1.3.1.1 PROFESSIONAL INFORMATION FOR MEDICINES FOR HUMAN USE

SCHEDULING STATUS

S5

1. NAME OF THE MEDICINE

MITIL TABLETS 5 mg

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet of MITIL TABLETS contains 5 mg prochlorperazine as a maleate salt.

Contains sugar: Lactose 63,7 mg

For full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Tablets

MITIL TABLETS are plain white, biconvex tablets.

4. CLINICAL PARTICULARS

4.1. Therapeutic indications

MITIL TABLETS are indicated in the control of mild and moderate mental and emotional disturbances, characterised by anxiety, tension and agitation.

These tablets are used in the treatment of Ménière's syndrome, labyrinthitis, vertigo and migraine. It is also particularly effective for the prevention and treatment of nausea and vomiting.

4.2. Posology and method of administration

Posology

Adults

PREVENTION OF NAUSEA AND VOMITING:

5 mg to 10 mg (1 to 2 tablets) of MITIL TABLETS two or three times a day.

TREATMENT OF NAUSEA AND VOMITING:

20 mg (4 tablets) of MITIL TABLETS given orally; further doses may be given as required.

TREATMENT OF MIGRAINE:

20 mg (4 tablets) of MITIL TABLETS at once followed, if required, by 10 mg (2 tablets) of MITIL TABLETS two hours later. In an established attack if the patient is unable to retain tablets, treatment may be administered in a different form (25 mg of prochlorperazine maleate suppository).

TREATMENT OF VERTIGO AS WELL AS THAT ASSOCIATED WITH MÉNIÈRES DISEASE:

15 mg to 30 mg (3 to 6 tablets) of MITIL TABLETS in divided doses; after several weeks the dose may gradually be reduced to 5 mg to 10 mg (1 to 2 tablets) of MITIL TABLETS daily.

TREATMENT OF PSYCHOSES:

12,5 mg (2½ tablets) of MITIL TABLETS twice a day for seven days adjusted gradually to 75 mg to 100 mg (15 to 20 tablets) of MITIL TABLETS daily according to the response. Some patients may be maintained on doses of 25 mg to 50 mg (5 to 10 tablets) of MITIL TABLETS daily.

TREATMENT OF NON-PSYCHOTIC ANXIETY DISORDERS:

5 mg to 10 mg (1 to 2 tablets) of MITIL TABLETS up to 3 to 4 times daily.

Special populations

Elderly population

Geriatric, emaciated and debilitated patients usually require a lower initial dose, the dosage being gradually increased as needed and tolerated.

Paediatric population

Tablets are not suitable for many paediatric patients' requirements and should not be given to children weighing less than 10 kg.

Method of administration

For oral administration.

4.3. Contraindications

MITIL TABLETS are contraindicated in:

- Patients with hypersensitivity to prochlorperazine maleate or to any excipients in MITIL TABLETS (see section 6.1),
- patients with pre-existing central nervous system depression or coma,

- patients with bone marrow suppression,
- patients with phaeochromocytoma,
- children weighing under 10 kg,
- concomitant use with medicines with central nervous system-depressant properties, including alcohol, general anaesthetics, hypnotics and sedatives, and opioid anaesthetics (see section 4.4 and 4.5).

Phenothiazines effects on the vomiting centre may mask the symptoms of overdosage of other medicines, or of disorders such as gastrointestinal obstruction (see section 4.5).

Safety in pregnancy and lactation has not yet been established therefore MITIL TABLETS are best avoided (see section 4.6).

4.4. Special warnings and precautions for use

Hypersensitivity

Hypersensitivity reactions including anaphylaxis, urticaria and angioedema have been reported with MITIL TABLETS use. In case of allergic reactions, treatment with MITIL TABLETS must be discontinued and appropriate symptomatic treatment initiated (see section 4.8).

Central Nervous System Depressants

Usage of MITIL TABLETS may lead to drowsiness and impaired concentration which is aggravated by the simultaneous intake of alcohol or other central nervous system depressant medicines (see section 4.3, 4.5 and 4.7).

Epileptic patients

Close monitoring is required in patients with a history of seizures or epileptic patients receiving anticonvulsant therapy as phenothiazines may lower the seizure threshold.

Dystonic reactions

Severe dystonic reactions have followed the use of MITIL TABLETS, particularly in children and adolescents. It should therefore be used with extreme care in children.

Neuroleptic Malignant Syndrome

It is imperative that treatment be discontinued in the event of unexplained fever, as this may be a sign of neuroleptic malignant syndrome (pallor, hyperthermia, autonomic dysfunction, altered consciousness, muscle rigidity). Signs of autonomic dysfunction, such as sweating and arterial instability, may precede the onset of hyperthermia and serve as early warning signs. Although neuroleptic malignant syndrome may be idiosyncratic in origin, dehydration and organic brain disease are predisposing factors.

Withdrawal and prolonged therapy

Acute withdrawal symptoms, including nausea, vomiting and insomnia, have very rarely been reported following the abrupt cessation of high doses of neuroleptics. Relapse may also occur, and the emergence of extrapyramidal reactions has been reported. Therefore, gradual withdrawal is advisable.

Avoid concomitant treatment with other neuroleptics (see section 4.5).

Mild symptoms resembling the withdrawal symptoms of dependence have been seen following the abrupt withdrawal of phenothiazines from patients receiving prolonged maintenance therapy.

MITIL TABLETS should be avoided in patients with:

- liver or renal dysfunction
- Parkinson's disease
- hypothyroidism
- cardiac failure
- myasthenia gravis
- prostatic hypertrophy
- a history of or active closed angle glaucoma
- agranulocytosis

MITIL TABLETS should be use with caution in patients with:

- impaired cardiovascular function,
- impaired cerebrovascular function
- impaired respiratory function
- diabetes mellitus,

Geriatric, emaciated or debilitated patients

Geriatric, emaciated, or debilitated patients usually require a lower initial dose, the dosage being gradually increased as needed and tolerated.

Eye examinations and monitoring of haematological parameters

Elderly and debilitated patients may be more prone to the adverse effects of MITIL TABLETS. Regular eye examinations and the monitoring of haematological parameters, including complete blood count, is advisable for patients receiving long term MITIL TABLETS therapy. The occurrence of unexplained infections or fever may be evidence of blood dyscrasia (see section 4.8) and requires immediate haematological investigation.

QT prolongation

Neuroleptic phenothiazines may potentiate QT interval prolongation which increases the risk of onset of serious ventricular arrhythmias of the torsade de pointes type, which is potentially fatal (sudden death). QT prolongation is exacerbated, in particular, in the presence of bradycardia, hypokalaemia, and congenital or acquired (i.e. drug induced) QT prolongation. The risk-benefit should be fully assessed before MITIL TABLETS treatment is commenced. If the clinical situation permits, medical and laboratory evaluations (e.g. biochemical status and ECG) should be performed to rule out possible risk factors (e.g. cardiac disease; family history of QT prolongation; metabolic abnormalities such as hypokalaemia, hypocalcaemia or hypomagnesaemia; starvation; alcohol abuse; concomitant therapy with other medicines known to prolong the QT interval) before initiating treatment with MITIL TABLETS and during the initial phase of treatment, or as deemed necessary during the treatment (see also sections 4.5 and 4.8).

Psychiatric disorders

As with all antipsychotic medicines, MITIL TABLETS should not be used alone where depression is predominant. However, it may be combined with antidepressant therapy to treat those conditions in which depression and psychosis coexist.

In schizophrenia, the response to neuroleptic treatment may be delayed. If treatment is withdrawn, the recurrence of symptoms may not become apparent for some time.

Photosensitivity

Because of the risk of photosensitisation, patients should be advised to avoid exposure to direct sunlight.

Skin reactions

To prevent skin sensitisation in those frequently handling preparations of phenothiazines, the greatest care must be taken to avoid contact of the medicine with the skin (see section 4.8).

Venous thromboembolism

Cases of venous thromboembolism (VTE) have been reported with antipsychotic medicines. Since patients treated with antipsychotics often present with acquired risk factors for VTE, all possible risk factors for VTE should be identified before and during treatment with MITIL TABLETS and preventative measures undertaken.

Hyperglycaemia

Hyperglycaemia or intolerance to glucose has been reported in patients treated with antipsychotic phenothiazines. Patients with an established diagnosis of diabetes mellitus or with risk factors for the development of diabetes who are started on MITIL TABLETS, should get appropriate glycaemic monitoring during treatment (see section 4.8).

Elderly

MITIL TABLETS should be used with caution in the elderly, particularly during very hot or very cold weather (risk of hyperthermia or hypothermia).

The elderly are particularly susceptible to postural hypotension. MITIL TABLETS should be used cautiously in the elderly owing to their susceptibility to medicines acting on the central nervous system and a lower initial dosage is recommended. There is an increased risk of drug-induced Parkinsonism in the elderly particularly after prolonged use. Care should also be taken not to confuse the adverse effects of MITIL TABLETS, e.g. orthostatic hypotension, with the effects due to the underlying disorder.

Increased mortality in elderly people with dementia:

Data from two large observational studies showed that elderly people with dementia who are treated with antipsychotics are at a small increased risk of death compared with those who are not treated. There are insufficient data to give a firm estimate of the precise magnitude of the risk, and the cause of the increased risk is not known.

MITIL TABLETS is not registered for the treatment of dementia-related behavioural disturbances.

Stroke:

In randomised clinical trials versus placebo performed in a population of elderly patients with dementia and treated with certain atypical antipsychotic medicines, a 3-fold increase of the risk of cerebrovascular events has been observed. The mechanism of such risk increase is not known.

An increase in the risk with other antipsychotic medicines or other populations of patients cannot be excluded. MITIL TABLETS should be used with caution in patients with stroke risk factors.

Paediatric population

Use with extreme care in children. Only to be used in children weighing over 10 kg (see section 4.3). MITIL TABLETS has been associated with dystonic reactions particularly after a cumulative dosage of 0.5 mg/kg.

Excipients

MITIL TABLETS contain lactose which may have an effect on the glycaemic control of patients with diabetes mellitus.

Patients with rare hereditary problems of galactose intolerance, total lactase deficiency or glucose-galactose malabsorption should not take MITIL TABLETS.

4.5. Interaction with other medicines and other forms of interaction

Most common interactions encountered with phenothiazines are adverse effects resulting from concomitant administration of medicines with similar pharmacological action.

Central nervous system depressants

Central nervous system depression may be enhanced by other medicines with central nervous system-depressant properties including alcohol, general anaesthetics, hypnotics and sedatives, and opioid anaesthetics (see section 4.3). Respiratory depression may occur.

Overdose of other medicines

Phenothiazines effects on the vomiting centre may mask the symptoms of overdosage of other medicines, or of disorders such as gastrointestinal obstruction (see section 4.3).

Adrenaline

Adrenaline must not be used in patients overdosed with MITIL TABLETS (see section 4.9). The action of adrenaline will be opposed by prochlorperazine.

Hypotensives

When given with other hypotensives, especially alpha adrenoceptor blocking antihypertensive medicines, a severe hypotensive effect can be produced. Phenothiazines reduce the antihypertensive action of guanethidine and other adrenergic neurone blockers.

Anticholinergics

Anticholinergic agents may reduce the antipsychotic effect of neuroleptics, and the mild anticholinergic effect of neuroleptics may be enhanced by other anticholinergic drugs, possibly leading to constipation, heat stroke, etc.

Dopaminergics

Where treatment for neuroleptic-induced extrapyramidal symptoms is required, anticholinergic anti-parkinsonian agents should be used in preference to levodopa, since neuroleptics antagonise the anti-parkinsonian action of dopaminergics.

Metoclopramide

Concomitant administration with metoclopramide may increase the risk of neuroleptic-induced extrapyramidal effects.

Interference with the absorption of neuroleptics

Some medicines interfere with absorption of neuroleptic agents: antacids, anti-Parkinson drugs and lithium.

Lithium

In patients treated concurrently with neuroleptics and lithium, there have been rare reports of neurotoxicity.

Hypoglycaemics

High doses of neuroleptics reduce the response to hypoglycaemic agents, the dosage of which might have to be raised.

QT prolonging medicines

There is an increased risk of arrhythmias when neuroleptics are used with concomitant QT prolonging medicines (including certain anti-dysrhythmics, antidepressants and other antipsychotics) and medicines causing electrolyte imbalance.

Desferrioxamine

Simultaneous administration of desferrioxamine and prochlorperazine has been observed to induce transient metabolic encephalopathy characterised by loss of consciousness for 48 – 72 hours.

Myelosuppressants

There is an increased risk of agranulocytosis when neuroleptics are used concurrently with medicines with myelosuppressive potential, such as carbamazepine or certain antibiotics and cytotoxics.

CYP2D6 inhibition

Some phenothiazines are potent inhibitors of CYP2D6. There is a possible pharmacokinetic interaction between inhibitors of CYP2D6, such as phenothiazines, and CYP2D6 substrates. Co-administration of phenothiazines with amitriptyline/amitriptylinoxide, a CYP2D6 substrate, may lead to an increase in the plasma levels of amitriptyline/amitriptylinoxide. Monitor patients for dose-dependent adverse reactions associated with amitriptyline/amitriptylinoxide.

Prochlorperazine, as contained in MITIL TABLETS, may oppose the action of the following medicines:

- amphetamine
- clonidine

Plasma concentrations of other medicines

Increases or decreases in the plasma concentrations of a number of medicines, e.g. propranolol, phenobarbital have been observed but were not of clinical significance.

4.6. Fertility, pregnancy and lactation

The safety of MITIL TABLETS in pregnancy and lactation has not been established therefore MITIL TABLETS are best avoided (see section 4.3).

Pregnancy

Animal studies are insufficient with respect to reproductive toxicity. However, potential harmful effect in animals cannot be ruled out. There is inadequate evidence of safety in pregnancy. Data from epidemiological studies do not suggest a risk of congenital malformations in children exposed in utero to MITIL TABLETS.

As a precautionary measure, MITIL TABLETS should be avoided during pregnancy.

Neuroleptics may occasionally prolong labour and at such time should be withheld until the cervix is dilated 3 – 4 cm. Possible adverse effects on the neonate include lethargy or paradoxical hyperexcitability, tremor and low Apgar score.

Neonates exposed to antipsychotics (including MITIL TABLETS) during the third trimester of pregnancy are at risk of adverse reactions including extrapyramidal and/or withdrawal symptoms that may vary in severity and duration following delivery. There have been reports of agitation, hypertonia, hypotonia, tremor, somnolence, respiratory distress, or feeding disorder. Consequently, newborns should be monitored carefully.

Breastfeeding

Phenothiazines may be excreted in milk, therefore breastfeeding should be suspended during treatment.

4.7. Effects on ability to drive and use machines

MITIL TABLETS may have a major influence on the ability to drive or operate machinery.

Usage of MITIL TABLETS may lead to drowsiness and impaired concentration which is aggravated by the simultaneous intake of alcohol or other central nervous system depressant medicines. Patients should be warned against operating vehicles or machinery or performing potentially hazardous tasks (see section 4.4).

4.8. Undesirable effects

a) Summary of the safety profile

Generally, adverse reactions occur at a low frequency; the most common reported adverse reactions are nervous system disorders.

b) Tabulated list of adverse reactions

System organ class	**Frequent**	**Less frequent**	**Frequency unknown** (cannot be estimated from the available data)
Blood and the lymphatic system disorders			Haemolytic anaemia, aplastic anaemia, thrombocytopenic purpura, potentially fatal agranulocytosis (within 4 – 10 weeks of starting treatment), mild leukopenia
Immune system disorders			Hypersensitivity reactions (urticaria, exfoliative dermatitis,

			erythema multiforme, contact sensitivity and angioedema), systemic-lupus-erythematosus-like syndrome and anaphylactic reactions
Endocrine disorders			Hyperprolactinaemia which may result in amenorrhoea, galactorrhoea, gynaecomastia and impotence, impaired body temperature regulation (hyperthermia, hypothermia)
Metabolism and nutrition disorders			Weight gain, hyperglycaemia and altered glucose tolerance, hyponatraemia, syndrome of inappropriate antidiuretic hormone secretion (SIADH).
Psychiatric disorders			Delirium, agitation, catatonic-like states, depression
Nervous system disorders			Insomnia, EEG changes and convulsions, extrapyramidal dysfunction (resulting in acute dystonia, Parkinsonism-like syndrome, akathisia, tardive dyskinesia, perioral tremor, oculogyric crisis)
Eye disorders			Blurred vision, mydriasis, miosis, deposition of pigment in the eyes
Cardiac disorders			Tachycardia (ventricular), electrocardiographic changes (including QT prolongation), ST depression, U-wave and T-wave changes, dysrhythmia (ventricular and atrial), A-V block, ventricular fibrillation, cardiac arrest, sudden death
Vascular disorders	Hypotension (usually postural)		Venous thromboembolism (including pulmonary embolism)
Respiratory, thoracic and mediastinal disorders			Nasal congestion, respiratory depression
Gastrointestinal disorders			Dry mouth, constipation
Hepatobiliary disorders			Jaundice, neuroleptic jaundice
Skin and subcutaneous tissue disorders			Photosensitivity reactions, deposition of pigment in the skin, contact skin sensitisations, skin rashes
Renal and urinary disorders			Difficulty with micturition, inhibition of ejaculation, impotence, and priapism

Pregnancy, puerperium and perinatal conditions			Drug withdrawal syndrome neonatal (see section 4.6)
General disorders and administrative site conditions			Neuroleptic malignant syndrome (hyperthermia, rigidity, autonomic dysfunction and altered consciousness) (see section 4.4).
Investigations			Minor abnormalities in liver function tests

c) Description of selected adverse reactions

Leukopenia

Mild leukopenia occurs in up to 30 % of patients on prolonged high dosage.

Acute dystonia or dyskinesias

These adverse reactions are usually not permanent and are more common in children and young adults, and they usually occur within the first 4 days of treatment or after dosage increases.

Akathisia

Characteristically occurs after large initial doses.

Parkinsonism

Parkinsonism is more common in adults and the elderly. It usually develops after weeks or months of treatment. One or more of the following may be seen: tremor, rigidity, akinesia or other features of Parkinsonism. Commonly just tremor.

Tardive dyskinesia

If this occurs it is usually, but not necessarily, after prolonged or high dosage. It can even occur after treatment has been stopped. Dosage should therefore be kept low whenever possible.

Ocular changes

Ocular changes and the development of metallic greyish-mauve coloration of exposed skin have been noted in some individuals mainly females, who have received chlorpromazine continuously for long periods (four to eight years). This could possibly happen with MITIL TABLETS.

Cardiac disorders

Dysrhythmias and tachycardias which may result in ventricular fibrillation or cardiac arrest have been reported during neuroleptic phenothiazine therapy, possibly related to dosage. Pre-existing cardiac disease, old age, hypokalaemia and concurrent tricyclic antidepressants may predispose patients to this.

There have been isolated reports of sudden death, with possible causes of cardiac origin (see section 4.4), as well as cases of unexplained sudden death, in patients receiving neuroleptic phenothiazines.

Hypotension

Hypotension, usually postural, commonly occurs. Elderly or volume depleted subjects are particularly susceptible; it is more likely to occur after intramuscular injection.

Jaundice

Jaundice, usually transient, occurs in a very small percentage of patients taking neuroleptics. A premonitory sign may be sudden onset of fever after one to three weeks of treatment followed by the development of jaundice. Neuroleptic jaundice has the biochemical and other characteristics of obstructive jaundice and is associated with obstruction of the canaliculi by bile thrombi; the frequent presence of an accompanying eosinophilia indicates the allergic nature of this phenomenon. Treatment should be withheld on the development of jaundice (see section 4.4).

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Healthcare providers are requested to report any suspected adverse drug reactions to SAHPRA via the Med Safety APP (Medsafety X SAHPRA) and eReporting platform (who-umc.org) found on SAHPRA website.

Aspen Pharmacare:

E-mail: Drugsafety@aspenpharma.com

Tel: 0800 118 088/+27 (0)11 239-6200

4.9. Overdose

Symptoms

Symptoms of phenothiazine overdose include drowsiness or loss of consciousness, acute hypotension, tachycardia, ECG changes, ventricular arrhythmias and hypothermia. Severe extrapyramidal dyskinesias may occur. Generalised vasodilatation may result in circulatory collapse.

Treatment

Activated charcoal should be given.

Raising the patient's legs may assist with generalised vasodilation symptoms. In severe cases of vasodilation, volume expansion by intravenous fluids may be needed; infusion fluids should be warmed before administration in order not to aggravate hypothermia. Positive inotropic agents such as dopamine may be tried if fluid replacement is insufficient to correct the circulatory collapse. Peripheral vasoconstrictor agents are not generally recommended. Avoid the use of adrenaline.

Ventricular or supraventricular tachy-arrhythmias usually respond to restoration of normal body temperature and correction of circulatory or metabolic disturbances. If persistent or life threatening, appropriate anti-arrhythmic therapy may be considered. Avoid lidocaine and, as far as possible, long-acting anti-arrhythmic medicines.

Pronounced central nervous system depression requires airway maintenance or, in extreme circumstances, assisted respiration. Severe dystonic reactions usually respond to procyclidine or orphenadrine administered intramuscularly or intravenously. Convulsions should be treated with intravenous diazepam.

Neuroleptic malignant syndrome should be treated with cooling. Dantrolene sodium may be tried.

There is no specific antidote. Treatment should be symptomatic and supportive.

5. PHARMACOLOGICAL PROPERTIES

5.1. Pharmacodynamic properties

Category and Class: A 2.6.1 Phenothiazines and their derivatives

Pharmacotherapeutic group: Antipsychotics, phenothiazines with piperazine structure

ATC code: N05AB04

Mechanism of action

Prochlorperazine, like its related molecules chlorpromazine and trifluoperazine, is a psychotherapeutic medicine believed to act at the subcortical level of the brain, principally it depresses the central nervous system.

Prochlorperazine is more potent than chlorpromazine but less so than trifluoperazine. The depressant action, hypotensive effect, antimuscarinic activity, potentiation of central nervous system depressants, and antihistaminic activity of prochlorperazine are all less than the respective effects of chlorpromazine.

6. PHARMACEUTICAL PARTICULARS

6.1. List of excipients

Lactose, magnesium stearate, microcrystalline cellulose, powdered vegetable stearin, starch maize.

6.2. Incompatibilities

Not applicable.

6.3. Shelf life

48 months.

6.4. Special precautions for storage

Store at or below 25 °C.

Protect from light.

Keep in original packaging until required for use.

6.5. Nature and contents of container

25 or 250 tablets are packed in a white polypropylene container and sealed with a white linear low density polyethylene snap-on cap with a tamper-proof tear-off seal together with a white foam insert and a leaflet.

25 or 250 tablets are packed in a round amber polyvinylchloride container and sealed with a white linear low density polyethylene snap-on cap with a tamper-proof tear-off seal and a leaflet.

Not all packs and pack sizes are necessarily marketed.

6.6. Special precautions for disposal and other handling

No special requirements.

7. HOLDER OF CERTIFICATE OF REGISTRATION

PHARMACARE LIMITED

Healthcare Park

Woodlands Drive

Woodmead 2191

0800 122 912 / +27 (0)11 239 6200

8. REGISTRATION NUMBER

J/2.6/184

9. DATE OF FIRST AUTHORISATION

20 April 1977

10. DATE OF REVISION OF TEXT

18 August 2025

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