PACKAGE LEAFLET: INFORMATION FOR THE USER

hameln

Midazolam 1 mg/ml solution for injection / infusion
Midazolam 2 mg/ml solution for injection / infusion
Midazolam 5 mg/ml solution for injection / infusion
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 or nurse.
- 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.

What is in this leaflet

1. WHAT MIDAZOLAM IS AND WHAT IT IS USED FOR

Midazolam belongs to a group of medicines called 'benzodiazepines'. Midazolam works quickly to make you feel sleepy or to put you to sleep. It also makes you calm and relaxes your muscles.

Midazolam is used in adults:
- as a general anaesthetic to put them to sleep or to keep them asleep.

Midazolam is also used in adults and children:
- to make them feel calm and sleepy if they are in intensive care. This is called 'sedation'.
- before and during a medical test or procedure where they are going to stay awake. It makes them feel calm and sleepy. This is called 'conscious sedation'.
- to make them feel calm and sleepy before they are given an anaesthetic.

2. WHAT YOU NEED TO KNOW BEFORE YOU ARE GIVEN MIDAZOLAM

You should not be given Midazolam:
- if you are allergic to midazolam or any of the other ingredients of this 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 for '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.

Warnings and precautions

Talk to your doctor or nurse before you are given Midazolam:
- if you are over 60 years of age.
- if you have a long term illness, such as breathing problems or kidney, liver or heart problems.
- if you have an illness that makes you feel very weak, run down and short of energy.
- if you have something called 'myasthenia gravis' where your muscles are weak.
- if you have a condition called 'sleep apnoea syndrome' (where your breathing stops when you are asleep.
- if you have ever had alcohol problems.
- if you have ever had drug problems.

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

Children
- Talk to your doctor or nurse if any of the above applies to your child.
- In particular, tell your doctor or nurse if your child has heart or breathing problems.

Other medicines and Midazolam

Tell your doctor or nurse if you are taking, have recently taken or might take any other medicines. This includes medicines that you buy without a prescription and herbal medicines. This is because Midazolam can affect the way some other medicines work. Also some other medicines can affect the way Midazolam works.

In particular, tell your doctor or nurse if you are taking any of the following medicines:
- Medicines for depression (antidepressants)
- 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 and Hepatitis C called 'protease inhibitors' (such as saquinavir, boceprevir, telaprevir)
- 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 applies to you (or you are not sure), talk to your doctor or nurse before you are given Midazolam.

Concomitant use of Midazolam 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 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.

Midazolam with alcohol

Do not drink alcohol if you have been given Midazolam. 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 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, do not breast-feed for 24 hours. This is because Midazolam may pass into your breast milk.

Driving and using machines

After having Midazolam, do not drive or use tools or machines until your doctor says you can.

This is because Midazolam 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.

The medicine can affect your ability to drive as it may make you sleepy or dizzy.
- 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 pharmacist if you are not sure whether it is safe for you to drive while taking this medicine.

Midazolam contains sodium

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

3. HOW MIDAZOLAM IS GIVEN

Midazolam 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 is not recommended for use in infants and babies under 6 months of age. However, if the doctor feels that it is necessary, it can be given to an infant or baby under 6 months who is in intensive care.

How Midazolam will be given to you

You will be given Midazolam 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).
- Into your back passage (rectum).

How much Midazolam will be given to you

The dose of Midazolam 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

After your treatment, you must be taken home by an adult who is able to look after you. This is because Midazolam may make you sleepy or forgetful. It may also affect your concentration and co-ordination.

If you are given Midazolam for a long time, such as in intensive care, your body may start to get used to the medicine. This means it may not work as well.

If you are given more Midazolam than you should

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 for sedation in intensive care

If you are given Midazolam 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" below).

If use of Midazolam is stopped

If you are given Midazolam for a long time, such as in intensive care, you may get withdrawal symptoms when you stop being given the medicine.

The following information is intended for healthcare professionals only:
PREPARATION GUIDE FOR:

hameln

Midazolam 1 mg/ml, 2 mg/ml, 5 mg/ml solution for injection / infusion

This is a summary of the information regarding the preparation of Midazolam 1 mg/ml, 2 mg/ml, 5 mg/ml solution for injection / infusion.

It is important that you read the entire contents of this guide prior to the preparation of this medicinal product.

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

1. PRESENTATION

Midazolam 1 mg/ml is supplied as a clear and colourless solution for injection in clear glass ampoules containing 2 ml, 5 ml, 10 ml and in clear glass vials containing 50 ml.

Midazolam 2 mg/ml is supplied as a clear and colourless solution for injection in clear glass ampoules containing 5 ml or 25 ml and in clear glass vials containing 50 ml.

Midazolam 5 mg/ml is supplied as a clear and colourless solution for injection in clear glass ampoules containing 1 ml, 2 ml, 3 ml, 5 ml, 10 ml or 18 ml.

2. PREPARATION

Dilution Instructions

This medicinal product must not be diluted with other solutions for parenteral use than those mentioned below.

With continuous intravenous infusion, midazolam injection solution may be diluted in a ratio of 15 mg midazolam to 100 - 1000 ml with one of the following infusion solutions: 0.9 % NaCl, 5 % and 10 % dextrose and Ringer's solution.

Chemical and physical in-use stability of the dilutions has been demonstrated for 3 days at room temperature.

These include:
- Mood changes
- Fits (convulsions)
- Headache
- Diarrhoea
- 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, this medicine can cause side effects, although not everybody gets them. The following side effects have been reported but their frequency is not known and cannot be estimated from the available data.

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:
- 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. 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.
- Muscle spasm around the voice box, causing choking.

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 mental problems
- Being less alert
- Feeling confused
- Feeling very happy or excited (euphoria).
- Changes in libido
- Feeling tired or sleepy or being sedated for a long time.
- Seeing or possibly hearing things that are not really there (hallucinations).
- Disturbance of consciousness (delirium)
- 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 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 or if it has been given too quickly. It is also more likely in children and elderly people.

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

Breathing
- Hiccups
- Being short of breath

Mouth, stomach and gut
- Dry mouth
- Constipation
- Feeling sick (nausea) or being sick (vomiting)

Skin
- 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.
- Swelling of the skin/mucous membrane (angioedema)
- The risk of falls and fractures is increased in those taking concomitant sedatives (including alcoholic beverages)
- Withdrawal symptoms (see 'Stopping Midazolam' in Section 3 above)
- Drug abuse

Elderly people
- Older people taking benzodiazepine medicines, like Midazolam, 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 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
- Your doctor or pharmacist is responsible for storing Midazolam. They are also responsible for disposing of any unused Midazolam correctly.
- 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/carton after "EXP:". The expiry date refers to the last day of that month.
- Do not use this medicine if the small glass bottle (ampoule/vial) or packaging is damaged.
- Keep the ampoules/vials in the outer carton in order to protect from light.
- Do not store above 25°C. Do not freeze.

6. CONTENTS OF THE PACK AND OTHER INFORMATION

What Midazolam contains
- The active substance is midazolam (as midazolam hydrochloride).

  In Midazolam 1 mg/ml, each 1 ml of liquid contains 1 mg of midazolam (as midazolam hydrochloride).

  In Midazolam 2 mg/ml, each 1 ml of liquid contains 2 mg of midazolam (as midazolam hydrochloride).

  In Midazolam 5 mg/ml, each 1 ml of liquid contains 5 mg of midazolam (as midazolam hydrochloride).
- The other ingredients are sodium chloride, hydrochloric acid and water for injections.

What Midazolam looks like and contents of the pack

Midazolam comes in a colourless glass ampoule/ vial (small bottle). It is a clear, colourless, liquid (solution for injection / infusion).

The following pack sizes are available for Midazolam 1 mg/ml solution for injection / infusion:
- 2 ml glass ampoules: packs of 5, 10, 25, 50 or 100
- 5 ml glass ampoules: packs of 5, 10, 25, 50 or 100
- 10 ml glass ampoules: packs of 5, 10, 25, 50 or 100
- 50 ml glass vials, closed with a bromobutyl rubber stopper: packs of 1, 5 or 10

The following pack sizes are available for Midazolam 2 mg/ml solution for injection / infusion:
- 5 ml glass ampoules: packs of 5, 10, 25, 50 or 100
- 25 ml glass ampoules: packs of 5, 10, 10x5, 5x10.
- 50 ml glass vial: packs of 1, 5 or 10

The following pack sizes are available for Midazolam 5 mg/ml solution for injection / infusion:
- 1 ml glass ampoules: packs of 5, 10, 25, 50 or 100
- 2 ml glass ampoules: packs of 5, 10, 25, 50 or 100
- 3 ml glass ampoules: packs of 5, 10, 25, 50 or 100
- 5 ml glass ampoules: packs of 5, 10, 25, 50 or 100
- 10 ml glass ampoules: packs of 5, 10, 25, 50 or 100
- 18 ml glass ampoules: packs of 5, 10, 25, 50 or 100

Not all pack sizes may be marketed.

Marketing Authorisation Holder

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Gloucester, GL3 4AG
United Kingdom

Manufacturer

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

UK (NI)	Midazolam 1 mg/ml, 2 mg/ml, 5 mg/ml solution for injection / infusion
DE	Midazolam-hameln 1 mg/ml, 2 mg/ml, 5 mg/ml Injektions-/ Infusionslösung
DK	Midazolam "hameln"
FI	Midazolam hameln 1 mg/ml, 5 mg/ml injektio-/infuusioneste, liuos
NL	Midazolam-hameln 1 mg/ml, 2mg/ml, 5 mg/ml oplossing voor injectie/infusie
SE	Midazolam hameln 1 mg/ml, 5 mg/ml, injektions-/infusionsvätska, lösning
BG	Midazolam hameln 1 mg/ml, 2 mg/ml, 5 mg/ml инжекционен/инфузионен разтвор
SK	Midazolam hameln 1 mg/ml, 2 mg/ml, 5 mg/ml injekčný/infúzny roztok
RO	Midazolam hameln 1 mg/ml, 2 mg/ml, 5 mg/ml soluţie injectabilă/perfuzabilă
SI	Midazolam hameln 1 mg/ml, 2 mg/ml, 5 mg/ml raztopina za injiciranje/ infundiranje
CZ	Midazolam hameln
AT	Midazolam-hameln 1 mg/ml, 2 mg/ml, 5 mg/ml Injektions- /Infusionslösung
NO	Midazolam hameln
PL	Midazolam hameln
HU	Midazolam hameln 1 mg/ml, 2 mg/ml, 5 mg/ml oldatos injekció/infúzió
HR	Midazolam hameln 1 mg/ml, 2 mg/ml, 5 mg/ml otopina za injekciju/infuziju

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From a microbiological point of view, unless the method of opening/dilution precludes the risk of microbial contamination, the product should be used immediately. If not used immediately, in-use storage times and conditions are the responsibility of the user.

3. INCOMPATIBILITIES

Compatibility must be checked before administration, if intended to be mixed with other drugs.

Midazolam precipitates in solutions containing bicarbonate. Theoretically, the midazolam injection solution is likely to be unstable in solutions of neutral or alkaline pH. If midazolam is mixed with albumin, amoxicillin sodium, ampicillin sodium, bumetanide, dexamethasone sodium phosphate, dimenhydrinate, floxacillin sodium, furosemide, hydrocortisone sodium succinate, pentobarbital sodium, perphenazine, prochlorperazine edisylate, ranitidine or thiopental sodium or trimethoprim-sulfamethoxazole, a white precipitate forms immediately.

A haze is formed immediately followed by a white precipitate with nafcillin sodium. With ceftazidime a haze is formed.

With methotrexate sodium a yellow precipitate forms. With clonidine hydrochloride an orange discoloration forms. With omeprazole sodium a brown discoloration forms, followed by a brown precipitate. With foscarnet sodium a gas is produced.

Midazolam should not be mixed with aciclovir, albumin, alteplase, acetazolam disodium, diazepam, enoximone, flecainide acetate, fluorouracil, imipenem, mezlocillin sodium, phenobarbital sodium, phenytoin sodium, potassium canrenoate, sulbactam sodium, theophylline, trometamol, urokinase.