

## **SUMMARY OF PRODUCT CHARACTERISTICS**

### **1 NAME OF THE MEDICINAL PRODUCT**

Promethazine Hydrochloride 25 mg Film-coated Tablets

### **2 QUALITATIVE AND QUANTITATIVE COMPOSITION**

Each tablet contains 25 mg of the active substance promethazine hydrochloride.

Excipient with known effect

Each tablet contains 179 mg of lactose monohydrate.

For full list of excipients, see section 6.1.

### **3 PHARMACEUTICAL FORM**

Film-coated tablet (Tablet)

White coloured, round, biconvex, bevelled edge film-coated tablets, debossed with 'L11' on one side and plain on other side.

### **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

- As an antiemetic

For short term use:

- Treatment of insomnia in adults
- As a paediatric sedative

## 4.2 Posology and method of administration

### Posology

#### *Paediatric population*

Not for use in children under the age of 6 years (see section 4.3).

#### *As an antihistamine in allergy:*

Children 6-10 years	25 mg as a single dose*. Maximum daily dose 25 mg.
Children over 10 years and adults (including elderly)	25 mg as a single dose*. Increasing to a maximum of 25 mg twice a day as required.

\*Single doses are best taken at night.

#### *As an antiemetic:*

Children 6-10 years	The use of promethazine hydrochloride liquid or Promethazine Hydrochloride 10 mg Film-coated Tablets is recommended.
Children over 10 years and adults (including elderly)	25 mg to be taken the night before the journey. To be repeated after 6-8 hours as required.

*As a paediatric sedative for short term use and for short term treatment of insomnia in adults:*

Children 6-10 years	25 mg as a single night time dose.
Children over 10 years and adults (including elderly)	25 mg or 50 mg as a single night time dose.

### Method of administration

For oral administration.

## **4.3 Contraindications**

- Promethazine hydrochloride should not be given to patients with a known hypersensitivity to promethazine, other phenothiazines, or to any other ingredients in the formulation of Promethazine hydrochloride
- Promethazine hydrochloride should not be used in patients in coma or suffering from CNS depression of any cause
- Promethazine hydrochloride is contraindicated for use in children less than 6 years of age (see section 4.4)
- Promethazine hydrochloride 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 Promethazine hydrochloride use. In case of allergic reaction, treatment with Promethazine hydrochloride must be discontinued and appropriate symptomatic treatment initiated (see section 4.8).

Promethazine hydrochloride 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 H1-antihistamines such as Promethazine hydrochloride due to the risk of sedation. Combined use with other sedative medicinal products is not recommended (see section 4.5).

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

Caution should be used in patients with:

- Asthma, bronchitis or bronchiectasis. Promethazine hydrochloride 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, hypokalaemia, 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).

#### QT interval

As phenothiazines can prolong the QT interval, caution is advised in treated 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.

#### Photosensitivity reactions

Due to the risk of photosensitivity, exposure to strong sunlight or ultraviolet light should be avoided during or shortly after treatment (see section 4.8).

#### Paediatric population

Promethazine must not be used in children less than six years of age due to the potential for fatal respiratory depression, psychiatric and CNS events (see section 4.3 and section 4.8).

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

#### Excipient(s) with known effect

This medicine contains lactose monohydrate. Patients with rare hereditary problems of galactose intolerance, total lactase deficiency or glucose-galactose malabsorption should not take this medicine.

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 anaesthetics, or alcohol.

The occurrence of unexplained infections or fever may be evidence of blood dyscrasia (see section 4.8) and requires immediate haematological 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 (hyperleukocytosis, granulocytopenia) are observed in the blood count.

#### **4.5 Interaction with other medicinal products and other forms of interaction**

Promethazine hydrochloride will enhance the action of any anticholinergic agent, tricyclic anti-depressant, sedative or hypnotic.

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

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

Promethazine hydrochloride 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.

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 moxifloxacin.

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/amitriptylinoloxime, a CYP2D6 substrate, may lead to an increase in the plasma levels of amitriptyline/amitriptylinoloxime. Monitor patients for dose-dependent adverse reactions associated with amitriptyline/amitriptylinoloxime.

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

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 Promethazine hydrochloride with drugs with anticholinergic properties enhances the anticholinergic effect.

## **4.6 Fertility, pregnancy and lactation**

### **Pregnancy**

The use of Promethazine hydrochloride 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

Promethazine hydrochloride is excreted in breast milk (see section 5.2). There are risks of neonatal irritability and excitement. Promethazine hydrochloride 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**

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

### **4.8 Undesirable effects**

The following CIOMS frequency rating is used: Very common ( $\geq 1/10$ ); common ( $\geq 1/100$  to  $< 1/10$ ); uncommon ( $\geq 1/1000$  to  $< 1/100$ ); rare ( $\geq 1/10\ 000$  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.

Frequency not known: Children less than 6 years of age also experienced psychomotor hyperactivity.

Frequency not known: Neuroleptic malignant syndrome, psychomotor hyperactivity.

#### 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.

Frequency not known: Children less than 6 years of age also experienced aggression and hallucination.

Frequency not known: Hallucinations, aggression.

#### 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, QT prolongation, 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](http://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, intellectual disability and cognition deficit in children less than 6 years of age 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). Prolonged QT interval and cases of severe arrhythmias with fatal outcome have been described in overdose of phenothiazines.

## 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 other suitable anticonvulsant.

In the event of overdose of Promethazine hydrochloride, 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 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**

Core tablet

Lactose monohydrate Maize starch Povidone K30 Magnesium stearate

Coating

Titanium dioxide (E171)

Hypromellose (E464)

Macrogol/Polyethylene glycol (E1521)

### **6.2 Incompatibilities**

Not applicable

### **6.3 Shelf life**

3 years

### **6.4 Special precautions for storage**

Store below 30oC. Store in the original package in order to protect from light.

#### **6.5 Nature and contents of container**

White opaque PVC-PVDC aluminium foil.

Available in blister packs of 28 and 56 tablets. Not all pack sizes may be marketed.

#### **6.6 Special precautions for disposal**

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

### **7 MARKETING AUTHORISATION HOLDER**

Crescent Pharma Limited  
Key House, Sarum Hill,  
Basingstoke, RG21 8SR  
United Kingdom

### **8 MARKETING AUTHORISATION NUMBER(S)**

PL 20416/1186

**9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION**

14/06/2024

**10 DATE OF REVISION OF THE TEXT**

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