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
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'.

Ozalin contains a very small amount of alcohol (ethanol). The ethanol is a component of the orange flavour in the formulation (in mg/5ml) which is added as 21.7 mg/ampoule. Ethanol is 70-80 % of the orange flavour, so ethanol is 15.2-17.4 mg/ampoule.
This medicine contains approximately 16 mg of alcohol (ethanol) per ampoule Ozalin (2 mg midazolam/ml and 10 mg /5 ml, respectively) which is equivalent to 16 mg/5 ml or 0,016 g/5 ml (0,0032 -> 0,32 % w/v or 3,2 ‰ w/v).
A dose of 10 mg Ozalin administered to a child 11 years of age and weighing 40 kg would result in exposure to 0,32 mg/kg of ethanol. The amount of 0,32 mg/kg in this medicine is equivalent to 0,2 ml of wine. (1/1000 of a glass of wine (210 ml, 10% w/v = 12,5% v/v)).
The amount of alcohol in this medicine is not likely to have an effect in adolescents, and its effects in children and infants are not likely to be noticeable.

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:
- General allergic reactions (skin reactions, heart and blood system reactions, wheezing).

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.
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 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.

OZALIN must be used immediately after opening the ampoule. Any portion of the contents remaining after use must be discarded.

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
PRIMEX PHARMACEUTICALS OY
Mannerheimintie 12 B
FI-00100 Helsinki
Finland

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

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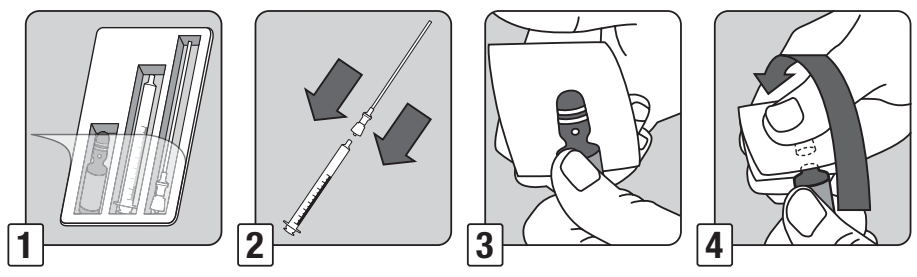
The following information is intended for healthcare professionals only:

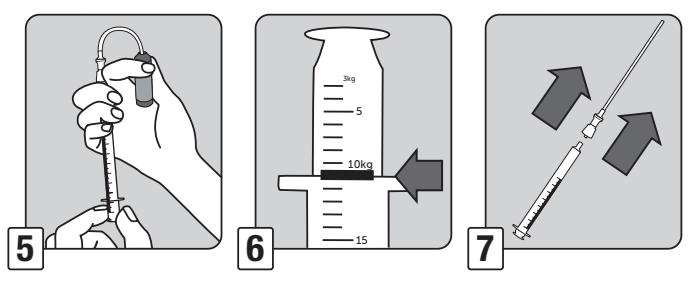
The solution should be visually inspected before use. Do not use this medicine if you notice any visible signs of deterioration in the solution or packaging. OZALIN should be only administered with its dedicated, specific oral applicator **graduated in kg**

How to open the ampoule

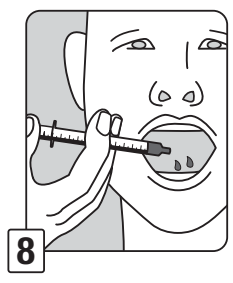


1. The administration to the patient requires use of the ampoule, the filter straw and the oral applicator.
2. Connect the filter straw on the end-piece of the oral applicator.
3. Tap the top of the ampoule to ensure all the liquid has flowed to the bottom. Cover the top of the ampoule with a compress 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.

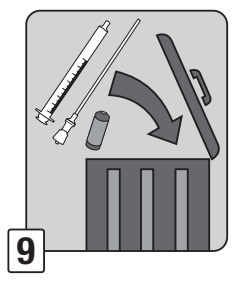
Preparation and administration of the solution



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 most cases of overdosing, monitoring of vital signs is sufficient.

In more severe cases of overdose, special attention should be paid to respiratory and cardiovascular functions in an intensive care unit.

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.

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