



**Mercy
Ships[®]**

Bringing Hope and Healing...

Formulary 2009-2011



**An Essential Medicines Dosing Guide
Based on the WHO Model Formulary**

CENTRAL NERVOUS SYSTEM

4.01 HYPNOTICS & ANXIOLYTICS

WHO MODEL FORMULARY 2008 NOTES:

The most widely used anxiolytics and hypnotics are the benzodiazepines. Treatment of anxiety should be limited to the lowest effective dose for the shortest possible time. The cause of insomnia should be established and appropriate treatment for underlying factors instituted before hypnotics are considered. Hypnotics may be of value for a few days but rarely longer than a week.

Tolerance and dependence (both physical and psychological) and subsequent difficulty in withdrawing the drug may occur after regular use for more than a few weeks. Patients with chronic anxiety, alcohol or drug dependence or those with personality disorders are more likely to become dependent. Anxiolytics and hypnotics should be prescribed in carefully individualized dosage and use should be limited to control of acute conditions such as panic attacks and acute anxiety and severe, incapacitating insomnia. There is usually no justification for prolonging treatment with anxiolytics and hypnotics for more than one to two weeks.

If used for longer periods, withdrawal should be gradual by reduction of the dose over a period of weeks or months, as abrupt discontinuation may produce confusion, toxic psychosis, convulsions or a condition resembling delirium tremens. The benzodiazepine withdrawal syndrome may develop at any time up to 3 weeks after stopping a long-acting benzodiazepine but may occur within a few hours in the case of a short-acting one. The syndrome is characterized by insomnia, anxiety, loss of appetite and body-weight, tremor, perspiration, tinnitus and perceptual disturbances. These symptoms may be similar to the original complaint and encourage further prescribing. Some symptoms may continue for weeks or months after stopping benzodiazepines.

Patients should be warned that their ability to drive or operate machinery may be impaired and that the effects of alcohol may be enhanced.

GENERIC (TRADE) NAME	CAT.	INDICATION/DOSE
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4.02 ANTIPSYCHOTIC MEDICINES

WHO MODEL FORMULARY 2008 NOTES:

Treatment of psychotic disorders is both pharmacological and psychosocial. Individual and community programmes for relearning old skills and developing new ones and for learning to cope with the illness should be initiated. Classes of antipsychotic drugs include phenothiazines (e.g. **chlorpromazine**), butyrophenones (for example **haloperidol**), thioxanthenes (e.g. flupentixol) and newer 'atypical' neuroleptics including clozapine and **risperidone**. The various antipsychotic drugs do not, in general, differ in their antipsychotic activity, but differ in range and quality of adverse effects (see below).

ACUTE PHASE TREATMENT. The administration of **chlorpromazine** or **haloperidol** will relieve symptoms such as thought disorder, hallucinations and delusions and prevent relapse. They are usually less effective in apathetic, withdrawn patients, but they can sometimes have an activating influence. Patients with acute schizophrenia generally respond better than those with chronic symptoms. In the acute phase chlorpromazine may be administered by intramuscular injection in a dose of 25–50 mg which can be repeated every 6–8 hours while observing the patient for possible hypotension. In most cases, however, IM injection is not needed and patients can be treated with an oral dose. Haloperidol may be administered in the acute phase. [Note: **Carbamazepine** is available on Mercy Ships list for prophylactic use in bipolar disorder (manic-depressive disorder) in patients unresponsive to lithium.]

MAINTENANCE THERAPY. Long-term treatment for schizophrenia may be necessary after the first episode to prevent the illness from becoming chronic. The lowest possible dose of antipsychotic drug that will prevent major exacerbations of florid symptoms is used for long-term management. Too rapid a dose reduction should be avoided. Intramuscular depot preparations such as **fluphenazine decanoate** [not on Mercy Ships list] may be used as an alternative to oral maintenance therapy especially when compliance with oral treatment is unreliable. Exacerbations of illness in patients on maintenance drug therapy can be precipitated by stress. Withdrawal of maintenance drug treatment requires careful surveillance since it is not possible to predict the course of the disease and the patient may suffer a relapse if treatment is withdrawn inappropriately. Further, the need for continuation of treatment may not be evident on withdrawal of treatment because relapse may be delayed for several weeks.

ADVERSE EFFECTS. Very common with long-term administration of antipsychotic medicines. Treatment of all patients on antipsychotics must be carefully and regularly reviewed. Hypotension and interference with temperature regulation, neuroleptic malignant syndrome and bone-marrow depression are the most life-threatening. Hypotension and interference with temperature regulation

GENERIC (TRADE) NAME	CAT.	INDICATION/DOSE
Chlorpromazine Tab 25mg (Largactil/Thorazine)	MSL IDA EML	Schizophrenia and other psychoses, mania, psychomotor agitation/violent behaviour, severe anxiety (adjunct): <i>By mouth</i> , Adult initially 25mg 3 times daily (or 75mg at night) adjusted according to response to usual maintenance dose 75-300mg daily (but up to 1g daily may be required in psychoses); Elderly (or debilitated) third to half adult dose; Child (childhood schizophrenia and autism) 1-5yo 500 micrograms/kg every 4-6 hours (max 40mg/DAY); 6-12yo third to half adult dose (max 75mg/DAY).
Chlorpromazine Inj 50mg/2ml (Largactil/Thorazine)	IDA EML	For relief of acute psychotic symptoms: <i>By deep IM inj undiluted</i> Adult 25-50mg every 6-8 hours; Child 500 micrograms/kg every 6-8 hours as needed (1-5 yo max 40mg/DAY, 6-12 yo max 75mg/DAY, in divided doses). Patient should remain supine and the blood pressure monitored for 30 minutes after IM injection.
Haloperidol Inj 5mg/ml (Serenace/Haldol)	EML	Acute psychotic symptoms: <i>By deep IM inj undiluted</i> Adult 2-10mg subsequent doses every 4-8 hours according to response (up to every hour if necessary) to total maximum of 18mg; severely disturbed patients may require initial dose of up to 18mg; Elderly (or debilitated) half adult dose; Child not recommended.

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4.03 ANTIDEPRESSANTS

WHO MODEL FORMULARY 2008 NOTES:

Tricyclic and related antidepressants and selective serotonin reuptake inhibitors (SSRIs) are the most widely used drugs in the treatment of depressive disorders. The response to antidepressant therapy is usually delayed with a lag-period of up to two weeks and at least six weeks before maximum improvement occurs. It is important to use doses that are sufficiently high for effective treatment, but not so high as to cause toxic effects. Low doses should be used for initial treatment in the elderly. The use of more than one antidepressant at a time is not recommended since this does not enhance effectiveness and may result in enhanced adverse effects/interactions.

Patients should be reviewed every 1-2 weeks at the start of treatment. Treatment should be continued for at least 4 weeks (6 weeks in the elderly) before considering whether to change to another antidepressant due to lack of efficacy. In the case of a partial response, treatment may be continued for a further 2 weeks (elderly patients may take longer to respond). Remission usually occurs after 3-12 months. Treatment at full therapeutic dose should be continued for at least 6 months, but preferably up to 12 months after resolution of symptoms (about 12 months in the elderly). Treatment should not be withdrawn prematurely otherwise symptoms are likely to recur. Patients with a history of recurrent depression should continue to receive maintenance treatment (for at least 5 years and possibly indefinitely). Lithium [not on Mercy Ships list] may be used as an alternative for maintenance treatment. Reduction in dose should be gradually carried out over a period of 4 weeks or longer if withdrawal symptoms emerge (6 months in patients who have been on long-term maintenance treatment).

Tricyclic and related antidepressants can be divided into those with more or less sedative effect. Those with sedative properties include **amitriptyline** and those with less sedative effects include imipramine [not on Mercy Ships list]. These drugs are most effective in the treatment of depression associated with psychomotor and physiological disturbances. Adverse effects include anticholinergic (more correctly antimuscarinic) symptoms of dry mouth, blurred vision, constipation and urinary retention. Arrhythmias and heart block can occur. Minimal quantities of tricyclic antidepressants should be prescribed at any one time (dangerous in overdose, high rate of fatality in the case of amitriptyline).

SSRIs (e.g. **fluoxetine**) characteristically cause gastrointestinal and sleep disturbances and hypersensitivity reactions including rash (may be a sign of an impending serious systemic reaction and discontinuation should be considered) but they are less sedating and have fewer anticholinergic (antimuscarinic) and cardiotoxic effects than tricyclic antidepressants. SSRIs are less toxic in overdose than the older tricyclic compounds, but there is some concern that SSRIs may increase suicidal ideation, especially in children and adolescents.

4.03a TRICYCLIC ANTIDEPRESSANTS [TCA]

[NOTE: Antidepressants may take at least TWO weeks to give effect, counsel patients accordingly to encourage compliance and avoid unreasonable expectations and disappointment.]

GENERIC (TRADE) NAME	CAT.	INDICATION/DOSE
Amitriptyline Hydrochloride Tab 25mg (Laroxyl)	IDA EML	Depression: <i>by mouth</i> Adult initially 75mg daily in divided doses <i>or</i> as a single dose at bedtime increased gradually as needed to 150-200mg daily (Elderly/adolescents half dose); not recommended in under 16 yo.

COMMENT/CAUTIONS:

- **Contraindications:** recent MI, arrhythmias (especially heart block); manic phase in bipolar disorders; severe liver disease; children; porphyria.
- **Adverse effects:** dry mouth, blurred vision, constipation, urinary retention. May cause drowsiness: caution patients to avoid driving/operate machinery.
- Do not use **TCA**s combined with **MAOIs** [Monoamine-oxidase inhibitor, none on the Mercy Ships list] unless under specialist supervision.

4.03b SELECTIVE SEROTONIN REUPTAKE INHIBITORS [SSRI]

GENERIC (TRADE) NAME	CAT.	INDICATION/DOSE
Fluoxetine Cap 20mg (Prozac) [SSRI]	IDA EML	Depression: <i>by mouth</i> Adult 20mg in the morning; child not recommended

COMMENT/CAUTIONS:

- A drug-free gap of ONE WEEK should be left after stopping **SSRI** (TWO WEEKS for paroxetine or sertraline, FIVE WEEKS for fluoxetine) before starting a **MAOI** [Monoamine-oxidase inhibitor, none on the Mercy Ships list]. A gap of TWO WEEKS is needed after stopping MAOI before starting another antidepressant.
- **Adverse effects:** diarrhoea, nausea/vomiting, headache, restlessness and anxiety. They tend to cause less sedation, cardiotoxicity and antimuscarinic effects. Caution use in epilepsy as it lowers the convulsion threshold.
- **Hyponatraemia** has been associated with all types of antidepressants (usually in the elderly). Consider in all patients who develop drowsiness, confusion or convulsions during treatment.

4.04 ANTIEPILEPTICS

WHO MODEL FORMULARY 2008 NOTES:

Treatment should always be started with a single drug, but the choice of an antiepileptic 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.

Initial dose of the drug of choice should be determined on the basis of the degree of urgency, the size and age of the patient. It should be increased gradually until an effective response is obtained. All antiepileptics commonly produce neurological adverse effects at too high a dose, and patients should be monitored closely for adverse effects to help in accurate dose titration. Except for phenytoin, it is rarely useful to measure plasma-drug concentrations as an aid to dose adjustment. Non-compliance because of inappropriate dosing and overdosing is a major impediment to effective antiepileptic treatment. Patients should ideally remain under supervision throughout treatment.

GENERALIZED TONIC-CLONIC, SIMPLE PARTIAL AND COMPLEX PARTIAL SEIZURES. **Carbamazepine**, **phenobarbital**, **phenytoin**, and **valproate** [not on Mercy Ships list] are widely used in the treatment of these conditions. However, each of these drugs is associated with dose-related and idiosyncratic adverse effects and monitoring of haematological and hepatic function is often advised, particularly for carbamazepine & valproate.

ABSENCE SEIZURES. Both **ethosuximide** and **valproate** [both not on Mercy Ships list] are widely used in the treatment of absence seizures (petit mal) and are usually well tolerated. However, ethosuximide can, rarely, cause lupus erythematosus and psychoses which call for immediate, but cautious, discontinuation. Absence seizures are commonly associated with tonic-clonic seizures and **valproate** is preferred since it is effective in both disorders.

TONIC, ATONIC AND ATYPICAL ABSENCE SEIZURES. **Phenobarbital** or **phenytoin** is widely used for tonic seizures, **valproate** [not on Mercy Ships list] for atonic and atypical absence seizures.

MYOCLONIC SEIZURES. **Valproate** [not on Mercy Ships list] is widely used and most effective for juvenile myoclonic seizures. However, both valproate and this type of seizure are associated with a high relapse rate and it is often necessary to continue therapy indefinitely. Other myoclonic seizures are often resistant to

treatment and some do not have an epileptic basis. **Valproate** can be of value here and other antiepileptic drugs may be useful in intractable cases.

INFANTILE SPASM (INFANTILE MYOCLONIC EPILEPSY). Infantile spasms, which are often associated with severe brain damage, can be resistant to antiepileptic drugs. **Valproate** [not on Mercy Ships list] is sometimes used.

FEBRILE CONVULSIONS. Brief febrile convulsions usually respond to sponging with tepid water and by giving an antipyretic such as paracetamol (section 5.01). Recurrent febrile convulsions or prolonged convulsions (those lasting 15 minutes or longer) are treated with **diazepam**, either rectally in solution or by intravenous injection, to prevent possible brain damage. *Intermittent prophylaxis*, with diazepam administered at the onset of fever, may prevent recurrence of febrile convulsions, but only in a small proportion of children and its routine use in this way is not recommended. Use of antiepileptics for *continuous prophylaxis* is controversial; it is probably indicated in only a small proportion of children including those whose first seizure occurred during the first 14 months of life, or who already have evident neurological abnormalities, or who have had previous prolonged or focal convulsions. **Phenobarbital** may be used for this purpose but careful clinical monitoring and dosage adjustment are necessary in order to minimize adverse effects risk. **Valproate** [not on Mercy Ships list] though effective is not recommended due to greater hepatotoxicity risk in young children.

STATUS EPILEPTICUS is a medical emergency which carries a high mortality rate. Initial management includes positioning the patient to avoid injury, supporting respiration including provision of oxygen, maintaining blood pressure, and the correction of any hypoglycaemia; maintenance of the airway and assisted ventilation are crucial even when the seizures are controlled, because the drugs used in its management may also depress respiration. The use of IV **thiamine** [not on WHO Model List] should be considered if alcohol abuse is suspected; **pyridoxine** should be administered if the status epilepticus is likely to be responsive to pyridoxine. IV **diazepam** is often effective in status epilepticus, acts rapidly and should be administered first, followed immediately by a loading dose of **phenytoin** which has a longer-acting effect. When cannulation is impossible, diazepam may be administered rectally as a solution (absorption from suppositories is too slow for treatment of status epilepticus). Intravenous **phenobarbital** is also effective but is more likely to cause respiratory depression; it is used in refractory cases but should be avoided in patients who have recently received oral phenobarbital. If seizures continue despite treatment, general anaesthesia may be required. The underlying cause must be identified and remedied in all cases.

[Mercy Ships note: Please refer to the WHO Formulary 2008 for the full notes including antiepileptics withdrawal and their use in pregnancy & breastfeeding.]

GENERIC (TRADE) NAME	CAT.	INDICATION/DOSE
Diazepam Inj 10mg/2ml (Valium) Avoid IM route - unreliable absorption. Caution: Respiratory depression.	PS MSL IDA EML	Status epilepticus, febrile convulsion: <i>By slow IV inj undiluted</i> (max rate 5mg/minute), Adult 10-20mg repeat if needed after 30-60 minutes (may be followed <i>by IV infusion</i> to max 3mg/kg over 24 hours); Child 200-300 micrograms/kg (or 1mg per year of age).
Diazepam Rectal Tube 2mg/ml, 1.25 or 2.5ml tubes Caution: Respiratory depression.	PS D	Status epilepticus, febrile convulsion: <i>By rectum</i> as rectal solution, Adult & Child > 10kg, 500 micrograms/kg, up to max 30mg (Elderly half dose), repeated after 12 hours if necessary.
Phenobarbital Tab 30mg [Phenobarbitone] (Gardenal)	PS IDA EML	<i>By mouth</i> Adult 60-180mg at night; Child 5-8mg/kg daily.
Phenobarbital Inj 100mg/ml, 2ml [Phenobarbitone] (Gardenal)	PS IDA EML	<i>By IV inj</i> diluted in 20ml WFI, Adult 10mg/kg at max rate 100mg/minute, max total dose 1g; Child 5-10mg/kg, at max rate 30mg/minute.
Phenytoin Sodium Tab 100mg (Dilantin)	IDA EML	<i>By mouth</i> , daily as single dose at night or in 2-3 divided doses given after food, Adult 200-300mg, max 500mg/DAY; Child 5-8mg/kg daily in 2 divided doses, max 300mg/DAY.
Phenytoin Sodium Inj 250mg/5ml (Dilantin Ready Mixed Inj)	IDA EML	Status epilepticus: <i>By slow IV undiluted</i> Adult loading dose 13-15mg/kg at max rate 50mg/minute; maintenance 100mg every 6 hours. Child loading dose 15mg/kg at max rate 1mg/kg/minute.
PS – Drugs subject to international control under the Convention on Psychotropic Substances (1971).		

COMMENT/CAUTIONS:

- **PS Psychotropic Substances.** Recording required in pharmacy/ward/OR.
- **Phenytoin:** Requires BP and ECG monitoring, max IV rate 50mg/minute to avoid cardiotoxicity and apnoea (fatalities reported when given IV too rapidly). Contraindicated in porphyria, sinus bradycardia, SA block, 2nd & 3rd degree AV block, and in patients with Stokes-Adams syndrome.
- **Phenytoin adverse effects:** sedation, mental depression, ataxia, nystagmus, allergic skin reactions, megaloblastic anaemia, osteomalacia.

4.05 ANTIMIGRAINE MEDICINES

WHO MODEL FORMULARY 2008 NOTES:

Chronic recurrent headache is associated with many disorders, both somatic and psychogenic. An accurate diagnosis must consequently be made before appropriate treatment can be initiated for migraine. Untreated, migraine attacks last for several hours and sometimes for as long as 3 days. Migraine headache is frequently accompanied by episodes of gastrointestinal disturbance including nausea and vomiting. The headache may be preceded or accompanied by aura (classical migraine) which is characterised by visual disturbances such as flickering lines and fragmented vision or sensory disturbances such as tingling or numbness; rarely, hemiparesis or impaired consciousness may occur. Migraine without aura (common migraine) is the more common form occurring in about 75% of patients who experience migraine.

Emotional or physical stress, lack of or excess sleep, missed meals, menstruation, alcohol and specific foods including cheese and chocolate are often identified as precipitating factors; oral contraceptives may increase the frequency of attacks. Avoidance of such precipitating factors can be of great benefit in preventing or reducing the frequency of attacks and should be addressed in detail. Women taking combined oral contraceptives who experience an onset or increase in frequency of headaches should be advised of other contraceptive measures.

The two principal strategies of migraine management are treatment of acute attacks and prophylactic treatment.

ACUTE MIGRAINE ATTACK. Treatment of acute attacks may be non-specific using simple analgesics; if nausea and vomiting are features of the attack, an antiemetic drug may be given. Treatment is generally by mouth; some drugs are available as suppositories which may be used if the oral route is not effective (poor oral bioavailability, or absorption from the gut impaired by vomiting), or not practicable (patient unable to take drugs orally). Excessive use of antimigraine medication (analgesics, 5HT₁ agonists [not included on WHO Model List] and ergotamine [not included on WHO Model List]) is associated with medication overuse headache (analgesic-induced headache); therefore, increasing consumption of these medicines needs careful management. Simple analgesics including NSAIDs (nonsteroidal anti-inflammatory drugs) can be effective in mild to moderate forms of migraine if taken early in the attack; most migraine headaches respond to **paracetamol** (acetaminophen), **acetylsalicylic acid** (aspirin) or an NSAID such as **ibuprofen** (see section 5.01). Peristalsis is often reduced during migraine attacks and, if available, a dispersible or effervescent preparation of the drug is preferred because of enhanced absorption compared with a conventional tablet. The risk of Reye syndrome due to acetylsalicylic acid in children can be avoided by giving paracetamol instead.

An antiemetic such as **metoclopramide**, given as a single dose orally or by IM injection at the onset of a migraine attack, preferably 10-15 minutes before the analgesic, is useful not only in relieving nausea but also in restoring gastric motility, thus improving absorption of the analgesic.

Specific antimigraine drugs, such as the 5HT1 agonist sumatriptan [not included on the WHO Model List and not available on the Mercy Ships list], are used when analgesics are ineffective; they act on 5HT (serotonin) 1B/1D receptors and can be used during the established headache phase of an attack. Ergot alkaloids should no longer be used; they are associated with many side effects and must be avoided in cerebrovascular or cardiovascular disease. Products which contain barbiturates or codeine are undesirable since they may cause physical dependence and withdrawal headaches.

GENERIC (TRADE) NAME	CAT.	INDICATION/DOSE
Amitriptyline Hydrochloride Tab 25mg (Laroxyl)	IDA EML	Migraine prophylaxis (unlicensed indication): <i>by mouth</i> Adult initially 10mg at bedtime increased gradually as needed to 50-75mg at bedtime.
Propranolol Hydrochloride Tab 40mg (Inderal/Avlocardyl)	IDA EML	Migraine prophylaxis: <i>by mouth</i> Adult 40mg 2-3 times daily, maintenance 80-160mg daily in divided doses.

COMMENT/CAUTIONS:

- Consider aspirin or paracetamol for acute attack pain relief.
- Consider metoclopramide for nausea & vomiting.

NOTE. For Antiemetics, see Chapter 01 Gastrointestinal System Section 1.02.

NOTE. For Antihistamines, see Chapter 03 Respiratory System Section 3.03 Antihistamines & Antiallergics.