NEW ZEALAND DATA SHEET

ADIRAMEDICA PROMETHAZINE 10 (PROMETHAZINE HYDROCHLORIDE 10 mg) AND ADIRAMEDICA PROMETHAZINE 25 (PROMETHAZINE HYDROCHLORIDE 25 mg) FILM COATED TABLETS

1 PRODUCT NAME

- AdiraMedica Promethazine 10 mg tablets
- AdiraMedica Promethazine 25 mg tablets

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

a) AdiraMedica Promethazine 10 contains Promethazine Hydrochloride 10mg as an active ingredient. This formulation contains Lactose monohydrate (sugars) as an excipient with known effect. For the full list of excipients see Section 6.1. List of excipients.

b) AdiraMedica Promethazine 25 contains Promethazine Hydrochloride 25mg as an active ingredient. This formulation contains Lactose monohydrate (sugars) as an excipient with known effect. For the full list of excipients see Section 6.1. List of excipients.

3 PHARMACEUTICAL FORM

Promethazine Hydrochloride 10mg & 25mg are blue coloured, round, biconvex, film coated tablets which are plain on both sides.

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 hay fever 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 (adults only) under the advice of a doctor or pharmacist. Do not use for more than 7 to 10 consecutive days.

Other:
Promethazine can be used as a preanesthetic medication for the prevention and control of post-operative vomiting.

4.2 DOSE AND METHOD OF ADMINISTRATION

This product should not be used in children under 6 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: 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: 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: 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 (promethazine hydrochloride), substances of similar chemical structure, for example other phenothiazines, or hypersensitivity to the other ingredients in the formulation of AdiraMedica Promethazine.

Promethazine is contraindicated for use in:

- newborns or premature infants
- children under 6 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 Interactions with Other Medicines and Other Forms of Interactions)
- 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 Interactions with Other Medicines and other forms of Interactions for additional information.

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 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

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 INTERACTIONS WITH OTHER MEDICINES AND OTHER FORMS OF INTERACTIONS

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 USEMACHINES

Promethazine considerably affects the ability to drive a vehicle and operate machines. Promethazine may cause drowsiness, dizziness and blurred vision.

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: Dry mouth, epigastric distress, loss of appetite, nausea, vomiting, constipation, diarrhea.

Nervous system: Sedation, restlessness, dizziness, lassitude, incoordination, fatigue,

somnolence.

Ocular: Blurred vision.

Less common reactions

Cardiovascular: Tachycardia, bradycardia, faintness.

Dermatological: Contact dermatitis (topical), photosensitization, urticaria, angioneurotic oedema, pruritus.

Hematological: Leucopenia, agranulocytosis, aplastic anemia, thrombocytopenic purpura..

Nervous-system: 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, somnolence, 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 preservatives used in Phenergan Elixir have been reported to cause hypersensitivity reactions (sodium metabisulphite, sodium sulphite, or sodium benzoate).

Reporting 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 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.

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

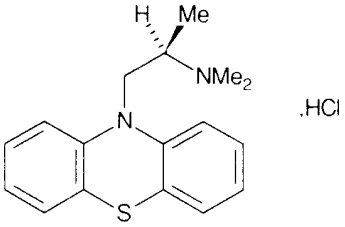
5.1 PHARMACODYNAMIC PROPERTIES

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.PRECLINICAL SAFETYDATA

No data available

6 PHARMACEUTICAL PARTICULARS

6.1 LIST OF EXCIPIENTS

Following are the list of excipients present in the formulation of 10 mg and 25 mg Promethazine hydrochloride tablets:

- Povidone
- Maize starch
- Lactose Monohydrate
- Magnesium stearate
- OPADRY complete film coating system 03B505083 Blue

6.2 INCOMPATIBILITIES

Not Applicable.

6.3 SHELF LIFE

24 months. The expiry date can be found on the packaging.

6.4 SPECIAL PRECAUTIONS FOR STORAGE

Store below 25°C, protect from light. Protect from moisture.

6.5 NATURE AND CONTENTS OF CONTAINER

Aluminium/Opaque PVC film blisters in packs of 50 tablets.

6.6 SPECIAL PRECAUTIONS FOR DISPOSAL

In New Zealand, any unused medicine or waste material should be disposed of by taking to your local pharmacy.

7 MEDICINE SCHEDULE

10’s blister pack: Pharmacy medicine
50’s blister pack: Pharmacist only medicine

8 SPONSOR

AdiraMedica Pty Ltd
C/O Core Business Services Ltd.
2 Khyber Pass Road, Grafton,
Auckland 1023, NZ

9 DATE OF FIRST APPROVAL

7 February 2023

10 DATE OF REVISION OF THE TEXT

23 May 2024 (Version 3)

SUMMARY TABLE OF CHANGES

Section Changed	Summary of new information
4.2 to 4.9, 5.1 to 5.3	The data sheet has been updated to include that the product is now contraindicated in children under 6 years of age (previously 2 years of age).