SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

Promazine 50 mg film-coated tablets

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains 50 mg of promazine hydrochloride.

Excipient(s) with known effect
Each tablet contains 120 mg of lactose monohydrate.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Film-coated tablet

Orange, round, biconvex film-coated tablets, embossed with 7Z2 on one side and plain on the reverse.

4. CLINICAL PARTICULARS

4.1. Therapeutic indications

Agitation and restlessness in the elderly.
Short-term adjunctive management of psychomotor agitation.

4.2. Posology and method of administration

To be taken orally.

ADULTS: For psychomotor agitation, 100-200 mg four times daily

ELDERLY: For agitation and restlessness, 25-50 mg four times daily.

These tablets are not recommended for use in children.

4.3. Contraindications

- Known sensitivity to phenothiazines or to any of the excipients
- Comatose states.
- CNS depression.

- Phaeochromocytoma.

4.4. Special warnings and precautions for use

Promazine should be used only with great caution in the following conditions; history of jaundice, blood dyscrasias (perform blood counts if unexplained infection or fever develops), renal and hepatic impairment, respiratory disease, Parkinsonism, epilepsy, hypothyroidism, depression, myasthenia gravis, prostatic hypertrophy, personal or a family history of angle-closure glaucoma.

As with other neuroleptics, caution is advised in patients with cardiovascular diseases and patients with a family history of QT prolongation.
Cases of venous thromboembolism (VTE) have been reported with antipsychotic drugs. 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 promazine and preventive measures undertaken.

As photosensitisation may occur with higher dosages, patients should avoid direct sunlight.
In patients with Parkinson's disease the anticholinergic side effects of promazine may be aggravated by anti-parkinsonian agents.

Concomitant use of promazine with other neuroleptics should be avoided.

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.

Promazine is not licensed for the treatment of dementia-related behavioural disturbances.

The elderly are particularly susceptible to the side effects of promazine especially sedation, hypotensive and temperature regulation effects.

Withdrawal of antipsychotic drugs after long-term therapy should always be gradual and closely monitored to avoid the risk of acute withdrawal syndromes or rapid relapse.

An approximately 3-fold increased risk of cerebrovascular adverse events has been seen in randomised placebo controlled clinical trials in the dementia population with some atypical antipsychotics. The mechanism for this increased risk is not known. An increased risk cannot be excluded for other antipsychotics or other patient populations. Promazine should be used with caution in patients with risk factors for stroke.

Excipients
Lactose
Patients with rare hereditary problems of galactose intolerance, total lactase deficiency or glucose-galactose malabsorption should not take this medicine.

4.5. Interactions with other medicinal products and other forms of interaction

The hypoglycaemic effect of sulphonylureas is possibly antagonised by phenothiazines.

The convulsive threshold of antiepileptics may be lowered if taken concomitantly with antipsychotic drugs.

An enhanced hypotensive effect can occur when antihypertensives are taken with antipsychotic drugs.

The antimuscarinic side effects of phenothiazines can be increased (but with reduced plasma concentrations) when taken with antimuscarinic drugs.

An increase in plasma concentration of antipsychotic drugs may occur if taken with ritonavir.

An enhanced sedative effect may occur if antipsychotics are taken with anxiolytics and hypnotic drugs.
An enhanced hypotensive effect may occur if calcium channel blockers are taken with antipsychotic drugs.

An increased risk of extrapyramidal effects and possibility of neurotoxicity may occur if lithium and phenothiazines are taken concomitantly.

There is an increased risk of CNS toxicity if sibutramine is taken concomitantly with antipsychotic drugs.

There is an increased risk of extrapyramidal effects if tetrabenazine and antipsychotics are taken together.

Cimetidine may enhance the effects of antipsychotic drugs.

There is an increased risk of extrapyramidal effects when antipsychotics are taken with metoclopramide.

The effects of antipsychotics may possibly be reduced by memantine.

Reduced absorption of phenothiazines with antacids and possibly with kaolin can occur.

Anaesthetics can cause an enhanced hypotensive effect when taken with antipsychotics.

Increased plasma concentrations and increased antimuscarinic effects can occur when tricyclics and phenothiazines are taken together.

An enhanced sedative and hypotensive effect can occur if opioid analgesics and antipsychotics are taken together.

There is an increased risk of convulsions if tramadol is taken with antipsychotics.

Sympathomimetics antagonise pressor action when taken with antipsychotics.

An enhanced sedative effect can occur if alcohol and antipsychotics are taken together.

The manufacturer of reboxetine advises caution with antipsychotics.

Concomitant use of promazine with drugs known to prolong the QT interval may increase the risk of ventricular arrhythmias, including Torsade de Pointes. Therefore concomitant use of these products is not recommended. Examples include certain antiarrhythmics, such as those of Class 1A (such as quinidine, disopyramide and procainamide) and Class III (such as amiodarone, sotalol and dofetilide), certain antimicrobials (sparfloxacin, moxifloxacin, erythromycin IV), tricyclic antidepressants (such as amitriptyline), certain tetracyclic antidepressants (such as maprotiline), other neuroleptics (e.g. phenothiazines, pimozide, sertindole and haloperidol), certain antihistamines (such as terfenadine), cisapride, bretylium and certain antimalarials such as quinine and mefloquine. This list is not comprehensive.

Concurrent use of drugs causing electrolyte imbalance is not recommended. Diuretics, in particular those causing hypokalaemia, should be avoided but, if necessary, potassium-sparing diuretics are preferred.

4.6. Fertility, pregnancy and lactation

Promazine should not be used in pregnancy, especially during the first trimester unless considered essential by the physician.
Neonates exposed to antipsychotics (including Promazine) 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.

Promazine should not be used during lactation.

4.7 Effects on ability to drive and use machines

Initial sedation may occur. Patients taking promazine should not drive or operate machinery unless the drug has been shown not to interfere with physical or mental ability. Patients should be advised not to drink alcohol due to the enhanced effects when combined with antipsychotics (see section 4.4).

4.8. Undesirable effects

Promazine exhibits side effects associated with phenothiazines in general including; nasal congestion, drowsiness, apathy, agitation, excitement, convulsions and insomnia, dizziness, headache, gastrointestinal disturbances, hypothermia.

Promazine may induce extrapyramidal side effects including dystonia, tremor, tardive dyskinesia and akathisia.

Antimuscarinic symptoms include: dry mouth, constipation, micturition difficulties and blurred vision.

Cardiovascular symptoms include: hypotension. Cardiac effects such as QT-interval prolongation, Torsade de Pointes, ventricular arrhythmias, including ventricular fibrillation and ventricular tachycardia, and cardiac arrest have been reported rarely.

Cases of sudden unexplained death have also occurred. These are class effects of neuroleptics.
Cases of venous thromboembolism, including cases of pulmonary embolism and cases of deep vein thrombosis have been reported with antipsychotic drugs- frequency unknown.

Sensitivity reactions such as agranulocytosis, leucopenia, allergic skin reactions, rashes. Photosensitisation and contact sensitisation.

Corneal and lens opacities and purplish pigmentation of the skin, cornea, conjunctiva, and retina.

Confusional states and epileptic fits can occur. Haemolytic anaemia and jaundice (including cholestatic jaundice).

Endocrine effects such as menstrual disturbances, galactorrhoea, gynaecomastia, impotence and weight gain.

Hypotension and interference with temperature regulation are dose-related side effects and are liable to cause dangerous falls and hypothermia or hyperthermia in the elderly.

Neuroleptic malignant syndrome (hyperthermia, fluctuating levels of consciousness, muscular rigidity, and autonomic dysfunction with pallor, tachycardia, labile blood pressure, sweating and urinary incontinence) is a rare but potentially fatal side effect of some drugs. If this occurs, antipsychotics should be discontinued.

Pregnancy, puerperium and perinatal conditions
Drug withdrawal syndrome neonatal (see 4.6) - frequency is not known.

Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the Yellow Card Scheme at: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store.

4.9. Overdose

Symptoms:

Drowsiness, confusion, hypotension and hypothermia may occur. Convulsions and coma are possible. Rarely there may be respiratory depression, rhabdomyolysis, renal failure and cardiac effects, including sinus tachycardia, QT and QRS prolongation, ventricular tachycardia and fibrillation, AV block, bundle branch block and torsade de pointes. Extra-pyramidal effects, including acute dystonic reactions, may occur but are not dose related. The adverse features seen with long-term therapeutic doses are not usually encountered after acute overdosage. Neuroleptic malignant syndrome may develop irrespective of the duration of therapy but is not usually a feature of poisoning.

Management:

The benefit of gastric decontamination is uncertain.

- Activated charcoal (50 g for adults; 10-15 g for children) should only be used within 1 hour of ingestion of a potentially toxic amount.
- Alternatively gastric lavage in adults may be carried out within 1 hour of a potentially life-threatening overdose.
- A clear airway and adequate ventilation should be maintained if indicated.
- Asymptomatic patients should be observed for at least 4 hours after ingestion, and blood pressure and pulse monitored.
- In symptomatic patients a 12 lead ECG should be carried out and cardiac rhythm monitored.
- Hypotension should be corrected. If severe hypotension persists, inotropes such as dopamine (2-10 micrograms/kg bodyweight/minute) or dobutamine (2.5-10 micrograms/kg body weight/minute) can be used.
- Convulsions may respond to intravenous diazepam (0.1-0.3 mg/kg body weight) or lorazepam (4 mg in an adult and 0.05 mg/kg in a child). Correct acid base and metabolic disturbances. Phenytoin (loading dose 15mg/kg IV infusion in adults and children) may be useful if fits are unresponsive to above measures. If seizures persist this may require intubation, paralysis and ventilation.
- Correct hypothermia.
- In patients with acute dystonic reactions Procyclidine (5 to 10 mg in adults) or benztropine (1 to 2 mg in adults) can be given. Diazepam (0.1-0.3 mg/kg bodyweight) is an alternative.
- Other measures as indicated by the patient's clinical condition.

5. PHARMACOLOGICAL PROPERTIES

5.1. Pharmacodynamic properties

ATC Code: N05A A03; Phenothiazines with aliphatic side-chain.

Promazine is a phenothiazine tranquilliser. It has a selective depression of the CNS centres responsible for the control of behaviour and wakefulness. Other properties include: anti-emetic, antipruritic, serotonic blocking, weak antihistaminic, alpha-adrenergic blocking, anticholinergic and dopamine inhibitory actions.

5.2. Pharmacokinetic properties

a) General characteristics: Promazine is absorbed readily from the GI tract and subjected to considerable first-pass metabolism in the gut wall.

b) Characteristics in patients: Promazine is extensively metabolised in the liver and excreted in the urine and bile. There is some evidence of enterohepatic recirculation.

5.3. Preclinical safety data

Preclinical information has not been included because the safety profile of promazine has been established after many years of clinical use. Please refer to section 4.

6. PHARMACEUTICAL PARTICULARS

6.1. List of excipients

Tablets contain
Lactose monohydrate
Maize starch
Maize starch (partially pregelatinised)
Magnesium stearate (E572)

Tablet coating
Hypromellose
Hydroxypropyl Cellulose
Talc (E553b)
Tartrazine (E102)
Titanium dioxide (E171)
Sunset yellow (E110)
Erythrosine (E127)

6.2. Incompatibilities

Not applicable.

6.3. Shelf life

36 months.

6.4. Special precautions for storage

Store below 25°C. Keep the container tightly closed.

6.5. Nature and contents of container

Polypropylene 'Securitainer' containing a polythene 'Jayfilla' and fitted with a polythene cap.

Polypropylene 'Securitainers' with LDPE lids.

Containers of 50, 100, 250 and 1,000 tablets.

Not all pack sizes may be marketed.

6.6. Instruction for use and handling

Not applicable.

7. MARKETING AUTHORISATION HOLDER

Teva UK Limited
Ridings Point,
Whistler Drive,
Castleford, WF10 5HX,
United Kingdom

8. MARKETING AUTHORISATION NUMBER

PL00289/0799

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

13 August 2009

10. DATE OF REVISION OF THE TEXT

16/02/2022