SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Cyclizine Hydrochloride 50mg Tablets

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains 50 mg cyclizine hydrochloride

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Tablet

White, circular, biconvex tablet with a break line on one side and plain on the other

The tablet can be divided into equal doses

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Cyclizine Hydrochloride Tablets are indicated for:-

- 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 Tablets 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

Method of administration:

Oral

Adults and children over 12 years of age:

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

Children 6- 12 years of age:

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

Children less than 6 years of age:

Cyclizine Hydrochloride are not recommended for use in children under 6 years of age.

Elderly

There have been no specific studies with Cyclizine Hydrochloride in the elderly. Experience has indicated that the normal adult dose is appropriate.

For the prevention of motion sickness, Cyclizine Hydrochloride should be taken 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

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

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, urinary retention, obstructive disease of the gastrointestinal tract, hepatic disease, phaeochromocytoma, hypertension, epilepsy and in males with possible prostatic hypertrophy.

Cyclizine should be used with caution in patients with severe heart failure or acute myocardial infarction. 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 4.3 and 4.5).

Cyclizine Hydrochloride contains lactose

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, antipsychotics, barbiturates.

Cyclizine Hydrochloride enhances the soporific 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)

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

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

Cyclizine is excreted in human milk; however, the amount has not been quantified.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 at dose levels of approximately 15 and 25 mg/kg/day. There is no experience of the effect of Cyclizine Hydrochloride 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 hydrochloride may have additive effects with alcohol and other central nervous system depressants, e.g. hypnotics and tranquillisers.

4.8 Undesirable effects

The following side effects have been reported with cyclizine hydrochloride:

Blood and lymphatic system disorders
Agranulocytosis, leucopenia, haemolytic anaemia, thrombocytopenia.

Immune system disorders
Hypersensitivity reactions, including anaphylaxis have occurred

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

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, tremor, convulsions, dizziness, decreased consciousness, transient speech disorders, paraesthesia, generalised chorea and Restless leg syndrome.

Ear and labyrinth disorders
tinnitus

Eye disorders
Blurred vision, oculogyric crisis

Cardiac disorders
Tachycardia, palpitations, arrhythmias

Vascular disorders
Hypertension, hypotension

Respiratory, thoracic and mediastinal disorders
Bronchospasm, apnoea

Gastrointestinal system disorders
Dryness of the mouth, nose and throat, constipation increased gastric reflux
Nausea, vomiting, diarrhea, stomach pain
Loss of appetite

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

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

Musculoskeletal and connective tissue disorders
Twitching, muscle spasms

Renal and urinary disorders
Urinary retention

General disorders and administration site conditions
Asthenia

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 the Yellow Card Scheme at Website: www.mhra.gov.uk/yellowcard.

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: R06AE03

Mechanism 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.

Pharmacodynamic effects

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

5.2 Pharmacokinetic properties

Absorption

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.

Distribution

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.

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.

Norcyclizine (a metabolite of cyclizine) is widely distributed throughout tissues and has a plasma elimination half-life of approximately 20 hours.

Biotransformation

The N-demethylated derivative, norcyclizine, has been identified as a metabolite of cyclizine. Norcyclizine has little antihistaminic (H_1) activity compared to cyclizine.

Elimination

The plasma elimination half-life was approximately 20 hours.

5.3 Preclinical safety data

Adverse reactions not observed in clinical studies but seen in animals at exposure levels similar to clinical exposure levels and with possible relevance to clinical use were as follows:

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 effect experience of the effect of Cyclizine Hydrochloride Tablets on human fertility.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Maize starch

Lactose monohydrate

Povidone (PVP K-30)

pregelatinised maize starch (Starch 1500)

magnesium stearate

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

3 years

6.4 Special precautions for storage

This medicinal product does not require any special storage conditions.

6.5 Nature and contents of container

PVC/PVdC-Aluminium Blister containing 1, 10, 28, 30, 40, 50, 84, 100 or 500 tablets
Polypropylene Container with Polypropylene Cap containing 100 tablets

Not all pack sizes may be marketed.

6.6 Special precautions for disposal

No special requirements for disposal

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7 MARKETING AUTHORISATION HOLDER

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TW4 5DQ
UK

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