FORMULARY OF NARCOTIC DRUGS AND PSYCHOTROPIC SUBSTANCES FOR ETHIOPIA

Second Edition

Ethiopian Food, Medicine and Healthcare Administration and Control Authority

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Contents

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 (Erythroxylon 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.

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 is believed that the health professionals who use this formulary will have a substantial reference opportunity on both controlled 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.

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

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.

PART I

NARCOTIC DRUGS

This Formulary will include information on the following: Codeine, cocaine, Diphenoxylate Fentanyl, Methadone, Morphine and Pethidine

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 throughout the CNS.

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.

COCAINE HYDROCHLORIDE

Topical solution, 4% (40mg/ml), 10 %(100mg/ml)

Indications: provide local anesthesia and vasoconstriction of accessible mucous membranes, especially in the oral, laryngeal, and nasal cavities

Cautions: Pregnancy, breast feeding and severely traumatized mucosa and sepsis.

Contraindications: known history of hypersensitivity to the drug or to the components of the topical solution.

Side effects: nausea, nervousness, unusual feelings of well-being, or restlessness

Dose and Administration: The dosage varies and depends upon the area to be anesthetized, vascularity of the tissues, individual tolerance, and the technique of anesthesia. The lowest dose needed to provide effective anesthesia should be administered. Dose should be reduced for children and for elderly and debilitated patients. Cocaine hydrochloride topical solution can be administered by means of cotton applicators or packs, instilled into a cavity, or as a spray.

Storage: Store at room temperature.

CODEINE PHOSPHATE

Tablet, 30 mg, Linctus, 15 mg/5ml

Indications: Antitussive in lower doses; treatment of mild to moderate pain.

Cautions: patients with asthma, hepatic and renal impairment, history of drug abuse and also in children, hypersensitivity reactions to other phenanthrene derivative opioid agonists.

Drug interactions: alcohol, CNS depressants, buprenorpine, monoamine oxidase (MAO) inhibitors, naltrexone, antidiarrhoeal agents.

Contraindications: children under 1 year old, productive cough, elderly, respiratory depression, head injury, acute alcoholism, acute asthma, heart failure secondary to chronic lung disease.

Side effects: constipation particularly troublesome in long term use; dizziness, nausea, vomiting; difficulty with micturation; ureteric or biliary spasm; dry mouth, headaches, sweating, facial flushing; dependence, euphoria, sedation, respiratory depression, circulatory collapse, anaphylactoid reaction.

Dose and Administration: Tablet, **Adult:** 10-20mg every 4 -6 hours. Maximum, 120mg in twentyfour hours.**Child:** (6-12 years of age), Oral, 5 to 10mg every four to six hours, not to exceed 60mg per day. ***Linctus*****, Adult**: 5-10ml 3 - 4 times daily.**Child** (but not generally recommended) 5-12 years, 2.5 - 5ml 3-4 times daily.

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

DIPHENOXYLATE HYDROCHLORIDE/ATROPINE SULPHATE

Tablet, 2.5 mg + 0.05 mg

Indications: acute diarrhea (adjunctive therapy)

Cautions: inflammatory bowel disease; severe colitis.

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

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

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

Dose and Administration: Oral: **Adult**: Diphenoxylate 5 mg 4 times/day until control achieved (maximum: 20 mg/day), then reduce dose as needed; some patients may be controlled on doses of 5 mg/day.**Child:** some authorities recommend that it should be avoided in children under 12 years. However, in certain circumstances

the following doses have been used: 4 - 8 years, 2. 5 mg upto 3 times daily, 9 - 12 years, 2.5 mg upto 4 times daily, 13 - 16 years, 5 mg upto 3 times daily.

Storage: store at room temperature and protect from light.

FENTANYL

Injection, 50mcg/ml

Indications: relief of pain,

Cautions:- inflammatory bowel disease; severe colitis.

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

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

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

Dose and Administration: Acute pain management: **Adult**: Severe: I.M, I.V: 50-100 mcg/dose every 1-2hours as needed; patients with prior opiate exposure may tolerate higher initial doses. Patient-controlled analgesia (PCA): I.V.: Usual concentration: 10mcg/ml. Demand dose: Usual: 10mcg; range: 10-50mcg. Lockout interval: 5-8 minutes. Mechanically-ventilate patients (based on 70 kg patient): Slow I.V.: 0.35-1.5mcg/kg every 30-60 minutes as needed; infusion: 0.7-10mcg/kg/hour

Storage:- store at room temperature and protect from light.

METHADONE HYDROCHLORIDE

Injection, 10 mg/ml, 20mg/ml in 1 ml ampoule

Tablet, 5 mg

Indications: for relief of severe pain, cough suppressant, opioid dependence.

Cautions: as for morphine. Methadone has a long half-life and accumulation may occur with repeated doses, especially in elderly or debilitated patients; caution in hepatic and renal impairment.

Drug interactions: as for morphine, and also fluconazole, zidovudine.

Contraindications: as for morphine, see notes above.

Side effects: as for morphine. Methadone has a more prolonged effect than morphine and readily accumulates with repeated doses. It may have a relatively greater respiratory depressant effect than morphine and, although

reported to be less sedating, repeated doses of methadone may result in marked sedation. It causes pain at injection sites; subcutaneous injection causes local tissue irritation and induration.

Dose and Administration: **Adult:**Analgesia: Oral: 2.5-10mg every 3-4 hours as needed.IV: initial: 2.5-10mg every 8-12 hours in opioid-naive patients also be administered by SC or IM injection.

Storage: store at room temperture.

MORPHINE SULPHATE

Tablets, 5mg, 10 mg, 15mg, 20mg, 30mg

Oral solution, 5mg/5ml, 20mg/5ml, 50mg/5ml

10 mg/5ml, 100 mg/5ml

Suppository, 10mg, 15mg, 20mg, 30mg

Granules for oral suspension, 30mg, 60mg, 100mg, 200mg per sachet

Capsule (modified release), 20mg, 50mg, 100mg, 200mg

Injection (as hydrochloride), 10 mg/ml, 20mg/ml in 1ml ampoule

Indications: analgesic, antidiarrhoeal, anaesthesia adjunt and antitussive; see also notes above.

Cautions: renal and hepatic impairment; elderly and debilitated, dependence; hypothyroidism; convulsive disorders; decreased respiratory reserve and acute asthma; hypotension, prostatic hypertrophy; pregnancy and breastfeeding, adrenocortical insufficiency, obstructive bowel disorders, myasthenia gravis, withdraw gradually, not drive or operate machinery; see also notes above.

Drug interactions: CNS depressants; e.g alcohol, anaesthetic agents; antidiarrheals; anticholinergics, antihypertensives; cimetidine; metoclopramide; MAO inhibitors.

Contraindications: acute respiratory depression, acute alcoholism, where risk of paralytic ileus; raised intracranial pressure or head injury; avoid injection in phaeochromocytoma; during labour, diarrhea caused by poisons, antibiotic-associated pseudomembranous enterocolitis, acute abdominal conditions and biliary colic; see also notes above.

Side effects: nausea, vomiting, constipation, drowsiness, also dry mouth, anorexia, spasm of urinary and biliary tract, bradycardia, tachycardia, palpitations, euphoria, decreased libido, rash, urticaria, pruritus, sweating, headache, facial flushing, vertigo, postural hypotension, hypothermia, hallucinations, confusion, tolerance & dependence, miosis, larger doses produce respiratory depression and hypotension.

Dose and Administration: Adult:*IM or SC:* 5 -15mg (usually 10 mg initially, based on an adult weighing 70 Kg); repeated 3-4 hourly as required. *IV*: 2.5 mg increments every 5 - 10 minutes, up to a maximum of 15 mg.*Oral:* 5 - 20 mg 4 hourly. When changing to a controlled release formulation, give the current total 24 - hour requirement in 2 divided doses. Controlled release tablets: Initially 10 - 20 mg twice daily, increased according to individual requirements.

Child*: IM or SC*: over one month old, 0.1-0.2 mg/kg.

Neonates: *IM or SC*: 0.1mg/kg. *Note: Facilities must be available to provide ventilatory support if necessary.*

Storage: Store at room temperature.

PETHIDINE HYDROCHLORIDE

Tablet, 50mg

Injection, 50mg/ml in 1 and 2ml ampoules

Indications: analgesia in moderate to severe pain including labour, anaesthesia adjunct; see also introduction notes.

Cautions: as for morphine above, also atrial fibrillation or other cardiac diseases where tachycardia might pose a problem.

Drug interactions: as for morphine, also MAO inhibitors, and cimetidine

Contraindications: as for morphine above, also renal failure or severe hepatic disease.

Side effects: as for morphine above; the effect on smooth muscle may be relatively less intense than with morphine and constipation occurs less frequently. Local reactions often follow injection of pethidine; general hypersensitivity reactions occur rarely. Pethidine given intravenously may increase the heart rate.

Dose and Administration: **Adult:** *Oral:* 50 - 150mg every 4 hours.*IM* (preferred), *SC:* 50 -150mg (usually 100mg) every three to four hour as needed**; Child**: *Oral or IM*: 0.5-2.0mg/kg/dose, repeated 8 hourly if required. Maximum 6mg/kg/day.

Storage: store at room temperature protect from light and from freezing.

PART II

PSYCHOTROPIC SUBSTANCES

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

DIAZEPAM

Tablet, 2mg, 5mg, 10mg

Suppository, 5mg, 10mg

Syrup, 2mg/5ml

Injection, 5mg/ml in 2ml ampoule

Indications: short-term treatment of anxiety or insomnia; adjunct in acute alcohol withdrawal; status epilepticus; febrile convulsions; muscle spasm; peri-operative use.

Cautions: elderly, in patients with impaired liver or kidney function, muscle weakness; elderly or debilitated patients; respiratory disease, history of alcohol abuse, marked personality disorder; pregnancy; breastfeeding; avoid prolonged use and abrupt withdrawal; porphyria.

Note:- drowsiness may affect performance of skilled tasks (e.g. driving); effects of alcohol enhanced.

Drug interactions: alcohol, antidepressants, antihistamines, antipsychotics, sedative, general anaesthetics, other hypnotics or sedatives, and opioid analgesics (sedation or respiratory and cardiovascular depression may be enhanced); fluvoxamine, ketoconazole, nefazodone (concurrent use may inhibit the hepatic metabolism of benzodiazepines that are metabolized by oxidation); plastic infusion tubing (diazepam may adheres to plastic infusion tubing), zidovudine, aminophylline.

Contraindications: preexisting CNS depression or coma, acute pulmonary insufficiency, or sleep apnoea, severe hepatic impairment; myasthenia gravis; respiratory depression; diazepam should not be used for the treatment of chronic psychosis or for phobic or obsessional states. Avoid injections containing benzyle alcohol in neonates.

Side effects: drowsiness and light headedness the next day; confusion and ataxia (especially in the elderly); amnesia; dependence; paradoxical increase in aggression; muscle weakness; occasionally headache, vertigo, salivation changes, gastrointestinal disturbances, visual disturbances, dysarthria, tremor, changes in libido, incontinence, urinary retention, blood disorders and jaundice, skin reactions raised liver enzymes, on IV injection, pain, thrombophlebitis and rarely apnea.

Dose and Administration: Oral:**Adult**: *Anxiety:* 2mg 3 times daily increased if necessary to 15 - 30 mg daily in divided doses; elderly (or debilitated) half adult dose.

Insomnia associated with anxiety: 5- 15 mg at bedtime.

Child: night terrors and somnambulism: 1 - 5 mg at bedtime.IM or slow IV injection (into a large vein, at a rate of not more than 5mg/minute): for severe acute anxiety, control of acute panic attacks, and acute alcohol

withdrawal, 10mg, repeated if necessary after not less than 4 hours.*Note: Only use intramuscular route when oral and intravenous routes not possible.*

Rectum as suppositories: anxiety when oral route not appropriate, 10 to 30mg (higher dose divided), dosage form not appropriate for less than 10mg.

Storage: at room temperature in light resistant container protect from freezing.

BROMAZEPAM

Tablet, 1.5mg, 3mg, 6mg

Indications: anxiety (short - term use, not more than two weeks)

Cautions:- elderly, in patients with impaired liver or kidney function, muscle weakness; elderly or debilitated patients; respiratory disease, history of alcohol abuse, marked personality disorder; pregnancy; breastfeeding; avoid prolonged use and abrupt withdrawal; porphyria.

Note:- drowsiness may affect performance of skilled tasks (e.g. driving); effects of alcohol enhanced.

Drug interactions:-alcohol, antidepressants, antihistamines, antipsychotics, sedative, general anaesthetics, other hypnotics or sedatives, and opioid analgesics (sedation or respiratory and cardiovascular depression may be enhanced); fluvoxamine, ketoconazole, nefazodone (concurrent use may inhibit the hepatic metabolism of benzodiazepines that are metabolized by oxidation); plastic infusion tubing (diazepam may adheres to plastic infusion tubing), zidovudine, aminophylline

Contraindications:- preexisting CNS depression or coma, acute pulmonary insufficiency, or sleep apnoea, severe hepatic impairment; myasthenia gravis; respiratory depression; diazepam should not be used for the treatment of chronic psychosis or for phobic or obsessional states. Avoid injections containing benzyle alcohol in neonates.

Side effects;- drowsiness and light headedness the next day; confusion and ataxia (especially in the elderly); amnesia; dependence; paradoxical increase in aggression; muscle weakness; occasionally headache, vertigo, salivation changes, gastrointestinal disturbances, visual disturbances, dysarthria, tremor, changes in libido, incontinence, urinary retention, blood disorders and jaundice, skin reactions raised liver enzymes, on IV injection, pain, thrombophlebitis and rarely apnea

Dose and Administration: *Oral:***Adult:** 6 to 18mg daily in divided doses; elderly (or debilitated) half adult dose; maximum (in exceptional circumstances in hospitalized patients) 60mg daily in divided doses.

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

ALPRAZOLAM

Tablet, 0.25mg, 0.5mg, 1mg

Indication: treatment of anxiety, panic disorder with or without agoraphobia; anxiety associated with depression.

Cautions, Drug interactions, Contraindications, **Side effects;** see under diazepam and also notes above.

Dose and Administration: *Oral:* **Adult:** 0.25 - 0.5mg 3 times daily (elderly or debilitated 0.25 mg 2-3 times daily), increased if necessary to a total of 3mg daily.

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

MEDAZEPAM

Capsule, 5mg, 10mg Medazepam is a long acting benzodiazepine with properties similar to those of diazepam.

Indications: used for short-term treatment of anxiety disorders.

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

Dose and Administration: *Oral:* **Adult*:*** 10-30mg daily in divided doses; in severe conditions up to 60mg daily has been given.

Storage: store at room temperature.

CHLORDIAZEPOXIDE

Tablet, 5mg, 10mg, 25mg

Indications: anxiety (short - term use); adjunct in acute alcohol withdrawal.

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

Dose and Administration: *Anxiety: Oral:* **Adult: 10mg** 3 times daily increased if necessary to 60 - 100mg daily in divided doses; elderly (or debilitated) half adult dose.

Note:the doses stated above refer equally to chlordiazepoxide and to its hydrochloride.

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

OXAZEPAM

Tablet, 10 mg

Indications: short-term management and relief of anxiety.

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

The elderly are more sensitive to CNS effects, use the smallest effective dose.

Dose and Administration: Oral**Adult:** Anxiety: 10 - 15 mg 2 - 4 times daily.*Insomnia*: 5 - 30 mg 1 - 2 hours before bedtime.*Psychotic patients and alcoholics:* 30 mg 3 to 4 times daily may be required.

Note: if used as hypnotic, it should be administered at least 1 to 2 hours before bed time as absorption is slower than with diazepam.

Storage: store at room temperature

PENTAZOCINE

Tablet, 50mg

Injection, 30mg/ml in 1ml ampoule

Indications: moderate to severe pain.

Cautions: as for morphine; pentazocine has weak opioid antagonist actions and may precipitate withdrawal symptoms if given to patients who are physically dependent on opioids.

Drug interactions: see under pethidine Hydrochloride.

Contraindications: see under Pethidine Hydrochloride and notes above; patients dependent on opioids; arterial or pulmonary hypertension, heart failure.

Side effects: as for morphine; also hallucinations, nightmares, thought distriburbances, hypertension, tachycardia, agranulocytosis, toxic epidermal necrosis.

Dose and Administration:*Oral*:**Adult:** Pentazocine hydrochloride 50mg every 3 - 4 hours preferably after food (range 25 - 100mg); maximum 600mg daily; **Child** 6 - 12 years 25 mg every 3-4 hours.*SC, IM, or IV injections:***Adult:** moderate pain, 30mg; severe pain 45 - 60 mg every 3 - 4 hours when necessary; **Child** over 1 year, *by S.C* or IM *injection*, up to 1mg/kg, *by IV injection* up to, 500 micrograms/kg.

Storage: at room temperature in a tight, light resistant container. Protect from freezing (Injection).

Notes: - Pentazocine exerts its agonist activity from their receptor binding sites and competitively inhibits their actions.

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.

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, amitryptylline, 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.

TEMAZEAPM

Capsules, 10mg, 15mg, 20mg, 30mg
Indications: short-term treatment of insomnia.
Cautions: elderly or debilitated patients; respiratory disease, renal and hepatic impairment.
Drug interactions: narcotic analgesics, barbiturates, phenothiazins, MAO inhibitors, cimetidine, ciprofloxacin, clozapine, and oral contraceptive.
Contraindications: narrow-angle glaucoma, pregnancy.
Side effects: confusion, dizziness, drowsiness, anxiety, headache, hangover, euphoria, rash, decreased libido, diarrhea, blurred vision, diaphoresis.
Dose and Administration: Adult: 15-30mg at bedtime.
Elderly or debilitated patients: 15mg
Storage: store at room temperature.

ZOLPIDEM

Tablet, 10mg

It is an imidazopyridine, chemically distinct from the benzodiazepines, but exhibiting selective high affinity for a benzodiazepine receptor subtype. Its sedative action predominates over its muscle relaxant and anticonvulsant activity (in contrast to the benzodiazepines), and its indication is for the treatment of insomnia.

Dose and Administration: Oral: **Adult:** 10mg at bedtime. Hepatic impairment and the elderly: 5 mg.

FLURAZEPAM

Capsule, 15 mg, 30 mg

Indications: short-term treatment of insomnia.

Cautions: elderly, pregnancy and children < 15 years.

Drug interactions: azole antifungals, ciprofloxacin, clarithromycin, diclofenac, doxycycline, erythromycin, isoniazide, protease inhibitor, quinidine, verapamil, cimetidine, clozapine, CNS depressants, digoxin, disulfiram, metoprolol.

Contraindications: narrow –angle glaucoma, pregnancy.

Side effects: chest pain, constipation, drowsiness, memory impairment, hangover effect, euphoria, hallucinations, rash, vomiting, diarrhea, nausea, blurred vision, tinnitus, and apnea.

Dose and Administration: Oral: Adult: 15-30 mg at bedtime. Elderly: 15mg at bedtime; avoid use if possible

Storage: store in light-resistant containers and at room temperature.

MIDAZOLAM HYDROCHLORIDE

Injection, 1mg/ml, 2 mg/ml in 5ml ampoule, 5 mg/ml in 2ml ampoule

Syrup, 2mg/ml

Tablet, 10 mg

Indications: preoperative sedation and provides conscious sedation prior to diagnostic or radiographic procedures; intravenous anesthesia (induction and maintenance).

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

Dose and Administration: Adult: Preoperative sedation: IM: 0.07 to 0.08 mg/kg 30-60 minutes prior to surgery/procedure; usual dose: 5mg.IV: 0.02-0.04mg/kg; repeat every 5 minutes as needed to desired effect or up to 0.1-0.2mg/kg. Conscious sedation: IV: initial; 0.5-2mg slow IV over at least 2 minutes; slowly titrate to effect by repeating doses every 2-3 minutes if needed; usual total dose: 2.5-5mg; use decreased doses in elderly.Anesthesia:IV: Induction: Unpremedicated patients: 0.3- 0.35mg/kg (up to 0.6mg/kg in resistant cases). Premeditated patients: 0.15-0.3 mg/kg.Maintenance: 0.05 to 0.3mg/kg as needed or continuous infusion 0.25 to 1.5mcg/kg/minute. Conscious sedation for procedures or preoperative sedation: Oral: 0.25-0.5 mg/kg as a single dose procedure, up to a maximum of 20 mg; administer 30-45 minutes prior to procedure. **Child< 6** years or less- cooperative patients may require as much as 1 mg/kg as a single dose; 0.25 mg/kg may suffice for child 6-16 years of age.

Storage: store at room temperature.

PENTOBARBITONE (PENTOBARBITAL)

Tablet, 10mg, 15mg, 30mg, 60mg and 100mg

Elixir, 20mg/5ml

Suppository (Sodium), 30mg, 60mg

Injection (sodium), *Injection (Sodium), 25mg/ml in 1ml ampoule, 100mg/ml in 1ml ampoule, 4%*

Indications: sedative/hypnotic; preanesthetic; high-dose barbiturate coma for treatment of increased intracranial pressure or status epilepticus unresponsive to other therapy.

Cautions: elderly, debilitated, renally impaired, hepatic dysfunction, or paediatric patients. Patients with depression or suicidal tendencies.

Drug interactions: other CNS depressants, ethanol, narcotic analgesics, antidepressants, or benzodiazepines, chloramphenicol, MAO inhibitors, valproic acid, griseofulvin, clarithromycin, vitamine D,xanthines such as aminophyline,caffiene,oxytriphyline,theophyline, cyclosporine, erythromycin, nevirapine, protease inhibitors, rifampin, oral contraceptives, oral anticoagulants.

Contraindications: hypersensitivity to barbiturates, hepatic impairment, respiratory disease involving dyspnea or airway obstruction particularly status asthmaticus, porphyria; pregnancy, breast feeding

Side effects: bradycardia, hypotension, drowsiness, CNS excitation or depression, lethargy, headache, insomnia, anxiety, dizziness, rash, nausea, vomiting, constipation, thrombocytopenia,ataxia and nystagmus(usually dose related), Rare: skin reactions, including Stevens-Johnson syndrome, photosensitivity; folic acid deficiency and megaloblastic anaemia. Prolonged use may lead to dependence, with a withdrawal syndrome on termination of treatment; also rickets and osteomalacia due to vitamin D deficiency, hypoprothrombinaemia and hepatitis.

Dose and Administration: Hypnotic: **Adult:** *Oral:* 100 to 320mg (base) at bedtime;*IM or IV*: 100 to 325mg. **Child:** dosage must be individualized by physician.

Sedative: Oral:**Adult:** daytime- 30-120mg (base) in two or three divided doses a day; **Child:** *daytime*, 2mg (base)/kg of body weight three times a day; Preoperative, 1 to 3mg (base) per kg of body weight. *IM or IV:* **Adult:**daytime, 30 to 120mg a day in two or three divided doses, preoperative *(IM),* 130-200mg sixty to ninety minutes before surgery. **Child:** preoperative*,* 1 to 3mg per kg of body weight, sixty-ninety minutes prior to surgery.

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

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. Anticonvulsants

Treatment should always be started with a single drug, but the choice of an anticonvulsant can only be made on an individual basis and will depend on the efficacy of the drug and the patient's

tolerance of treatment. If a drug fails to control the seizures after it has been used in full therapeutic dosage for an adequate period, or if it is not tolerated, it should be gradually substituted with another with the first drug being withdrawn only when the new regimen is mainly established. If monotherapy is ineffective, two drugs should be given in combination and several regimens may need to be tried before the most appropriate is found.

CLONAZEPAM

Injection, 1 mg/ml in 1ml ampoule

Tablet, 0.5 mg, 1mg, 2 mg

Indications: management of myoclonic and atonic/ akinetic seizures in children, and as an adjuvant agent in the management of other forms of epilepsy. It is used as an alternative to diazepam in the emergency treatment of status epilepticus.

Cautions: respiratory disease; hepatic impairment, renal impairment; elderly and debilitated; pregnancy; breastfeeding; avoid sudden withdrawal, porphyhria.

Drug interactions: acetazolamide, alcohol, carbamazepine, phenobarbital, phenytoin, ritonavir.

Contraindication: hypersensitivity to clonazepam.

Side effects: frequently - fatigue, drowsiness, ataxia and clumsiness, especially early in treatment. Paradoxical hyperkinesis, excitability, aggressiveness and other behavioral problems may occur, particularly in children with pre-existing brain damage or in patients with a history of aggressiveness. Other effects include headache and muscle weakness.

Dose and Administration: Adult: *Oral*: start with small doses and increase gradually to an optimum dose according to individual response. Initially 1mg at night for 4 nights, increased over 2 - 4 weeks to usual maintenance of 4 - 8 mg/day.*Status epilepticus: IV:* 1mg injected slowly, over 30 seconds; may be repeated as required. **Child:***Oral:* initially 0.05mg/kg/day in 3 divided doses, increased slowly if needed to a maximum of 0.3 mg/kg/day. Usual maintenance: < 1 year, 0.5 - 1mg/day; 1 - 5 years, 1 - 3mg/day; 5 - 12 years, 3 - 6mg/day, in 3 divided doses. *Status epilepticus:IV:* 0.5mg by slow injection.

Storage: store tablets at room temperature

Lorazepam

Tablet (Sublingual), 1mg, 2mg

Injection, 1mg, 4mg

Indications: conscious sedation for procedures; premedication; short-term use in anxiety or insomnia; status epilepticus, peri-operative febrile convulsions; convulsions due to poisoning.

Cautions: see under Diazepam; short acting; when given parenterally, facilities for managing respiratory depression with mechanical ventilation must be available

Drug interactions: alcohol, antidepressants, antihistamines, antipsychotics, sedative, general anaesthetics, other hypnotics or sedatives, and opioid analgesics (sedation or respiratory and cardiovascular depression may be enhanced); fluvoxamine, ketoconazole, nefazodone (concurrent use may inhibit the hepatic metabolism of benzodiazepines that are metabolized by oxidation); plastic infusion tubing (diazepam may adheres to plastic infusion tubing), zidovudine, aminophylline.

Contraindications: Hypersensitivity to lorazepam or any component of the formulation (cross-sensitivity with other benzodiazepines may exist); acute narrow-angle glaucoma; sleep apnea (pareteral); intra-arterial injection of parenteral formulation; several respiratory insufficiency (expect during mechanical ventilation); pregnancy

Side effects: drowsiness and light headedness the next day; confusion and ataxia (especially in the elderly); amnesia; dependence; paradoxical increase in aggression; muscle weakness; occasionally headache, vertigo, salivation changes, gastrointestinal disturbances, visual disturbances, dysarthria, tremor, changes in libido, incontinence, urinary retention, blood disorders and jaundice, skin reactions raised liver enzymes, on IV injection, pain, thrombophlebitis and rarely apnea.

Dose and Administration:Adult: By mouth, anxiety, 1–4 mg daily in divided doses.

Adult: *Insomnia associated with anxiety*, 1–2 mg at bedtime. **Adult**: By intramuscular or slow intravenous injection (into a large vein), acute panic attacks, 25–30 micrograms/kg (usual range 1.5–2.5 mg), repeated every 6 hours if necessary. *Child under 12 years: not recommended***.**

GENERAL INDEX

References

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2. "***Drug Information for the Health Care Professional***". Volume I, 14th edition, 1994
3. "***Model Formulary of Psychotropic Medicines for Africa***". United Nations International Drug Control Programme.
4. ***Ethiopian Medicine Formulary Second Edition,*** 2013.

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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