

Package leaflet: Information for the patient

Midazolam 1 mg/ml solution for injection/infusion in pre-filled syringe

midazolam (as midazolam hydrochloride)

Read all of this leaflet carefully before you are given 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 nurse. This includes any possible side effects not listed in this leaflet. See section 4.
- The full name of this medicine is Midazolam 1 mg/ml solution for injection/infusion in pre-filled syringe but within the leaflet it will be referred to as Midazolam injection.

What is in this leaflet:

1. What Midazolam injection is and what it is used for
2. What you need to know before you are given Midazolam injection
3. How Midazolam injection is given
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 contains the active substance midazolam, which 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 are given Midazolam injection

You must not be given Midazolam injection if:

- You are allergic to midazolam or any of the other ingredients of the medicine (listed in section 6).
- You are allergic to other benzodiazepine medicines, such as diazepam or nitrazepam.
- 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

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 specifically.
- 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 injection 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 effects of Midazolam injection, possibly leading to 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').

Other medicines and Midazolam injection.

Tell your doctor or nurse if you are taking, have recently taken or might start taking 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 (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 (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)
- the herbal medicine St John's Wort.



The following information is intended for healthcare professionals only:

Midazolam 1 mg/ml solution for injection/infusion in pre-filled syringe

Preparation of solution for infusion

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

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.

Operations

If you are going to have an anaesthetic for an operation or for dental treatment (including inhaled anaesthetics that you breathe in), 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

Tell your doctor if you are pregnant, think you may be pregnant or are planning to have a baby. Your doctor will decide if this medicine is suitable for you.

Midazolam injection 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 may pass into your breast milk.

Driving and using machines

Midazolam injection 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.

Do not drive while taking this medicine until you know how it affects you.

- It is an offence to drive if this medicine affects your ability to drive.
- However, you would not be committing an offence if:
 - The medicine has been prescribed to treat a medical or dental problem and
 - You have taken it according to the instructions given by the prescriber or in the information provided with the medicine and
 - It was not affecting your ability to drive safely.

Talk to your doctor or nurse 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.

Information on sodium content

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

3. How Midazolam injection is given

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.

How much Midazolam injection is given

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.

How Midazolam injection is given

Midazolam injection may be given to you in one of three 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).

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.

If too much Midazolam injection 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 treatment with 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.



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 Hartmann's solution or mixed with alkaline injections. Midazolam precipitates in hydrogen carbonate.

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

Midazolam injection is intended for single use only. Discard any excess contents. Use of this preparation for multiple administrations in the same or different patients is not recommended.

The following effects have been seen with Midazolam injection use, particularly in children and the elderly; restlessness, agitation, irritability, involuntary movements, hyperactivity, hostility, delusion, anger, aggressiveness, anxiety, nightmares, hallucinations (seeing and possibly hearing things that are not really there), psychoses (losing contact with reality), inappropriate behaviour, excitement and assault (these 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 injection 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
- 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 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
- hostility, anger or aggression
- 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
- 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
- hiccups.

Stomach, gut and mouth problems:

- feeling sick or being sick
- constipation
- dry mouth.



Shelf life and storage

Before opening

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

After dilution

Chemical and physical in-use stability of the dilutions has been demonstrated for 24 hours at room temperature (15°C-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

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.

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 nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the 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 Midazolam injection

Your doctor, pharmacist or nurse is responsible for storing Midazolam injection. The storage details are as follows:

- 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 label after "EXP". 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 injection if container is found leaking, solution is not clear with visible particles or any discoloration of the solution.

Do not throw away any medicines via wastewater or household waste. Your healthcare professional will throw away any medicines that are no longer being used. These measures will help protect the environment.

6 Contents of the pack and other information

What Midazolam injection contains

- The active substance is midazolam (as midazolam hydrochloride).
- The other ingredients include water for injections, sodium chloride, sodium hydroxide and concentrated hydrochloric acid.

Each 5 ml pre-filled syringe contains 5 mg of midazolam (as midazolam hydrochloride).

What midazolam injection looks like and contents of the pack

Midazolam injection is a clear, colourless to pale yellow solution filled in clear glass pre-filled syringe. Midazolam injection is available in pack containing 1 pre-filled syringe.

Marketing Authorisation Holder and Manufacturer

Marketing Authorisation Holder

Accord, Barnstaple, EX32 8NS, UK

Manufacturer

Accord Healthcare Limited
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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.

Disposal of waste

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