SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Phenergan 25mg/ml Solution for Injection.

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each ampoule contains 25 mg/ml of the active substance Promethazine hydrochloride.

Excipient(s) with known effect:
Also contains 0.5 mg of sodium sulphite anhydrous (E221) and 0.7 mg of sodium metabisulphite (E223).

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Solution for injection.

Phenergan Injection is a clean, bright, colourless or almost colourless solution.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

As symptomatic treatment for allergic conditions of the upper respiratory tract and skin including allergic rhinitis, urticaria and anaphylactic reactions to drugs and foreign proteins.

Sedation and treatment of insomnia in adults.

As an adjunct in preoperative sedation in surgery and obstetrics.

As a paediatric sedative.

4.2 Posology and method of administration

Adults: The usual dose is 25 – 50 mg. Maximum parenteral dose 100 mg.
Elderly: No specific dosage recommendations.
Paediatric population: 6.25 – 12.5 mg for children from 5 – 10 years by deep intramuscular injection. Not for use in children under 2 years of age (see section 4.3).

Method of administration
Deep intramuscular injection. In emergency, by slow intravenous injection after dilution of the 2.5% solution to 10 times its volume with water for injections immediately before use.

4.3 Contraindications

- Phenergan should not be given to patients with a known hypersensitivity to promethazine, other phenothiazines, or to other ingredients in the formulation of Phenergan.
- Phenergan should not be used in patients in coma or suffering from CNS depression of any cause.
- Promethazine is contraindicated for use in children less than two years of age because of the potential for fatal respiratory depression.
- Phenergan should be avoided in patients taking monoamine oxidase inhibitors up to 14 days previously.

4.4 Special warnings and precautions for use

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

Phenergan should be avoided in patients with liver or renal dysfunction, Parkinson's disease, hypothyroidism, cardiac failure, pheochromocytoma, myasthenia gravis, or prostate hypertrophy, or in patients with a history of narrow angle glaucoma or agranulocytosis.

Caution must be exercised when using H_1-antihistamines such as Phenergan due to the risk of sedation. Combined use with other sedative medicinal products is not recommended (see section 4.5).

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.

Close monitoring is required in patients with epilepsy or a history of seizures, as phenothiazines may lower the seizure threshold.

Phenergan Injection may increase glucose tolerance.

Caution should be used in patients with:

- asthma, bronchitis or bronchiectasis. Phenergan may thicken or dry lung secretions and impair expectoration.
- Severe coronary artery disease
- Epilepsy
- Bladder neck or pyloro-duodenal obstruction

Ototoxicity

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

It may also delay the early diagnosis of intestinal obstruction or raised intracranial pressure through the suppression of vomiting.

QT prolongation

Phenothiazine derivatives 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, hypokalemia, and acquired (i.e. drug induced) QT prolongation. If the clinical situation permits, medical and laboratory evaluations should be performed to rule out possible risk factors before initiating treatment with a phenothiazine derivative and as deemed necessary during treatment (see section 4.8).

Photosensitivity reactions

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

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

Excipient with known effect

Phenergan contains Sodium Sulphite and may rarely cause severe hypersensitivity reactions and bronchospasm.

Alcohol and alcohol-containing medicines should be avoided while on this medicine (see section 4.5).

Phenothiazines may be additive with, or may potentiate the action of, other CNS depressants such as opiates or other analgesics, barbiturates or other sedatives, general anesthetics, or alcohol.

The occurrence of unexplained infections or fever may be evidence of blood dyscrasia (see section 4.8), and requires immediate hematological investigation.

All patients should be advised that, if they experience fever, sore throat or any other infection, they should inform their physician immediately and undergo a complete blood count. Treatment should be discontinued if any marked changes (hyperleucocytosis, granulocytopenia) are observed in the blood count.

4.5 Interaction with other medicinal products and other forms of interaction

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

Alcohol should be avoided during treatment. Combination with alcohol enhances the sedative effects of H1 antihistamines.

Phenergan may cause hypotension, and dosage adjustment of antihypertensive therapy may therefore be required.

Phenergan may lower the convulsive threshold, and dosage adjustment of anticonvulsant medication may therefore be required.

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

Phenergan should be discontinued at least 72 hours before the start of skin tests as it may inhibit the cutaneous histamine response thus producing false-negative results.

Special caution is required when promethazine is used concurrently with drugs known to cause QT prolongation (such as antiarrhythmics, antimicrobials, antidepressants, antipsychotics) to avoid exacerbation of risk of QT prolongation.

Cytochrome P450 2D6 Metabolism: Some phenothiazines are moderate inhibitors of CYP2D6. There is a possible pharmacokinetic interaction between inhibitors of CYP2D6, such as phenothiazines, and CYP2D6 substrates. Co administration of promethazine 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.

Phenergan should be avoided in patients taking monamine oxidase inhibitors within the previous 14 days, and monamine oxidase inhibitors should be avoided while using Phenergan.

Seizure threshold-lowering drugs: Concomitant use of seizure-inducing drugs or seizure threshold-lowering drugs should be carefully considered due to the severity of the risk for the patient (see section 4.4).

Gastro-intestinal agents that are not absorbed (magnesium, aluminium and calcium salts, oxides and hydroxides): Reduced gastro-intestinal absorption of phenothiazines may occur. Such gastro-intestinal agents should not be taken at the same time as phenothiazines (at least 2 hours apart, if possible).

Drugs with anticholinergic properties: Concomitant use of Phenergan with drugs with anticholinergic properties enhances the anticholinergic effect.

4.6 Fertility, pregnancy and lactation

Pregnancy
The use of Phenergan is not recommended during pregnancy and in women of childbearing potential not using contraception, unless the potential benefits outweigh the potential risks. When promethazine has been given in high doses during late pregnancy, promethazine has caused prolonged neurological disturbances in the infant.

Advise patients to inform their healthcare provider of a known or suspected pregnancy. Advise patients to avoid becoming pregnant while receiving this medicine. Advise female patients of reproductive potential to use effective contraception.

There are no available animal studies regarding reproductive toxicity.

Breast-feeding
Phenergan is excreted in breast milk (see section 5.2). There are risks of neonatal irritability and excitement. Phenergan is not recommended for use in breast-feeding.

Fertility
There are no relevant fertility data in animals.

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 effects of the drug and do not suffer from disorientation, confusion, blurred vision or dizziness.

4.8 Undesirable effects

The following CIOMS frequency rating is used: Very common (≥1/10); common (≥1/100 to <1/10); uncommon (≥1/1000 to <1/100); rare (≥1/10,000 to ≥1/1000); very rare (<1/10 000), not known (cannot be estimated from the available data).

Immune system disorders

Frequency not known: Allergic reactions, including anaphylactic reaction, urticaria, angioedema.

Skin and subcutaneous tissue disorders
Frequency not known: Rash, photosensitivity reaction.

Nervous system disorders
Very common: Sedation or somnolence
Frequency not known: Dizziness, headaches, extrapyramidal effects including restless legs syndrome, muscle spasms and tic-like movements of the head and face.
Frequency not known: Dystonia, including oculogyric crisis, usually transitory are commoner in children and young adults, and usually occur within the first 4 days of treatment or after dosage increases.
Frequency not known: Anticholinergic effects such as ileus paralytic, risk of urinary retention, dry mouth, constipation, accommodation disorder.
The elderly are particularly susceptible to the anticholinergic effects and confusion due to promethazine.

Psychiatric disorders
Frequency not known: Agitation, confusional state, anxiety.
Frequency not known: Infants, newborns and premature are susceptible to the anticholinergic effects of promethazine, while other children may display paradoxical hyperexcitability, restlessness, nightmares, disorientation

Eye disorders
Frequency not known: Blurred vision

Gastrointestinal disorders
Frequency not known: Epigastric irritation/discomfort, dry mouth

Renal and urinary disorders
Frequency not known: Urinary retention

Metabolism and nutrition disorders
Frequency not known: Decreased appetite

Cardiac disorders
Frequency not known: Palpitations, arrhythmias (including QT prolongation and torsade de pointes)

Vascular disorders
Frequency not known: Hypotension

Respiratory, thoracic and mediastinal disorders
Frequency not known: Respiratory depression (see Section 4.4), nasal congestion

Hepatobiliary disorders
Frequency not known: Jaundice cholestatic

Blood and lymphatic system disorders
Frequency not known: Blood dyscrasias including haemolytic anaemia, agranulocytosis, leukopenia, eosinophilia, thrombocytopenia (including thrombocytopenic purpura).

General disorders and administration site conditions

Frequency not known: 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 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
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. High doses (supratherapeutic doses) can cause ventricular arrhythmias including QT prolongation and torsade de pointes (see section 4.8).

Management
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.

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

In the event of overdose of Phenergan, take all appropriate measures immediately.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Antihistamines for systemic use; Phenothiazine derivatives, ATC code: R06AD02

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

5.2 Pharmacokinetic properties

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

5.3 Preclinical safety data

No additional data of relevance to the prescriber.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Sodium sulphite anhydrous (E221)
Sodium metabisulphite (E223)
Water for injections

6.2 Incompatibilities

Not applicable

6.3 Shelf life

3 years

6.4 Special precautions for storage

Store in the original carton in order to protect from light.

6.5 Nature and contents of container

Cardboard carton containing either 10 x 1 ml ampoules or 10 x 2 ml ampoules.

Not all pack sizes may be marketed

6.6 Special precautions for disposal

Discoloured solutions should not be used.

7 MARKETING AUTHORISATION HOLDER

Opella POM UK Limited, trading as Opella
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Berkshire,
RG6 1PT,
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8 MARKETING AUTHORISATION NUMBER(S)

PL 61186/0003

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

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Date of latest renewal: 29 July 2002

10 DATE OF REVISION OF THE TEXT

22/09/2025