Package leaflet: Information for the patient

PHOENIX LABS

Cyclizine Lactate 50mg/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 pharmacist.
- This medicine has been prescribed for you. Do not pass it on to others. It may harm them, even if their symptoms are the same as yours.
- If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. See section 4.
- In this leaflet, Cyclizine Lactate 50mg/ml Injection will be called Cyclizine Injection.

What is in this leaflet

1. What Cyclizine Injection is and what is it used for

The name of your medicine is Cyclizine Lactate 50mg/ml Injection. It contains the active ingredient, 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).

Cyclizine Injection may be used by adults. Cyclizine Injection may be used if you:

- suffer from travel or motion sickness;
- have nausea caused by cancer treatment (radiotherapy) or other medicines;
- you have had an operation, as general anaesthetics can sometimes cause sickness.

Cyclizine 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 take Cyclizine Injection

Do not take Cyclizine Injection:

- if you have ever had an allergic reaction to cyclizine or any of the other ingredients of this medicine (listed in section 6). Allergic reactions 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 Cyclizine Injection may increase the toxicity of alcohol.

Warnings and precautions

Talk to your doctor or pharmacist before taking Cyclizine 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.

Children

Do not give this medicine to children under 18 years of age.

Other medicines and Cyclizine Injection

Tell your doctor or pharmacist if you are taking, have recently taken or might take 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.

Cyclizine Injection with Alcohol

Alcohol should be avoided when you are being treated with Cyclizine Injection.

Pregnancy and breast-feeding

You should not be given Cyclizine Injection if you are pregnant or planning to become pregnant or if you are breast-feeding.

Driving and using machines

Do not drive until you know how Cyclizine Injection affects you. It may make you feel dizzy. If it affects you in this way, do not drive or operate any machinery.

3. How to take Cyclizine Injection

You will be given Cyclizine Injection under supervision and your doctor will decide on a dose which is right for you.

Cyclizine 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 Cyclizine Injection by injection into a vein, approximately 20 minutes before the end of the operation.

If you take more Cyclizine 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,

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Information for the Healthcare Professional

PHOENIX LABS

SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Cyclizine Lactate 50 mg/ml Injection

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 1 ml ampoule contains 50 mg cyclizine lactate (equivalent to 37.25mg cyclizine).

Excipient(s) with known effect:

None.

For a full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Clear, colourless solution for injection.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Cyclizine Lactate 50mg/ml Injection 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 50mg/ml 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.

Cyclizine Lactate 50mg/ml Injection may be of value in relieving vomiting and attacks of vertigo associated with Meniere'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 50mg/ml Injection 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.

Older people

There have been no specific studies of Cyclizine Lactate 50mg/ml Injection 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 50mg/ml Injection 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 50mg/ml Injection 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 50mg/ml 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 50mg/ml Injection 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

Cyclizine Lactate 50mg/ml Injection may have additive effects with alcohol and other central nervous system depressants e.g. hypnotics, tranquillisers, anaesthetics, antipsychotics, barbiturates.

Cyclizine Lactate 50mg/ml Injection enhances the soporific effect of pethidine.

Cyclizine Lactate 50mg/ml Injection 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 50mg/ml Injection 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 50mg/ml Injection 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 100-90 days at dose levels of approximately 15 and 25 mg/kg/day. There is no experience of the effect of Cyclizine Lactate 50mg/ml Injection 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 50mg/ml Injection 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.

Cardiac disorders
Tachycardia palpitations, arrhythmias (see section 4.4).

Eye disorders
Blurred vision, oculogyric crisis.

Gastrointestinal system disorders
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
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
Hepatic dysfunction (see section 4.4),

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.

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.

Tell your doctor immediately if you notice any of the following:
- itching or skin rashes;
- swelling of the face, lips or throat;
- difficulty in breathing or wheeziness.

These may be signs of an allergic reaction.

Other side effects may include:
- 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;
- unpleasant sensation or an overwhelming urge to move the legs (also called Restless Legs Syndrome);
- 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;
- 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, 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 morelikely (agranulocytosis).

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 or pharmacist. This includes any possible side effects not listed in this leaflet. You can also report side effects directly 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.

5. How to store Cyclizine Injection

Your doctor or pharmacist will make sure your medicine is correctly stored and disposed of.

Keep this medicine out of the sight and reach of children.

Do not use Cyclizine Injection after the expiry date on the carton and on the ampoule label. The expiry date refers to the last day of that month. Do not store above 25°C, protect from light.

Once opened use immediately. Discard after use.

Medicines should not be disposed of via wastewater or household waste. These measures will help protect the environment.

6. Contents of the pack and other information

What Cyclizine Injection contains

- The active substance is cyclizine lactate (50mg/ml equivalent to 37.25mg cyclizine).
- The other ingredients are lactic acid and water for injection.

What Cyclizine Injection looks like and contents of the pack
Cyclizine Injection is a clear colourless solution and comes in sealed 1 ml clear glass containers called ampoules. Each ampoule contains 1 ml solution. Each box of Cyclizine Injection contains 5 ampoules.

Marketing Authorisation Holder
Phoenix Labs, Suite 12, Bunkilla Plaza, Bracetown Business Park
Clonee, Co. Meath, Ireland.

Manufacturer
Labiana Pharmaceuticals, S.L.U., C/ Casanova 31-27, Corbera de Llobregat, Barcelona, Spain.

This leaflet was last revised in **03/2021.**
If this leaflet is difficult to see or read, or you would like it in a different format, please contact Phoenix Labs, Suite 12, Bunkilla Plaza, Bracetown Business Park, Clonee, Co. Meath, Ireland.

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hypersensitivity hepatitis, cholestatic jaundice and cholestatic hepatitis have occurred in association with cyclizine.

Immune system disorders
Hypersensitivity reactions, including anaphylaxis have occurred.

Musculoskeletal and connective tissue disorders
Twitching, muscle spasms

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, restless leg syndrome, convulsions, dizziness, decreased consciousness,transient speech disorders, paraesthesia, paralysis* and generalised chorea.

*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).

Ear and labyrinth disorders
Tinnitus.

There have been rare case reports of patients experiencing depressed levels of consciousness/ loss of consciousness.

Psychiatric disorders
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
Urinary retention

Respiratory, thoracic and mediastinal disorders
Bronchospasm, apnoea

Skin and subcutaneous tissue disorders
Urticaria, pruritus, drug rash, angioedema, allergic skin reactions, fixed drug eruption, photosensitivity.

Vascular disorders
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.

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 50mg/ml Injection, 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.

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 (H1) 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

Mutagenicity
Cyclizine was not mutagenic in a full Ames test, including use of S-9microsomes 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 65 mg/kg in rats and 75 mg/kg in rabbits. The relevance of these studies to the human situation 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 100-90 days at dose levels of approximately 15 and 25 mg/kg/day. There is no experience of the effect of Cyclizine Lactate 50mg/ ml Injection 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

3 years.

The product should be used immediately and not stored after opening/reconstitution/dilution. If not used immediately, in-use storage times and conditions are the responsibility of the user.

6.4. Special Precautions for Storage

Do not store above 25ºC. Protect from light, keep the ampoule in the outer carton. For storage conditions after first opening of the medicinal product, see section 6.3

6.5 Nature and contents of container

1ml glass ampoules (Type 1). Each pack contains 5 ampoules.

6.6 Special precautions for disposal

No specialrequirements for disposal.

7 MARKETING AUTHORISATION HOLDER

Phoenix Labs
Suite 12, Bunkilla Plaza
Bracetown Business Park
Clonee, Co. Meath
Ireland

8 MARKETING AUTHORISATION NUMBER

PL 35104/0021

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 14 June 2018

10 DATE OF REVISION OF THE TEXT
16 March 2021