

VALOID™ Injection

Cyclizine lactate 50mg injection

Qualitative and Quantitative Composition

Valoid Injection contains 50mg cyclizine lactate in each 1mL ampoule.

Pharmaceutical Form

Injection solution.

Clinical Particulars

Therapeutic Indications

Valoid is indicated 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.

Intravenous Valoid is indicated pre-operatively in patients undergoing emergency surgery to reduce the hazard of regurgitation and aspiration of gastric contents during induction of general anaesthesia.

Valoid 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.

Posology and Method of Administration

For adult administration only:

50mg intramuscularly or intravenously, which may be repeated up to three times a day.

When used intravenously Valoid should be injected slowly undiluted into the bloodstream with only minimal withdrawal of blood into the syringe.

To prevent post-operative vomiting, the first dose should be given 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.

The Elderly:

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

Contra-indications

Valoid is contra-indicated in individuals who have previously reacted adversely to cyclizine.

Special Warnings and Special Precautions for Use

Because Valoid has anticholinergic activity, it may precipitate incipient glaucoma. It should be used with caution and appropriate monitoring in patients with glaucoma, obstructive disease of the gastrointestinal tract and in males with possible prostatic hypertrophy. Valoid may have a hypotensive effect.

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.

There have been no specific studies of Valoid in patients with hepatic and/or renal dysfunction.

There have been isolated case reports of transient paralysis occurring in patients using intravenous cyclizine. Two of the patients mentioned in these reports had an underlying neuromuscular disorder. Thus intravenous cyclizine should be used with caution in all patients in general, and in patients with underlying neuromuscular disorders in particular.

Potential for abuse:

In some countries the availability of Valoid Oral formulations as an over the counter sale has led to the misuse of cyclizine, predominantly by teenagers. The aim of abusers is to produce a state of disoriented exhilaration associated with hallucinations. Misuse may be by the oral or intravenous route. The concomitant misuse of Valoid with large amounts of alcohol is particularly dangerous, since the anti-emetic effect of cyclizine may increase the toxicity of alcohol.

Interaction with Other Medicaments and Other Forms of Interaction

Valoid may have additive effects with alcohol and other central nervous system depressants (e.g. hypnotics, tranquillizers).

Valoid enhances the soporific effect of pethidine.

Because of its anticholinergic activity cyclizine may enhance the side-effects of other anticholinergic agents.

Pregnancy and Lactation

Teratogenicity:

Some animal studies are interpreted as indicating that cyclizine may be teratogenic.

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 Valoid on human fertility.

Pregnancy and lactation:

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

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

Effects on Ability to Drive and Use Machines

Although studies designed to detect drowsiness did not reveal sedation in healthy adults who took a single oral therapeutic dose (50mg) 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 Valoid may have additive effects with alcohol and other central nervous system depressants, e.g. hypnotics and tranquillizers.

Undesirable Effects

Eye disorders: oculogyric crisis

General disorders and administration site conditions: asthenia. Injection site reactions including vein tracking, erythema, pain, thrombophlebitis and blisters. A sensation of heaviness, chills and pruritus have been reported rarely.

Hepatobiliary disorders: hepatic dysfunction, hypersensitivity hepatitis, cholestatic jaundice and cholestatic hepatitis.

Musculoskeletal and connective tissue disorders: twitching, muscle spasms

Nervous System Disorders: somnolence, headache, dystonia, dyskinesia, extrapyramidal motor disturbances, tremor, convulsions, dizziness, decreased consciousness, transient speech disorders, paraesthesia

Psychiatric disorders: disorientation, agitation

Respiratory, thoracic and mediastinal disorders: bronchospasm, apnoea

Skin and subcutaneous tissue disorders: urticaria, drug rash, angioedema

Vascular Disorders: hypertension, hypotension

Drowsiness, dryness of the mouth, nose and throat, blurred vision, tachycardia, urinary retention, constipation, restlessness, nervousness, insomnia and auditory and visual hallucinations have been reported, particularly when dosage recommendations have been exceeded.

Following oral administration, single case reports have been documented of:

- fixed drug eruption;
- generalised chorea;
- hypersensitivity hepatitis;
- agranulocytosis.

A single case of anaphylaxis has been recorded following intravenous administration of cyclizine co-administered with propanidid in the same syringe.

An increase in excitatory phenomena (tremor and muscle movements) has been reported when cyclizine has been given before propanidid and methohexitone anaesthesia.

Overdose

Symptoms:

Symptoms of acute toxicity from Valoid 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.

Treatment:

In the management of acute overdosage with Valoid, supportive measures for respiration and circulation should be performed if necessary. Convulsions should be controlled in the usual way with parenteral anticonvulsant therapy.

Pharmacological Properties

Pharmacodynamic Properties

Mode 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.

Pharmacodynamics:

Cyclizine produces its antiemetic effect within 2 hours and lasts approximately 4 hours.

Pharmacokinetic Properties

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 2 hours after medicine administration. The plasma elimination half life was approximately 20 hours.

Cyclizine is metabolised to its N-demethylated derivative, norcyclizine, which has little antihistaminic (H₁) activity compared to cyclizine. After a single oral 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.

Preclinical Safety Data**Mutagenicity:**

Cyclizine was not mutagenic in a full Ames test, including use of S9-microsomes.

Carcinogenicity:

No long-term studies have been conducted in animals to determine whether cyclizine has a potential for carcinogenesis.

Pharmaceutical Particulars***Shelf Life***

48 months

Special Precautions for Storage

Store below 25°C. Protect from light.

Package Quantities

Box of 5 x 1mL ampoules of Valoid Injection.

Pharmaceutical Precautions

No information is available on incompatibilities of Valoid with other products.

Medicines Classification

Prescription Only Medicine.

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