mg every 3 to 4 hours as needed preferably after food (range 25-100mg). The dose may be increased to 100 mg if necessary, but total daily dosage should not exceed 600mg. Parental, by subcutaneous, intramuscular, or intravenous injection, moderate pain, 30 mg, severe pain 45-60 mg every 3 to 4 hours as needed. Child over 1 year, by subcutaneous or intramuscular injection, up to 1 mg/kg, by intravenous injection up to 500 microgram per kg.

Children 6-12 years, by mouth 25mg every 3-4 hours preferably after food.

Obstetrical analgesia, Intramuscular, 30 mg as a single dose, or Intravenous, 20 mg administered when contractions become regular and repeated 2 to 3 times at 2 to 3 hour intervals as needed.

**Precautions:** *See under Morphine salts and notes above;* May antagonize the effects of Mu receptor agonists; Avoid in patients depend on opioids and in arterial or pulmonary hypertension and heart failure; and avoid in porphyria.

### **Drug Interaction**

As other opioid analgesics.

In addition to those contraindications pentazocine may precipitate occurrence to those contraindications pentazocine may precipitate occurrence of withdrawal symptoms. It may also increase cardiac work. Thus it is contraindicated or must be used with caution in patients physically dependent on opioid agonists and in patients with acute myocardial infarction, arterial or pulmonary hypertension, heart failure.

### **Side/Adverse Effects**

**Less Frequently:** Allergic reaction, respiratory depression, pounding heart beat, histamine release, increased blood pressure, antidiuretic effect, blurred vision, constipation, dizziness, feeling faint or light headedness, dry mouth, general feeling of discomfort, headache, hypotension, nervousness or restlessness, night mares, burning at site of injection, unusual tiredness or weakness, urethral spasm, (difficult or painful urination) frequent urge to urinate.

**More frequently:** Drowsiness, false sense of well-being, nausea or vomiting (occurs more frequently in ambulatory patients; are more frequent with initial doses, and are less likely to occur with subsequent doses), occasional hallucinations.

### **Dosage Form**

Tablets: 50 mg

Injection: 30mg.ml, in 1 ml ampoule

## **PART II**

### **PSYCHOTROPIC SUBSTANCES**

#### **A. Anxiolytics and Hypnotics**

##### **A1. Anxiolytics (antianxiety drugs/minor tranquilizers)**

Anxiolytics are drugs used to alleviate anxiety states. Most of the currently used drugs in this group are benzodiazepines. Although there is a tendency to prescribe these drugs to almost anyone with stress-related symptoms, unhappiness, or situational distress their use in such cases is often unjustified. They should be prescribed to patients with anxiety symptoms in the lowest therapeutic dose and for the shortest duration. Prolonged use may lead to dependence and tolerance and subsequent difficulty in withdrawing the drug.

The short acting ones are preferred only for patients who have difficulty falling asleep, while the long acting benzodiazepines are useful for insomnia.

Patients on benzodiazepines should be informed of the common consequences of treatment with these drugs e.g. impaired reflexes which may endanger driving or operating of machinery potentiation of the sedative effects of alcohol, dependence with prolonged use and the possibility of paradoxical effects (e.g. agitation and aggressiveness). Short acting benzodiazepines may induce rebound insomnia, anxiety, insomnia, nausea, vomiting, tachycardia anorexia, confusion, toxic psychosis, convulsion, and feeling of unreality.

Benzodiazepines can be classified according to their elimination half-life and duration of action.

Drug	Duration of Action	Elimination half-life (Hours)
ALPRAZOLAM	Short	6 –20
OXAZEPAM	Short	9-22
CHLORDIAZEPOXIDE	Long	7-46
DIAZEPAM	Long	14-90

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## **DIAZEPAM**

### ***Indications:***

Short-term use in anxiety or insomnia, adjunct in acute alcohol withdrawal status epilepticus, muscle spasm; peri-operative use, febrile convulsions.

### ***Dose:***

By mouth, anxiety, 2 mg 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

By intramuscular injection or slow intravenous injection (into large vein, at a rate of not more than 5 mg/minute), for severe anxiety, control of acute panic attacks and acute alcohol withdrawal, 10 mg, repeated if necessary after 4 hours.

**Note:** Only use intramuscular route when oral and intravenous routes not possible.

By rectum as suppositories, anxiety when oral route not appropriate, 10-30mg (higher dose divided), dose form not appropriate for less than 10mg.

By intravenous infusion: 10-20 mg at a rate of 0.5 ml (2.5mg) per 30 seconds, repeated if necessary after 30-60 minutes; may be followed by intravenous infusion to max. 3 mg/kg over 24 hrs. Child 200-300 micrograms/kg/

### ***Cautions:***

Respiratory disease, muscle weakness, history of drug abuse, marked personality disorder, pregnancy, breast feeding; reduce dose in elderly and debilitated and in hepatic impairment (avoid if severe), renal impairment avoid prolonged use (and abrupt withdrawal thereafter) special precautions for intravenous injection, porphyria. Driving: Drowsiness may affect performance of skilled tasks (e.g. driving) effects of alcohol enhanced.

### ***Contra-indications:***

Respiratory depression; acute pulmonary insufficiency; phobic or obsessional states chronic psychosis; porphyria, preexisting CNS depression or coma, severe hepatic impairment, myasthenia gravis.

### ***Interactions:***

Alcohol, Anaesthesia, Antidepressants, Antihistamines, Antipsychotics and opioid analgesics will have enhanced sedative effect with diazepam.

Isoniazid, fluvoxamine, ketoconazole, nefazodone (concurrent use may inhibit hepatic metabolism of benzodiazepins that are metabolized by oxidation); rifampicin increase metabolism of diazepam.

Phenytoin plasma concentrations increased or decreased by diazepam & Ritonavir increases plasma concentration of diazepam; plastic infusion.

### ***Side-effects:***

Drowsiness and light-headedness the next day; confusion and ataxia (especially in the elderly) amnesia may occur; dependence, paradoxical increase in aggression, muscle weakness and occasionally: headache, vertigo, hypotension, salivation changes, gastrointestinal disturbances rashes, visual disturbances changes in libido, urinary retention blood disorders and jaundice are reported: On intravenous injection, pain, thrombophlebitis, and rarely apnoea or hypotension.

### ***Dosage Form:***

2.5, 10 mg tablets  
2mg/5 ml syrup  
5,10 mg suppository  
5 mg/ml in 2 ml ampoules

## **BROMAZEPAM**

### ***Indication:***

Anxiety (short-term use)

### ***Dose:***

3-18 mg daily in divided doses; (elderly or debilitated) half adult dose; max. (in exceptional circumstances in hospitalized patients) 60 mg daily in divided doses.

Children – Not recommended

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***Cautions; Contraindications, side effects***

See under diazepam.

***Dosage Form:***

1.5mg, 3mg and 6 mg tablets.

**ALPRAZOLAM**

***Indications:***

Anxiety (short term use)

***Dose:***

*Adults:* 250-500 micrograms 3 times daily (elderly or debilitated 250 microgram 2-3 times daily), increased if necessary to a total of 3 mg daily.

*Children* - Not recommended

***Cautions, contraindications, side effects:***

See under diazepam

***Dosage Form:***

0.25mg, 0.5mg and 1mg tablet.

**MEDAZEPAM**

***Indication:***

Anxiety (short-term use)

***Dose:***

Anxiety, 15-30 mg daily in divided doses, increased in severe anxiety to max. 40 mg daily in divided doses; elderly (or debilitated) half adult dose.

***Caution; contraindications, side effects***

See under diazepam.

***Dosage Form:***

5 mg, 10 mg tablets

**CHLORDIAZEPOXIDE**

***Indication:***

Anxiety, (short term use), adjunct in acute alcohol withdrawal

***Dose:***

Anxiety, 10mg 3 times daily increased if necessary to 60 -100mg daily in divided doses. Elderly (or debilitated) half adult dose.

Children - Not recommended

**Note:** - The doses stated above refer equally to Chlordiazepoxide and its hydrochloride.

***Caution, contraindications, side effects, Drug interactions:***

See under diazepam

***Dosage Form:***

5mg, 10mg, 25mg tablets.

**OXAZEPAM**

***Indication***

Anxiety (short-term use)

***Dose***

Anxiety, 15-30 mg (elderly or debilitated 10 – 20 mg) 3-4 times daily. Insomnia associated with anxiety 15-25 mg (max. 50 mg) at bedtime, child not recommended.

***Cautions; Contra-indications; side effects***

See under Diazepam; short acting.

***Dosage Form***

10 mg tablet

**A2. Hypnotics**

Before a hypnotic is prescribed the causes of the insomnia should be established and where possible, underlying factors should be treated. However, it should be noted that some patients have unrealistic sleep expectations, and others under state their alcohol consumption, which is often the cause of insomnia.

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**Transient Insomnia:** may occur in those who normally sleep well and may be due to extraneous factors such as noise, shift work and jet lag. If a hypnotic is indicated one that is rapidly eliminated should be chosen, and only one or two doses should be given.

Short-term Insomnia is usually related to an emotional problem or serious medical illness. It may last for a few weeks, and may recur; a hypnotic can be useful but should not be given for more than three weeks (preferably only one week). Intermittent use is desirable with omission of some doses. A rapidly eliminated drug is generally appropriate.

Chronic insomnia is rarely benefited by hypnotics is more often due to mild dependence caused by injudicious prescribing. Psychiatric disorders such as anxiety, depression and abuse of drugs and alcohol are common causes. Sleep disturbance is very common in depressive illness and early wakening is a useful pointer. The underlying psychiatric complaint should be treated, adapting the drug regimen to alleviate insomnia.

For example, amitriptylline, prescribed for depression will also help to promote sleep if it is taken at night. Other causes of insomnia include daytime catnapping and physical causes such as pain, pruritus, and dyspnoea.

Hypnotics should not be prescribed indiscriminately and routine prescribing is undesirable. Ideally, they should be reserved for short courses in the acutely distressed. Tolerance to their effects develops within 3 to 14 days of continuous use and long-term efficacy cannot be assured. A major drawback of long-term use is that withdrawal causes rebound insomnia and precipitates a withdrawal syndrome.

Where prolonged administration is unavoidable hypnotics should be discontinued as soon as feasible and the patient warned that sleep may be disturbed for a few days before normal rhythm is re-established; broken sleep with vivid dreams and increased REM (Rapid Eye Movement) may persist for several weeks. This represents a mild form of dependence even if clinical doses are used.

**Children:** The prescribing of hypnotics to children except for occasional use such as for night terrors and somnambulism (sleep-walking) is not justified.

**Elderly:** Hypnotics should be avoided in the elderly who are at risk of becoming ataxic and confused and so liable to fall and injure themselves.

## **BENZODIAZEPINES**

Benzodiazepines used as hypnotics include nitrazepam, flunitrazepam, and flurazepam, which have a prolonged action and may give rise to residual effects on the following day; repeated doses tend to be cumulative.

Loprazolam, lormetazepam, and temazepam act for a shorter time and they have little or no hangover effect. Withdrawal phenomena however are more common with the short acting benzodiazepines.

Benzodiazepine anxiolytics such as diazepam given as a single dose at night may also be used as hypnotic.

## **TEMAZEAPM**

### ***Indications:***

Insomnia (short-term use); for peri-operative use.

### ***Dose:***

10-20 mg (severe insomnia, up to 30 – 40 mg) at bed time; elderly (or debilitated) 10mg at bed time maximum up to 20mg.

Children – Not recommended

### ***Cautions:***

Respiratory disease, muscle weakness history of drug or alcohol abuse, marked personality disorder, pregnancy, breast-feeding; reduce dose in elderly and debilitated, in hepatic and renal impairment; avoid prolonged use (and abrupt withdrawal there after); porphyria.

### ***Contraindications:***

Respiratory depression: acute pulmonary insufficiency; Myasthenia gravis, sleep apnoea syndrome; not for use alone to treat depression (or anxiety associated with depression) chronic psychosis; porphyria, sever hepatic impairment.

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**Side-effects:**

Drowsiness and light-headedness the next day; confusion and ataxia (especially in the elderly); dependence, amnesia.

**Dosage Form:**

10 mg, 15 mg, 20 mg, 30 mg tablet

**FLURAZEPAM HYDROCHLORIDE**

**Indication:** Short term use in insomnia

**Dose:**

*Adults:* 15-30mg at bedtime; elderly (or debilitated) 15 mg

*Children* - Not recommended

**Precautions:** respiratory disease, muscle weakness, history of drug or alcohol abuse, marked personality disorder, pregnancy and breast-feeding; reduce dose in elderly and debilitated, and in hepatic (avoid if severe) and renal impairment, avoid prolonged use (and abrupt withdrawal thereafter); porphyria.

**Interactions:** Ritonavir increases plasma concentration of flurazepam (Risk of extreme sedation and respiratory depression - avoid concomitant use)

- Anti-ulcer drugs (cimetidine) inhibits metabolism of benzodiazepines
- Alcohol, Anaesthetics, Opioid analgesics, Antidepressants, Antihistamines and Antipsychotics enhance sedative effect and Antihypertensives enhance Hypotensive effect of Flurazepam
- It antagonizes effect of Levodopa

**Contraindications:** respiratory depression, acute pulmonary insufficiency; severe hepatic impairment, myasthenia gravis, sleep apnoea syndrome; not for use alone to treat depression (or anxiety associated with depression) or chronic psychosis.

**Side Effects:** drowsiness and lightheadedness the next day; confusion and ataxia (especially in the elderly); amnesia may occur; dependence.

**Dosage Form:**

Capsule 15mg, 30mg

**PROMETHAZINE**

**Indications:**

Night sedation and insomnia (short-term use) or it is indicated as sedative Hypnotic.

**Dose:**

By mouth, 25 mg at bed time increased to 50 mg if necessary; child 2-5 years 15-20 mg (1-2 years on Doctors advice only), 5-10 years, 20-25 mg, at bed time.

**Caution:**

Epilepsy, prostatic hypertrophy; glaucoma and hepatic diseases, urinary retention, jaundice, pregnancy and breast feeding, in children and elderly, drowsiness.

**Contra-indications:**

Porphyria

**Drug Interactions:** alcohol, CNS depressants, anti cholinergics, antithyroid, epinephrine, extra pyramidal reaction causing medications, levodopa, metrizamide, and MAOIS.

**Side-effects:**

Headache, psychomotor impairment, anti-muscarinic effects such as urinary retention, dry mouth, blurred vision and gastro-intestinal disturbances occasional rashes and photosensitivity reactions have been reported; paradoxical stimulation may rarely occur, especially in high dosage or in children, hypersensitivity reaction (including bronchospasm, angioedema, and anaphylaxes).

**Dosage Form** – 25 mg tablet.

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## CHLORALHYDRATE

### **Indications:**

Insomnia (short-term use)

### **Dose:**

Insomnia, 0.5-1g (max. 2g) with plenty of water at bedtime; child 30-50 mg/kg up to a max. single dose of 1g.

### **Cautions:**

Respiratory disease, history of drug or alcohol abuse, marked personality disorder, pregnancy, breast-feeding; reduce dose in elderly and debilitated; avoid prolonged use (and abrupt withdrawal thereafter), avoid contact with skin and mucous membranes.

### **Contra-indication:**

Severe cardiac disease, gastritis, marked hepatic or renal impairment, pregnancy & breast-feeding, porphyria.

### **Interactions:**

Alcohol, Anaesthetics, Opioid analgesics, Antidepressants, Antihistamines, Antipsychotics will have enhanced sedative effect with chloral hydrate and Antihypertensives will have enhanced Hypotensive effect with chloral hydrate.

Chloral hydrate may transiently enhance anti coagulant effect of acenocoumarol and warfarin.

Concomitant administration of chloral hydrate and parenteral furosemide may displace thyroid hormone from binding sites.

### **Side-effect:**

Gastric irritation: abdominal distention and flatulence; occasionally; rashes headache, Ketonuria, excitement, delirium (especially in the elderly); dependence (may be associated with gastritis and renal damage) on prolonged use, vertigo, ataxia, staggering gait, light headedness, malaise, night mares, delirium (especially in the elderly), eosinophilia, reduction in white-cell count.

### **Dosage Form:**

Capsule 500 mg

Suppository 60 mg

Syrup 250 mg/5ml, 500 mg/5 ml, 1g/ml

## MIDAZOLAM

### **Indications:**

Sedation with amnesia and in conjunction with local anaesthesia; premedication, induction.

### **Dose:**

Sedation, by intravenous injection over 30 seconds, 2 mg (elderly 1-1.5 mg) followed after 2 minutes by increments of 0.5-1 mg if sedation not adequate: usual range 2.5-7.5 mg (about 70 micrograms/kg 30-60 minutes before surgery; usual dose 5 mg (2.5 mg in elderly Induction, below intravenous injection 200-300 microgram/kg (elderly 100-200 microgram/kg).

Sedation of patients receiving intensive care by intravenous infusion, initially 30-300 micrograms/kg given over 5 minutes then 30-200 microgram/kg).

Sedation of patients receiving intensive care by intravenous infusion, initially 30-300 micrograms/kg/hour, reduce dose (or omit initial dose) in hypovolaemia, Vasoconstriction, or hypothermia low doses may be adequate if opioid analgesic also used; avoid abrupt withdrawal after prolonged administration (safety after more than 14 days not established).

### **Cautions;**

Contra-indications; side effects see under diazepam.

### **Dosage Form:**

2 mg/ml in 5 ml ampoule

5 mg/ml in 2 ml ampoule

## PENTOBARBITAL/PENTOBARBITONE

### **Indications:**

Sedative, hypnotic and preanaesthetic medication to control certain convulsive syndromes.

### **Dose:**

Adult, sedative 30 mg 2 to 4 times daily or 100 mg as extended release tablet once, as hypnotic 100 mg at bedtime.



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Intramuscular preoperative sedative or hypnotic 150 to 200 mg.  
Intravenous, hypnotic or anticonvulsant 100 mg given as initial dose, with additional small doses at 1 minute intervals, if necessary up to a total of 500 mg. Rectal, sedative, 30 mg 2 to 3 times daily hypnotic 120 to 200 mg on retiring. Pediatric oral sedative, 2 mg/kg or 60 mg/m<sup>2</sup> body surface 3 times daily.

### **A3. Treatment of Benzodiazepine Dependence**

Withdrawal of benzodiazepines following either high dose or prolonged use should be gradual, as abrupt withdrawal may cause rebound anxiety and insomnia, delirium and even convulsions. The patient must be strongly motivated for treatment to be successful. Patients on high doses can tolerate 10% weekly reduction coupled with supportive counseling.

Hospitalized patients can tolerate reduction faster than 10% weekly. Patients with severe dependence on benzodiazepines should be referred to a specialist for proper treatment.

## **B. ANTIDEPRESSANTS**

Antidepressants are the basic drugs for the treatment of two important affective disorders: depression and mania.

The drugs of this class include:

- i. Tricyclics and related antidepressants;
- ii. Monoamine oxidase inhibitors (MAOI)
- iii. Lithium salts

Tricyclic antidepressants are generally considered to be more effective in endogenous depression while the MAOI exhibit greater effectiveness in neurotic or “atypical” depression. Lithium salts are more successfully used in the treatment of bipolar illness (manic depression), acute mania as well as unipolar illness (recurrent depression).

In addition to antidepressant treatment, attempts should be made identify the possible precipitating factors, such as psychological stress, physical illness or recent major loss.

Attempts should be made to help the patient overcome these stresses during treatment.

Causally related life changes or stressors have to be discussed with the patient, who should be given explanation and reassurance. The patient should be assisted to find solutions to his problems. Relatives and others who support a patient socially should be involved in the discussions whenever possible. Always inquire about suicidal ideas and if present, take precautions, for example hospitalization, vigilant 24 hour observation and nursing in a safe environment if the suicide risk is high.

### **B1. Tricyclic and Related Antidepressants**

There is no evidence that tricyclic and other related antidepressants differ significantly in their therapeutic efficacy. The choice of drugs should always be in relation to the special needs of the patient for example a sedating antidepressant in one with severe insomnia. Tricyclic antidepressants with potent anticholinergic effects should be avoided in patients who show low tolerance of such effects.

Although misuse and dependence on tricyclic antidepressants are virtually unknown prescribers should not stop the use of these drugs abruptly, because of rebound phenomena. When discontinuing treatment the dose should be reduced gradually over a period of weeks.

Amitriptyline and Imipramine are the two most commonly prescribed in these groups of drugs. Check the patients condition frequently in the early weeks of treatment, to detect any suicidal tendencies. Give few tablets at a time and involve family in supervising treatment because tricyclics are dangerous in overdose.

All tricyclics take 7-14 days to show therapeutic effects. In contrast, first adverse effects appear quickly, within 24-28 hours of administration.

Patients and relatives must be informed of the adverse effects and the delayed therapeutic benefit. In this way compliance with treatment will be improved. Treatment should be maintained at the optimum level for at least 4-6 weeks before lack of response is considered.

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Do not withdraw medication prematurely as this may lead to recurrence of symptoms. After improvement of symptoms, treatment should be continued for 6-9 months at a reduced dosage. Tricyclics with sedative properties are amitriptyline, doxepin, and trimipramine. Less sedative ones are imipramine, clomipramine and desipramine.

Tricyclics may be given one daily preferably at night. New compounds like mianserin may have fewer anticholinergic and cardiac adverse effects and therefore may be important in cases where such adverse effects are a major constraints; mianserin should however be used with precaution because of risk of blood dyscrasias. Where serum levels can be monitored the tricyclic antidepressants may be safely used in the elderly.

Overdose of a tricyclic may lead within 1-3 hours to unconsciousness, cardiac arrhythmias; fall in blood pressure, epileptic fits and even status epilepticus.

Stomach wash out, control of fits and maintenance of blood pressure must be carried out under medical specialist guidance.

Tricyclics diminish the action of anti-hypertensives such as bethanidine, clonidine, debrisoquine and guanethidine. Beta - adrenoreceptor-blocking drugs such as propranolol may be used with tricyclics.

Patients often experience dryness of mouth. They should be advised to take frequent sips of water. Patients should also be advised to rise up gradually from a recumbent position to reduce the effects of postural hypotension. They should be informed of transient blurring of vision. Patients and relatives should be educated regarding time lag between introduction of treatment and patient's improvement.

This may take up to two weeks.

## **AMITRIPTYLINE**

**Indications:** depressive illness, particularly where sedation is required; and Nocturnal enuresis in children and adults

### **Dose**

Children: 7-10 years 10-20 mg at bedtime for nocturnal enuresis 11-16 years 25-50 mg at bedtime for enuresis and depression; maximum period of treatment (including gradual withdrawal) 3 months full examination before further course.

**Adults:** Initially 75 mg daily in divided doses or as a single dose at night. Increase gradually to a maximum of 150-200 mg daily.

Enhance treatment dose 50-100 mg daily;

**Elderly and Adolescents:** Initially 30-75 mg daily in divided doses or as single dose at bedtime. Increase very gradually to a maximum of 100-125 mg daily.

### **Duration of therapy**

6-9 months maintenance treatment for depression. 10-12 weeks for nocturnal enuresis.

### **Side Effects**

Sedation, dry mouth, blurred vision, constipation, difficulty passing urine, postural hypotension, arrhythmias, tachycardia, syncope, sweating, tremor, rashes, impotence, agranulocytosis, leucopenia, thrombocytopenia and jaundice. May cause confusion in the elderly.

### **Precautions**

Amitriptyline should be used with caution in patients with the following conciliations: history of heart disease, cardiac conduction disorders, unexplained blackouts, Parkinson's disease, anticholinergic treatment programme, epilepsy, urinary retention prostatic hypertrophy, glaucoma, early pregnancy, diabetes and liver impairment, breast feeding, thyroid disease, phaeochromocytoma, history of mania, angle closure glaucoma.

### **Interactions with other drugs**

Sympathomimetics, anticholinergics, monoamine oxidase inhibitors, non-beta blocker antihypertensives (block hypotensive effects). Serum levels are reduced by antiepileptics. Potentiates effects of alcohol and other CNS depressants, antithyroid, phenothiazine, cimetidine, clonidine, guanethidine, extrapyramidal reaction causing medications.

### **Contraindications**

Arrhythmias (Heart block), recent myocardial infarction and mania.

### **Dosage Form:**

Tablets: 10,25 and 50 mg

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## AMITRIPRYLINE + CHLORDIAZEPOXIDE

See under Amitriptyline

**Dosage Form:** Capsule, 12.5mg + 5mg; 25mg + 10mg

## IMIPRAMINE

**Indication, cautions, contraindications, and side effects:** as for amitriptyline, but imipramine is considered less sedating.

**Dose:**

Depression, initially up to 75mg daily in divided doses increased gradually to 150-200mg (up to 300mg in hospital patients); up to 150mg may be given as a single dose at bed time; Elderly initially 10mg daily, increased gradually to 30-50mg daily, child not recommended for depression.

Nocturnal enuresis, child 7 years 25mg, 8-11 years 25-50mg, over 11 years 50-75mg at bedtime; maximum period of treatment (including gradual withdrawal) 3 months - full physical examination before further course.

**Dosage Form:**

Tablets: 10 and 25 mg

## CLOMIPRAMINE

**Indications, cautions, contraindications, and side effects,** as for amitriptyline. Clomipramine is specially indicated in patients with obsessional features and phobic symptoms in addition to depression, adjunctive treatment of cataplexy associated with narcolepsy. It is also considered to have less cholinergic effects.

**Dose:**

**Adults:** Initially 10mg daily, increased gradually as necessary to 30-150 mg daily in divided doses or as a single dose at bed time; maximum 250mg daily; Elderly initially 10mg daily increased carefully over approximately 10 days to 30-75mg daily.

**Child** - not recommended.

Phobic and obsessional states, initially 25mg daily (Elderly 10mg daily) increased over 2 weeks to 100-150mg daily, child not recommended.

Adjunctive treatment of cataplexy associated with Narcolepsy, initially 10mg daily gradually increased until satisfactory response (range 10-75mg daily).

**Dosage Form**

Capsules: 10,25 and 50 mg

## B2. Monoamine Oxidase Inhibitors (MAOI)

MAOIs' are used less frequently than other antidepressants. They are used when tricyclic antidepressants have failed. Atypical depression, depressions with phobic or hypochondriacal features respond best to MAOI. They may be useful in depressed patients with glaucoma.

These drugs when combined with tricyclic antidepressants or with tyramine in some foods precipitate dangerous rise in blood pressure. The danger persists up to 14 days after MAOI is discontinued. It is important to provide the patient with a list of drugs and foods, which may lead to this reaction. These drugs should only be prescribed and supervised by a consultant psychiatrist and when compliance instructions can be guaranteed.

The following information should be given to a patient who has to take MAOI, and a card containing these instructions should be given to him or her.

### PLEASE READ CAREFULLY

1. Do not eat cheese, chicken liver, broad bean pods, dried meat or fish, bananas, alcoholic beverages (especially red wine), marmot and yeast extract.
2. Eat only Fresh food and avoid food that has started becoming stale, especially such food as dried or smoked meat, fish or poultry. Avoid game.
3. Do not take any other Drug (including tablets, capsules, nose drops, inhalation, or suppositories) whether purchased by you or previously prescribed by your doctor without first seeing your

doctor or pharmacist. This includes all drugs for coughs, and colds, nose drops, pain relievers, tonics and laxatives.

4. Avoid alcoholic beverages.
5. Keep a careful note of any food or drink that disagrees with you, avoid it and tell your doctor. Report any unusual or severe symptoms to your doctor and follow any other advice given by him.

## LITHIUM

Lithium counteracts mood changes and is considered to be the only specific anti-treatment of bipolar disorders. Physical examination should be carried out before starting Lithium treatment. Test-urine for protein, sugar and casts; blood for electrolytes, urea, creatinine, full blood count and hemoglobin; thyroid function tests T3, T4 and TSH. If necessary pregnancy tests and ECG should be done.

This means that lithium treatment should be carried out in centers with specialist psychiatrists and facilities for laboratories if the treatment is to be safe.

The therapeutic serum levels are 0.8-1.2 mmol/L and prophylactic levels are 0.4-0.8 mmol/L. Blood samples should be taken 12 hours after last dose of lithium. Dosage of lithium can only be determined by titrating the daily dose against serum levels.

Once the therapeutic serum levels are reached; monitoring of serum level may be done once or twice weekly for stabilization. As the mania is controlled, dosage requirements tend to fall for the serum levels. Once the patients is stabilized prophylactic serum levels can be monitored every 6 and 8 weeks.

Every six months, serum electrolytes, urea, creatinine, full blood count and thyroid function test should be carried out. If tests show hypothyroidism stop lithium or give thyroxin supplements with lithium.

Always watch for toxic effects of Lithium. Where indicated, treatment can continue for 5 years or more. Patients should maintain a good fluid intake and should avoid dietary changes which might alter salt intake Lithium treatment is unsuitable for children.

## LITHIUM CARBONATE

### *Indications:*

Prevention of recurrent manic-depressive attacks, recurrent depression and for control of mania, treatment and prophylaxis of bipolar disorder, aggressive or self-mutilating behaviour.

**Dose:** adjusted to achieve a serum - lithium Concentration of 0.4 - 1 mmol/liter 12 hours after a dose on days 4-7 of treatment, then every week until dosage has remained constant for 4 weeks and every 3 months thereafter, doses are initially divided throughout the day, but once daily administration is preferred when serum-lithium concentration stabilized.

**Side Effects:** gastro-intestinal disturbances, fine tremor, renal impairment (particularly impaired urinary concentration and polyuria), polydipsia; also weight gain & edema (may respond to dose reduction); signs of intoxication are blurred vision, increasing gastrointestinal disturbances (anorexia, vomiting, diarrhea), muscle weakness, increased CNS disturbances (mild drowsiness and sluggishness increasing to giddiness with ataxia, coarse tremor, lack of co-ordination, dysarthria), and require withdrawal of treatment; with sever over dosage (serium-lithium concentration above 2 mmol/litre) hyperreflexia and hypertension of limbs, convulsions, toxic psychoses, syncope, renal failure, circulatory failure, coma, and occasionally death; goiter, raised antidiuretic hormone concentration, hypothyroidism, hypokalaemia, ECG changes, exacerbation of psoriasis, and kidney changes may also occur.

### *Precautions:*

Low salt diet, diarrhea and vomiting and dehydration can lead to toxicity. Use cutaneously in renal insufficiency. A high fluid intake should be maintained, measure serum-lithium concentration regularly (every 3 months on stabilized regimens), measure thyroid function every 6-12 months on stabilized regimens and advise patient to seek attention if symptoms of hypothyroidism develop (women are at greater risk) e.g. lethargy, feeling cold, maintain adequate sodium and fluid intake; test renal function before initiating and if evidence of toxicity, avoid in renal impairment, cardiac disease, and conditions with sodium imbalance such as Addison's disease, reduce dose or discontinue in diarrhea, vomiting and intercurrent infection (especially if sweating profusely); caution in pregnancy, breast

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feeding, elderly (reduce dose), diuretic treatment, myasthenia gravis; surgery; if possible avoid abrupt withdrawal.

***Interactions with other Drugs:***

Combination with diuretics may lead to toxicity particularly with thiazides. Use cautiously in combination with antipsychotic drugs. Concomitant use of iodine may lead to synergistic antithyroid effects.

***Contraindication:***

Marked renal impairment, cardiac failure and early pregnancy.

***Dosage Form:***

Tablets: 300 mg, 400mg

**LITHIUM TOXICITY & ITS MANAGEMENT**

Early symptoms of lithium intoxication are blurred vision, increasing gastrointestinal disturbances (anorexia, vomiting, diarrhea), increasing CNS disturbances (mild drowsiness and sluggishness increasing to giddiness with ataxia, coarse tremor, lack of coordination and dysarthria.).

Acute Lithium toxicity is characterized by coarse tremors, in coordination, slurred speech, disorientation, ataxia, confusion, convulsions, toxicity and coma which can lead to death.

1. If recently ingested, gastric lavage or indication of vomiting.
2. Osmotic diuresis with 31% urea or 10% mannitol or alkalization of urine with an agent such as sodium bicarbonate 245 mg or acetazolamide 750 mg.
3. Haemodialysis if life threatened
4. Restore fluid and electrolyte balance.

Inform patients that if they are in situations of water loss or deprivation such as excessive sweating, thirsting, vomiting, diarrhea, long exposure to strong sun or fever, this may lead to toxic levels of Lithium and therefore they should omit their dose and consult their doctor immediately.

**FLUOXETINE**

***Indication:***

See under Dose.

***Dose:***

- Depressive illness, 20mg daily; child not recommended
- Bulimia nervosa, 60mg daily; child not recommended
- Obsessive-compulsive disorder, initially 20mg daily, dose increase may be considered if no response after several weeks; maximum 60mg daily; child not recommended
- Premenstrual dysphoria disorder, 20mg daily for 6 months then reassess for benefit before continuing.

**N.B.** Consider the long half-life of fluoxetine when adjusting dosage (or in over dosage)

***Caution:***

Hepatic impairment, renal impairment (avoid if severe), epilepsy (avoid if poorly controlled), diabetes mellitus, pregnancy; long half-life (delayed response to dose change or cessation); rare reports of prolonged seizures with electro convulsive therapy, breast feeding, history of mania, cardiac disease, angle closure glaucoma, history of bleeding disorders, abrupt withdrawal should be avoided.

***Contra-indications:***

Breast-feeding, if the patient enters a manic phase.

***Side-effects:***

Rash (discontinue, treatment may be associated with vasculitis, anaphylaxis and pulmonary inflammation or fibrosis), nausea, vomiting, diarrhoea, anorexia with weight loss headache, nervousness, insomnia, anxiety, tremor, dry mouth, dizziness, hypomania, drowsiness, convulsions, fever, sexual dysfunction, sweating, other side-effects reported are vaginal bleeding on withdrawal, hyperprolactinemia, thrombocytopenia altered platelet function and abnormal bleeding confusion; rarely hyponatremia, possible changes in blood sugar, neuroleptic malignant syndrome like event, aplastic anemia, hemolytic anemia, cerebrovascular accident, pneumonia, GIT hemorrhage, pancreatitis, pancytopenia, thrombocytopenia.

***Dosage Form:***

20 mg, capsule

### C. ANTIPSYCHOTICS

Antipsychotic drugs (neuroleptics) have specific antipsychotic effects in both organic and functional psychosis. This specific antipsychotic effect is possibly mediated through central dopaminergic pathways. They have no effect on behavior changes that are not associated with psychotic condition. These drugs abolish or reduce hallucinations, delusions, agitation and psychomotor excitement in organic psychosis, schizophrenia, mania and other psychotic disorders. They are also used in maintenance treatment of schizophrenia. They can induce neurological adverse effects, in particular extrapyramidal effects.

The classes of antipsychotic drugs include phenothiazines, thioxanthenes and butyrophenones. All approximately are equally efficacious.

Patients who do not respond to one drug may respond to an agent from a different chemical class.

Chlorpromazine is preferred when sedation is required, haloperidol and trifluoperazine when sedation is undesired, fluphenazine decanoate and flupenthixol decanoate when depot preparations are required. Thioridazine is useful in the elderly and those patients who are very sensitive to extrapyramidal side effects. Chlorpromazine (100-200 mg) and haloperidol (5-10mg) can be given by intramuscular injection to produce a rapid calming effect in severely disturbed patients.

When extra pyramidal symptoms occur lower the dose of the antipsychotic or give anticholinergic medication or both. Sometimes there is a lower limit of antipsychotic dose below which side effects increase.

Before prescribing antipsychotics particularly for outpatients, the patient should be told of the common side effects of the drug and what to do when they occur.

Avoid prescriptions of more than one antipsychotic at a time. Regular use of antipsychotics with anticholinergics is not recommended. Use anticholinergics only when extrapyramidal side

effects occur. Patients' relatives should be informed on how to store the drug.

Antipsychotic drugs in general do not differ in range and quality of side effects, with a general tendency of the low-potency agents having less extrapyramidal side effects while the high potency agents like haloperidol have more extrapyramidal effects but less of the other side effects. These drugs can be used interchangeably in case of availability problems. There is no difference in antipsychotic effectiveness when dosage is adjusted to potency equivalence.

From a practical point of view, antipsychotic medications may be distinguished between low potency and high potency medications, as regards their side effects.

<b>Low Potency</b>	<b>Medium Potency</b>	<b>High Potency</b>
Chlorpromazine Thioridazine	Perphenazine Prochlorperazine	Haloperidol Fluphenazine Trifluoperazine

Low potency medications tend to be more sedating, cause more postural hypotension, and have more anticholinergic side effects, more allergic reactions, more likely to cause bone marrow toxicity, liver toxicity and a tendency to alter the body temperature. They are also more likely to cause ocular problems, more ejaculatory difficulties, spontaneous milk secretion and menstrual irregularities. They are also more epileptogenic. They have fewer tendencies to cause extrapyramidal side effects.

High potency antipsychotic medications have much less of the above unwanted effects but more extrapyramidal effects.

#### **C1. Extra pyramidal Side Effects**

Extra pyramidal side effects induced by antipsychotic drugs fall into four groups. They are acute dystonia, drug induced Parkinsonism, akathisia and tardive dyskinesia. The first three occur early in the course of treatment, particularly with high potency antipsychotic agents.

1. **Acute dystonia:** The common features are trismus tongue protrusion, grimacing, writhing, and twisting about, torticollis opisthotonos and oculogyric crises. In oculogyric crises the

eyes roll upwards and move to one side while the head tirts involuntarily backwards towards the same side. The dystonic reaction may develop within a few hours of use of a phenothiazine or other antipsychotics. Piperazine group of phenothiazines and butyrophenones are the most potent in causing acute dystonia. Young men are especially prone to dystonic reaction.

2. **Drug induced Parkinsonism:** This is the most common of the extrapyramidal reactions and is characterized by muscle weakness, facial immobility (expression less face), lack of associated movements when walking, rigidity of muscles, stooped posture salivation and tremors. This syndrome usually takes a few days or weeks to appear after starting treatment and sometimes diminishes with time even when the dose has not been reduced. The condition may be mistaken for blunting of affect or depression. Treatment with anticholinergic drug or reduction of the dose usually leads to improvement.
3. **Akathisia:** This is uncontrollable physical restlessness, subjective compulsion to keep moving, with unpleasant feeling of being unable to keep still. It usually occurs within the first 2-3 weeks of treatment. Treatment with anticholinergic drug is often not effective and dose reduction of the antipsychotic drug may be the only possible option. Benzodiazepines may be useful in controlling the syndrome.
4. **Tardive dyskinesia:** Although it is the least common of the extrapyramidal effects, it is the most serious. These reactions may not occur for months or even years after initiation of therapy. They may occur with all antipsychotic agents. Once established it does not always disappear when antipsychotics are stopped and may become worse when antipsychotics are discontinued abruptly. It develops slowly, characterized mainly by involuntary movements of the mouth and face, lips smacking, grimacing and movements of the tongue may occur. Chewing sucking movements and writhing and jerking movements are common.

This syndrome is common among those who have taken high doses of antipsychotic drugs for long durations, high doses of anticholinergic drugs, among elderly people and among patients with brain damage. There is no single known effective treatment.

## C2. **Malignant Neuroleptic Syndrome**

This is known to occur much more frequently than was previously thought and has significant mortality. It is characterized by increase body temperature (hyperthermia), fluctuating level of consciousness, muscular rigidity, autonomic dysfunction with pallor, tachycardia, fluctuating blood pressure, sweating and urinary incontinence. Drugs for which it has been reported include haloperidol, chlorpromazine, flupenthixol decanoate and possibly others.

Management: discontinue neuroleptic medication immediately. There is no proven effective treatment and the syndrome usually lasts for five to ten days after stopping medication. It may be unduly prolonged if depot preparations have been used. The following basic antipsychotics should be available, chlorpromazine, haloperidol, fluphenazine decanoate and thioridazine. Chlorpromazine is described in detail as a model antipsychotic.

### DOSAGE EQUIVALENT OF BASIC ANTIPSYCHOTICS

Basic Antipsychotic	Dosage Equivalence
Phenothiazine: Aliphatic	Chlorpromazine 100 mg
Piperazine	Fluphenazine 2 mg
	Trifluoperazine 5mg
Butyrophenones	Haloperidol 2 mg
Piperidines	Thioridazine 100 mg

## CHLORPROMAZINE HYDROCHLORIDE

### Indications:

- Treatment and maintenance therapy in schizophrenia
- Treatment of mania
- Treatment of other psychotic and delusional disorders, e.g. brief reactive psychosis or acute and transit psychotic disorders
- Control of disturbed behavior whether of organic or non-organic causation, associated with psychotic states.
- Used in low doses to treat anxiety states, but this is controversial because it may cause tardive dyskinesia.
- Antiemetic in palliative care.

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**Dose:**

**Adults:**

**Psychotic disorder:**

Orally, 10 to 25mg (base) two or four times a day, the dosage being increased by 20-50 mg 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

**Anxiety, pre-surgical**

Oral, 25 to 50mg (base) two or three hours before surgery, IM - 2.5 to 25mg one or two hours before surgery.

**Children (6 years and older):**

**Psychotic disorders:**

Oral, 0.5 mg 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.

**Duration of Therapy**

Most patients have to be maintained on the drug for 3-12 months after disappearance of psychotic symptoms. Brief reactive psychosis can have one episode and never relapse; such patients should not be treated with long-term maintenance treatment. History of relapse after the discontinuation of anti-psychotics is an indication for a longer than usual period of maintenance.

Where prior discontinuation of anti-psychotics did not lead to a relapse it is an indication for the gradual reduction of dosage, leading to the termination of treatment. Some patients may require prolonged maintenance with very low doses. E.g. Chlorpromazine 25-50 mg at bedtime.

**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 extra pyramidal 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 galactorrhea (female), gynecomastia and impotence (in male); hypothermia (decrease body temperature below normal); dry mouth; tachy cardia, urinal retention, increased appetite and weight gain, cholestatic jaundice, corneal capacity.

**Precautions:**

Cardiovascular diseases, respiratory diseases, phaeochromocytoma, Parkinson's disease, epilepsy, liver cirrhosis, hepatitis pregnancy, and renal failure, acute infection, breast feeding, 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 for it causes contact sensitization.

**Interaction With Other drugs**

Antacids decrease absorption of chlorpromazine. Propranolol and tricyclic antidepressants increase plasma levels of chlorpromazine, alcohol, CNS depressants, antithyroid agents, epinephrine, levodopa, lithium metrizamide, amphetamines, and anticonvulsants.

**Contraindications**

Central nervous system depression like in coma, bone marrow depression and liver failure, phaeochromocytoma, during pregnancy and breast-feeding.

**Dosage form**

Tablet 25 mg, 50 mg, 100 mg syrup, 25mg/5ml injection, 25 mg/ml in 1 and 2 ml ampoules 50 mg/ml in 2 ml ampoule Drop, 25 mg/ml in 10 ml bottle, 40 mg/ml in 10 ml and 30 ml bottles.

**FLUPHENAZINE DECANOATE**

**Indications:**

Maintenance therapy in chronic schizophrenia particularly where compliance with oral medication is poor and other psychosis.



**Dose:**

Given by deep intramuscular injection into the gluteal muscle. Start with test dose 12.5 mg or 6.25 mg in the elderly, then 4-7days, 12.5-100mg repeated at intervals of 14-35 days, adjusted according to response. Most average adults will require 25-50 mg administered at intervals of 3-5 weeks adjusted according to the response.

*Children* – Not recommended.

**Duration of Therapy, Precautions and interactions with other drugs**

As for chlorpromazine

**Adverse effects:**

As for chlorpromazine and Fluphenazine Hydrochloride, but less sedating, Extra-pyramidal reactions which occur more frequently than with chlorpromazine usually appear within few hours of administration and continue for about 2 days but may be delayed. With continuous use over several months the side effects may tend to vanish.

**Contraindications:**

Not to be used in children particularly younger children. Do not use in coma caused by central nervous system depressants or brain impairment, acute confusional states, Parkinson’s disease and in intolerance to anti-psychotics.

**Dosage Form**

Injections: 25 mg/ml ampoules of 1.0 ml (25 mg)  
(Depot, oily) 2.0 ml (50 mg)  
Also, 10 ml multi-dose vials are available

**FLUPHENAZINE HYDROCHLORIDE**

**Indications:** See under dose

**Dose:**

Schizophrenia and other psychoses, mania, initially 2.5-10 mg daily in 2-3 divided doses, adjusted according to response to 20 mg daily; doses above 20 mg daily (10 mg in elderly) only with special caution. Short-term adjunctive management of severe anxiety, psychomotor agitation, excitement and violent or dangerously impulsive behavior initially 1 mg twice daily, increased as necessary to 2 mg twice daily.

*Children* – Not recommended

**Cautions; contra-indications, Side-effects; Drug interactions;**

See under chlorpromazine Hydrochloride, but less sedating and fewer antimuscarinic or hypotensive symptoms, extrapyramidal symptoms, particularly dystonic reactions and akathisia, are more frequent, systemic lupus erythematosus avoid in depression, avoid in children.

**Dosage Form:**

1 mg tablet

**HALOPERIDOL**

**Indications:**

See under dose;

**Dose:**

By mouth, Schizophrenia and other psychoses, mania, short-term adjunctive management of psycho motor agitation, excitement, and violent or dangerously impulsive behavior, initially 1.5-3 mg 2-3 times 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 doses to a max, of 10 mg; adolescents up to 30 mg daily (exceptionally 60 mg). Agitation and restlessness in the elderly, initially 0.5-1.5mg once or twice daily. Short-term adjunctive management of severe anxiety, adults 500 micrograms twice daily, child not recommended. Intractable hiccup, 1.5 mg 3 times daily adjusted according to response, child not recommended. By intramuscular injection, 2-10 mg (increasing to 30 mg for emergency control) then 5 mg up to every hour if necessary (intervals of 4-8 hours may be satisfactory) Nausea and Vomiting 0.5-2 mg and elderly (or debilitated) initially half adult dose.

**Cautions; Contra-indications, side effects:**

See under chlorpromazine Hydrochloride but less sedating, and fewer antimuscarinic or hypotensive symptoms; pigmentation and photosensitivity reactions rare.

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Extrapyramidal symptoms, particularly dystonic reactions and akathisia are more frequent especially in thyrotoxic patients. Rarely weight loss. Avoid in Basal ganglia disease.

**Dosage Form:**

5 mg/ml in 1 ml ampoule  
2 mg/ml oral liquid  
1 mg, 2 mg, 5 mg tablet

**Information On Other Antipsychotics**

The following additional antipsychotic medications are also useful.

**HALOPERIDOL DECANOATE**

**Indications:**

As for Fluphenazine decanoate

**Dose:**

Deep intramuscular injection into the gluteal muscle 50 mg every four weeks if necessary. Increasing by 50 mg increments to 300 mg every 4 weeks. Lower doses for elderly patients (initially 12.5-25mg every 4 weeks)

*Children* – Not recommended

**Precautions and side effects:**

As for fluphenazine and Haloperidol. Gastrointestinal disturbances, weight loss and liver function alterations may rarely occur.

**Dosage Form:**

50 mg/ml; 100mg/ml injection (Depot, oily) in 1 ml ampoule.

**TRIFLUOPERAZINE**

**Indications:** See under Dose

**Duration of therapy, precautions, contraindications, side effects and interaction** with other drugs: As for Chlorpromazine; extra-pyramidal symptoms more frequent, especially at doses exceeding 6mg daily, pancytopenia, and thrombocytopenia.

**Dose:**

By mouth (reduce initial doses in elderly by at least half) Schizophrenia and other psychosis, short-term adjunctive management of psychomotor agitation, excitement, and violent or dangerously impulsive behaviour, initially 5mg twice daily, or 10mg daily in modified-release form, increased by 5mg after 1 week; then at intervals of 3 days, according to the response, child up to 12 years, initially up to 5mg daily in divided doses, adjusted according to response, age, and body weight.

Short term adjunctive management of severe anxiety, 2-4 mg daily in divided doses or 2-4 mg daily in modified release form, increased if necessary to 6mg daily; child 3-5 years up to 1mg daily, 6-12 years up to 4mg daily.

**Dosage Form:**

Tablets: 1 and 5 mg  
Capsules: 2 and 10 mg  
Syrup: 1 mg/5 ml  
Injections: 1 mg/ml ampoules, 2 mg/ml

**PIMOZIDE**

**Indication:**

See under dose

**Dose:**

Schizophrenia, initially 10 mg daily in acute conditions, adjusted according to response in increments of 2-4 mg at intervals of not less than 1 week; max. 20 mg daily, prevention of relapse, initially 2 mg daily (range 2-20 mg daily).

Monosymptomimetic hypochondriacal psychosis, paranoid psychosis, initially 4mg daily, adjusted according to response in increments of 2-4 mg at intervals of not less than 1 week; max. 16mg daily.

Mania, hypomania, short-term adjunctive management of excitement and psychomotor agitation, initially 10 mg daily adjusted according to the response in increments of 2-4 mg at intervals of not less than 1 week; max. 20mg daily.

Elderly: half usual starting dose.

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**Caution and Side effects:**

See under Chlorpromazine.

**Dosage Form:** Tablet, 2mg, 4mg, 10mg.

## THIORIDAZINE

**Indications:**

Under specialist supervision, second line treatment of schizophrenia in adults.

**Dose:**

50-300mg daily (initially in divided doses): maximum 600mg daily (in hospital patients only); child not recommended.

**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.

**Side-effects:**

See under Chlorpromazine Hydrochloride, but less sedating and extra pyramidal symptoms and hypothermia rarely occur, more likely to induce hypotension pigmentary retinopathy (with reduced visual acuity, brownish colouring of vision impaired night vision) occurs rarely with high doses – on prolonged use examinations for eye defects are required, sexual dysfunction, particularly retrograde ejaculation, may occur; avoid in porphyria.

**Drug interactions:** Antiepileptics (except carbamazepine), barbiturates, Antihypertensives and  $\beta$ -blockers, anticoagulant; anaesthetics, analgesics, anti-arrhythmics, anti bacterial, antidepressants, antifungals, antihistamines, antimalarials, other anti psychotics, antivirals, diuretics, lithium, pentamidine isetionate, sibutramine.

**Contra indications:** 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 and Drug interactions)
- A history of ventricular arrhythmias or Torsades de pointes

- Brady cardia or 2<sup>nd</sup> or 3<sup>rd</sup> degree heart block
- A family history of QTC interval prolongation
- Uncorrected hypokalaemia or hypomagnesaemia.

**Dosage Form:**

10,25,100mg tablets.

## D. ANTIEPILEPTICS

Anticonvulsant drugs should only be given when a proper diagnosis has been established. The aim of treatment is to stop all fits without causing adverse effects preferably using only one drug. Seizures may be controlled in more than three quarters of all treated epileptics and a quarter is considerably improved in seizure frequency and quality of life.

Epileptics normally well controlled on drugs, may have fits if they omit to take their drugs, alter their drinking habits, or experience some severe stress. Sleep deprivation may activate fits. Concomitant use of phenothiazine, tricyclic antidepressants and alcohol may lower seizure threshold. Menses also lower seizure threshold.

Treatment should be initiated with a low dose of one drug increasing over several weeks until control is achieved or adverse effects become intolerable.

If control is not achieved a second drug may be introduced increasing stepwise from a low dose over several weeks until control is achieved. At this stage the dose level of the second drug should be maintained while the first drug is slowly reduced. If no fits appear the first drug should be tapered off. But if the fits reappear, the two drugs will have to be used together.

Avoid combination of drugs with similar actions, for instance phenobarbitone and primidone. Where optimum serum levels of anticonvulsant can be obtained, combination of drugs may be avoided. Epileptics free of fits for at least three years on treatment, and with normal EEG, can have a gradual reduction of their drugs with the aim of eventually stopping medication. However patient's life style should always be taken into account before the decision to withdraw medication.

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## Children

Treatment follows the same principle as adults. Overprotection by restriction of activities must be avoided. Patients should be encouraged to socialize as normally as possible. Some antiepileptic drugs may interfere with learning and can lead to irritability and behavioral problems so the need to control fits should always be weighed against adverse effects of the drug in use.

## Status epilepticus

A patient is said to be in status epilepticus when seizures occur in succession with out intervening periods of recovery. The generalized tonic clonic (grand mal) form presents an immediate threat to the patient's life, because of respiratory obstruction, brain damage due to hypoxia and cardiac arrhythmia. Status epilepticus is a medical emergency, which carries a high mortality. Maintain the airway and assist ventilation even when the fits are controlled since the drugs used in its management may also depress respiration.

Intravenous diazepam is often effective but Phenytoin should be administered when feasible by the same route immediately afterwards. Diazepam may be administered rectally when annulations is impossible. Intravenous phenobarbitone is also effective and is preferred when status epilepticus occurs during withdrawal of oral phenobarbitone. When seizures continue despite treatment, general anaesthesia may be required.

Drugs may be administered through a nasogastric tube if necessary. Aim to start long-term antepileptic treatment in patients not currently on treatment, and continue in those already on treatment.

## PHENOBARBITONE

### Indications:

All types of epilepsy except petit mal seizures (absences) and also in status epilepticus.

Orally, several weeks (2-3) of therapy may be required to achieve maximum antiepileptic effect.

### Dose:

Adults: oral, 50-100mg every 12 hours daily

Children: oral, 15-50mg every 12 hours daily or 1-2 mg/kg of body weight every 8 hours daily.

Anticonvulsant, Adult, oral, 60-250mg per day as a single dose or in divided doses; IV 100-320mg, repeated if necessary up to a total dose of 600mg during a 24 hour period; children, oral, 1 to 6mg per kg of body weight per day as a single dose or in divided doses.

Status epilepticus- IV (slow), 10 to 20mg per kg of body weight, repeated, if necessary.

### Adverse Effects:

Drowsiness, lethargy, mental depression, respiratory depression, ataxia and allergic skin reactions, excitement, restlessness, confusion in the elderly and in child-hyperkinesia, irritability and learning difficulties. Megaloblastic anaemia may occur. Prolonged use of phenobarbitone may lead to dependence.

### Contraindications

Porphyria and hypersensitivity to barbiturates, respiratory depression.

### Interaction with other Drugs

Combination with phenytoin or sodium valproate increases sedation. Reduces plasma levels of tricyclic antidepressants, warfarin and dicumarol. Effectiveness of oral contraceptives may be reduced, paracetamol, isoniazid and chloramphenicol.

### Dosage Form:

Tablets: 10,15,30,60 and 100mg

Injection: 100 mg in 1 ml ampoules, 25 mg/ml

Elixir: 20 mg/5ml

## PHENYTOIN

### Indications

For all forms of epilepsy except petitmal (absences); trigeminal neuralgia.

### Dose:

#### Oral dosage Forms:

**Usual adult and adolescent dose:** Anticonvulsant - oral, initially, 100mg (for capsule or tablet) or 125mg (oral suspension) three times a day. The dosage being adjusted at seven to ten day intervals as needed and tolerated.

**Note:** For seriously ill or debilitated patients, or patients with impaired hepatic function, the total dose is often reduced

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**Usual Pediatric Dose:** Anticonvulsant - Initial: oral, 5mg per kg of body weight a day, divided into two or three doses, the dosage being adjusted as needed and tolerated but not to exceed 300mg a day.

**Maintenance:** oral, 4 to 8 mg per kg of body weight or 250mg per square meter of body surface area a day, divided into two or three doses.

**Usual geriatric dose** - Anti-convulsant - oral, initially 3 mg per kg of body weight a day, in divided doses, the dosage being adjusted according to serum phenytoin concentrations and the patient's response.

**Side Effects:**

Confusion, nausea and vomiting, dizziness, headache, tremor, and insomnia are fairly common. Nystagmus, diplopia, vertigo, ataxic gait and other cerebellar signs may occur at high dosages including acute confusional states. Hyperplasia of the gums develops in about 20% of those on chronic treatment. Peripheral neuritis, fever, hepatitis and folate deficiency anaemia. The latter effect can be avoided by periodic monitoring of serum folate level.

**Precautions:**

Pregnancy, hepatic impairment. Avoid sudden withdrawal.

**Interactions with other Drug**

Sulthiame, monoamine oxidase inhibitors and disulfiram increase phenytoin levels in plasma, by interfering with its liver metabolism. Carbamazepine lowers phenytoin plasma levels. Phenobarbitone and primidone also have complex interactions with phenytoin. Where possible check serum phenytoin when using it in combination with other anti-convulsants. It can reduce the effectiveness of oral contraceptives.

**Contra-indications:**

Prophyrias, cardiac function impairment, such as Adams-stokes syndrome, second and third degree AV block and sinus brady cardia.

**Dosage Form:**

Tablets: 50 and 100 mg

Capsules: 50 and 100 mg

Injection: powder for injection, 250mg in vial.

Suspension: 30 mg/5ml for oral use

## DIAZEPAM

**Indication**

Treatment of status epilepticus.

**Dose**

*Children:* 200-300 micrograms/kg body weight by slow intravenous injection

*Adult:* By slow intravenous injection 10-20 mg at a rate of 5 mg per minute. Repeat 30-60 minutes if necessary. May be followed by slow intravenous infusion to a maximum of 3mg/kg body weight over 24 hours. Once the status epilepticus has been controlled, the patient should be maintained on other antiepileptics.

*Elderly & debilitated:* 1/3 – 1/2 adult dose

**Side Effects:**

Respiratory depression and hypertension. Local reactions at injection site such as thrombophlebitis or venous thrombosis. (See also diazepam under anxiolytics).

**Precautions:**

Patients with chronic respiratory diseases and those with myasthenia gravis.

**Contraindications:**

Hypersensitivity to diazepam

**Dosage Form:**

Injections: 5 mg/ml in 2 ml ampoules

## CARBAMAZEPINE

**Indications:**

Partial and secondary generalized tonic-clonic seizures, some primary generalized seizures, trigeminal neuralgia; prophylaxis of bipolar disorder unresponsive to lithium.

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**Dose****Epilepsy:**

**Children:** under 1 year 100-200 mg;  
1-5 years 200 – 400 mg  
5 - 10 years 400 – 600 mg  
10-15 years 600-1,000 mg  
All in divided doses (preferably two)

**Adult:** Initially 100-200 mg twice daily increasing gradually up to a usual dose of 800-1200 mg daily depending on the patients needs. In some cases doses as high as 1600-2000 mg daily may be needed.

**Elderly and debilitated:** Reduce initial dose.

Trigeminal Neuralgia, initially 100mg, 1-2 times daily (but some patients may require higher initial dose), increased gradually according to response, usual dose 200mg 3-4 times daily up to 1-6 gm daily in some patients.

Prophylaxis of bipolar disorder unresponsive to lithium, initially 400mg daily in divided doses increased until symptoms controlled; usual range 400-600mg daily, maximum 1.6gm daily.

**Precautions:** Hepatic or renal impairment; cardiac disease. Skin reactions, history of hematological reactions to other drugs; glaucoma; pregnancy, breast-feeding, avoid abrupt withdrawal.

**Adverse Effects:**

Dizziness, drowsiness, ataxia, nystagmus, diplopia, jaundice, leucopenia, cardiac failure and skin allergy have been reported. Fluid retention may occur. Rarely severe bone marrow depression may occur necessitating immediate withdrawal of treatment, others include GIT intolerance, anorexia, abdominal pain, dry mouth, diarrhea, constipation, hepatitis, acute renal failure, toxic epidermal necrolysis.

**Interaction with other drugs;**

Interacts with monoamine oxidize inhibitors and may cause central nervous system excitation and hypertension. Lowers plasma levels of Phenytoin. It can reduce the effectiveness of oral contraceptives; others include acetazolamide, amitriptyline, chloroquine, chlorpromazine, ciclosporin, cimetidine, clomiperamine, and clonazepam.

**Contraindications:**

Previous sensitivity to carbamazepine or tricyclic anti depressants, porphyria, arterioventricular conduction disorders, history of bone marrow depression.

**Dosage Form:**

Tablets: 100, 200 mg  
Syrup: 100 mg/5ml

**D1. Other Anti-Epileptics**

The following additional antiepileptics: clonazepam, primidone and sodium valproate.

**CLONAZEPAM****Indications:**

All forms of epilepsy; myoclonus, status epilepticus.

**Dose:**

1mg (elderly, 500mcg), initially at night for 4 nights, increased over 2-4 weeks to a usual maintenance dose of 4-8mg daily in divided doses;

Child up to 1 year 250 mcg increased as above to 0.5-1mg

Child up to 1-5 years 250mcg increased to 1-3mg,

Child up to 5-12 years 500mcg increased to 3-6mg.

**Cautions:** respiratory disease, hepatic and renal impairment; elderly and debilitated; pregnancy and breast-feeding; avoid sudden withdrawal; porphyria.

**Interactions:** as diazepam

**Contraindications:** respiratory depression; acute pulmonary insufficiency.

**Side Effects:**

Drowsiness, fatigue, dizziness, muscle hypotonia, coordination disturbances; hypersalivation in infants, paradoxical aggression, irritability and mental changes, rarely blood disorders, abnormal liver function tests.

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**Dosage Form:**

Tablets: 0.5, 1mg and 2 mg  
Injection: 1mg/1 ml ampoule I.V.

**PRIMIDONE****Indications:**

All forms of epilepsy except petitmal (absence seizure)

**Dose:**

Epilepsy, Adult and Child over 9 years, initially, 125mg daily at bed time, increased by 125mg every 3 days to 500mg daily in 2 divided doses then increased by 250mg every 3 days to maximum 1.5gm daily in divided doses; child under 2 years, 250-500mg daily in 2 divided doses; 2-5 years, 500-750mg daily in 2 divided doses; 6-9 years 0.75-1gm daily in 2 divided doses.

**Side Effects; Cautions:** As for Phenobarbitone and may be more severe.

**Contraindications:** Prophyria

**Interactions with other drugs:**

Phenobarbitone, phenytoin and sodium valproate increase drowsiness when combined with primidone.

**Dosage Form:**

Tablet: 250 mg

**SODIUM VALPORATE****Indications:**

Epilepsy, particularly tonic clonic but also petit mal attacks and temporal lobe epilepsy.

**Dose:**

By mouth, initially, 600mg daily given in 2 divided doses, preferably after food, increasing by 200mg/day at 3 days intervals to a maximum of 2.5kg daily in divided doses, usual maintenance 1-2g daily (20-30mg/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 hematological parameters); over 20kg, initially 400mg daily in divided doses increased until control (usually in range of 20-30mg/kg daily); maximum 35mg/kg daily.

**Side Effects:**

Drowsiness, nausea, vomiting, increased appetite, weight gain, gastric irritation, acute liver disease or failure, muscle weakness and lethargy, hair loss, edema and thrombocytopenia.

**Precautions:**

Fetal hepatic failure has occurred, particularly in infants and children in the first 6 months of treatment. Liver function should be monitored and therapy withdrawn if significantly high levels of serum transaminases are detected, patients under 3 years of age, especially those with congenital metabolic disorders, organic brain disease mental retardation may be at particular risk of Hepatotoxicity.

**Interaction with other Drugs**

Raises serum phenobarbitone levels. Carbamazepine, phenytoin, phenobarbitone and primidone reduce plasma levels of sodium valproate.

**Contraindications**

Liver disease, pregnancy, pancreatitis, porphyria or family history of severe hepatic dysfunction.

**Dosage Form:**

Tablets: 200 and 500 mg

Syrup: 200 mg/5ml

**PARALDEHYDE****Indication:**

Status epilepticus

**Dose:**

By deep intramuscular injection, as or single dose, 5-10 ml; usual max. 20 ml daily with not more than 5 ml at any one site; child up to 3 months 0.5 ml, 3-6 months 1 ml, 6-12 months 1.5 ml, 1-2 years 2 ml, 3-5 years, 3-4 ml, 6-12 years 5-6 ml.

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By intravenous infusion, up to 4-5 ml diluted to 4% solution with sodium chloride intravenous infusion 0.9%.

By rectum, 5-10 ml, administered as a 10% enema in physiological saline; child as for intramuscular dose.

**Caution:**

Broncho pulmonary disease, hepatic impairment; avoid intramuscular injection near sciatic nerve (causes severe causalgia); intravenous route specialist centers only intensive care facilities.

**Side Effects:**

Rashes, pain and sterile abscess after intramuscular injection: rectal irritation after enema.

**Dosage Form:** Injection in 2ml, 5ml and 10 ml amps.

## ACETAZOLAMIDE

Acetazolamide is a carbonic anhydrase inhibitor, which is a second-line drug for both tonic-clonic and partial seizures. It is occasionally helpful in atypical absence, atonic and tonic seizures.

**Indication:**

See notes above.

**Dose:**

0.25-1g daily in divided doses, child 8-30mg/kg daily, maximum 750mg daily.

**Cautions:**

Avoid in severe renal impairment, pregnancy; not generally recommended for prolonged administration but if given monitor blood cell counts and plasma electrolyte concentration, pulmonary obstruction (risk of acidosis); avoid extravasations at injection site (risk of necrosis), elderly, pregnancy and breast feeding.

**Side Effects:**

Paraesthesia, hypokalaemia, lack of appetite, drowsiness and depression rashes and blood disorders occur (especially in the elderly), reduced libido metabolic acidosis and electrolyte

disturbances on long term therapy, hearing disturbances, malaena, glycosuria, haematuria, abnormal liver function, renal calculi, rarely photosensitivity, liver damage, flaccid paralysis reported.

**Dosage Form:** Tablet 125mg, 250mg.

## ETHOSUXIMIDE

**Indications:**

Absence seizures.

**Dose:**

Initially 500 mg daily, increased by 250 mg at intervals of 4-7 days to usual dose of 1-1.5g daily; occasionally up to 2g daily may be needed; child up to 6 years 250 mg daily, over 6 years 500 mg, increased gradually to a max., of 1 g daily.

**Cautions:**

Hepatic and renal impairment pregnancy and breast-feeding; avoid sudden withdrawal, porphyria.

**Side Effects:**

Gastrointestinal disturbances, drowsiness, dizziness, ataxia, dyskinesia, hiccup, photophobia, headache, depression and mild euphoria. Psychotic states, rashes, liver changes, and hematological disorders such as leucopenia and granulocytosis occur rarely; systemic lupus erythematosus reported.

**Dosage Form:**

250mg capsule

250mg/5 ml syrup

## E. DRUGS USED IN PARKINSONISM AND RELATED DISORDERS

In idiopathic Parkinson's disease, progressive degeneration of pigment containing cells of the substantia nigra leads to deficiency of neurotransmitter dopamine. This in turn results in neurohormonal imbalance in the basal ganglia, causing the characteristic signs and symptoms of the illness to appear.



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The pathogenesis of this process is still obscure and current drug therapy aims simply to correct the imbalance. Although this approach fails to prevent the progression of the disease, it greatly improves the quality and expectancy of life of most patients.

The patient should be advised at the outset of the limitations of treatments and possible side effects. About 10 to 20% of patients are unresponsive to treatment.

Antiparkinsonian drug carry a special risk of inducing confusion in the elderly. It is particularly important to initiate treatment with low doses and to use small increments.

## **E1. Dopaminergic Drugs**

### **LEVODOPA**

#### ***Indication:***

Parkinsonism (but not drug-induced extrapyramidal symptoms)

#### ***Dose:***

Initially 125-500 mg daily in divided doses after meals, increased according to response (but rarely used alone).

#### ***Cautions:***

Pulmonary disease, peptic ulceration, cardio-vascular disease diabetes mellitus, open angle glaucoma skin melanoma, psychiatric illness (avoid if severe). In prolonged therapy, psychiatric, hepatic, hematological, renal, and cardiovascular surveillance is advisable. Warn patients who benefit from therapy to resume normal activities gradually; avoid abrupt withdrawal.

#### ***Contra-indications:***

Closed angle glaucoma, pregnancy and breast-feeding.

#### ***Side-effects:***

Anorexia, nausea, vomiting, insomnia, agitation, postural hypotension (rarely labile hypertension), dizziness, tachycardia, arrhythmias, reddish discoloration of urine and other body fluids, rarely hypersensitivity; abnormal involuntary movements and psychiatric symptoms which include hypomania and psychosis may be dose-limiting occasionally depression, drowsiness and rarely headache peripheral neuropathy reported.

#### ***Dosage Form:***

250 mg, 500 mg tablet.

### **AMANTADINE**

#### ***Indications:***

Parkinsonism (but not drug-induced extrapyramidal symptoms); antiviral.

#### ***Dose:***

100 mg daily increased if necessary to 100 mg twice daily (not later than 4 pm) usually in conjunction with other treatment; max. 400 mg daily (with close supervision)

#### ***Cautions:***

Cardio-vascular, hepatic, or renal disease (avoid if severe), recurrent eczema, psychosis, elderly, pregnancy, breast-feeding. Avoid abrupt discontinuation.

#### ***Contra-indications:***

Epilepsy, gastric ulceration, severe renal impairment; pregnancy, breast-feeding.

#### ***Side-effects:***

Nervousness, inability to concentrate, insomnia, dizziness, convulsions hallucinations, gastro-intestinal disturbances, skin discoloration, dry mouth, peripheral edema rarely leucopenia, rashes.

#### ***Dosage Form:***

100 mg capsule

## **E2. Anti-Muscarinic drugs**

Antimuscarinic drugs (less correctly termed "Anti-cholinergics") are the other main class of drugs used in parkinson's disease. They are less effective than levodopa in idiopathic Parkinson's disease although they often usually supplement its action.

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Antimuscarinic drugs exert their anti-parkinsonian effect by correcting the relative central cholinergic excess thought to occur in Parkinsonism as a result of dopamine deficiency.

## **BENZHEXOL HYDROCHLORIDE**

### ***Indications:***

Parkinsonism; drug-induced extrapyramidal symptoms (but not tardive dyskinesia)

### ***Dose:***

1 mg daily; gradually increased; usual maintenance dose 5-15 mg daily in 3-4 divided doses; elderly preferably lower end of range.

### ***Cautions:***

Cardiovascular disease, hepatic or renal impairment; avoid abrupt discontinuation of treatment; drugs of this type are labile to abuse.

### ***Contra-indications:***

Untreated urinary retention, closed-angle glaucoma, gastrointestinal obstruction.

### ***Side Effects:***

Dry mouth, gastrointestinal disturbances, dizziness, blurred vision; less commonly urinary retention, tachycardia, hypersensitivity, nervousness and with high doses in susceptible patients, mental confusion, excitement and psychiatric disturbances which may necessitate discontinuation of treatment.

**Dosage Form:** Tablet 2 mg, 5mg

## **BENZTROPINE MESYLATE**

***Indications, Cautions, Contraindications, Side effects:*** See under Benzhexol Hydrochloride, but causes sedation rather than stimulation; avoid in children less than 3 years.

### ***Dose:***

By mouth, 0.5-1mg daily usually at bedtime, gradually increased; max. 6mg daily; usual maintenance dose 1-4 mg daily in single or

divided dose. By IM or IV injection 1-2mg, repeated if symptoms reappear, elderly lower end of range.

### ***Dosage Form:***

2mg tablet, 1mg/ml in 2ml ampoule.

## **ORPHENADRINE HYDROCHLORIDE**

***Indications; Cautions; Contra-indications, Side effects:*** see under Benzhexol Hydrochloride but more euphoric may cause insomnia; avoid in porphyria.

### ***Dose:***

150 mg daily in divided dose: gradually increased; max. 400 mg daily, elderly preferably lower end of range.

### ***Dosage Form:***

50 mg tablet

## **PROCYCLIDINE HYDROCHLORIDE**

***Indications; Cautions; Contra-indications; Side effects:*** See under Benzhexol hydrochloride.

### ***Dose:***

By mouth 2.5 mg 3 times daily, gradually increased necessary; usually max. 30 mg daily (60 mg daily in exceptional circumstances), elderly lower ends of range.

Acute dystonia, by intramuscular injection 5-10 mg repeated if necessary after 20 minutes; max. 20 mg daily; by intravenous injection, 5 mg (usually effective within 5 minutes); an occasional patient may need 10 mg or more and may require up to half an hour to obtain relief.

### ***Dosage Form:***

5 mg/ml, 2 ml ampoule

## **LEVODOPA + CARBIDOPA**

***Indications; Caution; Contra-indications; Side effects:***

See under levodopa

**Dose:**

Expressed as levodopa, initially 110-125 mg 304 times daily adjusted according to response; usual maintenance dose 0.75-1.5 gm daily in divided doses after food.

**Dosage Form:**

100 mg + 10 mg  
250 mg + 25 mg tablet

**F. CENTRAL NERVOUS SYSTEM STIMULANTS**

**METHYL PHENIDATE HYDROCHLORIDE**

**Indications:** Part of a comprehensive treatment programme for attention - deficit hyperactivity disorder when remedial measures alone prove insufficient (under specialist supervision).

**Dose:**

**Children:** Over 6 years, initially 5mg, 1-2 times daily, increased if necessary at weekly intervals by 5-10mg daily to maximum 60mg daily in divided doses; discontinue if no response after 1 month, also suspend periodically to assess child's condition (usually finally discontinued during or after puberty)

: Under 6 years not recommended

**N.B.** Evening dose: If effect wears off in evening (with rebound hyperactivity) a dose at bedtime may be appropriate (establish need with trial bedtime dose).

**Precautions:** mild hypertension (contra-indicated if moderate or severe)-Monitor BP; History of epilepsy (discontinue if convulsions occur); tics and Tourette Syndrome (use with caution)-discontinue if tics occur; monitor growth in children; avoid abrupt withdrawal; data on safety and efficacy of long term use not complete; porphyria, also periodic complete and differential blood and platelet counts is recommended.

**Interactions:** It may inhibit metabolism of Tricyclic Antidepressants & SSRIS, with Monoamine-oxidase inhibitors administration of Inotropics (dopamine & dopexamine) may cause hypertensive crisis. It increases plasma concentration of phenytoin and possibly of phenobarbital and primidone.

It antagonizes hypotensive effect of adrenergic neuron blockers and serious adverse events reported with concomitant methyl phenidate and clonidine.

It possibly enhances anticoagulant effect of warfarin and other coumarins.

**Contraindications:** Cardiovascular disease including moderate to severe hypertension, hyper excitability or agitated states, hyperthyroidism, history of drug or alcohol abuse, glaucoma, pregnancy and breast-feeding and may affect performance of skilled tasks (e.g. driving); effects of alcohol unpredictable.

**Side effects:** insomnia, restlessness, irritability and excitability, nervousness, night terrors, euphoria, tremor, dizziness, headache; convulsions, dependence and tolerance, sometimes psychosis; anorexia, gastro-intestinal symptoms, growth retardation in children; dry mouth, sweating, tachycardia (and anginal pain), palpitations, increased blood pressure; visual disturbances; cardiomyopathy reported with chronic use; central stimulants have provoked choreoathetoid movements, tics and tourette syndrome in predisposed individuals, sleep disturbances, rash, pruritus, urticaria, fever, arthralgia, alopecia, exfoliative dermatitis, erythema multiforme, thrombocytopenic purpura, thrombocytopenia, leucopenia, urinary disorders and very rarely liver damage.

**Dosage Form:**

Tablet: 5mg, 10mg, and 20mg

**GENERAL INDEX**

<u>A</u>		<u>L</u>	
Alprazolam	20	Lithium	34
Amitriptylline	30	Lithium carbonate	35
Acetazolamide	58	Levodopa	60
Amantadine	61	Levodopa+Carbidopa	63
Amitriptyline + Chlordiazepoxide	32	<u>M</u>	
<u>B</u>		Medazepam	20
Bromazepam	19	Methyl phenidate Hydrochloride	64
Benzhexol Hydrochloride	62	Morphine	8
		Midazolam	27
Benztropine Mesylate	62	Methadone	7
<u>C</u>		<u>O</u>	
Codeine phosphate	2	Oxazepam	21
Chloral hydrate	26	Orphenadrine Hydrochloride	63
Chlordiazepoxide	21	<u>P</u>	
Chlorpromazine Hydrochloride	41	Pentazocine	15
Clomipramine	32	Pethidine Hydrochloride	11
Carbamazepine	53	Pentobarbital	27
Clonazepam	55	Phenytoin	51
<u>D</u>		Phenobarbitone	50
Diazepam	18,53	Pimozide	47
<u>E</u>		Promethazine	25
Ethosuximide	59	Paraldehyde	57
<u>F</u>		Primidone	56
Fentanyl	4		
Flurazepam Hydrochloride	24		
Fluphenazine		Procyclidine Hydrochloride	63
Decanoate	43	<u>S</u>	
Fluphenazine Hydrochloride	44	Sodium Valporate	56
Fluoxetine	37	<u>T</u>	
<u>H</u>		Temazepam	23
Haloperidol	45	Thioridazine	48
Haloperidol Decanoate	46	Trifluoperazine	46
<u>I</u>		Tramadol hydrochloride	13
Imipramine	31		

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**Note**

This Formulary is subject to revision & amendment under any convincing circumstance, therefore the Authority welcomes comments, suggestions & amendments aiming at the improvement of the management of Narcotic Drugs and Psychotropic Substances.

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