SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

Cyclizine lactate 50 mg/ ml solution for injection

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 1 ml ampoule contains 50 mg cyclizine lactate.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Clear, colorless to slightly yellow solution for injection.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Cyclizine lactate is indicated in adults for the prevention and treatment of nausea and vomiting including:-

- Motion sickness when the oral route cannot be used.
- 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 lactate injection, by the intravenous route, is also indicated pre-operatively in patients undergoing emergency surgery inorder to reduce the hazard of regurgitation and aspiration of gastric contents during induction of general anaesthesia.

Cyclizine lactate may be of value in relieving vomiting and attacks of vertigo associated with Menière's disease and other forms of vestibular disturbance when the oral route cannot be used.

4.2 Posology and method of administration

Posology

For the prevention of postoperative nausea and vomiting, administer the first dose by slow intravenous injection 20 minutes before the anticipated end of surgery.

Adults

50 mg intramuscularly or intravenously up to three times daily.

When used intravenously, cyclizine lactate should be injected slowly into the bloodstream, with only minimal withdrawal of blood into the syringe.

For the prevention of postoperative nausea and vomiting, administer the first dose by slow intravenous injection 20 minutes before the anticipated end of surgery.

Cyclizine given intravenously, in half the recommended dose, increases the lower oesophageal sphincter tone and thereby reduces the hazard of regurgitation and aspiration of gastric contents if given to patients, undergoing emergency surgery, before induction of general anaesthesia.

Elderly

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

Paediatric population

Not licensed for use in children.

Method of Administration:

Intramuscularly or intravenously.

4.3 Contraindications

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

Cyclizine lactate 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 lactate 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, pheochromocytoma, hypertension, epilepsy and in males with possible prostatic hypertrophy. Cyclizine lactate injection may have a hypotensive effect.

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 lactate 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).

Case reports of paralysis have been received in patients using intravenous cyclizine. Some of the patients mentioned in these case reports had an underlying

neuromuscular disorder. Thus intravenous cyclizine should be used with caution in all patients and with particular care in patients with underlying neuromuscular disorders.

4.5 Interaction with other medicinal products and other forms of interaction

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

Cyclizine lactate enhances the soporific effect of pethidine.

Cyclizine lactate may counteract the haemodynamic benefits of opioid analgesics.

Because of its anticholinergic activity, cyclizine may enhance the side-effects of other anticholinergic drugs, and may have an additive antimuscarinic action with other antimuscarinic drugs, such as atropine and some antidepressants (both tricyclics and MAOIs).

Cyclizine lactate 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 lactate 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 lactate 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, sedation of short duration was reported by subjects receiving intravenous 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 lactate 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 (see section 4.4)
Ear and labyrinth disorders	Not known	Tinnitus. There have been rare case reports of patients experiencing depressed levels of consciousness/loss of consciousness.
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 Injection site reactions including vein tracking, erythema, pain, thrombophlebitis and blisters. A sensation of heaviness, chills and pruritus have been reported rarely. Anaphylaxis has been recorded following intravenous administration of cyclizine co-administered with propanidid in the same syringe.
Hepatobiliary disorders	Not known	Hepatic dysfunction (see section 4.4), 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,

System Organ Class	Frequency	Adverse Reactions
		drowsiness, incoordination, headache, dystonia, dyskinesia, extrapyramidal motor disturbances, restless legs syndrome, tremor, convulsions, dizziness, decreased consciousness, transient speech disorders, paraesthesia, paralysis* and generalised chorea.
Psychiatric disorders	Not known	Disorientation, restlessness or agitation, 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, pruritus, drug rash, angioedema, allergic skin reactions, fixed drug eruption, photosensitivity
Vascular disorders	Not known	Hypertension, hypotension

* Case reports of paralysis have been received in patients using intravenous cyclizine. Some of the patients mentioned in these case reports had an underlying neuromuscular disorder (see section 4.4).

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: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store.

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 overdosage with cyclizine lactate, 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 H1 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

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. 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 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

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 at dose levels up to 25 times the clinical dose level. In another study, cyclizine was negative at oral dose levels up to 65 mg/kg in rats and 75 mg/kg in rabbits. 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 at dose levels of approximately 15 and 25 mg/kg/day. There is no experience of the effect of cyclizine on human fertility.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Lactic acid

Water for injections

6.2 Incompatibilities

None known. In the absence of compatibility studies, this medicinal product must not be mixed with other medicinal products.

6.3 Shelf life

2 years

For single use only. Discard any unused product

6.4 Special precautions for storage

Do not freeze

Store below 25°C

Protect from light, keep the ampoule in the outer carton.

6.5 Nature and contents of container

1 ml clear glass ampoule.
Five or ten ampoules in a carton.
Not all pack sizes may be marketed.

6.6 Special precautions for disposal

No special instructions.

For single use only. Discard any unused product

7. MARKETING AUTHORISATION HOLDER

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TW4 5DQ
United Kingdom

8. MARKETING AUTHORISATION NUMBER(S)

PL 25298/0314

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

25/06/2024

10. DATE OF REVISION OF THE TEXT

29/08/2024