Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Phenergan 25 mg film-coated tablets

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Promethazine Hydrochloride 25 mg

Excipients - Contains Lactose Monohydrate 173.52mg

For a full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Film coated tablet.

Pale blue, circular biconvex tablet with bevelled edges marked 'PN25' on one side and the other plain.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

In the treatment of allergic conditions and reactions.
As an antiemetic.
As a tranquilliser.

4.2 Posology and method of administration

Route of Administration: Oral.

Adults including

The Elderly:

The usual daily dose is 25-75mg (1 to 3 tablets) either as a single daily dose at bedtime or in 3 divided doses, starting with the lower dose.
Maximum daily dose is 75mg

Children:

<u>As a tranquilliser:</u>
Children 6-12 years: 25mg (1 tablet) once daily at bedtime.
Children 2-5 years: Phenergan should not be used in children 2-5 years of age because of safety concerns (see sections 4.4, 4.8).
Children below 2 years: contraindicated (see section 4.3)

4.3 Contraindications

Phenergan should not be used in patients in pre-coma states, in a coma or suffering from CNS depression of any cause.
Phenergan should not be given to patients with a known hypersensitivity to promethazine or any of the excipients.
Phenergan should be avoided in patients with blood dycrasias and in patients taking monoamine oxidase inhibitors up to 14 days previously.

Promethazine is contraindicated for use in children less than two years of age because of the potential for fatal respiratory depression.

Phenergan should not be administered in patients with known, documented long QT syndrome, whether acquired or congenital (see sections 4.4 and 4.5).

4.4 Special warnings and precautions for use

Caution should be used in patients with pre-existing coronary insufficiency. Adjustment of dosage may be necessary to avoid postural hypotension, especially in the elderly.
Since the drug is metabolized in the liver, promethazine should be used cautiously in patients with hepatic impairment.

Prolonged treatment with this product may result in jaundice or blood dyscrasia necessitating regular monitoring of liver function and haemopoietic state.

Particular attention should also be paid to potential for inducing eye changes and myocardial conduction defects, especially if other concurrently administered drugs also have potential effects on these systems.

Due to the risk of photosensitivity, exposure to the sun or ultraviolet light should be avoided during or shortly after treatment.

Body temperature may fall during treatment with this product and special care should be exercised in this regard in the elderly.

Promethazine should only be used cautiously in epileptic patients, since central nervous stimulation may sometimes occur. Caution should also be exercised in patients with narrow angle glaucoma, renal insufficiency, bladder-neck or pyloro-duodenal obstruction.

Promethazine may thicken or dry lung secretions and impair expectoration. It should be used with caution in patients with asthma, bronchitis or bronchiectasis.

Promethazine may delay the elderly diagnosis of intestinal obstruction or increased intracranial pressure through the suppression of vomiting.

Promethazine may mask the warning signs of ototoxicity caused by ototoxic drugs e.g. salicylates.

There have been case reports of drug abuse with promethiazine. The risk of abuse is greater in patients with a history of drug abuse.

Neuroleptic malignant syndrome: As with neuroleptics, Neuroleptic Malignant Syndrome (NMS) characterized by hyperthermia, extrapyramidal disorders, muscle rigidity, altered mental status, autonomic nervous instability and elevated CPK, may occur. As this syndrome is potentially fatal, promethiazine must be discontinued immediately and intensive clinical monitoring and symptomatic treatment should be initiated.

Intravenous injection should be performed with extreme care to avoid extravasation or inadvertent intra-arterial injection, which could lead to necrosis and peripheral gangrene. If a patient complains of pain during intravenous injection, stop the injection immediately, as this may be a sign of extravasation or inadvertent intra-arterial injection. Intramuscular injection must also be performed carefully to avoid inadvertent subcutaneous injection, which could lead to local necrosis.

Paediatric population
Promethazine must not be used in children below two years of age due to the potential for fatal respiratory depression (see section 4.3).
Promethazine is not recommended in children aged 2-5 years of age due to the potential for hallucination, aggression and psychomotor hyperactivity (see section 4.8).

As phenothiazines can prolong the QT interval, caution is advised in treating patients with pronounced bradycardia, cardiovascular disease, with a hereditary form of prolongation of the QT interval and concomitant use with other products leading to QT prolongation. Phenergan can increase the risk of onset of serious ventricular arrhythmias of the torsade de pointes type, which is potentially fatal (sudden death).

The use of promethazine should be avoided in children and in adolescents with signs and symptoms suggestive of Reye's Syndrome.

Phenergan should not be used for longer than 7 days without seeking medical advice.

4.5 Interaction with other medicinal products and other forms of interaction

The product may potentiate the effects of alcohol and other central nervous system depressants. Alcohol should be avoided during treatment.

Phenergan may enhance the action of any anticholinergic agent, tricyclic antidepressant, sedative or hypnotic.

Attention is drawn to the fact that many psychotropic and anti-histamine drugs are of the phenothiazine group, and a combination of both may lead to toxicity. Potentiation of action may also occur with monoamine oxidase inhibitors and analgesics. Use of promethazine should be avoided in patients taking monoamine oxidase inhibitors up to 14 days previously. Antihypertensive therapy used concurrently may need adjustment of dosage to avoid hypotension, particularly in the elderly.

Promethazine may interfere with immunological urine pregnancy tests to produce false-positive or false-negative results.

Special caution is required when promethazine is used concurrently with other products leading to QT prolongation, including medicinal products such as antipsychotics i.e. some phenothiazines (chlorpromazine, levomepromazine), benzamides (sulpiride, amisulpride, tiapride), pimozide, haloperidol, droperidol, citalopram, halofantrin, methadone, pentamidine and moxifloxacine.

Promethazine should be discontinued at least 72 hours before commencing skin tests using allergen extracts, as the cutaneous histamine response may be inhibited.

Promethazine may lower the convulsion threshold. Dosage adjustment of anticonvulsant medication may be necessary.

Concurrent use of promethazine with other hepatotoxic medications may increase the potential for hepatotoxicity.

Concurrent use with other photosensitizing medications, e.g tetracyclines, may cause additive photosensitizing effects.

4.6 Fertility, pregnancy and lactation

Promethiazine should be used in pregnancy only if the potential benefits to the patient are weighed against the possible risk to the foetus.

When promethiazine has been given in high doses during late pregnancy, promethiazine has caused prolonged neurological disturbances in the infant.

The use of Phenergan is not recommended in the 2 weeks prior to delivery in view of the risk of irritability and excitement in the neonate.

Phenergan is excreted in breastmilk. There are risks of neonatal irritability and excitement. Phenergan is not recommended for use in breastfeeding.

4.7 Effects on ability to drive and use machines

Ambulant patients receiving Phenergan for the first time should not be in control of vehicles or machinery for the first few days until it is established that they are not hypersensitive to the central nervous system effects of the drug and do not suffer from disorientation, confusion or dizziness.

Because the duration of action may be up to 12 hours, patients should be advised that if they feel drowsy they should not drive or operate heavy machinery.

4.8 Undesirable effects

The following CIOMS frequency rating is used, when applicable:

Very common ≥10%; Common ≥1 and < 10%; Uncommon ≥0.1 and < 1%;
Rare ≥0.01 and < 0.1%; Very rare < 0.01%; Not known (cannot be estimated from available data).

Immune System Disorders
Frequency unknown: Allergic reactions, including urticaria, rash, pruritus, and anaphylactic reaction have been reported.

Skin and Subcutaneous Tissue Disorders
Frequency unknown: Photosensitivity reaction

Nervous System Disorders
Frequency unknown: Neuroleptic Malignant Syndrome, the elderly are particularly susceptible to the anticholinergic effects and confusion due to Phenergan, somnolence, dizziness, headaches, extrapyramidal effects including muscle spasm, tic-like movements of the head and face (akathisia, dystonia, tardive dyskinesia) especially in the presence of pre-existing brain damage, psychomotor hyperactivity.

Metabolism and Nutrition Disorders
Frequency unknown: Anorexia

Gastrointestinal Disorders
Frequency unknown: Epigastric discomfort, dry mouth

Eye Disorders
Frequency unknown: Blurred vision

Blood and Lymphatic System Disorders
Frequency unknown: Blood dyscrasias including haemolytic anaemia, agranulocytosis, thrombocytopenia (including thrombocytopenic purpura), eosinophilia

Renal and Urinary Disorders
Frequency unknown: Urinary retention

Psychiatric Disorders
Frequency unknown: Infants, newborns and premature are susceptible to the anticholinergic effects of promethazine, while other children may display paradoxical hyperexcitability, restlessness, nightmares, disorientation, aggression and hallucination.

Cardiac Disorders
Frequency unknown: Palpitations, arrhythmias, QT prolongation,torsade de pointes.
The effects of phenothiazines on the heart are dose related. ECG changes, with prolongation of QT interval and T-wave changes have been reported commonly in patients treated with moderate or high dose; they are reversible on reducing the dose. In a very small percentage of cases, they have been reported to precede serious arrhythmias, including ventricular tachycardia and fibrillation, which have also occurred after overdosage. Sudden, unexpected and unexplained deaths have been reported in patients receiving phenothiazines

Vascular disorders
Frequency unknown: Hypotension

Hepatobiliary disorders
Frequency unknown: Jaundice

General Disorders and Administration Site Conditions
Frequency unknown: Tiredness.

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 HPRA Pharmacovigilance, Website: www.hpra.ie.

4.9 Overdose

Symptoms of severe overdosage are variable. They are characterised in children by various combinations of excitation, ataxia, incoordination, athetosis and hallucinations, while adults may become drowsy and lapse into coma. Convulsions may occur in both adults and children. Coma or excitement may precede their occurrence. Tachycardia may develop. Cardiorespiratory depression is uncommon. If the patient is seen soon enough after ingestion, it should be possible to induce vomiting with ipecacuanha despite the antiemetic effect of promethazine; alternatively, gastric lavage may be used.

Prolonged QT interval and cases of severe arrhythmias with fatal outcome have been described in overdose of phenothiazines.

Treatment is otherwise supportive with attention to maintenance of adequate respiratory and circulatory status. Convulsions should be treated with diazepam or other suitable anticonvulsant.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Potent, long acting, antihistamine with additional anti-emetic central sedative and anticholinergic properties.

5.2 Pharmacokinetic properties

Promethazine is distributed widely in the body. It enters the brain and crosses the placenta. Promethazine is slowly excreted via urine and bile. Phenothiazines pass into the milk at low concentrations.

5.3 Preclinical safety data

No additional pre-clinical data of relevance to the prescriber.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Tablet core

Lactose monohydrate
Maize starch
Povidone K30
Magnesium stearate

Tablet Coating

Hypromellose
Macrogol 200
Indigo carmine (E132)
Titanium dioxide (E171)

6.2 Incompatibilities

Not applicable

6.3 Shelf life

3 years

6.4 Special precautions for storage

Do not store above 30°C. Store in original container in order to protect from light.

6.5 Nature and contents of container

PVDC coated uPVC film / aluminium foil blister strip in an outer box. Pack size 7, 10, 20, 28, 56 (28 tablets/strip) tablets.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal of a used medicinal product or waste materials derived from such medicinal product and other handling of the product

No special requirements.

7 MARKETING AUTHORISATION HOLDER

Opella Healthcare France SAS T/A Sanofi
82 Avenue Raspail
94250 Gentilly
France

8 MARKETING AUTHORISATION NUMBER

PA23180/011/002

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 1st April 1979

Date of last renewal: 1st April 2009

10 DATE OF REVISION OF THE TEXT

January 2026