PACKAGE INSERT FOR

MEDAZINE NAUSEA TABLETS

SCHEDULING STATUS:

S2

PROPRIETARY NAME (AND DOSAGE FORM):

MEDAZINE NAUSEA TABLETS (Tablets)

COMPOSITION:

Each tablet contains 50 mg cyclizine hydrochloride.

Inactive ingredients are colloidal silicon dioxide, lactose, magnesium stearate, maize starch, povidone and sodium starch glycollate.

Contains sugar (37 mg of lactose per tablet).

PHARMACOLOGICAL CLASSIFICATION:

A 5.7.2 Anti-emetics and antivertigo preparations.

PHARMACOLOGICAL ACTION:

Pharmacodynamic properties:

Cyclizine, a histamine H_1 -receptor antagonist of the piperazine class, is useful in the treatment of vertigo because of its anti-emetic and anticholinergic properties. The precise mechanism whereby cyclizine prevents or suppresses both nausea and vomiting from various causes is not known. Cyclizine reduces the sensitivity of the labyrinthine apparatus and increases lower oesophageal sphincter tone. It may cause

inhibition of the part of the midbrain collectively known as the emetic centre.

Effects develop within 30 minutes after oral administration, are maximal within 1 – 2 hours and, for cyclizine, last for 4 – 6 hours.

Pharmacokinetic properties:

Absorption:

H_1-blockers are well absorbed from the gastrointestinal tract. About 2 hours after administration, a single 50 mg oral dose of cyclizine results in a peak plasma concentration of about 70 ng/mℓ.

Distribution and metabolism:

Norcyclizine is the N-demethylated metabolite of cyclizine. Compared to cyclizine, norcyclizine has little antihistamine (H_1) activity. Norcyclizine is distributed widely throughout the tissues.

Elimination:

Cyclizine has a plasma elimination half-life of about 20 hours.

Following a single 50 mg dose of cyclizine, urine collected over the following 24-hour period contained less than 1 % of the total dose administered.

INDICATIONS:

MEDAZINE NAUSEA TABLETS is indicated for the treatment and prevention of nausea and vomiting, including nausea and vomiting induced by motion sickness,

narcotic analgesics, and vomiting associated with cancer chemotherapy and radiotherapy.

MEDAZINE NAUSEA TABLETS may be of value in relieving attacks of vertigo and vomiting associated with Ménière's disease and other labyrinthine disorders.

CONTRAINDICATIONS:

MEDAZINE NAUSEA TABLETS is contraindicated:

- In patients with known hypersensitivity to cyclizine, or who have previously reacted adversely to cyclizine, or to any of the inactive ingredients of **MEDAZINE NAUSEA TABLETS**..
- In pregnancy and lactation, as safety has not been established (see **"PREGNANCY AND LACTATION"**).
- During acute asthma attacks, because of its anticholinergic effects.

WARNINGS AND SPECIAL PRECAUTIONS:

MEDAZINE NAUSEA TABLETS may lead to impaired concentration and drowsiness, which may be aggravated by the concurrent intake of alcohol or other central nervous system depressants. Patients should be warned against performing potentially hazardous tasks or taking charge of vehicles or machinery where loss of concentration may lead to accidents (see **"Effects on the ability to drive and use machines"**).

Unless directed by a doctor, **MEDAZINE NAUSEA TABLETS** should not be used in conditions such as urinary retention, narrow angle glaucoma, prostatic hypertrophy,

chronic pulmonary disease, emphysema, difficult breathing and shortness of breath. **MEDAZINE NAUSEA TABLETS** should be used with caution in patients with hepatic disease, epilepsy and obstructive disease of the gastrointestinal tract.

Caution is required in patients with severe heart failure. In these patients, **MEDAZINE NAUSEA TABLETS** may cause a fall in cardiac output associated with increases in mean arterial pressure, heart rate and pulmonary wedge pressure.

MEDAZINE NAUSEA TABLETS should be avoided in porphyria.

There have been reports of either oral or intravenous abuse of cyclizine, as in **MEDAZINE NAUSEA TABLETS**, for its euphoric or hallucinatory effects. Since the antiemetic effect of cyclizine may increase the toxicity of alcohol, the concomitant misuse of large amounts of alcohol with **MEDAZINE NAUSEA TABLETS** is particularly dangerous (see **"INTERACTIONS"**).

MEDAZINE NAUSEA TABLETS may act as a cerebral stimulant in children and cause paradoxical central nervous system stimulation. In adults, symptoms of stimulation include nervousness, insomnia, tachycardia, muscle twitching, tremors and convulsions.

Large doses may also precipitate fits in epileptic patients. Furthermore, antihistamines, and therefore **MEDAZINE NAUSEA TABLETS**, may cause epileptiform seizures in patients with focal lesions of the cerebral cortex (see **"SIDE EFFECTS"**).

Anaphylaxis and allergy may occur. Blood dyscrasias including haemolytic anaemia and agranulocytosis have been reported (see **"SIDE EFFECTS"**).

There have been reports of insomnia and visual and auditory hallucinations, particularly when dosage recommendations have been exceeded (see **"SIDE EFFECTS"**).

Elderly patients may be more susceptible to the hypotensive and central nervous system effects of **MEDAZINE NAUSEA TABLETS** (see **"SIDE EFFECTS"**).

Antihistamines, including **MEDAZINE NAUSEA TABLETS**, may suppress positive skin test results.

No specific studies of **MEDAZINE NAUSEA TABLETS** have been performed in patients with renal and/or hepatic dysfunction.

Lactose:

MEDAZINE NAUSEA TABLETS contains lactose which may have an effect on the glycaemic control of patients with diabetes mellitus.

Patients with the rare hereditary conditions of galactose intolerance e.g. galactosaemia, Lapp-lactase deficiency or glucose-galactose malabsorption should not take **MEDAZINE NAUSEA TABLETS**.

Effects on the ability to drive and use machines:

In healthy adults who took a single oral therapeutic dose (50 mg) of cyclizine, as in **MEDAZINE NAUSEA TABLETS**, studies designed to detect drowsiness did not reveal sedation.

Until they have determined their own response, patients should not drive or operate machinery. Patients should be cautioned that alcohol and other central nervous system depressants, e.g. tranquilizers and hypnotics, may have additive effects with **MEDAZINE NAUSEA TABLETS**.

INTERACTIONS:

MEDAZINE NAUSEA TABLETS may increase the sedative effect of central nervous system depressants, including barbiturates, alcohol, narcotic analgesics, hypnotics, tranquilizers, anaesthetics and sedatives (see **"WARNINGS AND SPECIAL PRECAUTIONS"**).

The concomitant administration of **MEDAZINE NAUSEA TABLETS** may enhance the side effects of anticholinergic medicines, such as tricyclic antidepressants and atropine. If atropine and **MEDAZINE NAUSEA TABLETS** are used together, dizziness, restlessness and tachycardia may occur.

MEDAZINE NAUSEA TABLETS may mask the warning symptoms of damage caused by ototoxic medicines, such as aminoglycoside antibiotics.

MEDAZINE NAUSEA TABLETS may influence the metabolism of medicines in the

liver.

The antimuscarinic effects of antihistamines, such as **MEDAZINE NAUSEA TABLETS**, may be enhanced by monoamine oxidase inhibitors.

MEDAZINE NAUSEA TABLETS increases the soporific effect of pethidine.

PREGNANCY AND LACTATION:

As safety has not been established, **MEDAZINE NAUSEA TABLETS** is contraindicated in pregnancy and lactation (see **"CONTRAINDICATIONS"**).

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

DOSAGE AND DIRECTIONS FOR USE:

Adults and children over 12 years: 1 tablet (50 mg), may be repeated up to three times a day; not to exceed 4 tablets (200 mg) daily.

Children 6 to 12 years: ½ a tablet (25 mg) may be repeated up to three times a day; not to exceed 1½ tablets (75 mg) daily.

Motion sickness:

For the prevention of motion sickness, one tablet is taken one to two hours prior to departure. If necessary, this dose may be repeated three times daily. For children aged 6 to 12 years, the dosage is half the adult dosage.

Not recommended for children under 6 years of age.

The elderly:

No specific studies of cyclizine, as in **MEDAZINE NAUSEA TABLETS**, have been performed in elderly patients. Experience has indicated that the normal adult dosage is appropriate.

SIDE-EFFECTS:

Blood and lymphatic system disorders:

Frequency unknown: Blood dyscrasias, including haemolytic anaemia, agranulocytosis and leucopenia (see **"WARNINGS AND SPECIAL PRECAUTIONS"**).

Immune system disorders:

Frequency unknown: Hypersensitivity hepatitis, allergy, hypersensitivity reactions including anaphylaxis.

Psychiatric disorders:

Frequency unknown: Euphoria/elation, irritability, depression, nightmares, lassitude, disorientation, restlessness, nervousness, insomnia, visual and auditory hallucinations (particularly when dosage recommendations have been exceeded) (see **"WARNINGS AND SPECIAL PRECAUTIONS"**).

Nervous system disorders:

Frequent:	Sedation (including inability to concentrate and varying from slight drowsiness to deep sleep).
Frequency unknown:	Dizziness, incoordination, muscular weakness, headache, heaviness and weakness of the hands, tingling, generalised chorea, dystonia, somnolence, dyskinesia, tremor, extrapyramidal motor disturbances, convulsions, transient speech disorders, decreased consciousness, paraesthesia.

Eye disorders:

Frequency unknown:	Oculogyric crisis, blurred vision.

Ear and labyrinth disorders:

Frequency unknown:	Tinnitus.

Cardiac disorders:

Frequency unknown:	Tachycardia.

Vascular disorders:

Frequency unknown:	Hypertension, hypotension.

Respiratory, thoracic and mediastinal disorders:

Frequency unknown:	Tightness of the chest, apnoea, bronchospasm.

Gastrointestinal disorders:

Frequency unknown: Nausea, diarrhoea, vomiting, constipation, anorexia, epigastric pain, increased appetite, dryness of the mouth, nose and throat.

Hepatobiliary disorders:

Frequency unknown: Hypersensitivity hepatitis (see **"Immune system disorders"**), hepatic dysfunction, cholestatic jaundice, cholestatic hepatitis.

Skin and subcutaneous tissue disorders:

Frequency unknown: Fixed drug eruptions, medicine rash, urticaria, allergic skin reactions, angioedema.

Musculoskeletal, connective tissue and bone disorders:

Frequency unknown: Muscle spasms, twitching.

Renal and urinary disorders:

Frequency unknown: Difficulty in micturition, urinary retention, dysuria.

General disorders:

Frequency unknown: Asthenia.

KNOWN SYMPTOMS OF OVERDOSAGE AND PARTICULARS OF ITS TREATMENT:

Symptoms of acute toxicity stem from the effects of **MEDAZINE NAUSEA TABLETS** on the central nervous system. Such symptoms include dizziness, drowsiness, incoordination, hyperexcitability, weakness, disorientation, hyperkinesia, impaired judgement, extrapyramidal motor disturbances, hyperpyrexia, convulsions and respiratory depression. Ataxia, agitation and hallucinations may occur. Peripheral anticholinergic symptoms include blurred vision, dry mouth, nose and throat, urinary retention and tachycardia.

Overdosage may be fatal, especially in children. In children the main symptoms are central nervous system stimulation and antimuscarinic effects including ataxia, hallucinations, excitement, convulsions, muscle tremor, dry mouth, dilated pupils, facial flushing, and hyperpyrexia. Within 18 hours, cardiorespiratory collapse, deepening coma and death may occur. The usual symptoms in adults are convulsions, drowsiness and coma. Hypotension may also develop.

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

Treatment is symptomatic and supportive. If necessary, gastric lavage and supportive measures for circulation and respiration should be performed to manage

acute overdosage with **MEDAZINE NAUSEA TABLETS**. Convulsions should be controlled with parenteral anticonvulsant therapy.

IDENTIFICATION:

White, circular, flat, bevelled tablets with breakline on one side and plain on the other side.

PRESENTATION:

Securitainer of 200 tablets. Also packed in push-through blister packs of 10 tablets in cartons of 10 and 20 tablets.

STORAGE INSTRUCTIONS:

Store at or below 25 °C and protect from light.

KEEP OUT OF REACH OF CHILDREN.

REGISTRATION NUMBER:

27/5.7.2/0203

NAME AND BUSINESS ADDRESS OF THE HOLDER OF THE CERTIFICATE OF REGISTRATION:

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DATE OF PUBLICATION OF THIS PACKAGE INSERT:

16 March 1993

Revised: February 2013