

SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Valoid 50 mg Tablets
Cyclizine Hydrochloride 50 mg Tablets

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains 50 mg of cyclizine hydrochloride.

Excipient with known effect:
Lactose.

For a full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

White, biconvex, uncoated tablet, scored; coded T4A.

The scoreline is only 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 Hydrochloride 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.

Older people

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:

Oral

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 sections 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 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

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 and generalised chorea,

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 disorders

Dryness of the mouth, nose and throat, constipation increased gastric reflux.

Nausea, vomiting, diarrhoea 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, 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.

Management:

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

ATC Code: R06AE

Pharmacotherapeutic Group: Piperazine derivatives

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

H₁-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 (H₁) 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 Tablets on human fertility.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Lactose

Potato starch

Acacia

Magnesium stearate

6.2 Incompatibilities

None known

6.3 Shelf life

60 months

6.4 Special precautions for storage

Store below 25°C.

6.5 Nature and contents of container

Amber glass or polyethylene bottles with polyethylene tamper evident caps for pack size 100 tablets.

6.6 Special precautions for disposal

No special instructions

7 MARKETING AUTHORISATION HOLDER

Amdipharm UK Limited,
Capital House,
85 King William Street,
London EC4N 7BL,
United Kingdom

8 MARKETING AUTHORISATION NUMBER(S)

PL 20072/0241

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

01/1/2001 / 05/12/2005

10 DATE OF REVISION OF THE TEXT

27/03/2015