

Package leaflet: Information for the user

Lorazepam Macure 4 mg/ml solution for injection lorazepam

Read all of this leaflet carefully before you start using 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.
- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- 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.

What is in this leaflet

1. What Lorazepam Macure is and what it is used for
2. What you need to know before you use Lorazepam Macure
3. How to use Lorazepam Macure
4. Possible side effects
5. How to store Lorazepam Macure
6. Contents of the pack and other information

1. What Lorazepam Macure is and what it is used for

Lorazepam Macure contains lorazepam, which is a member of a group of medicines called benzodiazepines. It helps to relieve anxiety and muscle tension.

Lorazepam Macure is usually prescribed as pre-medication to help you to relax before an operation or before uncomfortable or prolonged investigations. It may also be used to relieve short periods of anxiety, excitement or agitation, and in the control of convulsions.

You must talk to a doctor if you do not feel better or if you feel worse.

Lorazepam Macure is not recommended for use in children under the age of 12 years except for status epilepticus.

2. What you need to know before you use Lorazepam Macure

Do not use Lorazepam Macure:

- If you are allergic to benzodiazepines, including lorazepam or any of the other of this medicine (listed in section 6).
- If you have severe breathing or chest problems.
- If you have myasthenia gravis (a disease causing weakened muscles and excessive tiredness).
- If you have serious liver problems.
- If you suffer from sleep apnoea (breathing problems when you are asleep).

If you are an out-patient you should not be given Lorazepam Macure 4 mg/ml solution for injection unless you have somebody to take you home.

Lorazepam Macure contains benzyl alcohol and should not be used in infants or young children up to 3 years old.

Warnings and precautions

Talk to your doctor or nurse before using Lorazepam Macure if:

- You are pregnant or trying to become pregnant.
- You are breast-feeding, since the drug may pass into breast milk.
- You abuse or have in the past abused drugs or alcohol.
- You have a personality disorder. If so, you have a greater chance of becoming dependent on lorazepam.
- You have any kidney or liver problems.
- You have suffered from depression in the past since it could re-occur during treatment with lorazepam.
- You are currently suffering from depression, since lorazepam may increase any suicidal feelings, which you may have.
- You suffer from breathing problems.
- You suffer from an eye problem called glaucoma.
- You enter hospital for treatment.

Rare cases of severe allergic reactions have been reported. An allergic reaction may include a rash, itching, difficulty breathing or swelling of the face, lips, throat or tongue. If you experience any of these events, contact your doctor immediately.

Other medicines and Lorazepam Macure

Tell your doctor if you are using, have recently used or might use any other medicines, including medicines obtained without a prescription, since they may affect the way lorazepam works.

Lorazepam may also affect the way other drugs work.

In particular, you should tell your doctor if you are taking any other sedative, anti-anxiety drugs, antidepressants, strong pain killers (e.g. opioids, methadone), drugs for epilepsy, antihistamines, drugs for mood or mental disorders (e.g. chlorpromazine, clozapine and haloperidol), drugs for respiratory diseases, drugs for gout (probenecid). The dose of these drugs may need to be reduced before you can take lorazepam.

You should also tell your doctor if you are taking a drug called scopolamine, which may be used for gut problems or before an operation.

Use of lorazepam at the same time as opioids (strong pain killers, medicines for substitution therapy and some cough medicines) increases the risk of drowsiness, difficulties in breathing (respiratory depression), coma and may be life-threatening. Because of this, use of lorazepam at the same time as opioids should only be considered when other treatment options are not possible.

However if your doctor does prescribe lorazepam together with opioids the dose and duration of treatment should be limited by your doctor.

Please tell your doctor about all opioid medicines you are taking, and follow your doctor's dose recommendation closely. It could be helpful to inform friends or relatives to be aware of the signs and symptoms stated above. Contact your doctor when experiencing such symptoms.

Lorazepam Macure with food and drink and alcohol

You should avoid alcohol for at least 24 to 48 hours after receiving Lorazepam Macure. Please refer to section 3.

Pregnancy, breast-feeding and fertility

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 taking this medicine.

Benzodiazepines, including lorazepam, may cause damage to the foetus if taken during early pregnancy. If you take this medicine during late pregnancy or during labour, your baby, when born, may be less active than other babies, have a low body temperature, be floppy or have breathing or feeding difficulties for a while. Your baby's response to the cold might be temporarily impaired also. If this medicine is taken regularly in late pregnancy, your baby may develop withdrawal symptoms after birth. The drug may pass into breast milk.

Driving and using machines

Do not drive or use machinery within 24 to 48 hours of receiving lorazepam.

The medicine can affect your ability to drive as it may make you sleepy or dizzy.

- Do not drive while taking this medicine until you know how it affects you.
- It is an offence to drive if this medicine affects your ability to drive.
- However, you would not be committing an offence if:
 - The medicine has been prescribed to treat a medical or dental problem and
 - You have taken it according to the instructions given by the prescriber or in the information provided with the medicine and
 - It was not affecting your ability to drive safely

Talk to your doctor or pharmacist if you are not sure whether it is safe for you to drive while taking this medicine.

Lorazepam Macure contains benzyl alcohol and propylene glycol

This medicine contains 21 mg benzyl alcohol in each 1 ml of solution for injection.

Benzyl alcohol may cause allergic reactions.

Ask your doctor for advice if you are pregnant or breast-feeding or if you have a liver or kidney disease. This is because large amounts of benzyl alcohol can build-up in your body and may cause side effects (called "metabolic acidosis").

Benzyl alcohol has been linked with the risk of severe side effects including breathing problems (called "gasping syndrome") in young children.

Do not give to your newborn baby (up to 4 weeks old), unless recommended by your doctor.

This medicine contains 840 mg propylene glycol in each 1 ml of solution for injection.

If your child is less than 5 years old, talk to your doctor or pharmacist before giving them this medicine, in particular if they use other medicines that contain propylene glycol or alcohol. If they suffer from a liver or kidney disease, your doctor may carry out extra checks while they are taking this medicine.

3. How to use Lorazepam Macure

Always use this medicine exactly as your doctor has told you. Check with your doctor if you are not sure.

Your doctor will give you Lorazepam Macure, by injecting it into one of your veins (intravenously) or into one of your muscles. Lorazepam Macure may be diluted with water or saline just before it is given to you. The amount of Lorazepam Macure you are given will depend on how much you weigh and why it is being given to you:

The recommended dose is:

- Before an operation or investigation, you will usually be given 0.05 mg of Lorazepam Macure for each kilogram that you weigh (e.g. if you weigh 70 kilograms you will receive 3.5 mg of Lorazepam Macure).
- For anxiety or excitement, the usual dose is 0.025 to 0.03 mg for each kilogram that you weigh (e.g. if you weigh 70 kilograms you will probably receive 1.75 to 2.1 mg of Lorazepam Macure).
- When Lorazepam Macure is used to control convulsions a dose of 4 mg is usually given intravenously to adults. A lower dose of 2 mg given intravenously is usually given to control convulsions in children.

Your doctor may prescribe a different dose or length of treatment, especially if you are elderly.

Some people feel sleepy after receiving Lorazepam Macure.

Therefore, you may need to stay in hospital for at least 8 hours, or overnight, after receiving your injection. If you are to leave hospital shortly after receiving Lorazepam Macure you should have someone with you.

Lorazepam Macure is usually only prescribed for one or two doses, or for a short course of treatment.

This reduces the risk of becoming dependent on lorazepam, or suffering unpleasant effects when you stop taking it (See 'If you stop using Lorazepam Macure', below).

If you stop using Lorazepam Macure

- After you have finished your prescribed treatment with Lorazepam Macure, your doctor will decide whether or not you need further treatment.
- Following a course of treatment your dose of Lorazepam Macure may be reduced slowly. This allows your body to get used to being without Lorazepam Macure, and reduces the risk of unpleasant effects.
- On stopping Lorazepam Macure, you may experience symptoms such as headaches, muscle or stomach pains, anxiety, tension, depression, restlessness, sweating, sleep problems, confusion or irritability. If these symptoms do occur, they do not usually last for long. If you suffer from any of these symptoms, ask your doctor for advice.
- If you suffer from any of the following symptoms; loss of the sense of reality, tinnitus (ringing sounds in your ears), numbness or tingling of your arms or legs, vomiting, twitching, hallucinations, convulsions, or effects on sight, hearing or touch, ask your doctor for advice immediately.

If you have any further questions on the use of this medicine, ask your doctor or nurse.

4. Possible side effects

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

Reasons for stopping Lorazepam Macure

It is very important that you immediately contact your doctor if you develop any of the following symptoms:

- Anaphylactic (severe allergic) reactions such as swelling of the face, tongue, lips or throat (angioedema), which may cause difficulty breathing; swelling of the extremities (hands or feet)

- A serious allergic reaction which causes swelling of your face or throat (angioedema)
- Develop signs of jaundice (yellowing of the skin or the whites of the eyes)
- Difficulty breathing
- Thoughts of harming or killing yourself
- Changes in your mental state.

Other side effects that may occur are:

Very common: may affect more than 1 in 10 people

- Drowsiness, sedation
- Tiredness.

Common: may affect up to 1 in 10 people

- Confusion, depression, unmasking of depression
- Lack of muscle coordination, dizziness
- Muscle weakness
- Lack of energy.

Uncommon: may affect up to 1 in 100 people

- Nausea
- Changes in sex drive, impotence, decreased orgasm.

Not known: frequency cannot be estimated from available data

Contact your doctor if you develop any of the following symptoms:

- Blood disorders which can include lower levels of red blood cells, white blood cells and platelets (known as blood dyscrasias). Symptoms of this include unexplained bruising, bleeding, pale skin, weakness and/or breathlessness, mouth ulcers and/or frequent infections.
- Allergic (hypersensitivity) reactions
- Abnormally concentrated urine
- Low levels of sodium in the blood
- Loss of inhibitions, feelings of great happiness or well-being (euphoria), thoughts or attempts of suicide
- Anxiety, agitation, excitation, hostility, aggression, rage, sleep disturbances/insomnia, sexual arousal, and hallucinations
- Extrapyramidal symptoms, involuntary trembling, vertigo, visual disturbances (including double vision and blurred vision), slurred speech, headache, vomiting, fits, memory loss, coma
- Low blood pressure
- Reduced breathing rate, shortness of breath, temporary cessation of breathing, including during sleep, worsening of sleep
- Worsening of chronic obstructive lung disease
- Constipation
- Increases in liver enzymes, which may affect the way your liver works (will be detected by blood tests)
- Allergic skin reactions, hair loss
- Hypothermia
- Pain or redness at the injection site.

Reporting of side effects

If you get any side effects, talk to your doctor 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. By reporting side effects you can help provide more information on the safety of this medicine or search for MHRA Yellow Card in the Google Play or Apple App Store.

5. How to store Lorazepam Macure

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

Store and transport refrigerated (2-8°C). Keep in the outer carton to protect from light.

Do not use this medicine after the expiry date which is stated on the label and on the carton after EXP.

The expiry date refers to the last day of that month.

Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.

6. Contents of the pack and other information

What Lorazepam Macure contains

- The active substance is lorazepam; each 1 ml of solution contains 4 mg lorazepam.
- The other ingredients are macrogol, benzyl alcohol and propylene glycol.

What Lorazepam Macure looks like and contents of the pack

A clear, colourless or almost colourless hypertonic solution, free from visible particles.

1ml solution in a Type I glass ampoule (2ml capacity) with a one-point-cut opening.

Box of 5 or 10 ampoules.

Not all pack sizes may be marketed.

Marketing Authorisation Holder

Macure Pharma ApS

Hejrevej 39, 2400 Copenhagen NV, Denmark

Manufacturer

Medochemie Ltd (Ampoule Injectable Facility), 48 Iapetou Street, Agios Athanassios Industrial Area, Agios, Athanassios, Limassol, 4101, Cyprus

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The following information is intended for medical or healthcare professionals only:

Posology and method of administration

Posology

Dosage and duration of therapy should be individualised. The lowest effective dose should be prescribed for the shortest time possible.

Treatment in all patients should be withdrawn gradually to minimise possible withdrawal symptoms.

Method of administration

Lorazepam Macure can be given intravenously or intramuscularly. However, the intravenous route is to be preferred. Care should be taken to avoid injection into small veins and intra-arterial injection.

Absorption from the injection site is considerably slower if the intramuscular route is used and as rapid an effect may be obtained by oral administration of lorazepam.

Lorazepam Macure should not be used for long-term chronic treatment.

Chemical and physical in-use stability has been demonstrated for 1 hour at 2-8°C. From a microbiological point of view, unless the method of opening/dilution precludes the risk of microbial contamination, the product should be used immediately. If not used immediately, in-use storage times and conditions are the responsibility of the user.

Preparation of the injection

Lorazepam injection is slightly viscous when cool. It must be inspected visually for the presence of particles or discolouration prior to administration. It should not be mixed with other drugs in the same syringe.

Intramuscular administration

Dilution with an equal volume of diluent is recommended. The diluent should be 0.9% sodium chloride, 5% glucose or water for injections.

Intravenous administration

Lorazepam injection should always be diluted with an equal volume of one of the following diluents: 0.9% sodium chloride, 5% glucose or water for injection.

Do not use if solution has developed a colour or a precipitate.

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

Dosage

1. Premedication

Adults: 0.05 mg/kg (3.5 mg for an average 70 kg man).

By the intravenous route the injection should be given 30-45 minutes before surgery when sedation will be evident after 5-10 minutes and maximal loss of recall will occur after 30-45 minutes.

By the intramuscular route the injection should be given 1-1½ hours before surgery when sedation will be evident after 30-45 minutes and maximal loss of recall will occur after 60-90 minutes.

Paediatric population: Lorazepam Macure is not recommended in children under 12.

2. Acute anxiety

Adults: 0.025-0.03 mg/kg (1.75-2.1 mg for an average 70 kg man). Repeat 6 hourly.

Paediatric population: Lorazepam Macure is not recommended in children under 12.

3. Status epilepticus

Adults: 4 mg intravenously

Paediatric population: 2 mg intravenously

Elderly: The elderly may respond to lower doses and half the normal adult dose may be sufficient.

Patients with renal or hepatic impairment

Lower doses may be sufficient in these patients. Use in patients with severe hepatic insufficiency is contraindicated.

Incompatibilities

In the absence of compatibility studies, this medicinal product must not be mixed with other medicinal products other than those mentioned above.