Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Cyclizine hydrochloride Cipla 50mg Tablets

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains 50 mg of cyclizine hydrochloride.

Excipients with known effect:

Each tablet contains 37 mg of lactose monohydrate

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Tablet

White to off white, circular shaped, flat bevelled uncoated tablet with central break line on one side and plain on other.

The tablet can be divided into equal halves.

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

Cyclizine hydrochloride 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.
- Vomiting associated with radiotherapy, especially for breast cancer since cyclizine does not elevate prolactin levels.

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

4.2 Posology and method of administration

Posology

Route of administration: oral

Adults and Children over 12 Years:

50 mg orally, which may be repeated up to three times a day.

Children 6 – 12 Years:

25 mg orally, which may be repeated up to three times a day.

Children less than 6 years of age:

Cyclizine Hydrochloride tablets are not recommended for children less than 6 years of age.

Use in the Elderly:

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

To prevent motion sickness Cyclizine hydrochloride should be taken about one to two hours before departure.

4.3 Contraindications

Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.

4.4 Special warnings and precautions for use

As with other anticholinergic agents, Cyclizine hydrochloride may precipitate incipient glaucoma and it should be used with caution and appropriate monitoring in patients with glaucoma, obstructive disease of the gastrointestinal tract, hepatic disease, epilepsy and in males with possible prostatic hypertrophy.

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.

Cyclizine should be avoided in porphyria.

There have been reports of abuse of cyclizine, either oral or intravenous, for its euphoric or hallucinatory effects. The concomitant misuse of Cyclizine hydrochloride 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).

Isolated cases of transient paralysis have been reported in patients with underlying neuromuscular disease/epilepsy. Therefore caution should be applied when using cyclizine.

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

4.5 Interaction with other medicinal products and other forms of interaction

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

Cyclizine hydrochloride 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

In the absence of any definitive human data, the use of Cyclizine hydrochloride in pregnancy is not advised.

Breast-feeding

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

Fertility

There are no data available on the effects of cyclizine hydrochloride on human fertility.

There was no evidence of impaired fertility in male and female rats administered cyclizine (see section 5.3).

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

4.8 Undesirable effects

Blood and lymphatic system disorders
Agranulocytosis

Cardiac disorders
Tachycardia

Eye disorders
Blurred vision, oculogyric crisis

Gastrointestinal system disorders
Dryness of the mouth, nose and throat, constipation

General disorders and administration site conditions
Asthenia

Hepatobiliary disorders
Hepatic dysfunction, hypersensitivity hepatitis, cholestatic jaundice and cholestatic hepatitis have occurred in association with cyclizine.

Immune system disorders
Hypersensitivity reactions, including anaphylaxis have occurred

Musculoskeletal and connective tissue disorders
Twitching, muscle spasms

Nervous system disorders
Effects on the central nervous system have been reported with cyclizine these include somnolence, headache, dystonia, dyskinesia, extrapyramidal motor disturbances, tremor, convulsions, dizziness, decreased consciousness, transient speech disorders, paraesthesia and generalised chorea.

Psychiatric disorders
Disorientation, restlessness, nervousness, insomnia and auditory and visual hallucinations have been reported, particularly when dosage recommendations have been exceeded.

Renal and urinary disorders
Urinary retention

Respiratory, thoracic and mediastinal disorders
Bronchospasm, apnoea

Skin and subcutaneous tissue disorders
Urticaria, drug rash, angioedema, allergic skin reactions, fixed drug eruption

Vascular disorders
Hypertension

Reporting of suspected adverse reactions:
Reporting suspected adverse reactions after authorisation 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 via HPRA Pharmacovigilance, Earlsfort Terrace, IRL - Dublin 2; Tel: +353 1 6764971; Fax: +353 1 6762517. Website: www.hpra.ie; E-mail: medsafety@hpra.ie.

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 hydrochloride, 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

Pharmacotherapeutic group: Piperazine derivatives, ATC code: R60AE03

Mode of Action:

Cyclizine is a histamine H_1 receptor antagonist of the piperazine class which is characterised by a low incidence of drowsiness. It possesses anticholinergic and antiemetic properties. The exact mechanism by which cyclizine can prevent or suppress both nausea and vomiting from various causes is unknown. Cyclizine increases lower oesophageal sphincter tone and reduces the sensitivity of the labyrinthine apparatus. It may inhibit the part of the midbrain known collectively as the emetic centre.

Pharmacodynamics:

Cyclizine produces its antiemetic effect within two hours and last approximately four hours.

5.2 Pharmacokinetic properties

H_1-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.

In healthy adult volunteers the administration of a single oral dose of 50 mg cyclizine resulted in a peak plasma concentration of approximately 70 ng/mL occurring at about two hours after drug administration. The plasma elimination half-life was approximately 20 hours.

The N-demethylated derivative, norcyclizine, has been identified as a metabolite of cyclizine. Norcyclizine has little antihistaminic (H_1) activity compared to cyclizine. It is widely distributed throughout the tissues and has a plasma elimination half-life of approximately 20 hours.

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 90-100 days. There is no experience of the effect of Cyclizine Hydrochloride on human fertility.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Lactose Monohydrate (200 Mesh)
Maize Starch
Sodium Starch Glycolate (Primojel) (Type A)
Povidone (PVP K-30)
Colloidal Anhydrous Silica
Magnesium Stearate

6.2 Incompatibilities

Not applicable

6.3 Shelf life

24 Months

6.4 Special precautions for storage

This medicinal product does not require any special temperature storage conditions.

6.5 Nature and contents of container

PVC with aluminum foil blister. Pack size: 100 tablets

6.6 Special precautions for disposal

No special requirements.

7 MARKETING AUTHORISATION HOLDER

Cipla (EU) Limited
Hillbrow House
Hillbrow Road
Esher
Surrey KT10 9NW
United Kingdom

8 MARKETING AUTHORISATION NUMBER

PA1809/011/001

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 9th January 2015

10 DATE OF REVISION OF THE TEXT