

Package leaflet: Information for the user

Ozalin® 2 mg/ml, oral solution in single-dose container Midazolam

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 pharmacist.
- If your child gets any side effects, talk to your child's doctor or pharmacist. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

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

1. What Ozalin is and what it is used for

Ozalin contains midazolam. It belongs to the group of medicines known as benzodiazepines.

Ozalin is used in infants, children and adolescents from 6 months to 17 years old for moderate sedation:

- before a therapeutic or diagnostic procedure, to relieve anxiety, distress and agitation related to the procedure,
- as premedication before anaesthesia.

2. What you need to know before your child receives Ozalin

Do not use Ozalin:

- if your child is allergic to midazolam, to benzodiazepines or to any of the other ingredients of this medicine (listed in section 6),
- if your child has a neuromuscular disease which causes severe weakness of the muscles (myasthenia gravis),
- if your child has severe difficulty breathing,
- if your child has an illness causing frequent interruption of breathing during sleep (sleep apnoea syndrome),
- if your child has severe liver problems.

Warnings and precautions

Talk to your doctor or pharmacist before your child receives Ozalin

- if your child has a long term illness (such as breathing problems or kidney, liver or heart problems),
- if your child is in poor general health,
- if your child has a history of alcoholism or drug addiction,
- if your child is under the age of 6 months.

Other medicines and Ozalin

Tell your doctor or pharmacist if your child is taking, has recently taken or might take any other medicines and in particular if your child is taking any of the following medicines:

- medicines used to treat bacterial infections (antibiotics), e.g. erythromycin, clarithromycin, telithromycin, roxithromycin,
- medicines used to treat fungal infections (antifungals), e.g. ketoconazole, voriconazole, fluconazole, itraconazole and posaconazole,
- medicines used to treat stomach ulcers (antiulcer), e.g. cimetidine and ranitidine,
- medicines used to treat epilepsy (antiepileptics), e.g. phenytoin and carbamazepine,
- medicines used to treat high blood pressure (antihypertensives), e.g. diltiazem and verapamil,
- medicines used to treat HIV and AIDS, e.g. saquinavir, including combinations containing ritonavir and efavirenz,
- medicine used to prevent nausea and vomiting, e.g. aprepitant,
- medicine used to reduce fat in the blood, e.g. atorvastatin,
- medicines used to treat depression that make you sleepy (sedative antidepressants),
- other medicines to treat depression (antidepressant), e.g. fluvoxamine,
- medicine used to treat cystic fibrosis, e.g. ivacaftor,
- medicine used to treat urinary incontinence, e.g. propiverine,
- medicine used to treat mycobacterial infections such as tuberculosis, e.g. rifampicin
- medicine used as anaesthetic, e.g. inhalation anaesthetics, propofol, ketamine, etomidate,
- sleep inducing medicines (hypnotics),
- medicines used as strong pain killers (narcotic analgesics), e.g. fentanyl,
- medicines for cough relief (antitussives) or used to treat dependence on opiate drugs (substitutive treatment) that contain opioids,
- medicines used to treat specific mental disorders such as psychosis (antipsychotics),
- medicines that contain benzodiazepines used to treat anxiety or sleep disturbances (benzodiazepines used as anxiolytics or hypnotics),
- medicines to treat allergies (antihistamines),
- herbal medicines, e.g. St. John's wort, purple coneflower, turmeric rhizome.

Ozalin with food, drink and alcohol

General fasting guidelines should be respected before sedation.

Your child must not drink alcohol while taking Ozalin. Alcohol may increase the sedative effects of this medicine and make them very sleepy.

Your child must not drink grapefruit juice while taking Ozalin. Grapefruit juice may increase the sedative effects of this medicine and make them very sleepy

Pregnancy and breast-feeding

Pregnancy

If your child is pregnant or you think she is pregnant, ask your doctor for advice before this medicine is given to her.

Breast-feeding

If your child is a breast-feeding mother, she should be informed of the need to suspend breast-feeding in the 24 hours that follow administration of midazolam as midazolam passes in small quantities into breast milk.

Driving and using machines

Ozalin may make your child sleepy, forgetful or affect his/her concentration and co-ordination. Your child should not drive vehicles, ride a bicycle or use tools or machines before fully recovering. Please discuss with your doctor if you need further advice.

Ozalin contains sodium, ethanol and gammadex

This medicine contains less than 1 mmol (23 mg) of sodium per ampoule, that is to say that this medicine is essentially 'sodium-free'.

This medicine contains a maximum of 17.4 mg of alcohol (ethanol, component of the orange flavour) in each dosage unit, ampoule of 5 mL, which is equivalent to 3.5 mg/mL (ethanol/solution) or 0.32 % w/v.

The amount of ethanol in 1 ampoule of 5 mL of this medicine (17.4 mg) is equivalent to 0.2 mL of wine. The amount of ethanol in 2 ampoules of 5 mL of this medicine (34.8 mg) is equivalent to 0.4 mL of wine, at the maximum posology of 20 mg of midazolam.

The small amount of alcohol in this medicine will not have any noticeable effects.

This medicine contains 400 mg of gammadex in each ampoule which is equivalent, at the recommended dosing, to 10 mg/kg/day and is below the permitted daily exposure. Therefore, even if Ozalin would be inadvertently used with 0.5 mg/kg dose, the amount of gammadex would not exceed the permitted daily exposure.

3. How to use Ozalin

Instruction for use

Ozalin must be given by mouth.

Ozalin will be given to your child by a healthcare professional. It will be given in a place that has the equipment needed to monitor your child and to treat any side effects.

Ozalin is not for self-administration.

Your child should be accompanied by an adult upon discharge and leave the treatment room only after receiving authorisation from the doctor.

4. Possible side effects

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

The following side effects may occur when administering midazolam. Their frequency has not been determined. It cannot be estimated on the basis of data currently available.

Nervous system disorders:

- Prolonged/over sedation,
- Agitation, restlessness, hostility, rage or aggression, excitement, confusion, euphoria (an excessive feeling of happiness or excitement), or hallucinations (seeing and possibly hearing things that are not really there),
- Drowsiness, somnolence,
- Dizziness,
- Difficulty in co-ordinating muscles,
- Vertigo,
- Speech disorders,
- Dry mouth,
- Salivation,
- Urinary incontinence,
- Headache,
- Temporary memory loss.

Immune system disorders

- Hypersensitivity reactions and angioedema may occur in susceptible individuals.

- **Chest pain as a sign of a serious allergic reaction called Kounis syndrome has been observed.**

Cardiac disorders:

- Modified heart rate (slow or accelerated heart rate).

Respiratory disorders:

- Laryngospasm (tightening of the vocal cords causing difficult and noisy breathing), breathing difficulties (slow breathing), wheezing,
- Noisy breathing,
- Hiccups.

Gastrointestinal disorders:

- Vomiting,
- Nausea.

Eye disorders:

- Blurred vision,
- Double vision.

Skin disorders:

- Itching, skin rash with red, raised, itchy bumps (urticarial reaction),
- Skin rash.

General disorders and administration site conditions:

- Unusual tiredness
- Feeling of weakness.

Reporting of side effects

If your child gets any side effects, talk to your child's doctor or pharmacist. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the national reporting system.

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 Ozalin

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

Do not use this medicine after the expiry date which is stated on the ampoule label, the blister or the carton after EXP. The expiry date refers to the last day of that month.

Store in the original package in order to protect from light. Do not store above 25°C. Do not refrigerate or freeze.

6. Contents of the pack and other information

What Ozalin contains

- The active substance is midazolam.
- The other ingredients are: citric acid monohydrate, gammadex, sucralose, orange flavour (contains notably 70-80% ethanol), sodium hydroxide (for pH-adjustment), water for injections

What Ozalin looks like and contents of the pack

Ozalin is presented as one 5 ml amber glass ampoule, one filter straw and one oral applicator packaged together into an individual blister.

Ozalin is marketed as 3 different presentations:

- pack of one blister
- pack of five blisters
- pack of ten blisters

Not all pack sizes may be marketed.

Marketing Authorisation Holder and Manufacturer

Marketing Authorisation Holder

ISTITUTO GENTILI S.R.L.

Via San Giuseppe Cottolengo 15
20143 Milan
Italy

Manufacturer

VALDEPHARM

Parc Industriel d'Incarville, 27106 Val-De-Reuil – France

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

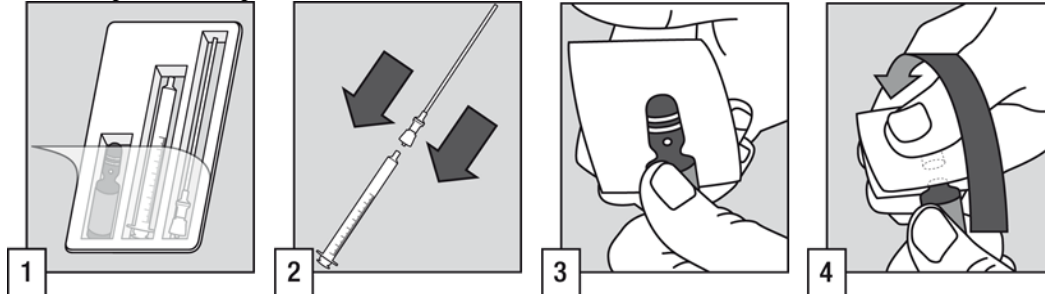
Austria	OZASED® 2 mg/ml Lösung zum Einnehmen im Einzeldosisbehältnis
Belgium	Ozalin 2 mg/ml solution buvable en récipient unidose / drank in verpakking voor éénmalig gebruik / Lösung zum Einnehmen im Einzeldosisbehältnis
Denmark	Ozalin 2 mg/ml oral opløsning i enkelt-dosisbeholder
Finland	Ozalin 2 mg/ml oraaliliuos kerta-annospakkaus
France	Ozalin 2 mg/ml solution buvable en récipient unidose
Germany	Ozalin 2 mg/ml Lösung zum Einnehmen im Einzeldosisbehältnis
Greece	Ozalin 2 mg/ml πόσιμο διάλυμα σε περιέκτη μίας δόσης
Ireland	Ozalin 2 mg/ml oral solution in single-dose container
Italy	Ozased 2 mg/ml soluzione orale in contenitore monodose
Norway	Ozalin 2 mg/ml mikstur, oppløsning i endosebeholder
Poland	OZASED, 2 mg/ml, roztwór doustny w pojemniku jednodawkowym
Portugal	Ozalin 2 mg/ml solução oral em recipiente unidose
Spain	Ozalin 2 mg/ml solución oral en envase unidosis
The Netherlands	Ozalin 2 mg/ml drank in verpakking voor eenmalig gebruik

This leaflet was last revised

The following information is intended for healthcare professionals only:

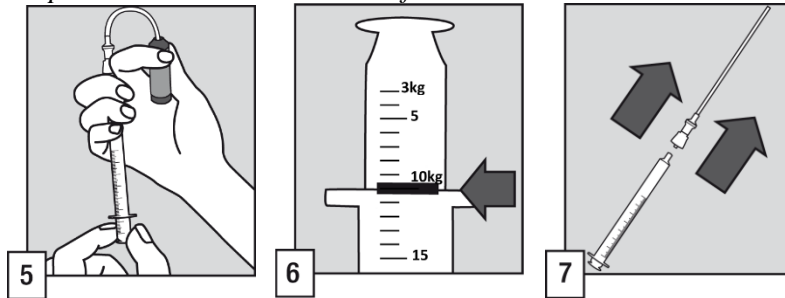
The solution should be visually inspected before use. Do not use this medicine if you notice any visible signs of deterioration in the solution or packaging. Ozalin should be only administered with its dedicated, specific oral applicator **graduated in kg**

How to open the ampoule

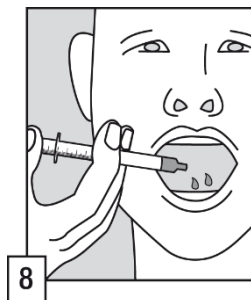


- (1) The administration to the patient requires use of the ampoule, the filter straw and the oral applicator.
- (2) Connect the filter straw on the end-piece of the oral applicator.
- (3) Tap the top of the ampoule to ensure all the liquid has flowed to the bottom. Cover the top of the ampoule with a compress and place the thumb of one hand on the white dot.
- (4) Hold the ampoule firmly with the white dot pointing upwards and facing you. Push back on the neck of the ampoule and it will open easily.

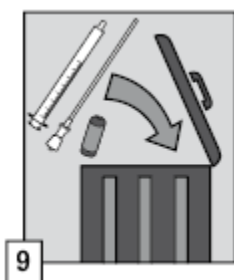
Preparation and administration of the solution



- (5) Insert the filter straw into the ampoule. Before adjusting the dosage and in order to eliminate the possible air in the filter straw, a short pumping with the applicator (fill and empty) of the solution inside the ampoule is recommended.
- (6) While holding the ampoule in an upright position, fill the oral applicator to the graduation mark corresponding to the **weight of the patient in kilograms (kg)**. Align the line mark with the top of the flange to take the correct dose.
- (7) Remove the filter straw from the end piece of the oral applicator.



- (8) Empty the contents of the oral applicator into the patient's mouth. The solution should be swallowed immediately.



- (9) After use, discard the ampoule, filter straw, oral applicator and any unused contents into a container prepared for this purpose according to the local requirements for controlled substances and pharmaceutical accessories.

Dosage

The dose must be adapted to the patient's weight.

Ozalin should be used orally at a single dose of 0.25 mg/kg in children from the age of six months. The maximum dose should not exceed 20 mg of midazolam (corresponding to 2 ampoules), even for children and adolescents weighing more than 80 kg.

In obese children and adolescents, the dose should be given according to actual body weight, up to the limit of 20 mg.

The oral applicator is **graduated in kilograms, from 3 kg to 40 kg body weight**, with three types of graduation marks:

- A small graduation mark corresponding to 1 kg, *i.e.*: 0.25 mg of midazolam,
- An intermediate graduation mark corresponding to 5 kg, *i.e.*: 1.25 mg of midazolam,
- A large graduation mark corresponding to 10 kg, *i.e.*: 2.50 mg of midazolam

For patients above 40 kg, 2 ampoules are needed. The minimal dose to be sampled from an ampoule should correspond to a 3 kg dose. For patients weighing 41 and 42 kg, needing more than one ampoule, take a dose lower than 40 kg in the first ampoule and the supplement to dose in the second ampoule, see examples below:

- For a patient of 41 kg, it is recommended to take 30 kg in the first ampoule and 11 kg in the second ampoule
- For a patient of 42 kg, take a dose corresponding to 30 kg in the first ampoule and 12 kg in the second ampoule.

The oral applicator and filter straw are single use sampling and administration devices.

Ozalin should be administered on average 30 minutes before the procedure or anaesthesia.

Ozalin is not recommended in new-borns (preterm and term) and in infants under 6 months of age.

In case of overdose, vomiting should be induced (as soon as possible and in any event within an hour of the oral administration of midazolam) if the patient is conscious, or gastric lavage undertaken while protecting the airways if the patient is unconscious. If gastric lavage is not effective, activated charcoal should be administered to reduce absorption.

Flumazenil, a benzodiazepine antagonist, is indicated in case of severe intoxication accompanied by respiratory depression or coma. This treatment should only be administered under close supervision and in accordance with local guidelines.