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 given to children under 6 years of age. This product should be given to children aged between 6 and 11 years only on the advice of a doctor, pharmacist or nurse practitioner (see Section 4.4 Special Warnings and Precautions for Use). Dosage varies according to the condition being treated and the individual's response.

Do not halve tablet. Dose equivalence when the tablet is divided has not been established.

ALLERGIC DISORDERS

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

Adults and children over 12 years: 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.

Adults and children over 12 years: 10 mg to 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, to every 4 to 6 hours to a maximum daily dose of 25 mg.

Adults and children over 12 years: 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.

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))
- women who are lactating/breastfeeding.
- 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.

4.4 SPECIAL WARNINGS AND PRECAUTIONS FOR USE

Warnings

- Do not use Promethazine hydrochloride in children below 6 years of age. Fatal respiratory depression has been associated with use in children under 2 years of age
- Promethazine hydrochloride should be used with caution, if at all, in patients with history if hypertensive crisis.
- Solar dermatitis has been reported following oral doses of Promethazine in patients with eczema or a tendency to rheumatism.
- Epileptic patients may experience increased severity of convulsions.

Identified precautions

Caution is advised in patients with:

- cardiovascular disease
- hepatic insufficiency renal failure or insufficiency 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. (See Section 4.7 EFFECTS ON ABILITY TO DRIVE AND USE MACHINES)

QT interval prolongation has been reported with phenothiazines. Refer to SECTION 4.5 'INTERACTIONS WITH OTHER MEDICINES AND OTHER FORMS OF INTERACIONS' for additional information.

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

with a history of drug abuse.

Promethazine delays 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.

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

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.

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).

Paediatric use

Do not use Promethazine hydrochloride in children under 6 years of age due to the potential for fatal respiratory depression. The use of Promethazine should be avoided in children and adolescents with signs or symptoms of Reye's Syndrome. 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. Children may experience paradoxical excitation with promethazine.

Effects on laboratory tests
No data available.

4.5 INTERACTIONS WITH OTHER MEDICINES AND OTHER FORMS OF INTERACTIONS

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. (This information is taken from MEDSAFE New Zealand Data Sheet: Phenergan®).

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

Effects on fertility

No data available.

Use in pregnancy – 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. There are risks of neonatal irritability and excitement in breastfed neonates. Therefore, it should not be used for breastfeeding women.

4.7 EFFECTS ON ABILITY TO DRIVE AND USE MACHINES

Patients receiving Promethazine hydrochloride 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. This medication may cause drowsiness and may increase the effects of alcohol. If affected do not drive a motor vehicle or operate machinery
Promethazine considerably affects the ability to drive a vehicle and operate machines.

4.8 ADVERSE EFFECTS (UNDESIRABLE EFFECTS)

<u>CNS Effects</u>

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.

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.

Hepatic: Jaundice.

Musculoskeletal: Extrapyramidal symptoms.

Nervous-system: Tinnitus, euphoria, nervousness, insomnia, convulsive seizures, oculogyric crises, excitation, catatonic-like states, hysteria, extrapyramidal symptoms, tardive dyskinesia, Neuroleptic Malignant Syndrome (NMS).

Respiratory: Marked irregular respiration.

Immunological: Very rare cases of allergic reactions, including urticaria, rash and pruritus have been reported.

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 disorders: Blood dyscrasias including haemolytic anaemia, 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.

Reporting suspected adverse effects

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

4.9 OVERDOSE

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 hyperesthesia 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.

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

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 analgesic.

Clinical trials

No data available

5.2 PHARMACOKINETIC PROPERTIES

Absorption

Promethazine hydrochloride is well absorbed from the GI tract and from parenteral sites 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 hydrochloride is widely distributed within body tissues. It is highly bound to plasma proteins (76-93%). Promethazine crosses the blood-brain barrier, and the placenta and is excreted in breast milk.

Metabolism

Promethazine hydrochloride is metabolized in the liver. Promethazine undergoes extensive metabolism, predominantly to promethazine sulfoxide, and also to N- desmethylpromethazine.

Excretion

Promethazine hydrochloride is slowly excreted via urine and 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.

5.3 PRECLINICAL SAFETY DATA

Genotoxicity

No data available.

Carcinogenicity

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

23 Feb 2023

10 DATE OF REVISION OF THE TEXT

SUMMARY TABLE OF CHANGES

Section Changed	Summary of new information