NEW ZEALAND DATA SHEET

1. PRODUCT NAME

NAUSICALM, Cyclizine hydrochloride 50 mg tablet

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains 50 mg of cyclizine hydrochloride.

Excipient with known effect: Lactose monohydrate.

For a full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

White, circular, biconvex, uncoated tablets with a score line on one side, plain on the other.

The tablets can be divided into two halves.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

NAUSICALM is indicated in adults and children over 6 years of age for the prevention and treatment of nausea and vomiting including:

- motion sickness.
- nausea and vomiting caused by narcotic analgesics and by general anaesthetics in the post-operative period.
- nausea and vomiting associated with radiotherapy, especially for breast cancer since cyclizine does not elevate prolactin levels.

NAUSICALM may be of value in relieving vomiting and attacks of vertigo associated with Meniere's disease and other forms of vestibular disturbance.

4.2 Dose and method of administration

Route of administration: Oral

Dose
Adults and children over 12 years: one tablet (50 mg) up to three times daily.

Children 6 – 12 years: half a tablet (25 mg) up to three times daily.

Paediatric population
Children under 6 years: Not recommended.

Use in the elderly
There have been no specific studies of cyclizine in the elderly. Experience has indicated that normal adult dosage is appropriate.

Use in hepatic impairment

Use with caution and monitor closely in patients with hepatic disease.

4.3 Contraindications

NAUSICALM should not be given to individuals with known hypersensitivity to cyclizine or to any of the excipients listed in section 6.1.

Cyclizine is contraindicated in the presence of acute alcohol intoxication. The anti-emetic properties of cyclizine may increase the toxicity of alcohol.

4.4 Special warnings and precautions for use

General
Cyclizine has anticholinergic effects and may precipitate pre-existing conditions that are likely to be exacerbated by anticholinergic activity.

Cyclizine should be used with caution and with appropriate monitoring in patients with glaucoma, urinary retention, obstructive disease of the gastrointestinal tract, hepatic disease, pheochromocytoma, hypertension, epilepsy and in males with possible prostatic hypertrophy.

Cyclizine may have a hypotensive effect. It may also exacerbate gastrointestinal obstructive disorders and cause dry mouth and constipation.

Cyclizine may precipitate incipient glaucoma.

It has been suggested that the anticholinergic effect of antihistamines such as cyclizine may reduce the volume and cause thickening of bronchial secretions, resulting in obstruction of respiratory tract. Cyclizine should be administered cautiously in patients with asthma or chronic obstructive pulmonary disease.

Heart failure
Cyclizine should be used with caution in patients with severe heart failure. In such patients, cyclizine may cause a fall in cardiac output associated with increases in heart rate, mean arterial pressure and pulmonary wedge pressure.

Hereditary enzyme deficiency
Patients with rare hereditary problems of galactose insufficiency, the Lapp lactase deficiency or glucose-galactose malabsorption should not take this medicine.

Renal and hepatic impairment
There have been no specific studies in hepatic and/or renal dysfunction.

Use in porphyria
Cyclizine should be avoided in porphyria.

Epilepsy
Cyclizine should be administered with caution in patients with epilepsy.

Sunlight
Cyclizine may increase sensitivity to sunlight.

Abuse and misuse
There have been reports of abuse of cyclizine, either oral or intravenous, for its euphoric or hallucinatory effects. The concomitant misuse of cyclizine with large amounts of alcohol is particularly dangerous, since the antiemetic effect of cyclizine may increase the toxicity of alcohol (see also Section 4.5 Interactions).

Nervous system
Nervous system side effects of cyclizine have included drowsiness and sedation in many patients. Motor skills may be impaired. Cyclizine may also cause restlessness, excitation, nervousness and insomnia. Extrapyramidal effects may occur and dystonic reactions have been reported after single doses of cyclizine.

4.5 Interaction with other medicines and other forms of interaction

Cyclizine may have additive effects with alcohol and other central nervous system depressants e.g. hypnotics, tranquillisers.

Cyclizine enhances the sedating effect of pethidine.

Cyclizine hydrochloride may counteract the haemodynamic benefits of opioid analgesics.

Because of its anticholinergic activity cyclizine may enhance the side- effects of other anticholinergic drugs and have an additive antimuscarinic action with other antimuscarinic drugs, such as atropine and some antidepressants (both tricyclics and MAOIs) and clozapine.

Cyclizine hydrochloride may mask the warning signs of damage caused by ototoxic drugs such as aminoglycoside antibacterials.

4.6 Fertility, pregnancy and lactation

Pregnancy
Pregnancy Category B3. Some animal studies are interpreted as indicating that cyclizine may be teratogenic. In the absence of any definitive data, the use of cyclizine in pregnancy is not advised.

Breast-feeding
Cyclizine is excreted in human milk; however, the amount has not been quantified. The use of cyclizine in breastfeeding women is not recommended.

Fertility
There is no experience of the effect of cyclizine on human fertility.

4.7 Effects on ability to drive and use machines

Studies designed to detect drowsiness did not reveal sedation in healthy adults who took a single oral therapeutic dose (50 mg) of cyclizine.

Patients should not drive or operate machinery until they have determined their own response.

Although there are no data available, patients should be cautioned that cyclizine may have additive effects with alcohol and other central nervous system depressants (e.g. hypnotics and tranquillisers).

4.8 Undesirable effects

Adverse reactions are ranked under heading of frequency, the most frequent first, using the following convention: Very common: (≥1/10); Common (≥1/100 to <1/10); Uncommon (≥1/1,000 to <1/100); Rare (≥1/10,000 to <1/1,000); Very rare (<1/10,000); Not known: cannot be estimated from the available data.

Blood and lymphatic system disorders
Agranulocytosis, leucopenia, haemolytic anaemia, thrombocytopenia (frequency not known)

Cardiac disorders
Tachycardia, palpitations, arrhythmias (frequency not known).

Ear and labyrinth disorder
Tinnitus (frequency not known).

Eye disorders
Blurred vision, oculogyric crisis (frequency not known).

Gastrointestinal disorders
Dryness of the mouth, nose and throat, constipation increased gastric reflux, nausea, vomiting, diarrhoea, stomach pain, loss of appetite (frequency not known).

General disorders and administration site conditions
Asthenia (frequency not known).

Hepatobiliary disorders
Hepatic dysfunction, hypersensitivity hepatitis, cholestatic jaundice and cholestatic hepatitis have occurred in association with cyclizine (frequency not known).

Immune system disorders
Hypersensitivity reactions, including anaphylaxis have occurred (frequency not known).

Musculoskeletal and connective tissue disorders
Twitching, muscle spasms (frequency not known).

Nervous system disorders
Effects on the central nervous system have been reported with cyclizine these include somnolence, drowsiness, incoordination headache, dystonia, dyskinesia, extrapyramidal motor disturbances, restless leg syndrome, tremor, convulsions, dizziness, decreased consciousness, transient speech disorders, paraesthesia and generalised chorea (frequency not known).

Psychiatric disorders
Disorientation, restlessness, nervousness, euphoria, insomnia and auditory and visual hallucinations have been reported, particularly when dosage recommendations have been exceeded (frequency not known).

Renal and urinary disorders
Urinary retention (frequency not known).

Respiratory, thoracic and mediastinal disorders
Bronchospasm, apnoea (frequency not known).

Skin and subcutaneous tissue disorders
Urticaria, drug rash, angioedema, allergic skin reactions, fixed drug eruption photosensitivity (frequency not known).

Vascular disorders
Hypertension, hypotension (frequency not known).

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
Symptoms of acute toxicity from cyclizine arise from peripheral anticholinergic effects and effects on the central nervous system.

Peripheral anticholinergic symptoms include, dry mouth, nose and throat, blurred vision, tachycardia and urinary retention. Central nervous system effects include drowsiness, dizziness, incoordination, ataxia, weakness, hyperexcitability, disorientation, impaired judgement, hallucinations, hyperkinesia, extrapyramidal motor disturbances, convulsions, hyperpyrexia and respiratory depression.

An oral dose of 5 mg/kg is likely to be associated with at least one of the clinical symptoms stated above. Younger children are more susceptible to convulsions. The incidence of convulsions, in children less than 5 years, is about 60% when the oral dose ingested exceeds 40 mg/kg.

Treatment
In the management of acute overdosage with cyclizine, supportive measures for respiration and circulation should be performed if necessary. Convulsions should be controlled in the usual way with parenteral anticonvulsant therapy.

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

ATC Code: R60AE03

Pharmacotherapeutic Group: Piperazine derivatives

Mode of Action:
The active ingredient-cyclizine is a piperazine derivative with the general properties of H1- blocking drugs but is used as an anti-emetic in a variety of clinical situations including drug- induced and

motion sickness, vertigo, post- operative vomiting and radiation sickness. The mechanism of the anti-emetic effect is unclear. Cyclizine also possesses anticholinergic activity but does not have marked sedative effects.

5.2 Pharmacokinetic properties

Absorption

H1-blockers are well absorbed from the GI tract. Following oral administration effects develop within 30 minutes, are maximal within 1-2 hours and last, for cyclizine, for 4-6 hours.

Biotransformation

Cyclizine is extensively N-demethylated to norcyclizine *in vivo.*

Distribution

Norcyclizine is widely distributed throughout the tissues and has a plasma half-life of less than 1 day.

Elimination

After a single dose of 50 mg cyclizine given to a single adult male volunteer, urine collected over the following 24 hours contained less than 1% of the total dose administered.

5.3 Preclinical safety data

Mutagenicity

Cyclizine was not mutagenic in a full Ames test, including use of S9- microsomes but can nitrosate *in vitro* to form mutagenic products.

Carcinogenicity

No long-term studies have been conducted in animals to determine whether cyclizine has a potential for carcinogenesis. However, long-term studies with cyclizine administered with nitrate have indicated no carcinogenicity.

Teratogenicity

Some animal studies are interpreted as indicating that cyclizine may be teratogenic. The relevance of these studies to the human situation is not known.

Fertility

In a study involving prolonged administration of cyclizine to male and female rats there was no evidence of impaired fertility after continuous treatment for 90 to 100 days. There is no experience of the effect of cyclizine on human fertility.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Potato starch
Lactose monohydrate
Gum acacia
Magnesium stearate

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

36 months.

6.4 Special precautions for storage

Store below 30 °C.

6.5 Nature and contents of container

PVC/PVDC/Al blister strips.
Pack sizes of 6, 10, 50 and 100 tablets
Not all pack sizes may be marketed.

6.6 Special precautions for disposal

No special requirements

7. MEDICINE SCHEDULE

Pharmacist Only Medicine
Blister packs of 6

Prescription Only Medicine
Blister packs of 10
Blister packs of 50
Blister packs of 100

8. SPONSOR

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9. DATE OF FIRST APPROVAL

13/04/2006

10. DATE OF REVISION OF THE TEXT

09/05/2024

Summary table of changes

Section changed	**Summary of new information**
4.1, 4.2	Editorial changes
4.3, 4.4, 4.5, 5.6, 4.8,4.9	Safety update