

Data Sheet

Promethazine Winthrop®

Name of Medicine

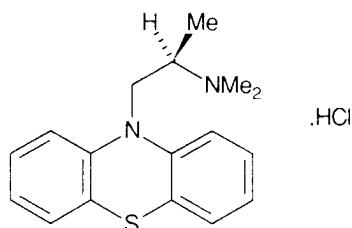
Promethazine Winthrop Elixir

Non-proprietary Name

Promethazine hydrochloride BP

Chemical Structure

Promethazine hydrochloride has the following structural formula:



CAS Number

58-33-3

Description

Promethazine hydrochloride is a white or faintly yellow, practically odourless, crystalline powder. It is very soluble in water, freely soluble in alcohol and in chloroform, and practically insoluble in ether.

Promethazine Winthrop Elixir contains promethazine hydrochloride 5 mg/5 mL. Promethazine Winthrop Elixir also contains maltitol solution, acesulfame potassium, sodium benzoate, sodium citrate, citric acid, sodium sulfite, sodium metabisulfite, ascorbic acid, caramel and orange juice flavour.

Pharmacology

Promethazine, a phenothiazine derivative, is a long acting antihistamine with mild atropine-like anticholinergic effects and some antiserotonin effects, and because of its marked effect on the central nervous system (CNS), it acts as an antiemetic, hypnotic, tranquilliser, and a potentiator of anaesthetics, hypnotics, sedatives and analgesics.

Pharmacokinetics

Promethazine is well absorbed after oral administration. Peak plasma concentrations are reached 2 to 3 hours after administration by this route, although there is low systemic bioavailability after oral administration, due to high first-pass metabolism in the liver. Promethazine crosses the blood-brain barrier and the placenta, and is distributed into breast milk. It is highly bound to plasma proteins (76-93%). Promethazine undergoes extensive metabolism, predominantly to promethazine sulfoxide, and also to N-desmethylpromethazine. It is excreted slowly via the urine and bile, mainly as metabolites. Elimination half-lives of 5 to 14 hours have been reported. The antihistamine action has been reported to be between 4 and 12 hours.

Indications

Allergies: Treatment of allergic conditions including some allergic reactions to drugs, urticaria and allergic contact dermatitis, and allergic reactions to insect bites and stings.

Upper respiratory tract: Relief of excessive secretion in the upper respiratory tract as a result of hayfever and allergic rhinitis.

Nausea and vomiting: Antiemetic for vomiting from various causes, including postoperative vomiting, irradiation sickness, drug induced nausea and motion sickness.

Sedation: For short term use under the advice of a doctor or pharmacist. Do not use for more than 7 to 10 consecutive days.

Other: Promethazine has sedative effects and can be used in the symptomatic management of measles and chicken pox. Promethazine can be used as a preanaesthetic medication for the prevention and control of post operative vomiting.

Contraindications

Promethazine is contraindicated for use in patients with a history of hypersensitivity to the drug substance, substances of similar chemical structure or hypersensitivity to the other ingredients. Promethazine Winthrop Elixir should not be given to patients with allergies to sodium metabisulfite, sodium sulfite or sodium benzoate.

Promethazine is contraindicated for use in:

- newborns or premature infants
- children under 2 years of age (see Precautions)
- lactating women
- patients taking monoamine oxidase inhibitors (MAOIs) (see Interactions with Other Medicines)
- jaundice induced by other phenothiazine derivatives
- patients who have received high doses of other CNS depressants and/or are comatose.

Refer to 'Interactions with Other Medicines' for additional information.

Precautions

Caution is advised in patients with:

- cardiovascular disease
- impaired hepatic function
- renal failure or impairment
- acute or chronic respiratory impairment
- epilepsy
- hypertensive crisis
- narrow-angle glaucoma
- stenosing peptic ulcer
- symptomatic prostatic hypertrophy
- bladder neck obstruction
- pyloroduodenal obstruction

Promethazine may cause drowsiness and may increase the effects of alcohol. Drowsiness may continue the following day. Those affected should not drive or operate machinery; alcohol should be avoided.

QT interval prolongation has been reported with phenothiazines. Refer to 'Interactions with Other Medicines' for additional information.

Use in Pregnancy (Category C)

Promethazine, owing to its pharmacological effects, has caused or may be suspected of causing, harmful effects on the human foetus or neonate without causing malformations. These effects may be reversible. When promethazine has been given in high doses during late pregnancy, promethazine has caused prolonged neurological disturbances in the infant. Promethazine should

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

Use in Lactation

Promethazine is excreted in breast milk. Therefore it should not be used for breastfeeding women.

Paediatric Use

Children may experience paradoxical excitation with promethazine.

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

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

Caution should be exercised when administering promethazine to children as there is potential for central and obstructive apnoea and reduced arousal. Excessive dosages of antihistamines in children may cause hallucinations, convulsions and sudden death.

Use in the Elderly

The elderly may experience paradoxical excitation with promethazine. The elderly are more likely to have CNS depressive side effects, including confusion and are more susceptible to the antimuscarinic effects of antihistamines, including hypotension (see Contraindications).

Interactions with Other Medicines

Promethazine may cause drowsiness and may enhance the sedative effects of CNS depressants (including alcohol, barbiturates, hypnotics, opioid analgesics, anxiolytic sedatives and neuroleptics), and have additive antimuscarinic actions with other antimuscarinic drugs (atropine, tricyclic antidepressants). Interactions between promethazine and monoamine oxidase inhibitors and tricyclic antidepressants (TCAs) may prolong and intensify the anticholinergic and CNS depressive effects

Warnings

Hypertensive crisis: Promethazine should be used with caution, if at all, in these patients.

Solar dermatitis has been reported following oral doses of Promethazine Winthrop in patients with eczema or a tendency to rheumatism.

Epilepsy: Epileptic patients may experience increased severity of convulsions.

Effects on Ability to Drive and Use Machinery

Ambulant patients receiving Promethazine Winthrop 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 medicine and do not suffer from disorientation, confusion or dizziness.

Adverse Effects

CNS Effects

CNS depressive effects of promethazine include sedation and impaired performance (impaired driving performance, poor work performance, incoordination, reduced motor skills, and impaired information processing). Performance may be impaired in the absence of sedation and may persist the morning after a night-time dose.

The CNS stimulatory effects of promethazine may include anxiety, hallucinations, appetite stimulation, muscle dyskinesias and activation of epileptogenic foci.

High doses of promethazine may cause nervousness, tremor, insomnia, agitation, and irritability.

Anticholinergic Effects

Side effects of promethazine associated with cholinergic blockage include dryness of the eyes, mouth and nose, blurred vision, urinary hesitancy and retention, constipation and tachycardia.

More common reactions

Gastrointestinal: Dry mouth, epigastric distress, loss of appetite, nausea, vomiting, constipation, diarrhoea
Nervous system: Sedation, restlessness, dizziness, lassitude, incoordination, fatigue
Ocular: Blurred vision

Less common reactions

Cardiovascular: Tachycardia, bradycardia, faintness
Dermatological: Contact dermatitis (topical), photosensitization, urticaria, angioneurotic oedema, pruritus
Haematological: Leucopenia, agranulocytosis, aplastic anaemia, thrombocytopenic purpura.
Hepatic: Jaundice
Musculoskeletal: Extrapyramidal symptoms
Nervous-system: Tinnitus, euphoria, nervousness, insomnia, convulsive seizures, oculogyric crises, excitation, catatonic-like states, hysteria, extrapyramidal symptoms, tardive dyskinesia
Respiratory: Marked irregular respiration

Severe or life-threatening reactions

Agranulocytosis, anaphylaxis.

The preservatives used in Promethazine Winthrop Elixir have been reported to cause hypersensitivity reactions (sodium metabisulphite, sodium sulphite, or sodium benzoate).

Dosage and Administration

This product should not be used in children under 2 years of age (see Precautions).

Dosage varies according to the condition being treated and the individual's response.

Allergic disorders

Children: 2 – 5 years: 5 to 15 mg (5 to 15 mL) as a single dose at night, or 5 mg two to three times daily.

Children: 6 – 12 years: 10 to 25 mg (10 to 25 mL) as a single dose at night, or 10 mg two to three times daily.

Sedation

Children: 2 – 5 years: 5 to 15 mg (5 to 15 mL).

Children: 6 – 12 years: 10 to 25 mg (10 to 25 mL).

Given as a single dose at night.

Travel sickness

Children 2 – 5 years: 5 mg (5 mL).

Children: 6 – 12 years: 10 mg (10 mL).

To be taken the night before travel and repeated after 6 to 8 hours on the following day if required.

Nausea and vomiting

Children: 2 – 5 years: 5 mg (or 5 mL) every 4 to 6 hours to a maximum daily dose of 15 mg (or 15 mL).

Children: 6 – 12 years: 10 mg (or 10 mL) every 4 to 6 hours to a maximum daily dose of 25 mg (or 25 mL).

Overdosage

The chief sign of acute poisoning from ingestion of an overdose of Promethazine Winthrop is unconsciousness, which is commonly delayed. In addition, convulsions, hallucinations, delirium, acute anxiety, psychotic reactions, extreme hyperaesthesia and hyperalgesia with extensor plantar responses may occur. Anticholinergic action may cause tachycardia, flushed skin, dry mouth and sometimes mydriasis and urinary retention.

In adults, CNS depression is more common, with drowsiness, coma, convulsions, progressing to respiratory failure or cardiovascular collapse.

In infants and children, CNS stimulation predominates over CNS depression causing ataxia, excitement, tremors, psychoses, hallucinations, convulsions and possibly hyperpyrexia, which may be followed by deepening coma and cardiorespiratory collapse.

Treatment

Similar to that of other phenothiazines. Symptomatic supportive therapy is indicated and maintenance of adequate ventilation should be instituted if necessary.

In case of overdose, contact the Poisons Information Centre.

Presentation and Storage Conditions

Elixir

5 mg/5 mL. Sugar free, alcohol free, orange flavoured, 100 mL. Store below 25°C. Protect from light.

Medicine Classification

Pharmacist Only Medicine

Name and Address of the Sponsor

sanofi-aventis new zealand limited

Level 8, James and Wells Tower

56 Cawley Street

Ellerslie

Auckland

Telephone: (09) 580 1810

Date of Preparation

25 February 2009