SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Cyclizine hydrochloride 50mg tablets

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains 50mg of cyclizine hydrochloride.

Excipient with known effect:

Also contains lactose monohydrate (46.5mg/tablet).

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

White to off white round tablets with breakline on one side and plain on other side.

The breakline is to facilitate breaking for ease of swallowing and not to divide into equal doses.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Cyclizine hydrochloride is indicated in adults and in children aged 6 years and over 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 may be of value in relieving vomiting and attacks of vertigo associated with Menière's disease and other forms of vestibular disturbance.

4.2 Posology and method of administration

Posology

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

Elderly

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

Paediatric population

Children less than 6 years of age:

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

Children 6 to 12 years of age:

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

Children over 12 years of age:

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

Adults

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

Method of administration

For oral administration

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 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 sections 4.3 and 4.5).

Cyclizine hydrochloride tablet contains lactose monohydrate.

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 (50mg) of cyclizine.

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

Although there is no data available, patients should be cautious that cyclizine hydrochloride 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.

The following undesirable effects have been reported with a frequency of Not known.

System Organ Class	**Frequency**	**Adverse reactions**
Blood and lymphatic system disorders	Not known	Agranulocytosis, leucopenia, haemolytic anaemia, thrombocytopenia.
Cardiac disorders	Not known	Tachycardia palpitations, arrhythmias
Ear and labyrinth disorders	Not known	Tinnitus.
Eye disorders	Not known	Blurred vision, oculogyric crisis
Gastrointestinal system disorders	Not known	Dryness of the mouth, nose and throat, constipation, increased gastric reflux, nausea, vomiting, diarrhoea, stomach pain, loss of appetite.
General disorders and administration site conditions	Not known	Asthenia

Hepatobiliary disorders	Not known	Hepatic dysfunction, hypersensitivity hepatitis, cholestatic jaundice and cholestatic hepatitis have occurred in association with cyclizine.
Immune system disorders	Not known	Hypersensitivity reactions, including anaphylaxis have occurred.
Musculoskeletal and connective tissue disorders	Not known	Twitching, muscle spasms
Nervous system disorders	Not known	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.
Psychiatric disorders	Not known	Disorientation, restlessness, nervousness, euphoria, insomnia and auditory and visual hallucinations have been reported, particularly when dosage recommendations have been exceeded.
Renal and urinary disorders	Not known	Urinary retention
Respiratory, thoracic and mediastinal disorders	Not known	Bronchospasm, apnoea
Skin and subcutaneous tissue disorders	Not known	Urticaria, drug rash, angioedema, allergic skin reactions, fixed drug eruption, photosensitivity
Vascular disorders	Not known	Hypertension, hypotension

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 website www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store. By reporting side effects, you can help provide more information on the safety of this medicine

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.

Management

In the management of acute over dosage 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 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 50mg cyclizine resulted in a peak plasma concentration of approximately 70ng/mL occurring at about two hours after drug administration. The plasma elimination half-life was 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. It is widely distributed throughout the tissues and has a plasma elimination half-life of approximately 20 hours.

Elimination

After a single dose of 50mg 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 at dose levels up to 25 times the clinical dose level. In another study, cyclizine was negative at oral dose levels up to 65mg/kg in rats and 75mg/kg in rabbits. The relevance of these studies in humans 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 90-100 days at dose levels of approximately 15 and 25 mg/kg/day. There is no experience of the effect of cyclizine hydrochloride Tablets on human fertility.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Lactose monohydrate,

Sodium starch glycolate

Povidone –K30

Silica colloidal anhydrous

Magnesium stearate

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

4 years

In-use-90 days

6.4 Special precautions for storage

Store below 25°C.

Keep the bottle in the outer carton in order to protect from light.

6.5 Nature and contents of container

White opaque HDPE bottle with a child resistant closure, containing 100 tablets.

6.6 Special precautions for disposal

No special instructions.

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

7 MARKETING AUTHORISATION HOLDER

Strandhaven Limited t/a Somex Pharma

Ilford, Essex

IG3 8BS, UK.

8 MARKETING AUTHORISATION NUMBER(S)

PL15764/0135

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

11/10/2024

10 DATE OF REVISION OF THE TEXT

11/10/2024