NEW ZEALAND DATA SHEET

1. ALLERSOOTHE ELIXIR

Allersoothe 5 mg/5mL Elixir

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Allersoothe Elixir: Each 5 mL of the elixir contains 5 mg of promethazine hydrochloride.

Excipients with known effect:

For the full list of excipients, see section 6.1

3. PHARMACEUTICAL FORM

Elixir liquid.

Allersoothe Elixir is a clear, orange, syrupy liquid with banana and vanilla flavour. Each 5 mL of the elixir contains 5 mg of promethazine hydrochloride.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

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

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

3. Anti-emetic for vomiting from various causes including post-operative vomiting, irradiation sickness, drug induced nausea and motion sickness

4. Sedation - for short term use in adults under the advice of a doctor or pharmacist. Do not use for more than 7-10 consecutive days

5. Promethazine can be used as a pre-anaesthetic medication for the prevention and control of post-operative vomiting.

4.2 Dose and method of administration

Dose

Allersoothe should not be used in children less than six years of age. The dosage varies according to the condition being treated and the patient's response:

Allergic disorders

Children 6-12 years of age: 10-25 mg (10-25 mL) as a single dose at night or 10 mg (10 mL) 2-3 times daily.

Children over 12 years and adults: 25-75 mg as a single dose at night or 10-20 mg 2-3 times daily.

Sedation

Give as a single dose at night.

Adults: 25-75 mg

Travel sickness

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

Children 6-12 years of age: 10 mg (10 mL)

Children over 12 years and adults: 25 mg

Nausea and vomiting

Children 6-12 years of age: 10 mg (10 mL) every 4-6 hours to a maximum daily dose of 20 mg (20 mL)

Children over 12 years and adults: 25 mg every 4-6 hours to a maximum daily dose of 100 mg.

4.3 Contraindications

• Patients with hypersensitivity to promethazine, substances with a similar chemical structure or to any of the excipients.

• Patients who are allergic to sodium benzoate.

• New born and premature infants

• Children under 6 years of age

• Women who are breast feeding

• Patients who have received high doses of other CNS depressants and/or are comatose

• Patients suffering from CNS depression of any cause.

• Allersoothe should not be given for jaundice induced by other phenothiazine derivatives.

• Allersoothe should be avoided in patients who have been taking monoamine oxidase inhibitors within the previous 14 days.

4.4 Special warnings and precautions for use

Caution is advised in patients with:

• cardiovascular disease

• acute or chronic respiratory impairment (including asthma, bronchitis and bronchiectasis) as promethazine may thicken or dry lung secretions and impair expectoration

• epilepsy

• hypertensive crisis

• stenosing peptic ulcer

• symptomatic prostatic hypertrophy

• bladder neck obstruction

• pyloroduodenal obstruction

Hypersensitivity reactions including anaphylaxis, urticaria and angioedema have been reported with promethazine use. In case of allergic reaction, treatment with promethazine must be discontinued and appropriate symptomatic treatment initiated.

Promethazine should be avoided in patients with 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 due to the risk of sedation. Combined use with other sedative medicinal products is not recommended (see section 4.5 Interactions with other medicines).

Prolonged administration of any phenothiazine may result in tardive dyskinesia, particularly in the elderly and children.

As agranulocytosis has been reported, regular monitoring of the complete blood count is

recommended. The occurrence of unexplained infections or fever may be evidence of blood dyscrasia and requires immediate hematological 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 (hyperleucocytosis, granulocytopenia) are observed in the blood count.

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 and alcohol-containing medicines should be avoided during treatment.

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 anesthetics, or alcohol.

QT interval prolongation has been reported with phenothiazines.

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 Undesirable effects).

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 promethazine 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

Promethazine should be avoided in patients with liver dysfunction.

Use in renal impairment

Promethazine should be avoided in patients with renal dysfunction.

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 6 years of age, due to the potential for fatal respiratory depression, psychiatric and CNS events (see Section 4.3 Contraindications and 4.8 Adverse Effects).

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.

Drugs known to cause QT Prolongation: 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.

Promethazine should be discontinued at least 3 days before the start of skin tests as it may inhibit the cutaneous histamine response thus producing false-negative results.

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/ amitriptylinoxide, a CYP2D6 substrate, may lead to an increase in the plasma levels of amitriptyline/ amitriptylinoxide. Monitor patients for dose-dependent adverse reactions associated with amitriptyline/amitriptylinoxide. Promethazine is contraindicated in patients taking monoamine oxidase inhibitors within the previous 14 days. Monoamine

oxidase inhibitors should be avoided while using promethazine.

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.

Gastrointestinal agents that are not absorbed: Reduced gastrointestinal absorption of phenothiazines may occur. Such gastrointestinal 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 with drugs with anticholinergic properties enhances the anticholinergic effect.

4.6 Fertility, pregnancy and lactation

Pregnancy (Category C)

The use of promethazine is not recommended during pregnancy and in women of childbearing potential not using contraception, unless the potential benefits outweigh the potential risks.

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.

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 may cause drowsiness and may increase the effects of alcohol. Drowsiness may continue the following day. Those affected should not drive or operate machinery. Patients receiving Allersoothe 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 reacting 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, somnolence

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: Rash, photosensitivity reaction

Hepatobiliary disorders: Jaundice

Renal and urinary disorders: Urinary retention

Nervous system disorders: Neuroleptic malignant syndrome, headaches, tic-like movements of the head and face, extrapyramidal effects including muscle spasm 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. Anticholinergic effects such as ileus paralytic, risk of urinary retention, accommodation disorder The elderly are particularly susceptible to the anticholinergic effects and confusion due to promethazine. Children less than 6 years of age also experienced psychomotor hyperactivity.

Immune system disorders: Allergic reactions, including anaphylactic reaction, urticaria, angioedema

Metabolism and nutrition disorders: Anorexia, decreased appetite

Blood and lymphatic system disorders: Blood dyscrasias including haemolytic anaemia, eosinophilia, thrombocytopenia

Psychiatric disorders: Agitation, confusional state Infants, newborns and premature are susceptible to the anticholinergic effects of promethazine, while other children may display paradoxical hyperexcitability, restlessness, nightmares, disorientation. Children less than 6 years of age also experienced aggression and hallucination

Cardiac disorders: Palpitations, arrhythmias, QT Prolongation, torsade de pointes

Vascular disorders: Hypotension

General disorders and administration site conditions: Tiredness

Respiratory, thoracic and mediastinal disorders: Respiratory depression, nasal congestion

Gastrointestinal disorders: Epigastric discomfort

Severe or life-threatening reactions

Agranulocytosis, anaphylaxis.

The preservative (sodium benzoate) used in Allersoothe Elixir has been reported to cause hypersensitivity reactions.

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://pophealth.my.site.com/carmreportnz/s/.

4.9 Overdose

Symptoms of severe overdosage are variable. They are characterized in children by various

combinations of excitation, ataxia, incoordination, athetosis and hallucinations, reversible 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. The chief sign of acute poisoning from ingestion of an overdose of promethazine 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.

High doses can cause ventricular arrhythmias including QT prolongation and torsade de pointes (see Section 4.8 Undesirable effects).

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 the event of overdose of promethazine, take all appropriate measures immediately.

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

Promethazine, a phenothiazine derivative, is a long acting antihistamine with mild atropine-like anticholinergic effects and some anti-serotonin effects. Because of its marked effect on the central nervous system (CNS), it acts as an anti-emetic, hypnotic, tranquiliser and a potentiator of

anaesthetics, hypnotics, sedatives and analgesics. The antihistamine action has been reported to last for between 4 and 12 hours.

5.2 Pharmacokinetic properties

Promethazine is well absorbed after oral dosing with peak plasma concentrations being reached 2- 3 hours after administration. Due to high first pass metabolism in the liver there is low systemic bioavailability after oral administration. It is widely distributed in the body, entering the brain and crossing the placenta. It is highly bound to plasma proteins (76-93%).
Promethazine undergoes extensive metabolism and is slowly excreted via urine and bile, mainly as metabolites. Elimination half-lives of 5-14 hours have been reported. Phenothiazines pass into breast milk at low concentrations.

5.3 Preclinical safety data

No data available.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Colouring

Quinoline yellow, sunset yellow FCF.

Flavour

Banana flavour 10, vanillin

Other excipient

Citric acid, disodium edetate, glycerol, hyetellose, propyl gallate, propylene glycol, purified water q.s (to 1 mL), sodium citrate, sodium benzoate.

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

18 months from date of manufacture stored at or below 25ºC.

6.4 Special precautions for storage

Store below 25°C. Protect from light.

6.5 Nature and contents of container

Bottles of 100 mL

6.6 Special precautions for disposal

No special requirements for disposal.

7. MEDICINE SCHEDULE

Pharmacist only medicine.

8. SPONSOR

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9. DATE OF FIRST APPROVAL

9 July 2009

10. DATE OF REVISION OF THE TEXT

11 June 2024

SUMMARY TABLE OF CHANGES

Date	**Section(s) Changed**	**Change (s)**
October 2020	4	Instructions for use in children for sedation removed
September 2022	4.1	Medsafe data sheet update request.
September 2022	4.5, 4.8	Correction of typographical errors and formatting.
June 2024	4.2, 4.4, 4.5 4.3, 4.4, 4.5, 4.6, 4.8, 4.9	Revised to convey that the product is contraindicated in children below 6 years of age. Revised as per datasheet of reference product