NEW ZEALAND DATA SHEET

1 PHENERGAN TABLETS AND PHENERGAN ELIXIR

Phenergan Tablets 10 mg and 25 mg

Phenergan Elixir 5 mg/5 mL

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Promethazine hydrochloride

Phenergan Elixir contains promethazine hydrochloride 5 mg/5 mL.

Excipients of known effect: maltitol solution, sodium benzoate, sodium sulfite, sodium metabisulfite

Phenergan tablets contain 10 mg or 25 mg of promethazine hydrochloride.

Excipients with known effect: lactose.

For the full list of excipients, see Section 6.1 List of excipients.

3 PHARMACEUTICAL FORM

ELIXIR

5 mg/5 mL. Sugar free, alcohol free, orange flavoured.

TABLETS

10 mg: Circular, film-coated biconvex tablets with bevelled edges, pale blue in colour, one face impressed 'PN' above '10', the reverse face plain.

25 mg: Circular, film-coated biconvex tablets with bevelled edges, pale blue in colour, one face impressed 'PN' above '25', the reverse face plain.

4 CLINICAL PARTICULARS

4.1 THERAPEUTIC 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 in adults 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.

4.2 DOSE AND METHOD OF ADMINISTRATION

Dose

This product should not be used in children under 2 years of age (see Section 4.4 Special warnings and precautions for use).

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.
Adults: 25 to 75 mg as a single dose at night, or 10 to 20 mg two to three times daily.

Sedation
Adults: 25 to 75 mg as a single dose at night.

Travel sickness

Children 2 – 5 years: 5 mg (5 mL).
Children: 6 – 12 years: 10 mg (10 mL).
Adults: 25 mg.

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).
Adults: 25 mg every 4 to 6 hours to a maximum daily dose of 100 mg.

4.3 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. Phenergan 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 less than 2 years of age (see Section 4.4 Special warnings and precautions for use)
- lactating women
- patients taking monoamine oxidase inhibitors (MAOIs) up to 14 days previously (see Section 4.5 Interaction with other medicines and other forms of interaction)
- jaundice induced by other phenothiazine derivatives
- patients in coma or suffering from CNS depression of any cause or who have received high doses of other CNS depressants.

Refer to ‘Section 4.5 Interaction with other medicines and other forms of interaction for additional information.

4.4 SPECIAL WARNINGS AND PRECAUTIONS FOR USE

Caution is advised in patients with:

- cardiovascular disease
- acute or chronic respiratory impairment as promethazine may thicken or dry lung secretions and impair expectoration
- epilepsy
- hypertensive crisis
- narrow-angle glaucoma

- stenosing peptic ulcer
- symptomatic prostatic hypertrophy
- bladder neck obstruction
- pyloroduodenal obstruction

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

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

Promethazine may increase the effects of alcohol. Alcohol should be avoided during treatment.

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

There have been case reports of drug abuse with promethazine. The risk of abuse is greater in patients with a history of drug abuse.

As with neuroleptics, Neuroleptic Malignant Syndrome (NMS) characterized by hyperthermia, extrapyramidal disorders, muscle rigidity, altered mental status, autonomic nervous instability and elevated CPK, may occur. As this syndrome is potentially fatal, promethazine must be discontinued immediately and intensive clinical monitoring and symptomatic treatment should be initiated.

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

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

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

Epilepsy: Epileptic patients may experience increased severity of convulsions.

Use in hepatic impairment

Caution is advised in patients with hepatic insufficiency.

Use in renal impairment

Caution is advised in patients with renal failure or insufficiency.

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 must not be used in children under 2 years of age, due to the potential for fatal respiratory depression (see Section 4.3 Contraindications).

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 Section 4.3 Contraindications).

4.5 INTERACTION WITH OTHER MEDICINES AND OTHER FORMS OF INTERACTION

Promethazine will enhance the action of any anticholinergic agent, tricyclic antidepressant, sedative or hypnotic. Promethazine may cause drowsiness and will 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. Alcohol should be avoided during treatment. Combination with alcohol enhances the sedative effects of H1 antihistamines. Promethazine may interfere with immunological urine pregnancy tests to produce false-positive or false-negative results.

4.6 FERTILITY, PREGNANCY AND LACTATION

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

Breast-feeding

Promethazine is excreted in breast milk. There are risks of neonatal irritability and excitement. Therefore it should not be used for breastfeeding women.

Fertility

No data available.

4.7 EFFECTS ON ABILITY TO DRIVE AND USE MACHINES

Promethazine considerably affects the ability to drive a vehicle and operate 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 medicine and do not suffer from disorientation, confusion or dizziness.

4.8 UNDESIRABLE 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 disorders:	Dry mouth, epigastric distress, loss of appetite, nausea, vomiting, constipation, diarrhoea
Nervous system disorders:	Sedation, restlessness, dizziness, lassitude, incoordination, fatigue
Eye disorders:	Blurred vision

Less common reactions

Cardiovascular:	Tachycardia, bradycardia, faintness
Skin and subcutaneous tissue disorders:	Contact dermatitis (topical), urticaria, angioneurotic oedema, pruritus
Haematological:	Leucopenia, agranulocytosis, aplastic anaemia, thrombocytopenic purpura.
Nervous system disorders:	Tinnitus, euphoria, nervousness, insomnia, convulsive seizures, oculogyric crises, excitation, catatonic-like states, hysteria, tardive dyskinesia,
Respiratory:	Marked irregular respiration

Reactions with frequency unknown

Skin and subcutaneous tissue disorders:	Photosensitivity reaction
Hepatobiliary disorders:	Jaundice
Renal and Urinary Disorders:	Urinary retention
Nervous system disorders:	Neuroleptic Malignant Syndrome, somnolence, headaches, tic-like movements of the head and face, extrapyramidal symptoms including muscle spasm, the elderly are particularly susceptible to the anticholinergic effects and confusion due to promethazine
Immune system disorders:	Allergic reactions, including urticaria, rash, pruritus, and anaphylactic reaction have been reported
Metabolism and Nutrition Disorders:	Anorexia
Blood and lymphatic system	Blood dyscrasias including haemolytic anaemia,

disorders:	agranulocytosis
Psychiatric disorders:	Infants, newborns and premature are susceptible to the anticholinergic effects of promethazine, while other children may display paradoxical hyperexcitability, restlessness, nightmares, disorientation
Cardiac disorders:	Palpitations, arrhythmias
Vascular disorders:	Hypotension
General disorders and administration site conditions:	Tiredness

Severe or life-threatening reactions

Agranulocytosis, anaphylaxis.

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

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Healthcare professionals are asked to report any suspected adverse reactions https://nzphvc.otago.ac.nz/reporting/ .

4.9 OVERDOSE

Symptoms of severe overdosage are variable. The chief sign of acute poisoning from ingestion of an overdose of Phenergan 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.

For advice on the management of overdose please contact the National Poisons Centre on 0800 POISON (0800 764766).

5 PHARMACOLOGICAL PROPERTIES

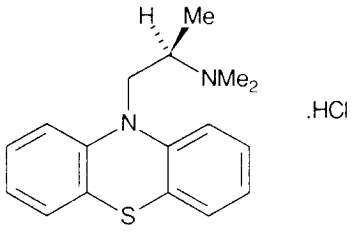
5.1 PHARMACODYNAMIC PROPERTIES

Pharmacotherapeutic group: Antihistamines for systemic use; ATC code: R06AD02

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.

Chemical Structure

Promethazine hydrochloride has the following structural formula:



CAS Number

58–33-3

Mechanism of Action

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.

5.2 PHARMACOKINETIC PROPERTIES

Absorption

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.

Distribution

Promethazine crosses the blood-brain barrier and the placenta, and is distributed into breast milk. It is highly bound to plasma proteins (76-93%).

Elimination

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.

Pharmacokinetic/pharmacodynamic relationship

The antihistamine action has been reported to be between 4 and 12 hours.

5.3 PRECLINICAL SAFETY DATA

No data available

6 PHARMACEUTICAL PARTICULARS

6.1 LIST OF EXCIPIENTS

Elixir

Phenergan Elixir contains maltitol solution, acesulfame potassium, sodium benzoate, sodium citrate, citric acid, sodium sulfite, sodium metabisulfite, ascorbic acid, caramel and orange juice flavour.

Tablets

Phenergan Tablets contain lactose, starch maize, povidone, magnesium stearate, hypromellose, macrogol 200 and blue opaspray.

6.2 INCOMPATIBILITIES

Not applicable.

6.3 SHELF LIFE

Elixir

18 months from date of manufacture

3 months opened

Tablets

60 months from date of manufacture

6.4 SPECIAL PRECAUTIONS FOR STORAGE

Elixir

Store below 25°C. Protect from light.

Tablets

Store below 30°C.

6.5 NATURE AND CONTENTS OF CONTAINER

Phenergan elixir is available in 100 mL bottles.

Phenergan 10 mg and 25 mg tablets are available in packs of 25 and 50.

6.6 SPECIAL PRECAUTIONS FOR DISPOSAL

No special requirements for disposal.

7 MEDICINE SCHEDULE

Pharmacist Only Medicine

8 SPONSOR

sanofi-aventis new zealand limited

Level 8, James and Wells Tower
56 Cawley Street
Ellerslie
Auckland

Telephone: (09) 580 1810

9 DATE OF FIRST APPROVAL

Tablets: 31 December 1969

Elixir: 5 May 1998

10 DATE OF REVISION OF THE TEXT

18 December 2020

Summary table of changes

Section changed	Summary of new information
4.1	The sedation indication has been updated to to include adults.
4.2	Dose and method of administration has been updated to remove the children population from sedation.