

Package leaflet: Information for the user

Midazolam 2 mg/ml Solution for Injection or Infusion Midazolam 5 mg/ml Solution for Injection or Infusion

Midazolam (as Midazolam hydrochloride)

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

What is in this leaflet

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

1. What Midazolam Injection is and what it is used for

Midazolam Injection belongs to a group of medicines known as benzodiazepines. 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.

This medicine is used for:

- 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 use Midazolam Injection

You must not be given Midazolam Injection:

- if you are allergic (hypersensitive) to midazolam or any of the other ingredients of the medicine (listed in section 6).
 - if you are allergic to other benzodiazepine medicines, such as diazepam or nitrazepam.
 - if you have severe breathing problems and you are going to have Midazolam Injection for conscious sedation.
- You must not be given Midazolam Injection if any of the above apply to you. If you are not sure, talk to your doctor or nurse before you are given this medicine.

Warnings and precautions

Talk to your doctor or nurse before using Midazolam Injection

Children and babies

If your child is going to be given this medicine:

- It is particularly important to tell your doctor or nurse if your child has cardiovascular disease (heart problems). Your child will be carefully monitored and the dose will be adjusted specially.
- Children must be carefully monitored. For infants and babies under 6 months this will include monitoring of breathing and oxygen levels.

Adults

Talk to your doctor or nurse before you are given Midazolam if:

- You are over 60 years of age.
- You have a long term illness (such as breathing problems or kidney, liver or heart problems).
- You are debilitated (have an illness that makes you feel very weak, run down and short of energy).
- You have a condition called 'sleep apnoea syndrome' (where your breathing stops when you are asleep), so you may be closely monitored.
- You have myasthenia gravis (a neuromuscular disease causing muscle weakness).
- You regularly drink large amounts of alcohol or you have had problems with alcohol use in the past. Alcohol can increase the clinical effects of midazolam, possibly including severe sedation that could result in coma or death.
- You regularly take recreational drugs or you have had problems with drug use in the past.
- You are pregnant or think you may be pregnant (see 'Pregnancy and breast-feeding').

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 Injection.

Other medicines and Midazolam Injection

Tell your doctor or nurse if you are taking, have recently taken or might take any other medicines. This includes 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 or antipsychotics (medicines for depression or schizophrenia)
- narcotic analgesics (very strong pain killers)
- cough medicines (such as ones containing codeine)
- antihistamines (used to treat allergies)
- medicines to treat fungal infections (ketoconazole, voriconazole, fluconazole, itraconazole, posaconazole)
- macrolide antibiotics (such as erythromycin, clarithromycin or roxithromycin)
- medicines used to treat high blood pressure and heart disease (such as diltiazem, verapamil and methyldopa)
- medicines for HIV (efavirenz or protease inhibitors, such as saquinavir) medicines for Hepatitis C (protease inhibitors such as boceprevir and telaprevir)
- atorvastatin (used to treat high cholesterol)
- rifampicin (used to treat mycobacterial infections such as tuberculosis)
- ticagrelor (used to prevent heart attack)
- herbal medicine St John's Wort.
- Carbamazepine (used to treat epilepsy and bi-polar disorder)

- phenytoin (used to treat epilepsy)
- prepatent (used to stop you feeling or being sick).

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 Injection.

Concomitant use of Midazolam Injection 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 Midazolam Injection 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.

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 Injection.

Midazolam Injection with alcohol

Do not drink alcohol if you have been given Midazolam Injection. This is because alcohol can increase the sedative effect of Midazolam Injection and may cause problems with your breathing.

Pregnancy and breast-feeding

If you are pregnant or breast-feeding, think you may be pregnant or are planning to have a baby, ask your doctor or nurse for advice before taking this medicine.

Midazolam may harm your unborn baby when used in early pregnancy. When high doses are administered during late pregnancy, labour or caesarean section, you might have an inhalation risk and your baby might have an irregular heartbeat, state of low muscle tone (hypotonia), feeding difficulties, a low body temperature and difficulty in breathing. With prolonged administration during late pregnancy, your baby may develop a physical dependence and risk of withdrawal symptoms after birth.

Do not breast-feed for 24 hours after being given Midazolam Injection. This is because Midazolam Injection may pass into your breast milk.

Driving and using machines

Midazolam may make you sleepy, dizzy, forgetful or affect your concentration and co-ordination. This may affect your performance at skilled tasks such as driving or using machines.

- Do not drive or use machinery until you are completely recovered. Your doctor should advise you when you can start these again.
- Midazolam Injection may make you sleepy, forgetful or affect your concentration and co-ordination. This may affect your performance at skilled tasks such as driving or using machines.
- You should always be taken home by a responsible adult after your treatment.

Talk to your doctor or pharmacist if you are not sure whether it is safe for you to drive while taking this medicine

Lack of sleep or alcohol consumption may further impair your alertness. You should always be taken home by a responsible adult after your treatment.

Important information about some of the ingredients of Midazolam

Midazolam Injection is essentially 'sodium free' as it contains less than 1 mmol sodium (23 mg) per ampoule (small glass bottle).

3. How to use Midazolam Injection

Midazolam Injection should be given only by experienced healthcare professionals (doctor or nurse). It should be given in a place (hospital, clinic or surgery) equipped to monitor and support the patient's breathing, heart and circulation (cardiovascular function) and recognise the signs of and manage the expected side effects of anaesthesia.

Normal adult dose

Your doctor will decide on a suitable dose for you. The dose you are given will depend on why you are being treated and the type of sedation needed. Your weight, age, your state of health, how you respond to Midazolam Injection and whether other medicines are needed at the same time will also influence the dose that you are given.

If you need strong painkillers, you will be given these first and then be given Midazolam Injection. Your doctor will decide on a suitable dose for you.

Midazolam Injection may be given to you in one of four different ways:

- by slow injection into a vein (intravenous injection)
- through a tube into one of your veins (intravenous infusion)
- by injection into a muscle (intramuscular injection)
- into your back passage (rectum).

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 Injection 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 Injection into a vein. When Midazolam Injection is used for premedication (to cause relaxation, calm and drowsiness before an anaesthetic) it may be given into the back passage (rectum).

If too much midazolam is given

Your medicine will be given to you by a doctor or nurse. If you are accidentally given too much Midazolam Injection you may:

- Feel drowsy.
- Lose your co-ordination (ataxia) and reflexes.
- Have problems with your speech (dysarthria).
- Have involuntary eye movements (nystagmus).
- Develop low blood pressure (hypotension).
- Stop breathing (apnoea) and suffer cardiorespiratory depression (slowed or stopped breathing and heartbeat) and coma.

Stopping Midazolam Injection

If you receive long term treatment with Midazolam Injection (are given the medicine for a long time) you may:

- Become tolerant to Midazolam Injection. The medicine becomes less effective and does not work as well for you.
- Become dependent upon this medicine and get withdrawal symptoms (see below).

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

The following effects have been seen with Midazolam use particularly in children and the elderly; restlessness, agitation, irritability, involuntary movements, hyperactivity, nervousness, hostility, delusion, anger, aggressiveness, anxiety, nightmares, hallucinations (seeing and possibly hearing things that are not really there), psychoses (losing contact with reality) and inappropriate behaviour (these reactions are also known as paradoxical reactions, which are outcomes that are opposite to the effects normally expected for the drug). If you experience these, your doctor will consider stopping Midazolam treatment.

Withdrawal symptoms:

Benzodiazepine medicines, like Midazolam Injection, may make you dependent if used for a long time (for instance in intensive care). This means that if you stop treatment suddenly, or lower the dose too quickly, you may get withdrawal symptoms. The symptoms can include:

- headache
- diarrhoea
- muscle pain
- feeling very worried (anxious), tense, restless, confused or bad-tempered (irritable)
- problems with sleeping (insomnia)
- mood changes
- hallucinations (seeing and possibly hearing things that are not there)
- fits (convulsions).

In severe cases of withdrawal, the following can occur: a feeling of losing contact with reality, numbness and tingling of the extremities (e.g. hands and feet), feeling sensitive to light, noise and touch.

4. Possible side effects

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

The following side effects have been reported with this medicine (frequency not known).

Stop having Midazolam Injection 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, 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 (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 problems:

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

Effects on behaviour:

- restlessness, agitation, irritability
- nervousness, anxiety
- agitation
- restlessness
- hostility, anger, aggression or assault
- excitement.
- hyperactivity
- changes in libido
- inappropriate behaviour

Muscle problems:

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

Mental and Nervous system problems:

- confusion, disorientation
- emotional and mood disturbances
- involuntary movements
- euphoria (an excessive feeling of happiness or excitement)
- nightmares, abnormal dreams
- hallucinations (seeing and possibly hearing things that are not really there)
- psychoses (losing contact with reality)
- 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 Injection you were given. You may experience this after your treatment. In isolated cases this has been prolonged (lasted for a long time).
- Drug dependence, abuse.

Heart and circulation problems:

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

Breathing problems:

- shortness of breath
- hiccup.

Stomach, gut and mouth problems:

- feeling sick or being sick

- constipation
- dry mouth.

Skin problems:

- rash
- hives (lumpy rash)
- itchiness.

Injection site problems:

- redness
- swelling of the skin
- blood clots or pain at the injection site.

Injury:

- 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).

General:

- tiredness (fatigue).

Elderly patients:

- 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 when the injection is given too quickly or at a high dose.

Unexpected reactions:

unexpected (paradoxical) reactions such as restlessness, agitation, irritability, involuntary movements (including muscle tremor), hyperactivity, nervousness, hostility, delusion, anger, aggressiveness, anxiety, nightmares, hallucinations (seeing and possibly hearing things that are not really there), psychoses (losing contact with reality) and inappropriate behaviour, excitement and assault have occurred with midazolam. These reactions may occur with high doses and/or when the injection is given rapidly. These reactions occur most commonly in children and the elderly.

Patients with severe kidney disease:

- patients with severe kidney disease are more likely to experience side effects.

If any of the side effects become serious or troublesome, or if you notice any side effects not listed in this leaflet, please tell your doctor or nurse.

Reporting of side effects

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. You can also report side effects directly via

Ireland

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 Midazolam Injection

Your doctor or pharmacist is responsible for storing Midazolam Injection. They are also responsible

for disposing of any unused Midazolam Injection correctly.

This medicinal product does not require any special temperature storage conditions
Keep this medicine out of the sight and reach of children.

Keep the ampoules (small glass bottle) in the outer carton in order to protect from light.

Do not use this medicine after the expiry date (EXP) which is stated on the pack. The expiry date refers to the last day of that month.

6. Contents of the pack and other information

What Midazolam Injection contains

The active substance in **Midazolam Injection** is midazolam (as midazolam hydrochloride).
Midazolam Injection comes in two different strengths

Midazolam 2 mg/ml solution for injection or infusion contains 2 mg of the active ingredient midazolam (as the hydrochloride) in each millilitre (ml). Midazolam 5 mg/ml solution for injection or infusion contains 5 mg of midazolam (as the hydrochloride) in each ml. Both strengths of solution also contain the inactive ingredients sodium chloride, hydrochloric acid, sodium hydroxide and water for injections.

The other ingredients in both strengths are sodium chloride, hydrochloric acid, sodium hydroxide and water for injections.

What Midazolam Injection looks like and contents of the pack

Midazolam 2 mg/ml solution for injection or infusion is a clear, colourless or slightly yellow solution for injection or infusion.

Midazolam 5 mg/ml solution for injection or infusion is available in 1 ml, 2 ml and 5 ml glass ampoules.
Midazolam 2 mg /ml solution for injection or infusion is available in 5 ml glass ampoules. The glass ampoules come in pack sizes of 10 or 20's. Not all pack sizes may be marketed.

Marketing Authorisation Holder and Manufacturer

Marketing Authorisation Holder

Accord Healthcare Ireland Limited
Euro House
Euro Business Park
Little Island
Cork T45 K857
Ireland

Manufacturer

Accord Healthcare Polska Sp.z o.o.,
ul. Lutomska 50,95-200 Pabianice, Poland

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

Name of the Member state	Name of the medicinal product
Ireland	Midazolam 2 mg/ml solution for injection or infusion Midazolam 5 mg/ml solution for injection or infusion
United Kingdom	Midazolam 2 mg/ml solution for injection or infusion Midazolam 5 mg/ml solution for injection or infusion

This leaflet was last revised in July 2023.

The following information is intended for medical or healthcare professionals only

Midazolam 2 mg/ml Solution for Injection or Infusion
Midazolam 5 mg/ml Solution for Injection or Infusion
Midazolam (as Midazolam hydrochloride)

Please refer to the Summary of Product Characteristics for full prescribing information.

Presentation

Midazolam 2 mg/ml Solution for Injection or Infusion contains 2 mg of the active ingredient midazolam (as the hydrochloride) in each millilitre (ml). Midazolam 5 mg/ml Solution for Injection or Infusion contains 5 mg of midazolam (as the hydrochloride) in each ml. Both strengths of solution also contain the inactive ingredients sodium chloride, hydrochloric acid, sodium hydroxide and water for injections.

The other ingredients in both strengths are sodium chloride, hydrochloric acid, sodium hydroxide and water for injections.

Midazolam Solution for Injection or Infusion is a clear, colourless or slightly yellow solution for injection or infusion.

Midazolam 5 mg/ml Solution for Injection or Infusion is available in 1 ml, 2 ml and 5 ml glass ampoules. Midazolam 2 mg /ml Solution for Injection or Infusion is available in 5 ml glass ampoules. The glass ampoules come in pack sizes of 10 or 20's. Not all pack sizes may be marketed.

Shelf life and storage

For single use only.

Midazolam Solution for Injection or Infusion is stable, both physically and chemically, for up to 24 hours at 2°C-8°C when mixed aseptically with 500ml infusion fluids containing Dextrose 4% with Sodium Chloride 0.18%, Dextrose 5% or Sodium Chloride 0.9%. Diluted product should be discarded if not used within 24 hours.

Do not use the product if the solution is discoloured.

From a microbiological point of view, the product should be used immediately. 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 to 8°C, unless dilution has taken place in controlled and validated aseptic conditions.

Incompatibilities

Admixture with Hartmann's solution is not recommended as the potency of midazolam decreases.

Special precautions for storage

This medicinal product does not require any special temperature storage conditions. Keep the container in the outer carton in order to protect from light.

This healthcare professional leaflet was last revised in July 2023