

PACKAGE LEAFLET

Package leaflet: Information for the patient

Midazolam 1 mg/ml solution for injection/infusion in pre-filled syringe 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 nurse.
- 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 1 mg/ml Solution for injection/infusion in pre-filled syringe is and what it is used for
2. What you need to know before you are given Midazolam 1 mg/ml Solution for injection/infusion in pre-filled syringe
3. How to use Midazolam 1 mg/ml Solution for injection/infusion in pre-filled syringe
4. Possible side effects
5. How to store Midazolam 1 mg/ml Solution for injection/infusion in pre-filled syringe
6. Contents of the pack and other information

1. What Midazolam 1 mg/ml Solution for injection/infusion in pre-filled syringe is and what it is used for

Midazolam 1 mg/ml Solution for injection/infusion in pre-filled syringe contains contains Midazolam. This belongs to a group of medicines called 'benzodiazepines'.

Midazolam 1 mg/ml Solution for injection/infusion in pre-filled syringe works quickly to make you feel sleepy or to put you to sleep. It also makes you calm and relaxes your muscles.

Midazolam 1 mg/ml Solution for injection/infusion in pre-filled syringe is used in adults:

- As a general anaesthetic to put you to sleep or to keep you asleep.

Midazolam 1 mg/ml Solution for injection/infusion in pre-filled syringe is also used in adults and in children (≥ 12 years age):

- To make you feel calm and sleepy if you are in intensive care. This is called 'sedation'.
- Before and during a medical test or procedure where you are going to stay awake. It makes you feel calm and sleepy. This is called 'conscious sedation'.
- To make you feel calm and sleepy before you are given an anaesthetic.

2. What you need to know before you are given Midazolam 1 mg/ml Solution for injection/infusion in pre-filled syringe

You must not be given Midazolam 1 mg/ml Solution for injection/infusion in pre-filled syringe if:

- You are allergic (hypersensitive) to midazolam or any of the other ingredients of this medicine (listed in Section 6: Contents of the pack and other information).
- You are allergic to other benzodiazepine medicines, such as diazepam or nitrazepam.
- You have severe breathing problems **and** you are going to have Midazolam 1 mg/ml Solution for injection/infusion in pre-filled syringe for 'conscious sedation'.

You must not be given Midazolam 1 mg/ml Solution for injection/infusion in pre-filled syringe 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

Check with your doctor or nurse before you are given Midazolam 1 mg/ml Solution for injection/infusion in pre-filled syringe 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 have an illness that makes you feel very weak, run down and short of energy.
- You have something called ‘myasthenia gravis’ where your muscles are weak.
- You have sleep apnoea
- You have ever had alcohol problems.
- You have ever had drug problems.

If any of the above apply to you (or you are not sure), talk to your doctor or nurse before you are given Midazolam 1 mg/ml Solution for injection/infusion in pre-filled syringe.

If your child (≥ 12 years age) is going to be given this medicine:

- Talk to your doctor or nurse if any of the above applies to your child (≥ 12 years age).
- In particular, tell your doctor or nurse if your child has heart or breathing problems.

Other medicines and Midazolam 1 mg/ml Solution for injection/infusion in pre-filled syringe

Please tell your doctor or nurse if you are taking or have recently taken any other medicines. This includes medicines that you buy without a prescription and herbal medicines. This is because Midazolam 1 mg/ml Solution for injection/infusion in pre-filled syringe can affect the way some other medicines work. Also some other medicines can affect the way Midazolam 1 mg/ml Solution for injection/infusion in pre-filled syringe works.

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

- Medicines for depression.
- Hypnotic medicines (to help you sleep).
- Sedatives (to make you feel calm or sleepy).
- Tranquilliser medicines (for anxiety or to help you sleep).
- Carbamazepine or phenytoin (these may be used for fits or seizures).
- Rifampicin (for tuberculosis).
- Medicines for HIV called ‘protease inhibitors’ (such as saquinavir).
- Antibiotics called ‘macrolides’ (such as erythromycin or clarithromycin).
- Medicines to treat fungal infections (such as ketoconazole, voriconazole, fluconazole, itraconazole, posaconazole).
- Strong pain killers.
- Atorvastatin (for high cholesterol).
- Anti-histamines (for allergic reactions).
- St John’s Wort (a herbal medicine for depression).
- Medicines for high blood pressure called ‘calcium channel blockers’ (such as diltiazem).

If any of the above apply to you (or you are not sure), talk to your doctor or nurse before you are given Midazolam 1 mg/ml Solution for injection/infusion in pre-filled syringe.

Midazolam 1 mg/ml Solution for injection/infusion in pre-filled syringe with drink and alcohol

Do not drink alcohol if you have been given Midazolam 1 mg/ml Solution for injection/infusion in pre-filled syringe. This is because it may make you feel very sleepy and cause problems with your breathing.

Pregnancy and breast-feeding

- Talk to your doctor before you are given Midazolam 1 mg/ml Solution for injection/infusion in pre-filled syringe if you are pregnant or think you may be pregnant. Your doctor will decide if this medicine is suitable for you.

- After you have been given Midazolam 1 mg/ml Solution for injection/infusion in pre-filled syringe, do not breast-feed for 24 hours. This is because Midazolam 1 mg/ml Solution for injection/infusion in pre-filled syringe may pass into your breast milk.

Driving and using machines

- After having Midazolam 1 mg/ml Solution for injection/infusion in pre-filled syringe, do not drive or use tools or machines until your doctor says you can.
- This is because Midazolam 1 mg/ml Solution for injection/infusion in pre-filled syringe may make you feel sleepy or forgetful. It may also affect your concentration and co-ordination. This may affect you being able to drive or use tools and machines.
- After your treatment, you must be taken home by an adult who can look after you.

Midazolam 1 mg/ml Solution for injection/infusion in pre-filled syringe contains sodium

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

3. How to use Midazolam 1 mg/ml Solution for injection/infusion in pre-filled syringe

Midazolam 1 mg/ml Solution for injection/infusion in pre-filled syringe will be given to you by a doctor or nurse. It will be given to you in a place that has the equipment needed to monitor you and to treat any side effects. This might be a hospital, clinic or doctor's surgery. In particular, your breathing, heart and circulation will be monitored.

Midazolam 1 mg/ml Solution for injection/infusion in pre-filled syringe is not recommended for use in infants and children < 12 years age.

How Midazolam 1 mg/ml Solution for injection/infusion in pre-filled syringe will be given to you

You will be given Midazolam 1 mg/ml Solution for injection/infusion in pre-filled syringe in one of the following ways:

- By slow injection into a vein (intravenous injection).
- Through a drip into one of your veins (intravenous infusion).
- By injection into a muscle (intramuscular injection).

How much Midazolam 1 mg/ml Solution for injection/infusion in pre-filled syringe will be given to you

The dose of Midazolam 1 mg/ml Solution for injection/infusion in pre-filled syringe varies from one patient to another. The doctor will work out how much to give you. It depends on your age, weight and general health. It also depends on what you need the medicine for, how you respond to treatment, and whether you are going to be given other medicines at the same time.

After being given Midazolam 1 mg/ml Solution for injection/infusion in pre-filled syringe

After your treatment, you must be taken home by an adult who is able to look after you. This is because Midazolam 1 mg/ml Solution for injection/infusion in pre-filled syringe may make you sleepy or forgetful. It may also affect your concentration and co-ordination.

If you are given too much Midazolam 1 mg/ml Solution for injection/infusion in pre-filled syringe

Your medicine will be given to you by a doctor or nurse. This means it is unlikely that you will be given too much. However, if you are given too much by mistake, you may notice the following:

- Feeling sleepy and losing your co-ordination and reflexes.
- Problems with speaking and unusual eye movements.
- Low blood pressure. This may make you feel dizzy or light-headed.
- Slowing or stopping of your breathing or heart beat and being unconscious (coma).

Long term use of Midazolam 1 mg/ml Solution for injection/infusion in pre-filled syringe for sedation in intensive care

If you are given Midazolam 1 mg/ml Solution for injection/infusion in pre-filled syringe for a long time, the following may happen:

- It may start to work less well.
- You may become dependent on the medicine and get withdrawal symptoms when you stop having it (see “Stopping Midazolam 1 mg/ml Solution for injection/infusion in pre-filled syringe” below).

If you stop using Midazolam 1 mg/ml Solution for injection/infusion in pre-filled syringe

If you are given Midazolam 1 mg/ml Solution for injection/infusion in pre-filled syringe for a long time, such as in intensive care, you may get withdrawal symptoms when you stop being given the medicine. These include:

- Mood changes.
- Fits (convulsions).
- Headache.
- Muscle pain.
- Problems with sleeping (insomnia).
- Feeling very worried (anxious), tense, restless, confused or bad tempered (irritable).
- Seeing and possibly hearing things that are not really there (hallucinations).

Your doctor will lower your dose gradually. This will help to stop withdrawal symptoms from happening to you.

4. Possible side effects

Like all medicines, Midazolam 1 mg/ml Solution for injection/infusion in pre-filled syringe can cause side effects, although not everybody gets them. The following side effects may happen with this medicine. The following side effects have been reported (frequency not known, cannot be estimated from the available data).

Stop having Midazolam 1 mg/ml Solution for injection/infusion in pre-filled syringe 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:

- A severe allergic reaction (anaphylactic shock). The signs may include a sudden rash, itching or lumpy rash (hives) and swelling of the face, lips, tongue or other parts of the body (angioedema). 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). The signs may include chest pain.
- Breathing problems, sometimes causing the breathing to stop.
- Choking and sudden blockage of the airway (laryngospasm).

Life-threatening side effects are more likely in adults over 60 years, and in people who already have breathing or heart problems. These side effects are also more likely if the injection is given too fast or at a high dose.

Other possible side effects:

Nervous system and Psychiatric disorders

- Being less alert.
- Feeling confused.
- Feeling very happy or excited (euphoria).
- Changes in sexual drive
- Feeling tired or sleepy or being sedated for a long time.
- Seeing or possibly hearing things that are not really there (hallucinations).
- Headache.

- Feeling dizzy.
- Difficulty co-ordinating muscles.
- Fits (convulsions) in premature and new-born babies.
 - Temporary memory loss. How long this lasts depends on how much Midazolam 1 mg/ml Solution for injection/infusion in pre-filled syringe you were given. Occasionally this has lasted for a long time.
 - Feeling agitated, restless, angry or aggressive. You may also have muscle spasms or shaking of your muscles that you cannot control (tremors). These effects are more likely if you have been given a high dose of Midazolam 1 mg/ml Solution for injection/infusion in pre-filled syringe or if it has been given too quickly. It is also more likely in children and elderly people.

Cardiac and Vascular disorders

- Fainting.
- Slow heart rate.
- Redness of the face and neck (flushing).
- Low blood pressure. This may make you feel dizzy or light-headed.

Respiratory disorders

- Hiccups.
- Being short of breath.

Gastrointestinal disorders

- Dry mouth.
- Constipation.
- Feeling sick (nausea) or being sick (vomiting).

Skin and subcutaneous tissue disorders

- Feeling itchy.
- Rash, including a lumpy rash (hives).
- Redness, pain, blood clots or swelling of the skin where the injection was given.

General

- Allergic reactions including skin rash and wheezing.
 - Withdrawal symptoms (see 'Stopping Midazolam 1 mg/ml Solution for injection/infusion in pre-filled syringe' in Section 3 above).
- Falling and breaking bones. The risk is increased if you take other medicines at the same time which are known to cause drowsiness (for example calming or sleeping drugs), or alcohol.

Elderly people

- Older people taking benzodiazepine medicines, like Midazolam 1 mg/ml Solution for injection/infusion in pre-filled syringe, have a higher risk of falling and breaking bones.
- Life-threatening side effects are also more likely to happen in adults over 60 years.

Reporting of side effects

If any of the side effects gets serious, or if you notice any side effects not listed in this leaflet, please tell your doctor or nurse. 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 1 mg/ml Solution for injection/infusion in pre-filled syringe

- 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.
- This medicinal product does not require any special temperature storage conditions. Store in the outer box in order to protect from light.
- The product is for single use and any excess solution should be discarded. Do not use Midazolam 1 mg/ml Solution for injection/infusion in pre-filled syringe 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 1 mg/ml Solution for injection/infusion in pre-filled syringe contains

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

Each ml of solution contains midazolam hydrochloride corresponding to 1 mg midazolam.

Each 5 ml pre-filled syringe contains midazolam hydrochloride corresponding to 5 mg midazolam.

What Midazolam 1 mg/ml Solution for injection/infusion in pre-filled syringe looks like and contents of the pack

Midazolam 1 mg/ml Solution for injection/infusion in pre-filled syringe is a clear, colourless to pale yellow solution free from foreign particles filled in clear glass prefilled syringe.

Midazolam 1 mg/ml Solution for injection/infusion in pre-filled syringe available in pack containing 1 pre-filled syringe.

Marketing Authorisation Holder and Manufacturer

Marketing Authorisation Holder

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

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Or

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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, 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.

The dose of Midazolam 1 mg/ml Solution for injection/infusion in pre-filled syringe must be calculated accurately for each patient. Only a part of the medicine might be required and please pay attention to the accuracy of dose required for each patient based on body weight.

When the quantity of drug to be injected requires to be adjusted based on the patient's body weight, use the graduated pre-filled syringes to reach the required volume by discarding the excess before injection in case of i.v. or i.m. bolus injection.

Shelf life and storage

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

Before opening

Store in the original package in order to protect from light

After dilution

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

From the microbiological point of view, the diluted product 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.