

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

Prothiazine 25 mg Tablets

Prothiazine Syrup

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

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

Each 5ml syrup contains 5mg of the active substance Promethazine hydrochloride.

For full list of excipients, see section 6.1

3. PHARMACEUTICAL FORM

Prothiazine tablets are purple, round, and biconvex.

Prothiazine syrup is a clear orange-colored liquid.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Antihistaminic, Antiemetic, Sedative.

4.2 Posology and method of administration

Route of administration: Oral.

Not for use in children under the age of 2 years (see section 4.3).

For treatment of allergies:

Children aged 2-5 years:

5-15 ml of syrup in one dose, to be taken at night or 5 ml two to three times a day. Do not administer more than 15 ml per day.

Children aged 6-12 years:

10-25 ml of syrup in one dose to be taken at night, or 10 ml twice a day. Do not administer more than 25 ml per day.

Children above the age of 12 and adults:

Begin treatment by taking one tablet at night. The dosage can be increased to a maximum of one tablet twice a day, as required.

For treatment and prevention of nausea and vomiting:

Children aged 2-5 years:

5 ml of syrup every 4-6 hours up to a maximum of 15 ml per day.

Children aged 6-12 years:

A dose of 10 ml of syrup; wait 4-6 hours before administering another dose. Up to two doses per day can be administered (a total of 20 ml per day).

Children above the age of 12 and adults:

One tablet every 4-6 hours, up to a maximum of 4 tablets per day.

For short-term use as a sedative, with the doctor's instruction only:

Children aged 2-5 years:

5-15 ml of syrup as a single dose to be taken at night, at bedtime.

Children aged 6-12 years:

10-20 ml of syrup as a single dose to be taken at night, at bedtime.

Children above the age of 12 and adults:

One to three tablets as a single dose, to be taken at night, at bedtime.

4.3 Contraindications

Prothiazine should not be used in patients in coma or suffering from CNS depression of any cause.

Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.

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

Prothiazine should be avoided in patients taking monoamine oxidase inhibitors up to 14 days previously.

4.4 Special warnings and precautions for use

Prothiazine may thicken or dry lung secretions and impair expectoration.

It should therefore be used with caution in patients with asthma, bronchitis or bronchiectasis.

Use with care in patients with severe coronary artery disease, narrow angle glaucoma, epilepsy or hepatic and renal insufficiency.

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

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

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.

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).

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

Prothiazine tablets contain lactose. Patients with rare hereditary problems of galactose intolerance, total lactase deficiency or glucose-galactose malabsorption should not take this medicine.

Prothiazine syrup contains sucrose, sorbitol and glucose. Patients with rare hereditary problems of fructose intolerance, glucose-galactose malabsorption or sucrase-isomaltase insufficiency should not take this medicine.

4.5 Interaction with other medicinal products and other forms of interaction

Prothiazine will enhance the action of any anticholinergic agent, tricyclic antidepressant, sedative or hypnotic. Alcohol should be avoided during treatment.

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

4.6 Fertility, pregnancy and lactation

Prothiazine should not be used in pregnancy unless the physician considers it essential. The use of Prothiazine is not recommended in the 2 weeks prior to delivery in view of the risk of irritability and excitement in the neonate.

Available evidence suggests that the amount excreted in milk is insignificant.

However, there are risks of neonatal irritability and excitement.

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 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 ($\geq 1/10000$ to $< 1/1000$); very rare ($< 1/10000$), not known (cannot be estimated from the available data).

Side effects may be seen in a few patients: drowsiness, dizziness, restlessness, headaches, nightmares, tiredness, and disorientation. Anticholinergic side effects such as blurred vision, dry mouth and urinary retention occur occasionally. Infants are susceptible to the anticholinergic effects of promethazine, while other children may display paradoxical hyperexcitability.

The elderly are particularly susceptible to the anticholinergic effects and confusion due to promethazine. Other side-effects include urticaria, rash, pruritus, anorexia, gastric irritation, palpitations, hypotension, arrhythmias, QT prolongation, torsade de pointes, extrapyramidal effects, restless legs syndrome, muscle spasms and tic-like movements of the head and face. Anaphylaxis, jaundice and blood dyscrasias including haemolytic anaemia rarely occur. Photosensitive skin reactions have been reported. 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. Any suspected adverse events should be reported to the Ministry of Health according to the National Regulation by using an online form <https://sideeffects.health.gov.il/>

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. Cardiorespiratory depression is uncommon. High doses (supratherapeutic doses) can cause ventricular arrhythmias including QT prolongation and torsade de pointes (see section 4.8). 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.

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 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

Prothiazine tablets: Lactose, Maize starch, Methocel E5, Povidone 25, Magnesium stearate, Purified talc, Diethyl Phthalate, Propylene glycol, Polyvinyl acetate phthalate, Colloidal silicone dioxide, Titanium dioxide, Indigo carmine, Ponceau 4R.

Prothiazine syrup: Sucrose, sorbitol solution, Liquid glucose, Disodium hydrogen Phosphate, Ethanol, Ascorbic acid, Citric acid, Orange flavour 926, Methyl hydroxybenzoate, Propyl hydroxybenzoate, Sunset yellow, Purified water.

6.2 Incompatibilities

Not applicable

6.3 Shelf life

The expiry date of the product is indicated on the packaging materials.

Prothiazine syrup: Shelf life after first opening: 22 days

6.4 Special precautions for storage

Store below 25°C.

7. MARKETING AUTHORISATION HOLDER and MANUFACTURER

CTS CHEMICAL INDUSTRIES LTD, ISRAEL

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