

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 belongs to a certain group of sedative-hypnotic medicines, called benzodiazepines.

Lorazepam Macure can be used in adults and adolescents above 12 years of age:

- as a sedative to initiate certain interventions (premedication), such as small or large surgical procedures or certain extensive physical examinations.
- in people who suffer from severe fears or tension and for any reason can not take any tablets.

Lorazepam Macure can also be used in adults, adolescents, children and infants from 1 month and older:

- in the control of status epilepticus.

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

You should not be given Lorazepam Macure:

- If you are allergic to the active substance, other benzodiazepines, benzodiazepine-like substances or any of the other ingredients of this medicine (listed in section 6);
- If you suffer from myasthenia gravis (a disease causing weakened muscles and excessive tiredness);
- If you suffer from severe breathing disorders;
- If you suffer from sleep apnoea syndrome (breathing problems when you are asleep);
- If you have severe liver problems.

Lorazepam Macure may not be injected into an artery.

Children

Children under 12 years old are not allowed to use Lorazepam Macure except for the control of status epilepticus. For status epilepticus, Lorazepam Macure must not be used in neonates.

Warnings and precautions

Talk to your doctor or nurse before using Lorazepam Macure:

- If you suffer from chronic breathing disorders.
- If your liver or kidney function is reduced.
- If you are elderly or debilitated.
- If you suffer from epilepsy.
- If you suffer from "green star" (acute narrow angle glaucoma).
- If you are planning a pregnancy or are pregnant.
- If you are breast-feeding, since the drug may pass into breast milk.

For 24 hours after Lorazepam Macure administration, you should stay under observation. Early walking (within 8 hours after Lorazepam Macure use) can make you fall and injure.

A reduction of alertness may also last for more than 24 hours, for example if you are older or use other medicines.

If you are an outpatient and Lorazepam Macure is used for a short-term procedure, you must be accompanied by a responsible adult upon discharge from the hospital.

You may not drive vehicles or take activities requiring attention during 24-48 hours after administration. You may not remember what you have experienced, during a certain period of time after Lorazepam Macure administration.

After treatment you may experience that you do not remember what you experienced during a certain period after receiving Lorazepam Macure.

Patients with mental disorders

Lorazepam Macure is not a first choice in the treatment of mental disorders. Lorazepam Macure should not be used without adequate antidepressant therapy in depressed patients.

Benzodiazepines may have an disinhibitory effect in depressed patients and may cause suicidal tendencies.

You must gradually reduce Lorazepam Macure treatment.

Use of Lorazepam Macure may result in dependence

Use of benzodiazepines may result in physical or psychological dependence. To reduce the risk of dependence, the lowest effective dose of Lorazepam Macure should be used and the duration of the therapy should be as short as possible.

If you stop the treatment suddenly you may experience withdrawal symptoms: headache, muscle ache, extreme fear, tension, restlessness, confusion, irritability, mood swings, depression and insomnia.

You may also temporarily return to the symptoms for which you temporarily received Lorazepam Macure (see also "If you stop using Lorazepam Macure" in section 3).

Tolerance

This medicine can lose its effect after repeated use for several weeks.

Elderly or debilitated patients and children

Elderly and children may experience reactions that are completely opposite to what you expect from Lorazepam Macure treatment, such as: restlessness, excitement, aggressiveness, delusions, rage attacks,

nightmares, certain mental disorders (psychoses) inappropriate and other opposing behaviour. If these reactions occur, your doctor will stop the treatment.

Children may be allergic to some of the excipients in Lorazepam Macure (see section “Lorazepam Macure contains benzyl alcohol, polyethylene glycol and propylene glycol”).

Other medicines and Lorazepam Macure

Tell your doctor if you are using, have recently used or might use any other medicines.

Concomitant use of the following medicinal products may enhance Lorazepam Macure calming/relieving effect:

- scopolamine (a medicine for motion sickness and gut problems),
- anti-psychiatric medicine,
- sleeping pills,
- sedative and / or tranquilizers,
- anti-depressants,
- muscle-relaxants,
- some highly active prescription analgesics (narcotic analgesics),
- anti-epileptic medicine,
- medicines used for breathing problems (theophylline/aminophylline),
- medicine that cause general or local anaesthesia (anesthetics),
- medicine used in allergies or motion sickness (antihistamines),
- medicine used to treat gout and high levels of uric acid in the blood (e.g. probenecid),
- disulfiram (a medicine used to treat chronic alcoholism),
- metronidazole (an antibiotic).

Concomitant use of lorazepam and 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, concomitant use should only be considered when other treatment options are not possible.

However if your doctor does prescribe Lorazepam Macure together with opioids the dose and duration of concomitant 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

Lorazepam Macure calming / relieving effect can be enhanced by the simultaneous use of alcoholic beverages. This may persist up to 48 hours after Lorazepam Macure administration.

You should not intake any alcohol 48 hours after Lorazepam Macure administration.

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.

You should only use Lorazepam Macure during pregnancy if this is strictly necessary, for the shortest possible period at the lowest possible dose.

Lorazepam passes into breast milk in small amounts. Breast-feeding is not recommended while taking Lorazepam Macure.

There are no data on possible effects of lorazepam administered by injection or infusion on female fertility.

In addition, Lorazepam Macure contains benzyl alcohol, a preservative that can cross the placenta and pass into breast milk. Lorazepam Macure also contains propylene glycol (see “Lorazepam Macure contains benzyl alcohol, propylene glycol and polyethylene glycol”).

Driving and using machines

To control a vehicle or operate a machine, you must be able to react and make decisions well and quickly. You must also be able to move quickly and accurately.

If you receive Lorazepam Macure, control of these skills can be lowered because Lorazepam Macure can adversely affect the alertness, responsiveness, memory and accuracy of muscle movements.

Therefore, you cannot drive a vehicle or perform other activities requiring attention 24 to 48 hours after administration.

Lorazepam Macure contains benzyl alcohol, propylene glycol and polyethylene glycol

Lorazepam Macure contains 21 mg benzyl alcohol, 840 mg propylene glycol and 189 mg polyethylene glycol in each ml.

Ask your doctor or pharmacist for advice if your child is below 5 years of age, if you have liver or kidney disease or if you are pregnant or breast-feeding. This is because the excipients may cause side effects. Your doctor may need to adjust the dose if you or your child use other medicines that contain benzyl alcohol, propylene glycol or alcohol.

Benzyl alcohol may cause allergic reactions.

Benzyl alcohol has been linked with the risk of severe side effects including breathing problems (called “gasping syndrome”) in young children. Medicines containing benzyl alcohol should not be given to newborn babies (up to 4 weeks old) and should not be used for more than a week in young children (less than 3 years old), unless advised by your doctor or pharmacist.

If you are pregnant or breast-feeding, do not take this medicine unless recommended by your doctor.

Your doctor may carry out extra checks while you are taking this medicine.

If you suffer from liver or kidney disease, do not take this medicine unless recommended by your doctor.

Your doctor may carry out extra checks while you are taking this medicine.

There have been reports of polyethylene glycol toxicity (e.g., acute tubular necrosis) during administration of lorazepam. This includes when lorazepam is administered at doses higher than recommended.

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.

1. Premedication

The recommended dose you will normally be given into a vein (intravenously) is based on body weight (0.044 mg per kg body weight), up to a total of 2 mg, 15 to 20 minutes before the expected procedure. Sometimes higher doses up to 4 mg can be administered.

The recommended dose given into a muscle (intramuscularly) is 0.05 mg per kg body weight with a maximum of 4 mg, at least 2 hours before the expected procedure.

2. Treatment of symptoms of severe anxiety and tension in people who cannot take tablets

The recommended dose is 2 to 4 mg, i.e. 0.05 mg per kg body weight. If necessary, the dose may be repeated after 2 hours. The injection will be given into a vein (intravenously) or into a muscle (intramuscularly).

3. Status epilepticus

Dose in adults: 4 mg intravenously.

Elderly (over 65 years): The elderly may respond to lower doses; thus, half the normal dose for adults may be sufficient.

Dosage in adolescents, children and infants from 1 month of age: 0.1 mg/kg body weight intravenously with a maximum of 4 mg/dose.

If the epileptic seizure lasts longer than 10-15 minutes, the doctor may decide to administer one more dose. A maximum of 2 doses may be administered.

Your child should not be given more than two repeated doses on a single day, if your child is below 5 years of age.

Use in children

Lorazepam Macure should not be used in children under 12 years except for the control of status epilepticus. For status epilepticus, it should not be used in neonates (see also section 2).

Use in elderly and debilitated patients

Your doctor will prescribe a lower dose. In addition, your doctor will check you regularly and adjust the dose according to your response.

Patients with kidney or liver disorders

Lorazepam Macure should not be used in patients with severe liver disorders. When Lorazepam Macure is used in patients with mild to moderate liver or kidney disorders, your doctor may prescribe a lower dose.

If you use more Lorazepam Macure than you should

If you are given more medicine than you should, you may experience symptoms such as sleepiness, mental confusion and lethargy when mildly overdosed, and low blood pressure, difficulty in controlling movements, breathing problems and coma, in severe cases.

Treatment of overdose will mainly consist of supportive measures, including maintenance of breathing and monitoring of your fluid balance (how much fluid you take in and pass out).

If you stop using Lorazepam Macure

You should discontinue or stop the treatment following doctor's instructions only.

If you are being treated for the symptoms of severe anxiety and the treatment is discontinued suddenly, you should consider the possible occurrence of one or more of the following withdrawal symptoms: headache, muscle ache, extreme fear, anxiety, tension, excitement, restlessness, confusion, irritability, mood swings, sweating, depression, and insomnia.

In more serious cases, withdrawal symptoms may include: loss of feelings, loss of reality, where the (familiar) environment seems unreal, alienation of self and self-esteem (depersonalisation), numbness and tingling of the arms and legs, greatly increased sensitivity to light, noise and touch, increased hearing, ear pains, involuntary movements, vomiting, delusions (hallucinations) or attacks of falling disease (epileptic attacks).

Also, the symptoms for which you received Lorazepam Macure may temporarily return to an elevated degree.

To minimize the risk of these symptoms occurring, it is recommended to gradually reduce the dose when discontinuing the treatment.

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. Side effects usually occur at the start of treatment and gradually disappear during treatment or when the dose is reduced.

The following side effects were reported after using lorazepam:

Very common: may affect more than 1 in 10 people

- fatigue.

Common: may affect up to 1 in 10 people

- sleepiness during daytime,
- drowsiness,
- dizziness,
- coordination problems,
- vomiting,
- muscle weakness.

Uncommon: may affect up to 1 in 100 people

- confusion,
- depression,
- emotional flattening,
- sleep disturbances,
- headache,
- decreased alertness,
- visual disturbances,
- double vision (diplopia),
- nausea,
- gastrointestinal problems,
- skin reactions, hair loss,
- change in sex drive.

Rare: may affect up to 1 in 1,000 people

- blood anomaly (dyscrasia),
- temporary memory loss,
- contradictory reactions,
- decreased blood pressure (hypotension),
- elevated blood pressure (hypertension),
- liver disease related abnormalities.
- psychiatric disorders: excitation (agitation), nervousness, irritability, aggressiveness, suspicion, rage attacks, nightmares, observations of things that are not there (hallucinations), severe mental illness

in which control over behaviour and behaviour is disturbed (psychosis), inappropriate behaviour. These side effects occur mainly in children and older people.

Other side effects:

- sudden hypersensitivity reactions (within minutes or hours), including breathing difficulties, skin rashes and fainting (anaphylactic/anaphylactoid reactions). Can be life-threatening.
- blood abnormality (thrombocytopenia, agranulocytosis, pancytopenia),
- pain, burning sensation, redness and inflammation at the site of injection have been reported,
- dependence may occur after repeated use for several weeks (see section 2),
- breathing difficulties in severe anaesthesia may occur,
- withdrawal symptoms occurs after discontinuation of treatment (see section “If you stop using Lorazepam Macure”),
- swelling,
- suicidal thoughts or attempts,
- difficult to speak,
- seizures,
- coma,
- lowered body temperature.

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

HPRA Pharmacovigilance

Website: www.hpra.ie

By reporting side effects, you can help provide more information on the safety of this medicine.

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 in order to protect from light.

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.

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 use this medicine if you notice visible particles in the solution.

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 propylene glycol (E1520), polyethylene glycol 400 (macrogol 400), and benzyl alcohol.

What Lorazepam Macure looks like and contents of the pack

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

Lorazepam Macure is packed in Type I (Ph.Eur), clear glass ampoule of 2 ml filling capacity.

Each ampoule contains 1 ml of solution.

The ampoules are placed in moulded polyvinyl chloride trays, which are then sealed by a protective PE transparent foil. The polyvinyl chloride trays are inserted in a carton box together with a leaflet.

Lorazepam Macure is supplied in packs of 5 and 10 ampoules of 1 ml solution.

Not all pack sizes may be marketed.

Marketing Authorisation Holder

Macure Pharma ApS
Hejrevej 39
2400 Copenhagen NV
Denmark

Manufacturer

Medochemie Ltd
48 Iapetou Street, Agios Athanassios Industrial Area
4101 Agios Athanassios, Limassol
Cyprus

This medicinal product is authorised in the Member States of the EEA under the following names:

Netherlands	Lorazepam Macure 4 mg/ml oplossing voor injectie
Denmark	Lorazepam Macure
Sweden	Lorazepam Macure 4 mg/ml injektionsvätska, lösning
Finland	Lorazepam Macure 4 mg/ml injektioneste, liuos
Norway	Lorazepam Macure
Austria	Lorazepam Macure 4 mg/ml Injektionslösung
Germany	Lorazepam Macure 4 mg/ml Injektionslösung
Belgium	Lorazepam Macure 4 mg/ml solution injectable/ oplossing voor injectie/ Injektionslösung
Ireland	Lorazepam Macure 4 mg/ml solution for injection
Italy	Lorazepam Macure
Slovenia	Lorazepam Macure 4 mg/ml raztopina za injiciranje

This leaflet was last revised in September 2024.

The following information is intended for healthcare professionals only:

Instruction for use

Lorazepam Macure is slightly viscous when cool.

Intramuscular administration:

In order to facilitate intramuscular administration, dilution with an equal volume of a compatible solution is recommended, such as sodium chloride 9 mg/ml (0.9%) solution for injection, glucose 50 mg/ml (5%) and water for injection.

Lorazepam Macure can be also administered undiluted, if given deeply in a large muscle mass.

Intravenous administration:

In case of intravenous administration, Lorazepam Macure should always be diluted with an equal volume of one of the following diluents: sodium chloride 9 mg/ml (0.9%) solution for injection, glucose 50 mg/ml (5%) and water for injection.

The injection rate should not exceed 2 mg / min. Parenteral medicines must be inspected visually for the presence of particles or discolourations prior to administration.

Instructions for dilution for intravenous use

Extract the desired amount of Lorazepam Macure into the syringe, then slowly extract the desired volume of diluent. Retract the piston slightly to provide an additional mixing space. Immediately mix the contents by repeatedly twisting the syringe until a homogeneous solution has formed. Do not shake vigorously as this will cause air bubbles.

Lorazepam Macure should not be mixed with other drugs in the same syringe. Do not use if solution has developed a colour or a precipitate (see section 4.2).

No special requirements for disposal. Any unused medicinal product or waste material should be disposed of in accordance with local requirements.