

PATIENT INFORMATION LEAFLET
Midazolam 1 mg/ml Solution for Injection or Infusion
Midazolam 5 mg/ml Solution for Injection or Infusion
midazolam

Read all of this leaflet carefully before you start taking 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 your 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 or pharmacist or nurse. This includes any possible side effects not listed in this leaflet. See section 4

What is in this leaflet:

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

1. What midazolam is and what it is used for

Midazolam 1 mg/ml & 5 mg/ml Solution for Injection or Infusion contains Midazolam. Midazolam belongs to a group of medicines known as benzodiazepines (sedatives).

It is a short acting medicine that is used to induce sedation (a very relaxed state of calm, drowsiness or sleep) and relieves anxiety and muscle tension.

- Conscious sedation (an awake but very relaxed state of calm or drowsiness during a medical test or procedure) in adults and children
- Sedation of adults and children, in intensive care units
- Anaesthesia in adults, used alone or with other medicines.
- Premedication medicine used to cause relaxation, calm and drowsiness before an anaesthetic) in adults and children.

2. What you need to know before you take midazolam

Do not use midazolam

- If you are allergic (hypersensitive) to midazolam, group of medicines known as benzodiazepines or any other ingredients in the midazolam solution for injection
 - If you have severe difficulties with your breathing and that you are to undergo conscious sedation.
- You must not be given midazolam if any of the above applies to you. If you are not sure, talk to your doctor or nurse before you are given this medicine.

Take Special Care with midazolam

Midazolam should be used only when age- and size-appropriate resuscitation facilities are available. Administration of midazolam may depress myocardial contractility (ability of heart muscle to contract) and cause apnoea (pauses in breathing). Severe cardio respiratory adverse events have occurred on rare occasions. 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.

Special care needs to be taken if midazolam is used in babies or children. Let your doctor know if your child has a cardiovascular disease. Your child will be carefully monitored and the dose will be adjusted specially. Patients under 6 months old in sedation in Intensive Care Unit are more likely to develop breathing problems, so they will be dosed very gradually and their breathing and oxygen levels observed.

When midazolam 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 of the patient.

The use of midazolam is not recommended in neonates and children up to 6 months of age.

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

Before midazolam is given, let your doctor or nurse know if you:

- are over 60 years of age
- have a long term illness or are debilitated (for example, chronic respiratory problems, renal, hepatic or cardiac disorders).
- have a myasthenia gravis (neuromuscular disease characterized by a muscle weakness).
- have a history of alcohol or drug abuse.
- are taking any other medicines including those not prescribed by your doctor (for more information see section 'Using other medicines')
- are pregnant or think being pregnant.

If any of the above applies to you, or if you are not sure, talk to your doctor or nurse before you are given midazolam.

Long term treatment

If you receive long-term midazolam, you may become tolerant (midazolam becomes less effective) or you may become dependent upon this medicine.

After treatment for a long time (such as in an intensive care unit) the following withdrawal symptoms may occur: headaches, muscle pain, anxiety, tension, restlessness, confusion, irritability, inability to sleep, mood changes, hallucinations and convulsions. Your doctor will reduce your dose gradually to avoid these effects happening to you.

Using other medicines:

Please tell your doctor if you are taking or have recently taken any other medicines, including medicines obtained without a prescription and herbal medicines.

This is extremely important, as using more than one medicine at the same time can strengthen or weaken the effect of the medicines involved.

In particular, tell your doctor or nurse if you are taking any of the following medicines:

- tranquilisers (for anxiety or to help you sleep)
- hypnotics (medicines to make you sleep)
- sedatives (to make you feel calm or sleepy)
- antidepressants (medicines for depression)
- narcotic analgesics (very strong pain killers)
- antihistamines (used to treat allergies)
- medicines to treat fungal infections (ketoconazole, voriconazole, fluconazole, itraconazole, posaconazole)
- macrolide antibiotics (such as erythromycin or clarithromycin)
- diltiazem (used to treat high blood pressure)
- medicines for HIV called protease inhibitors (such as saquinavir)
- atorvastatin (used to treat high cholesterol)
- rifampicin (used to treat mycobacterial infections such as tuberculosis)
- the herbal medicine St. John's Wort.

If any of the above apply to you, or if you are not sure, talk to your doctor or nurse before you are given midazolam.

Operations

If you are going to have an inhaled anaesthetic (one that you breathe in) for an operation or for dental treatment, it is important to tell your doctor or dentist that you have been given midazolam.

Using midazolam with food and drink

While you are using midazolam you must not drink any alcohol, since alcohol can markedly increase the sedative effect of midazolam.

Pregnancy and breast-feeding and fertility:

- If you are pregnant or breast-feeding or think you may be pregnant, ask your doctor or pharmacist for advice before taking this medicine. Your doctor will decide if you should be given this medicine or not. during late pregnancy, labour or caesarean section, you might have an inhalation risk and your baby might have an irregular heart beat, hypotonia (state of low muscle tone), feeding difficulties, a low body temperature and respiratory depression (difficulty in breathing).
- 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.
- Midazolam may pass into breast milk, therefore, if you are breast feeding you should not do so for 24 hours after receiving this medicine.

Driving and using machines:

This medicine may make you sleepy, forgetful or affect your concentration and co-ordination. This may affect your performance at skilled tasks, e.g. driving or operating machinery. After midazolam administration you should not drive a vehicle or operate a machine until completely recovered. Your doctor should advise you when you can start these again. You should always be accompanied to home by a responsible adult after your treatment.

Important information about some of the ingredients of midazolam solution for injection

This medicinal product contains less than 1 mmol sodium (23 mg) per dose i.e. essentially 'sodium free'.

3. How to use midazolam

Midazolam should be administered only by experienced physicians in a setting fully equipped for the monitoring and support of respiratory and cardiovascular function and by persons specifically trained in the recognition and management of expected adverse events.

Dosage and route of administration

Your doctor will decide on a suitable dose for you. Doses vary considerably and will depend on the planned treatment and the sedation required. Your weight, age, general condition of health, concomitant medication, response to the drug and whether other medicines are required at the same time will also influence the dose that you receive.

If you are to receive strong painkillers, you will receive these first and then have your midazolam dose adjusted specially for you.

Midazolam is given slowly, by injection into a vein (intravenously), by a drip (infusion), injection into a muscle (intramuscular) or via rectal administration.

You should always be taken home by a responsible adult after your treatment.

Children and babies

- In infants and babies under 6 months of age midazolam is only recommended for sedation in intensive care units. The dose will be given gradually into a vein.
- Children 12 years and under will usually be given midazolam into a vein. When midazolam is used for premedication (to cause relaxation, calm and drowsiness before an anaesthetic) it may be given into the back passage (rectum).

If you use more midazolam than you should

Your medicine will be given by a doctor or nurse.

If you accidentally got an overdose, this could lead to sleepiness, ataxia (in coordination of voluntary muscular action), dysarthria (speech disorder) and nystagmus (involuntary eye movements), loss of reflexes, apnoea (suspension of breathing), hypotension (low blood pressure), cardio respiratory depression and in rare cases coma. Overdose may require intense vital sign monitoring and symptomatic treatment of cardio respiratory effects and use of benzodiazepine antagonist.

If you stop using midazolam

Sudden discontinuation of treatment can be accompanied by withdrawal symptoms such as headache, muscular pain, anxiety, tension, restlessness, confusion, mood swings, hallucinations & convulsions, rebound insomnia, irritability and convulsions. Since the risk of withdrawal symptoms occurring is greater if treatment is discontinued abruptly, dose should be reduced gradually when treatment is being discontinued.

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

4. Possible side effects

Like all medicines midazolam can cause side effects, although not everybody gets them. The following undesirable effects have been reported (frequency not known).

Stop having midazolam and see a doctor straight away if you notice any of the following side effects. They can be life-threatening and you may need urgent medical treatment:

- Anaphylactic shock (a life-threatening allergic reaction). Signs may include a sudden rash, itching or lumpy rash (hives) and swelling of the face, lips, tongue or other parts of the body. You may also have shortness of breath, wheezing or trouble breathing.
- Heart attack (cardiac arrest). Signs may include chest pain which may spread to your neck and shoulders and down your left arm.
- Breathing problems or complications (sometimes causing the breathing to stop).
- Choking and sudden blockage of the airway (laryngospasm).

Life-threatening side effects are more likely to occur in adults over 60 years of age and those who already have breathing difficulties or heart problems, particularly if the injection is given too fast or at a high dose

Other possible side effects***Immune System disorders:***

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

Psychiatric disorders

- confusion
- euphoria (an excessive feeling of happiness or excitement)
- hallucinations (seeing and possibly hearing things that are not really there)
- agitation
- restlessness
- hostility, rage or aggression
- excitement
- drug dependence, abuse.

Nervous system disorders :

- drowsiness and prolonged sedation
- reduced alertness
- headache
- dizziness

- difficulty co-ordinating muscles
- fits (convulsions) in premature infants and new-born babies
- temporary memory loss. How long this lasts depends on how much midazolam you were given. You may experience this after your treatment. In isolated cases this has been prolonged (lasted for a long time).

Cardiac and Vascular disorders :

- low blood pressure
- slow heart rate
- redness of the face and neck (flushing), fainting or headache.

Gastrointestinal disorders:

- nausea
- vomiting
- constipation
- dry mouth.

Skin and subcutaneous tissue disorders:

- rash
- hives (lumpy rash)
- itchiness.

Musculoskeletal and connective tissue disorders:

- muscle spasms and muscle tremors (shaking of your muscles that you cannot control).

General disorders and administration site conditions:

- tiredness (fatigue)
- redness
- swelling of the skin
- blood clots or pain at the injection site.

Injury Poisoning and Procedural Complications:

- Patients taking benzodiazepine medicines are at risk of falling and breaking bones. This risk is increased in the elderly and those taking other sedatives (including alcohol).

Reporting of suspected adverse reactions:

If you get any side effects, talk to your doctor, pharmacist or nurse. 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 midazolam injection

- Keep this medicine out of the sight and reach of children.
- Do not use midazolam after the expiry date (EXP) which is stated on the carton and ampoule. The expiry date refers to the last day of that month.
- Store in the original package in order to protect from light.
- The product is for single use and any remaining solution should be discarded. Do not use midazolam solution for injection or infusion if container is found leaking, solution is not clear with visible particles or any discoloration of the solution.

Medicines should not be disposed of via wastewater or household waste. Ask your pharmacist how to dispose of medicines no longer required. These measures will help to protect the environment.

6. Contents of the pack and other information

What midazolam contains:

The active ingredient is midazolam (as midazolam hydrochloride).

For 1 mg/ml

Each ml of solution for injection contains 1 mg of midazolam (as midazolam hydrochloride)

Presentations 5 ml

Amount of midazolam 5 mg

For 5 mg/ml

Each ml of solution for injection contains 5 mg of midazolam (as midazolam hydrochloride)

Presentations 1 ml 3 ml 10 ml

Amount of midazolam 5 mg 15 mg 50 mg

The other ingredients include water for injections, sodium chloride, sodium hydroxide (for pH adjustment) and concentrated hydrochloric acid (for pH adjustment).

What midazolam solution for injection looks like and contents of the pack:

Midazolam solution for injection is a clear colourless to pale yellow solution filled in a clear glass ampoule.

Midazolam solution for injection is available in pack of 10 X 5 ml ampoules for 1 mg/ml formulation

Midazolam solution for injection is available in pack of 10 X 1ml, 10 X 3 ml, 10 X 10 ml and 1 X 10 ml ampoules for 5 mg/ml formulation.

The ampoule are available in blister/ tray pack.

Not all pack sizes may be marketed.

Manufacturing authorisation holder and manufacturer:

Accord Healthcare Limited,
Sage House, 319 Pinner Road,
North Harrow,
Middlesex, HA1 4HF,
UK

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

Name of the member state	Name of the medicinal product
Austria	Midazolam Accord 1 mg/ml, Injektionslösung oder Infusionslösung
	Midazolam Accord 5 mg/ml, Injektionslösung oder Infusionslösung
Belgium	Midazolam Accord Healthcare 1 mg/ml, solution pour injection ou perfusion/ oplossing voor injectie of infusie/ Lösung zur Injektion oder Infusion
	Midazolam Accord Healthcare 5 mg/ml, solution pour injection ou perfusion/ oplossing voor injectie of infusie/ Lösung zur Injektion oder Infusion
Cyprus	Midazolam Accord 1 mg/ml, ενέσιμο διάλυμα ή διάλυμα για έγχυση
	Midazolam Accord 5 mg/ml, ενέσιμο διάλυμα ή διάλυμα για έγχυση
Czech Republic	Midazolam Accord 1 mg/ml, injekční roztok nebo infuzi
	Midazolam Accord 5 mg/ml, injekční roztok nebo infuzi
Germany	Midazolam Accord 1 mg/ml Injektionslösung oder Infusionslösung
	Midazolam Accord 5 mg/ml Injektionslösung oder Infusionslösung
Denmark	Midazolam Accord 1 mg/ml, injektions og infusionsvæske, opløsning
	Midazolam Accord 5 mg/ml, injektions og infusionsvæske, opløsning
Estonia	Midazolam Accord 1 mg/ml, injekcinis ar infuzinis tirpalas
	Midazolam Accord 5 mg/ml, injekcinis ar infuzinis tirpalas
Greece	Midazolam Accord 1 mg/ml, ενέσιμο διάλυμα ή διάλυμα για έγχυση

	Midazolam Accord 5 mg/ml, ενέσιμο διάλυμα ή διάλυμα για έγχυση
Spain	Midazolam Accord 1 mg/ml, para inyección o infusión
	Midazolam Accord 5 mg/ml, para inyección o infusión
Finland	Midazolam Accord 1 mg/ml, injektio- tai infuusioneste/ Lösning för injektion och infusion
	Midazolam Accord 5 mg/ml, injektio- tai infuusioneste/ Lösning för injektion och infusion
Hungary	Midazolam Accord 1 mg/ml, oldatos injekció/ infúzió
	Midazolam Accord 5 mg/ml, oldatos injekció/ infúzió
Ireland	Midazolam 1 mg/ml, Solution for Injection or Infusion
	Midazolam 5 mg/ml, Solution for Injection or Infusion
Italy	Midazolam Accord 1 mg/ml, Soluzione per Iniezione o Infusione
	Midazolam Accord 5 mg/ml, Soluzione per Iniezione o Infusione
Latvia	Midazolam Accord 1 mg/ml, šķīdums injekcijām vai infūzijām
	Midazolam Accord 5 mg/ml, šķīdums injekcijām vai infūzijām
Malta	Midazolam 1 mg/ml, Solution for Injection or Infusion
	Midazolam 5 mg/ml, Solution for Injection or Infusion
The Netherlands	Midazolam Accord 1 mg/ml, oplossing voor injectie of infusie
	Midazolam Accord 5 mg/ml, oplossing voor injectie of infusie
Norway	Midazolam Accord 1 mg/ml, oppløsning til injeksjon og infusjon
	Midazolam Accord 5 mg/ml, oppløsning til injeksjon og infusjon
Poland	Midazolam Accord
Portugal	Midazolam Accord
Sweden	Midazolam Accord 1 mg/ml, Lösning för injektion och infusion
	Midazolam Accord 5 mg/ml, Lösning för injektion och infusion
Slovenia	Midazolam Accord 1 mg/ml, raztopina za injiciranje ali infundiranje
	Midazolam Accord 5 mg/ml, raztopina za injiciranje ali infundiranje
Slovak Republic	Midazolam Accord 1 mg/ml, injekčný alebo infúzny roztok
	Midazolam Accord 5 mg/ml, injekčný alebo infúzny roztok
United Kingdom	Midazolam 1 mg/ml, Solution for Injection or Infusion
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The leaflet was last approved in xx/yyyy.

The following information is intended for medical or healthcare professionals only

Preparation of solution for infusion

Midazolam injection can be diluted with 0.9% sodium chloride solution, 5% or 10% glucose solution, or Ringer or Hartmann solution. In case of continuous intravenous infusion, midazolam injection solution may be diluted in the range of 0.015 to 0.15 mg per ml with one of the solution mentioned above.

. These solutions remain stable for 24 hours at room temperature, and 3 days at 8°C. Midazolam injection must not be mixed with any solution other than those listed above. In particular, midazolam injection must not be diluted with 6% w/v dextran (with 0.9% sodium chloride) in glucose or mixed with alkaline injection injections. Midazolam precipitates in hydrogen carbonate.

The solution for injection should be examined visually before administration. Only solutions without visible particles should be used.

Shelf Life and storage

Midazolam Injection 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 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 product or waste material should be disposed of in accordance with local requirements.