Package leaflet: Information for the user

Midazolam Sandoz 1 mg/ml, oplossing voor injectie of infusie
Midazolam Sandoz 5 mg/ml, oplossing voor injectie of infusie

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, pharmacist 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, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet
1. What [nationally completed name] is and what it is used for
2. What you need to know before you use [nationally completed name]
3. How to use [nationally completed name]
4. Possible side effects
5. How to store [nationally completed name]
6. Contents of the pack and other information

1. What [nationally completed name] is and what it is used for

[Nationally completed name] contains the active substance midazolam and belongs to a group of medicines known as benzodiazepines. It is a short-acting medicine that induces sedation – a state of calm, drowsiness or sleep - and relieves anxiety and muscle tension. It has anticonvulsant effects and causes loss of memory for recent events.

[Nationally completed name] is used for:
- conscious **sedation** during a medical test or procedure, in adults and children
- sedation in intensive care units, in adults and children
- **anaesthesia** in adults, used alone or with other anaesthetic medicines
- sedation before induction of anaesthesia, in adults and children

2. What you need to know before you are given [nationally completed name]

You must not be given [nationally completed name]
if you are/have:
- **allergic** to:
  - midazolam or any of the other ingredients of this medicine (listed in section 6)or

  - other medicines also belonging to the group of so called benzodiazepines. These have active substance names ending with “azepam”, such as diazepam, nitrazepam
- **acute** or **severe breathing problems** and you are going to have [nationally completed name] for conscious sedation

If you are not sure, talk to your doctor or nurse before you are given this medicine.

Warnings and precautions
[Nationally completed name] should be used only when age- and size-appropriate resuscitation facilities are available due to the possibility of life-threatening side effects, see also section 4. Administration of [nationally completed name] may depress myocardial contractility and cause apnoea (suspension of breathing). Severe cardiorespiratory adverse events have occurred. These have included respiratory depression, apnea, respiratory and/or cardiac arrest. To avoid such incidents, the injection should be given slowly and the dose should be as low as possible.

When [nationally completed name] is given as a premedication, you will be checked closely to how you respond and to ensure you have received the right dose as the sensitivity varies depending on the patient.

Paradoxical reactions and anterograde amnesia (loss of memory for recent events) have been reported to occur with midazolam (see section 4.).

Long term treatment:
If you receive long-term [nationally completed name], you may become tolerant meaning that [nationally completed name] becomes less effective or you may become dependent upon this medicine.
After treatment for a long time (such as in an intensive care unit) withdrawal symptoms may occur. Your doctor will reduce your dose gradually to avoid this happening to you. See section 3 under the headline “Stopping [nationally completed name]” for further information.

Talk to your doctor or nurse before [nationally completed name] is given if you are/have:
- **over 60 years** of age
  Patients of this age require lower doses and careful monitoring for changes in vital functions.
- a **long term illness** or are **debilitated**, such as
  - breathing problems
    Please note that [nationally completed name] must not be used in breathing problems described above under “You must not be given [nationally completed name]”.
  - kidney failure
  - reduced liver or heart function

  Debilitated patients or those with long term illness require lower doses and careful monitoring for changes in vital functions.
- a certain **muscle weakness** called myasthenia gravis

- a history of **alcohol or drug abuse**
  [Nationally completed name] should be avoided in patients with such history
  - taking any other medicines including those not prescribed by your doctor, see "Other medicines and [nationally completed name]" for more information
- a **temporary absence of breathing during sleep** (sleep apnoea)
- pregnant or think to be pregnant.

Children
Special care needs to be taken if [nationally completed name] is used in babies or children.
Tell your doctor or nurse if your child is to be given this medicine and:
- has heart and respiratory problems
  Your child will be carefully monitored and the dose will be adjusted specially.
- is under 6 months of age or a preterm infant
  - [nationally completed name] is only recommended in children under 6 months for sedation in intensive care units.
  - Very gradual dosing and special monitoring of breathing and oxygen levels is required, because these patients are more likely to develop breathing problems.

Other medicines and [nationally completed name]
Tell your doctor or nurse if you are taking or have recently taken any other medicines.

Inform your doctor or nurse if you are using any of the following medicines, as they may intensify the effects of [nationally completed name]:
- medicines which calm, induce sleep, relax muscles or treat anxiety and mental disorders
- medicines to aid sleep or those used during anaesthesia, such as etomidate, ketamine, propofol
- medicines to treat mental or anxiety disorders, with sedative effects
- medicines to treat depression
- Carbamazepine or phenytoin (these can be given in the event of convulsions or seizures)
- medicines to treat strong pain or coughing, or used in substitutive treatment
- medicines to treat allergies and sleep disturbances called antihistamines
- medicines to treat fungal infections, with active substance names ending in "azole", such as ketoconazole, voriconazole, fluconazole, itraconazole, posaconazole
- medicines to treat bacterial infections with active substance names ending in "mycin", such as erythromycin, clarithromycin
- diltiazem: a medicine to treat high blood pressure and heart disorders
- medicines to treat high blood pressure which act in the brain
- medicines to treat HIV infections with active substance names ending in "navir", such as saquinavir
- medicines to treat Hepatitis C virus infections ending in "previr", such as boceprevir, telaprevir
- atorvastatin: a medicine to lower cholesterol levels
- rifampicin: a medicine to treat tuberculosis
- St. John's wort: a herbal medicine to treat depression

- inhaled anaesthetics

[Nationally completed name] with food and drink and alcohol
Do not drink any alcohol if you have been given [nationally completed name]. Alcohol can markedly increase the sedative effect of [nationally completed name] and may cause problems with your breathing.

Pregnancy and breast-feeding and fertility
- **Pregnancy**
  Talk to your doctor if you are pregnant, or think you are pregnant. Your doctor will decide if this medicine is suitable for you.
  If your doctor decides that you should be given this medicine during late pregnancy, labour or caesarean section, you might have inhalation risk and your baby might have an irregular heartbeat, hypotonia (resistance to movement in a muscle), feeding difficulties, a low body temperature and respiratory depression.
  If you have passed through prolonged treatment during last phase of pregnancy with this medicine, your baby may develop physical dependence and risk of withdrawal symptoms after birth.

- **Breast-feeding**
  Do not breast-feed for 24 hours after being given [nationally completed name] as it may pass into your breast milk.

- **Fertility**
  [nationally completed name] does not affect fertility according to present data.

Driving and using machines
- **Do not drive or use machines** until you are completely recovered. Your doctor should advise as to when you may resume these activities.
- You should always be taken home by a responsible adult following treatment.

[Nationally completed name] can cause sleepiness, forgetfulness or affect concentration and co-ordination. This may affect your performance at skilled tasks such as driving or operating machinery.

Important information about some of the ingredients of [nationally completed name]
This medicine contains less than 1 mmol sodium (23 mg) per ml, i.e. essentially “sodium-free”.

3. How to take [nationally completed name]

This medicine should be given only by an experienced doctor or nurse. It should be given in a hospital, clinic or surgery, equipped to:
- monitor and support the patient’s breathing, heart and circulation
- recognise and manage expected side effects of anaesthesia

The recommended dose is:
The doctor will decide the dose individually dependent on:
- reason for your treatment
- type of sedation required
- patient's age, weight and general state of health
- concomitant medication
- how you react to [nationally completed name]
- whether other medicines are needed at the same time

If you are to receive strong pain killers, you will receive these first and then have your [nationally completed name] dose individually adjusted.

Route and method of administration
- intravenous: by slow injection into a vein
- infusion: through a tube into one of your veins
- intramuscular: by injection into a muscle
- rectal: into your rectum

[Nationally completed name] will usually be given into the vein in children 12 years and younger. It may be given into the rectum in this age group if being used for sedation before anaesthesia. Please note the information in section 2, under the heading "Children".

Instructions for proper use
[Nationally completed name] is **compatible** with the following solutions for infusion:
- sodium chloride 0.9 % (9 mg/ml) solution
- glucose 5 % (50 mg/ml) solution
- glucose 10 % (100 mg/ml) solution
- Ringer solution
- Hartmann's solution

[Nationally completed name] is **not compatible** with the following solutions for infusion:
- dextran 6% w/v (with 0.9% sodium chloride) in dextrose
- alkaline solutions for injection. Midazolam precipitates in sodium bicarbonate.

To avoid potential incompatibility with other solutions, [nationally completed name] must not be mixed with other solutions except those mentioned above.
[Nationally completed name] ampoules are for single use only. Discard any unused solution.
The ampoule and the solution should be visually inspected prior to use. Only intact ampoules and clear solutions without particles and discoloration should be used.

If you receive more [nationally completed name] than you should
Inform your doctor, who will treat you appropriately, if you experience signs of overdose:
- feeling drowsy
- difficulty in controlling movements or speaking
- loss of reflexes
- involuntary eye movements
- low blood pressure (can cause dizziness or lightheadedness)
- slowed or stopped breathing or heartbeat

- loss of consciousness (coma)

Overdose may require intense monitoring of vital signs, symptomatic treatment of cardiorespiratory effects and use of a benzodiazepine antagonist.

Stopping [nationally completed name]

If [nationally completed name] is given for a long time:

- the medicine may become less effective and not work as well
- you may become dependent upon this medicine and get withdrawal symptoms
  If treatment is stopped suddenly, or the dose lowered too quickly, you may get the following **withdrawal symptoms**:
  - headache
  - muscle pain
  - anxiety
  - tension
  - restlessness
  - confusion
  - irritability
  - difficulty sleeping
  - mood swings
  - hallucinations: seeing and possibly hearing things that do not exist
  - fits

Your doctor will reduce your dose gradually to avoid these effects occurring.

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. The following side effects may occur with this medicine (frequency not known, cannot be estimated from the available data):

STOP having [nationally completed name] and see/tell your doctor straight away if you notice any side effect, highlighted in bold print. They can be life-threatening and you may need urgent medical treatment.

- **severe allergic reaction (anaphylactic shock)**
  Signs are sudden rash, itching or nettle-rash; swelling of the face, lips, tongue or other parts of the body. You may also have shortness of breath, wheezing or trouble breathing, or a pale skin, a weak and rapid pulse, or feeling of loss of consciousness. Additionally, you may experience chest pain, which can be a sign of a potentially serious allergic reaction called kounis syndrome.
- **heart attack**
  Signs are chest pain which may spread to your neck and shoulders and down your left arm.
- **breathing problems** or complications
- **larynx spasm**

These life-threatening side effects are more likely in patients over 60 years of age, or patients with breathing or heart problems. This occurs particularly if the injection is given too fast or at a high dose.

You may experience any of the other following side effects listed below.

Nervous system and mental disorders
- reduced alertness
- confusion
- excessive feeling of happiness or excitement (euphoria)
- changes in sex drive
- tiredness, drowsiness and prolonged sedation
- seeing and possibly hearing things that are not exist (hallucinations)
- headache
- dizziness
- difficulty co-ordinating muscles
- fits in premature infants and new-born babies
- temporary memory loss has been reported. The duration of memory loss depends upon duration of treatment and dose. You may experience this after your treatment. In isolated cases, this has lasted for a long time.
- Restlessness, hostility, anger or aggression. You may also experience muscle cramps or muscle tremors without having control over them. These effects are more likely if you have received a high dose of [nationally completed name] or if it has been administered too quickly. It is also more likely in children and older people.
- Contact your doctor if you notice that you become dependent on this medicine or if you notice that you become insensitive to the effects and therefore need to increase the dose.

Heart and circulatory conditions
- slow heart rate
- cardiac arrest
- redness of the face and neck,
- fainting
- low blood pressure. This can cause dizziness and a light feeling in the head.
- clotting or inflammation of a vein (thrombophlebitis, thrombosis)

Respiratory system disorders
- hiccups
- shortness of breath, breathlessness

Gastrointestinal disorders
- dry mouth
- constipation
- nausea, vomiting

Skin and subcutaneous disorders

- itching
- skin rash, nettle-rash
- skin reddening and pain at the injection site

General disorders and administration site disorders
- Allergic reactions including rash and wheezing
- Withdrawal symptoms (see ' Stopping [nationally completed name] in section 3)
- Falling and fractures. The risk is increased if you are simultaneously taking other medicines known to cause drowsiness (e.g. tranquilizers or sleep aids), or if you are simultaneously taking alcohol.

Elderly
Elderly people taking a benzodiazepine group drug, such as [nationally completed name], have a higher risk of falling and bone fractures.
Life-threatening side effects are more likely in adults over 60 years of age.

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 national reporting system listed in Appendix V*. By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store [nationally completed name]

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 and on the carton after “EXP”. The expiry date refers to the last day of that month.

Store in the original packaging in order to protect from light.

After opening of the ampoule:
From a microbiological point of view, the medicinal product should be used immediately. If not used immediately, in-use storage times and conditions are the responsibility of the user.

After dilution:
Chemical and physical in-use stability of the dilutions has been demonstrated for 24 hours at room temperature (15 – 25°C) or for 3 days at +2 °C to +8 °C.
From a microbiological point of view, the product should be used immediately after dilution. If not used immediately, in-use storage times and conditions prior to use are the responsibility of the user and would normally not be longer than 24 hours at 2°C to 8°C unless dilution has taken place in controlled and validated aseptic conditions.

Midazolam ampoules are intended for single use. Discard any unused solution.

Do not use this medicine if you notice that the ampoule is found leaking, or the solution is not clear and not free from particles or if you notice any discoloration of 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 [nationally completed name] contains

The active substance is midazolam.

[1 mg/ml solution for injection or infusion]:
Each ampoule of 5 ml solution for injection or infusion contains 5 mg of midazolam (as hydrochloride).

[5 mg/ml solution for injection or infusion]:
Each ampoule of 1 ml solution for injection or infusion contains 5 mg of midazolam (as hydrochloride).
Each ampoule of 3 ml solution for injection or infusion contains 15 mg of midazolam (as hydrochloride).
Each ampoule of 10 ml solution for injection or infusion contains 50 mg of midazolam (as hydrochloride).

[1 mg/ml solution for injection or infusion]:
The other ingredients are sodium chloride, hydrochloric acid and water for injections.

[5 mg/ml solution for injection or infusion]:
The other ingredients are sodium chloride, hydrochloric acid, sodium hydroxide and water for injections.

What [nationally completed name] looks like and contents of the pack

This medicinal product is a clear, slightly yellow solution contained in a clear glass ampoule.

[1 mg/ml solution for injection or infusion]:
Pack sizes:
5 x 5 ml
[5 mg/ml solution for injection or infusion]:
Pack size:
5 x 1 ml
5 x 3 ml
5 x 10 ml

Not all pack sizes may be marketed.

Houder van de vergunning voor het in de handel brengen en fabrikant

Houder van de vergunning voor het in de handel brengen
Sandoz B.V., Veluwezoom 22, 1327 AH Almere, Nederland

Fabrikant
Salutas Pharma GmbH
Otto-von-Guericke Allee 1
39179 Barleben
Duitsland

Sandoz GmbH
Biochemiestraße 10
6250 Kundl
Oostenrijk

EVER Pharma Jena GmbH
Otto-Schott-Straße 15
07745 Jena
Duitsland

Ever Pharma Jena GmbH,
Brüsseler Straße 18,
07747, Jena
Duitsland

In het register ingeschreven onder:

Midazolam Sandoz 1 mg/ml, oplossing voor injectie of infusie	RVG 110832.
Midazolam Sandoz 5 mg/ml, oplossing voor injectie of infusie	RVG 110837.

Dit geneesmiddel is geregistreerd in lidstaten van de EEA onder de volgende namen:

Nederland	Midazolam Sandoz 1 mg/ml, oplossing voor injectie Midazolam Sandoz 5 mg/ml, oplossing voor injectie
Polen	Midazolam Sandoz
Slovenië	Midazolam Lek 1 mg/ml raztopina za injiciranje ali infundiranje Midazolam Lek 5 mg/ml raztopina za injiciranje ali infundiranje

Deze bijsluiter is voor het laatst goedgekeurd in augustus 2023.

The following information is intended for healthcare professionals only

Preparation of solution for infusion
[Nationally completed name] can be diluted with 0.9% sodium chloride solution, glucose 50 mg/ml (5%) or 100 mg/ml (10%) solution, or Ringer or Hartmann solution at a ratio of 15 mg of midazolam to 100-1,000 ml of infusion solution. These solutions remain stable for 24 hours at room temperature, and 3 days at +2 °C to +8 °C. [Nationally completed name] must not be mixed with any solution other than those listed above. In particular, [nationally completed name] must not be diluted with 6% w/v dextran (with 0.9% sodium chloride) in dextrose or mixed with alkaline injection injections. Midazolam precipitates in sodium bicarbonate.

The ampoule and the solution should be visually inspected prior to use. Only intact ampoules and clear solutions without particles and discoloration should be used.

Shelf life and storage
[Nationally completed name] ampoules are intended for single use only.

Ampoule before opening
Store in the original package in order to protect from light

Ampoule after dilution
Chemical and physical in-use stability of the dilutions has been demonstrated for 24 hours at room temperature (15 – 25°C) or for 3 days at +2 °C to +8 °C.

From the microbiological point of view, the dilutions should be used immediately. If not used immediately, in-use storage times and conditions prior to use are at the responsibility of the user and would normally not be longer than 24 hours at +2 to +8 °C, unless dilution has taken place in controlled and validated aseptic conditions.
In case of continuous intravenous infusion, midazolam injection solution may be diluted in the range of 0.015 to 0.15 mg with one of the solution mentioned above.

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