Package leaflet: Information for the user

Valoid® 50 mg/ml Injection
Cyclizine Lactate

Read all of this leaflet carefully before you start taking this medicine because it contains important information for you.
- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor or nurse.
- If you get any side effects, talk to your doctor or nurse. This includes any possible side effects not listed in this leaflet. See section 4.

The name of your medicine is Valoid 50 mg/ml Injection. It will be referred to as Valoid Injection for ease hereafter.

What is in this leaflet

1. WHAT VALOID INJECTION IS AND WHAT IT IS USED FOR
The name of your medicine is Valoid Injection. Valoid Injection contains the active substance cyclizine lactate, which belongs to a group of medicines called antihistamines which can be used to help stop you feeling sick (nausea) or being sick (vomiting).

Valoid Injection may be used by adults.
Valoid Injection may be used if you suffer from travel or motion sickness; nausea caused by cancer treatment (radiotherapy) or other medicines; or if you have had an operation, as general anaesthetics can sometimes cause sickness.

Valoid Injection can also be used to treat sickness caused by some inner ear problems such as Meniere's disease.

2. WHAT YOU NEED TO KNOW BEFORE YOU ARE GIVEN VALOID INJECTION
Do not use this medicine:
• if you are allergic to cyclizine lactate or any of the other ingredients of this medicine (listed in section 6)
• if you have allergic reactions which include mild symptoms such as itching and/or rash. More severe symptoms include swelling of the face, lips, tongue and/or throat with difficulty in swallowing or breathing
• if you have been drinking alcohol. The anti-vomiting properties of Valoid Injection may increase the toxicity of alcohol.

Warnings and precautions
Talk to your doctor or nurse before you are given Valoid Injection if you:

- suffer from an eye disease caused by a rise of pressure within the eye (glaucoma)
- suffer from urinary retention (experience difficulty passing urine)
- have an obstructive bowel condition
- have any **liver problems**
- suffer from phaeochromocytoma (tumour of the medulla of the adrenal glands)
- suffer from high blood pressure
- have **epilepsy**
- are a man and you suffer from an enlarged prostate gland (difficulty or slowness passing urine)
- have been told your heart is not working properly (heart failure)
- suffer from an inherited disorder which can lead to a sensitivity to sunlight (porphyria)
- suffer from **low blood pressure.**

Other medicines and Valoid Injection
Tell your doctor if you are taking any other medicines especially the following:

- medicines for problems such as **depression**, anxiety or difficulty in sleeping
- strong **painkillers** such as pethidine
- any medicine which belong to a group of medicines called anticholinergics.

Please tell your doctor if you are taking or have recently taken any other medicines including those you have obtained without a prescription.

Valoid Injection with food, drink and alcohol
Alcohol should be avoided when you are being treated with Valoid Injection.

Pregnancy and breast-feeding
If you are pregnant or breast-feeding, think you may be pregnant or are planning to have a baby, ask your doctor for advice before you are given this medicine.

Driving and using machines
You can drive while being treated with Valoid Injection but do not drive until you know how it affects you. It may make you feel dizzy. If it affects you in this way, **do not** drive or operate any machinery.

3. HOW VALOID INJECTION WILL BE GIVEN TO YOU
You will be given Valoid Injection under supervision and your doctor will decide on a dose which is right for you.
Valoid injection can be given as a slow injection into a vein (intravenously) or by injection into a muscle (intramuscularly).
The recommended dose for adults is:

- 50 mg up to three times a day.

For prevention of sickness after a normal operation:
Your doctor will give the first dose of Valoid by injection into a vein, approximately 20 minutes before the end of the operation. The use of the injectable form of cyclizine has been associated with cases of transient paralysis following administration of the medicine. The onset of paralysis is usually within minutes of administration, affects the limbs, and fully resolves within hours of discontinuation of the medicine.

If you receive more Valoid Injection than you should
As this medicine is given to you by a doctor, it is very unlikely that an overdose will happen. Should an overdose occur, the doctor will treat any symptoms that follow. Symptoms of overdose include dry mouth, nose and throat, blurred vision, fast or irregular heartbeat, difficulty passing urine, drowsiness, dizziness, lack of balance and coordination, weakness, excitability, disorientation, impaired judgement, hallucinations, muscle spasm, involuntary movements, convulsions, high temperature and difficulty breathing.

4. POSSIBLE SIDE EFFECTS
Like all medicines, this medicine can cause side effects, although not everybody gets them.

If you notice:
- itching or skin rashes
- swelling of the face, lips or throat
- difficulty in breathing or wheeziness.

Tell your doctor immediately. These may be signs of an allergic reaction.

The following side effects are reported for either compound with a not known frequency (frequency cannot be estimated from the available data)

Side effects may include
- skin rashes or itching
- muscle twitches, spasms or tremors
- restlessness
- decrease in muscle tone that can cause irregular body movements
- unusual body movements, particularly of your hands, arms or legs
- lack of coordination
- blurred vision or involuntary rolling of the eyes
- paralysis especially in patient who are already suffering from disorder of nerves and muscles
- convulsions, seizures
- nervousness
- seeing or hearing things that are not really there (hallucinations)
- ringing in the ears
- euphoria
- headache

- fast heartbeat, irregular heartbeat
- drowsiness or general feelings of weakness/tiredness
- a dry mouth, nose or throat
- heartburn (reflux)
- stomach pain
- nausea
- vomiting
- diarrhoea
- loss of appetite
- difficulty in passing water
- constipation
- difficulty in sleeping
- being confused, disorientated or unaware
- dizziness
- decreased consciousness/loss of consciousness
- temporary difficulty in speaking
- high blood pressure
- low blood pressure
- pins and needles
- yellowing of the skin and the whites of your eyes (jaundice)
- a red or brownish patch which appears at the same spot each time you take the medicine
- inflammation of the liver (hepatitis) or problems with the liver
- injection site reactions such as redness, pain, swelling or blistering
- sensations of heaviness, flushing, feeling cold or agitated or experiencing a decrease in blood pressure
- reduced rate of breathing (apnoea)
- reduction in the production of a type of white blood cell making infection more likely (agranulocytosis)
- unpleasant sensation or an overwhelming urge to move the legs (also called Restless Legs Syndrome).

If you feel very tired, experience unexpected bruising or bleeding or more infections (e.g. colds and sore throats) than usual please tell your doctor. Your doctor may decide to conduct tests on your blood periodically as a result of these symptoms.

Reporting of side effects
If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet.
You can also report side effects directly 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.
By Reporting side effects, you can help provide more information on the safety of this medicine.

5. HOW TO STORE VALOID INJECTION
Keep this medicine out of the sight and reach of children.

Valoid Injection will be stored by the hospital pharmacy before it is given to you. They will follow the instructions below. Valoid Injection should be stored in a safe place below 25°C and protected from light. The injection should not be used if there are any particles floating in it or after the "EXP" date on the carton and label.

6. CONTENTS OF THE PACK AND OTHER INFORMATION

What Valoid Injection contains

Valoid injection comes as a 1 ml ampoule containing 50 mg of the active ingredient, cyclizine lactate, dissolved in sterile water.
The injection also contains the inactive ingredient, lactic acid.

What Valoid Injection looks like and contents of the pack

Valoid Injection is a clear, colourless solution. Each pack contains 5 ampoules.

Marketing Authorisation Holder

Amdipharm UK Limited,
Dashwood House,
69 Old Broad Street, London,
EC2M 1QS, United Kingdom

Alternative Manufacturer

Cenexi,
52 Rue Marcelet Et Jacques Gaucher,
Fontenay-Sous Bois, F-94120, France

Valoid is a registered trademark of Amdipharm Mercury International Limited.

This leaflet was last revised in January 2024.

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

Valoid 50 mg/ml Injection
Cyclizine Lactate 50 mg/ml 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, colourless solution for injection.

4. CLINICAL PARTICULARS

4.1. Therapeutic indications

Valoid 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.
- Valoid injection, by the intravenous route, is also indicated pre-operatively in patients undergoing emergency surgery in order 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.

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, Valoid 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 Valoid 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.

Valoid 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, Valoid 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. Valoid 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 Valoid 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. Interactions with other medicinal products and other forms of interaction

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

Valoid enhances the soporific effect of pethidine.

Valoid 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).

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

4.6. Fertility, pregnancy and lactation

<u>Pregnancy</u>

In the absence of any definitive human data, the use of Valoid 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 Valoid 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 Valoid 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, malaise Injection site reactions including vein tracking, erythema, pain, thrombophlebitis and blisters. A sensation of heaviness, chills, flushing, agitation and pruritus have been reported rarely. Rapid IV administration can lead to symptoms similar to overdose.

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, drowsiness, incoordination, headache, dystonia, dyskinesia, extrapyramidal motor disturbances, restless leg 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, website: 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 Valoid, 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.

Pharmacodynamics 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 Valoid 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.

6.4. Special precautions for storage

Store below 25ºC

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

6.5. Nature and contents of container

1ml neutral glass ampoules. Five ampoules in a carton.

6.6. Special precautions for disposal

No special requirements

7. MARKETING AUTHORISATION HOLDER

Amdipharm UK Limited,
Dashwood House,
69 Old Broad Street, London,
EC2M 1QS, United Kingdom

8. MARKETING AUTHORISATION NUMBER

PL 20072/0010

9. DATE OF FIRST AUTHORISATION/RENEWAL OF AUTHORISATION

Date of first authorisation: 05 December 2005

Date of latest renewal: 31 October 2008

10. DATE OF REVISION OF THE TEXT

January 2024