# Summary of Product Characteristics

## 1 NAME OF THE MEDICINAL PRODUCT

Promethazine Hydrochloride Injection BP 2.5% w/v

## 2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 1ml of solution contains 2.5% w/v (25mg per ml) of Promethazine Hydrochloride

For a full list of excipients, see section 6.1

## 3 PHARMACEUTICAL FORM

Solution for injection.
Clear, colourless or almost colourless sterile aqueous solution.

## 4 CLINICAL PARTICULARS

### 4.1 Therapeutic Indications

In the treatment of allergic conditions and reactions.
As an anti-emetic.
As a tranquilliser.

### 4.2 Posology and method of administration

Promethazine Hydrochloride Injection B.P. is for administration by deep intramuscular injection. In adults only, it may also be administered by slow intravenous injection after dilution to 10 times its volume with Water for Injections.

Adults : The usual adult dose is 25 - 50mg by deep intramuscular injection. In emergency situations, a dose of 25 - 50mg may be administered by slow intravenous injection after dilution to 10 times its volume with Water for Injections. The maximum dose parenterally is 100mg.

Children : 5 - 10 years only. As a tranquilizer; 6.25 - 12.5mg daily by deep intramuscular injection.

Elderly : No specific dosage recommendation, although promethazine should be used cautiously in the elderly owing to their susceptibility to drugs acting centrally on the nervous system.

### 4.3 Contraindications

Promethazine Hydrochloride Injection BP should not be used in patients who are in coma or suffering from CNS depression of any cause. It must not be given to patients who are hypersensitive to Promethazine Hydrochloride or to any of the ingredients in the formulation. It should be avoided in patients with existing blood dyscrasias and in patients taking monoamine oxidase inhibitors within the previous 14 days.
Promethazine Hydrochloride Injection BP is contraindicated for use in children less than two years of age due to the potential for fatal respiratory depression.

## 4.4 Special warnings and precautions for use

Caution should be used in patients with pre-existing coronary insufficiency, narrow angle glaucoma, hepatic and renal insufficiency and in those receiving anti-hypertensive therapy. Caution should be used in epileptic patients, since central nervous stimulation may occasionally occur. As Promethazine Hydrochloride is metabolised in the liver, it should be used cautiously in patients with hepatic impairment.

Prolonged treatment with this product may result in jaundice and blood dyscrasias 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 have potential effects on these systems.

Caution should be exercised in patients with bladder neck or pyloro-duodenal obstruction.

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

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

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

Use of this product at high (relative or absolute) doses may induce extra pyramidal side effects e.g. dyskinesia, akathisia, dystonia, especially in the presence of pre-existing brain damage. These are likely to be particularly severe in children. Children may also display paradoxical hyperexcitability.

Although prolonged administration of Promethazine hydrochloride may result in tardive dyskinesia, particularly in the elderly, the injectable form is intended only for short term usage. In an attempt to minimise the possibility of the development of such a syndrome, major tranquilliser therapy should be reserved for these patients for whom it is essential, the dosage used should be the lowest commensurate with optimal benefit and duration of treatment should not extend beyond that necessary for the patient.

There is no known treatment for tardive dyskinesia. The antipsychotic drug may mask it, as may anticholinergic agents. Although the latter do not predispose to tardive dyskinesia, they should not be used routinely to mask the Parkinsonian effects of antipsychotic drugs as they may mask the early signs of tardive dyskinesia.

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

Allergic and photosensitivity reactions have been reported following use of this product.
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.

Phenothiazines should be used with caution in patients with cardiac disease or cardiac arrhythmias.

The use of Promethazine Hydrochloride should be avoided in children and adolescents with signs and symptoms suggestive of Reye's Syndrome.
Neuroleptic malignant syndrome: The syndrome may occur with the use of any neuroleptic agent. Symptoms include clouding of consciousness, rigidity and other extrapyramidal effects, and autonomic dysfunction, most importantly hyperpyrexia. Treatment involves the immediate cessation of neuroleptic therapy and symptomatic management as appropriate.

Promethazine hydrochloride should not be used in children under 2 years of age due to the potential for fatal respiratory depression.

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

Promethazine Hydrochloride may enhance the action of any anticholinergic agent, tricyclic antidepressant, sedative or hypnotic. Alcohol should be avoided during treatment. Promethazine Hydrochloride may cause hypotension, and dosage adjustment of antihypertensive therapy may therefore be required. Patients, especially if they are elderly, on anti-hypertensive therapy may require adjustment of dosage to avoid postural hypotension.

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. Promethazine Hydrochloride should be avoided in patients taking M.A.O.I's up to 14 days previously.

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

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

Promethazine Hydrochloride may lower the convulsive threshold and dosage adjustment of anticonvulsant medication may therefore be required. Promethazine Hydrochloride injection may increase glucose tolerance.

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.

## 4.6 Fertility, pregnancy and lactation

Because the safety of Promethazine Hydrochloride in pregnancy has not been established, it should not be used during pregnancy unless considered essential by the physician. Promethazine Hydrochloride crosses the placenta and its use is not recommended in the two weeks prior to delivery in view of the risk of irritability and excitement in the neonate. Promethazine Hydrochloride appears in the milk of nursing mothers receiving the drug and the risk of neonatal irritability and excitement should be considered if Promethazine Hydrochloride is administered to nursing mothers.

## 4.7 Effects on ability to drive and use machines

Promethazine Hydrochloride may impair the mental and/or physical abilities required for driving or operating machinery. Ambulant patients receiving promethazine Hydrochloride 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 or dizziness.

## 4.8 Undesirable effects

Possible side effects include drowsiness, dizziness, restlessness, headaches, nightmares, tiredness, disorientation, bradycardia, tachycardia and hypotension. Anticholinergic side effects such as blurred vision, dry mouth and urinary retention occur occasionally. Use of this product at high (relative or absolute) doses may induce extra pyramidal side effects e.g. dyskinesia, akathisia, dystonia, especially in the presence of pre-existing brain damage. These are likely to be particularly severe in children. Children may also display paradoxical hyperexcitability.

Prolonged administration of this product may result in persistent or tardive dyskinesias particularly in the elderly. Other side effects in the elderly include anorexia, gastric irritation, palpitations and arrhythmia.

The effect of phenothiazines on the heart is dose related. ECG changes with prolongation of QT interval and T- wave changes have been reported commonly in patients treated with moderate to high doses; they are reversible on reducing the dose. In a very small number of cases they have been reported to precede serious arrhythmias, including ventricular tachycardia and fibrillation, which have also occurred after dosage. Sudden, unexpected and unexplained deaths have been reported in hospitalised psychotic patients receiving phenoziathines.

Very rare cases of allergic reactions, including urticaria, rash and pruritus have been reported. Photosensitive skin reactions have been reported and strong sunlight should be avoided during treatment.

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, Earlsfort Terrace, IRL - Dublin 2; Tel: +353 1 6764971; Fax: +353 1 6762517. Website: www.hpra.ie; E-mail: medsafety@hpra.ie.

## 4.9 Overdose

Symptoms of overdosage are variable. In children, there may be various combinations of excitation, ataxia, incoordination, athetosis and hallucinations, whereas adults may become drowsy and lapse into coma.

Convulsions may occur in both adults and children and coma or excitement may precede their occurrence. Cardiorespiratory depression is not 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 Hydrochloride; alternatively, gastric lavage may be used.

There is no specific antidote and treatment is symptomatic and supportive. Convulsions should be treated with diazepam or suitable anticonvulsant. A patent airway should be established and attention should be directed at maintaining adequate respiratory and circulatory status.

# 5 PHARMACOLOGICAL PROPERTIES

## 5.1 Pharmacodynamic properties

Promethazine hydrochloride is a phenothiazine derivative. It has a prolonged antihistamine action with additional antiemetic, anticholinergic and sedative effects.

## 5.2 Pharmacokinetic properties

Promethazine hydrochloride is well absorbed after oral or intramuscular administration. The drug is distributed widely in the body and it enters the brain and crosses the placenta. It is extensively metabolised in the liver and is excreted via urine and bile, mainly as metabolites. The antihistamine action of promethazine hydrochloride has been reported to last for between 4 and 12 hours.

## 5.3 Preclinical safety data

No further relevant information other than that which is included in other sections of the Summary of Product Characteristics.

# 6 PHARMACEUTICAL PARTICULARS

## 6.1 List of excipients

Sodium Metabisulphite
Anhydrous Sodium Sulphite
Sodium chloride
Water for Injections

## 6.2 Incompatibilities

Promethazine hydrochloride has been reported to be incompatible with solutions of a number of compounds including aminophylline, barbiturates, benzylpenicillin salts, carbenicillin, heparin, hydrocortisone sodium succinate, morphine sulphate, alkalis and some contrast media.

## 6.3 Shelf life

Unopened: 3 years.
The product should be used immediately after opening.

## 6.4 Special precautions for storage

Protect from light. Keep ampoules in outer carton.
Do not store above 25$^{o}$C.

## 6.5 Nature and contents of container

1 ml and 2 ml clear glass ampoules, glass type I Ph. Eur. borosilicate glass packed in cardboard cartons to contain 10 x 1 ml ampoules and 10 x 2 ml ampoules.

## 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

If only part of the contents of an ampoule is used, the remaining solution should be discarded.
For single use only.

## 7 MARKETING AUTHORISATION HOLDER

Mercury Pharmaceuticals (Ireland) Ltd
4045 Kingswood Road
Citywest Business Park
Co Dublin
Ireland

## 8 MARKETING AUTHORISATION NUMBER

PA0073/053/004

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

Date of first authorisation: 02 June 1988

Date of last renewal: 02 June 2003

## 10 DATE OF REVISION OF THE TEXT

July 2015