NEW ZEALAND DATA SHEET

1 PRODUCT NAME

NAUSICALM

Cyclizine hydrochloride 50 mg tablet

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains 50 mg 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 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

Adults and children over 12 years: one tablet up to three times daily
Children 6 – 12 years: half a tablet up to three times daily
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.

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.

4.4 Special warnings and precautions for use

Potential anticholinergic effects
As with other anticholinergic agents, cyclizine should be used with caution and appropriate monitoring in patients with glaucoma, obstructive disease of the gastrointestinal tract and in males with possible prostatic hypertrophy.

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.

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
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).

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 soporific effect of pethidine. Because of its anticholinergic activity cyclizine may enhance the side-effects of other anticholinergic drugs.

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
It is not known whether cyclizine or its metabolite are excreted in human milk.

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

a. Summary of the Safety Profiles

Urticaria, drug rash, drowsiness, dryness of the mouth, nose and throat, blurred vision, tachycardia, urinary retention, constipation, restlessness, nervousness, insomnia and auditory and visual hallucinations have been reported, particularly when dosage recommendations have been exceeded.

b. Summary of Adverse Reactions

Blood and lymphatic system disorders
Agranulocytosis

Psychiatric disorders
Disorientation, agitation

Nervous system disorders
Somnolence, headache, dystonia, dyskinesia, extrapyramindal motor disturbances, tremor, convulsions, dizziness, decreased consciousness, transient speech disorders, paraesthesia, generalised chorea.

Eye disorders
Oculogyric crisis

Vascular disorders
Hypertension, hypotension

Respiratory, thoracic and mediastinal disorders
Bronchospasm, apnoea

Hepatobiliary disorders
Hepatic dysfunction, hypersensitivity hepatitis, cholestatic jaundice and cholestatic hepatitis.

Skin and subcutaneous tissue disorders
Urticaria, drug rash, angioedema, fixed drug eruption.

Musculoskeletal and connective tissue disorders
Twitching, muscle spasms

General disorders and administration site conditions
Asthenia. Injection site reactions including vein tracking, erythema, pain, thrombophlebitis and blisters. A sensation of heaviness, chills and pruritus have been reported rarely.

c. Description of selected adverse reactions

Single case reports have been documented of fixed drug eruption, generalised chorea, hypersensitivity hepatitis and agranulocytosis.

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, gastric lavage and supportive measures for respiration and circulation should be performed if necessary. Convulsions should be controlled in the usual way with parenteral anticonvulsant therapy.

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 H_1- 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

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

B. 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.

C. 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.

D. 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^{o}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

January 2017

SUMMARY TABLE OF CHANGES

Version	Date	Change	Approval Date
1.0	01/2017	Reformat.	07/02/2017