

PACKAGE LEAFLET: INFORMATION FOR THE PATIENT

Midazolam 5mg/ml Solution for Injection/Infusion

Midazolam

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.
- 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.

This product will be referred to as Midazolam Injection from here on.

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 you will be given 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 contains Midazolam. Midazolam belongs to a group of medicines called benzodiazepines which can cause sedation (sleepiness) and relieve anxiety.

It is used:

- to sedate patients during minor surgical and dental operations, and medical procedures such as passing a tube into the stomach or bladder
- to sedate patients in intensive care unit
- as an anaesthetic in high risk and elderly patients
- by injection into a muscle to provide pre medication for some patients prior to surgery.

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 other benzodiazepines or to any of the other ingredients of this medicine (listed in section 6).
- 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.

Children

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 of age this will include monitoring of breathing and oxygen levels.

Warnings and precautions:

Talk to your doctor or nurse before you are given Midazolam Injection.

Adults

Before Midazolam Injection is given, let your doctor or nurse know if:

- you are over 60 years of age
- you suffer from a lung or breathing disorder
- you have a problem with your kidneys or liver
- have a long-term illness or debilitated (have an illness that makes you feel very weak, run down and short of energy)
- you have ever been diagnosed as suffering from a personality disorder
- you regularly drink large amounts of alcohol or you have had problems with alcohol use in the past
- 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”)
- you suffer from a condition called myasthenia gravis (which causes severe weakness of the muscles)
- you suffer from heart disease or you have an abnormally low volume of blood in the circulation (for example, due to haemorrhage, dehydration or severe burns).
- you are taking any medicine from the group of medicines known as opioids: taking these medicines with Midazolam Injection may result in sedation, difficulties in breathing (respiratory depression), coma and may be fatal. Even if opioids are prescribed, your doctor may need to change the dose, the duration of treatment or monitor you regularly.

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

Other medicines and Midazolam Injection:

Tell your doctor or nurse if you are using, have recently used or might use any other medicines.

This is extremely important because some medicines can strengthen or weaken the effects of others. In particular, tell your doctor or nurse if you are taking any of the medicine following:

- strong pain relievers, such as codeine or pethidine
- diltiazem, nifedipine or verapamil (used for angina or high blood pressure, verapamil may also be used to control irregular heartbeats)
- medicines to treat high blood pressure like minoxidil, moxonidine, sodium nitroprusside, hydralazine, calcium channel blockers, beta blockers, alpha blockers and ACE inhibitors
- medicines known as water pills or diuretics
- the anti-fungal medicines ketoconazole, voriconazole, fluconazole, posaconazole or itraconazole
- erythromycin, roxithromycin, clarithromycin, quinupristin/dalfopristin and telithromycin (macrolide antibiotics)
- any other benzodiazepine drugs, such as diazepam or temazepam
- hypnotics (medicines that make you sleep)
- sedatives (medicines that make you feel calm or sleepy)
- antidepressants (medicines for treatment of depression)
- medicines for epilepsy (fits) such as phenytoin and carbamazepine
- antihistamines (used to treat allergies)
- medicines used in HIV infections called protease inhibitors (such as saquinavir) and efavirenz
- atorvastatin (used to treat high cholesterol levels in blood)
- rifampicin (used to treat mycobacterial infections such as tuberculosis)
- herbal medicine St John's Wort

- ciclosporin used to suppress the immune system
- medicines used to treat cancer such as nilotinib
- medicines effective against vomiting and nausea, such as nabilone.

If you are already taking one of these medicines, speak to your doctor before you receive 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.

Operations

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

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 for advice before taking this medicine.

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.

Breast- feeding

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 will affect your ability to drive and operate machinery. You should speak to your doctor for advice on when you will be able to drive, operate machines or resume normal activities.

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, if you have received midazolam injection.

The medicine can affect your ability to drive as it may make you sleepy or dizzy.

- do not drive after receiving 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 been given 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 after receiving this medicine.

Midazolam Injection contains Sodium

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

3. HOW YOU WILL BE GIVEN MIDAZOLAM INJECTION

Midazolam Injection will be given only by experienced doctors and trained people in a setting fully equipped for life support and who will recognize and be able to treat known side effects if they happen.

Midazolam Injection may be administered by intravenous injection (injection into a vein) or by intravenous infusion (given by a drip into a vein).

Your doctor will give this medicine to you and decide on the dose to be given based on the particular procedure they are doing, the degree of sleep (sedation) required, your weight, your response to the medication.

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

Use in Children

- 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 anesthetic) it may be given into the back passage (rectum).

If you think you have been given more Midazolam Injection than you should have.

This is unlikely as your injection will be administered by a doctor or nurse. If you are concerned about the dose, discuss it with your doctor.

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 heart beat) and coma.

If you stop using Midazolam injection:

- if you are given midazolam injection for a long time you may:
 - become tolerant to it. 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.

Withdrawal symptoms:

Benzodiazepine medicines, like midazolam injection, may make you dependent if used for a long time. This means that if you stop treatment suddenly, or lower the dose too quickly, you may get withdrawal symptoms. The symptoms can include: headache; 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).
If you have any further questions on the use of this product ask your doctor or pharmacist.

4. POSSIBLE SIDE EFFECTS

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

Serious side effects

Stop having midazolam injection and see your 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 have shortness of breath, wheezing or troubled 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.
- general allergic reactions (skin reactions, heart and blood system reactions, wheezing)
- 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:

The following side effects have been reported since the marketing of midazolam injection

Not known (frequency cannot be estimated from the available data):

- confusion
- euphoria (an excessive feeling of happiness or excitement)
- hallucinations (seeing and possibly hearing things that are not really there)
- drowsiness and prolonged sedation
- reduced alertness
- headache
- dizziness or fainting
- fits (convulsion) in premature infants and new-born babies
- fits (convulsion) due to withdrawal of drug
- temporary memory loss - how long this occurs depends on how much midazolam was given to you. You may experience this temporary memory loss after your treatment. In isolated cases temporary memory loss had been prolonged (lasted for a long time)
- agitation, restlessness, hostility, rage or aggression and excitement particularly in children and older patients
- Hiccup
- dry mouth
- hives (lumpy rash)
- potential drug dependence and withdrawal syndrome
- abuse of Midazolam

- low blood pressure
- slow heart rate
- redness of face and neck (flushing)
- inflammation of veins, clotting in blood vessels(thrombophlebitis and thrombosis)
- feeling of sick or being sick
- constipation
- dry mouth
- Injection site problems (Injection site redness, swelling of the skin, pain at the injection site)
- tiredness (fatigue)
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- muscle spasms and muscle tremors (shaking of muscles that you cannot control)
- difficulty coordinating muscles
- involuntary movements
- Falls and fractures

Older people:

- Older patients taking benzodiazepine medicines have a higher risk of falling and breaking bones.
- Potential drug dependence, abuse and withdrawal. If you have received Midazolam injection for a long time, you may find yourself becoming addicted and experience withdrawal symptoms once discontinued. If you have symptoms of agitation, anxiety and restlessness, speak to 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 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

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 carton and ampoule label after “Exp”. The expiry date refers to the last day of that month.

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

Do not store above 25°C.

Do not use the ampoule if it is damaged or the contents are discoloured.

If only part used, discard the remaining solution.

Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.

6. CONTENTS OF THE PACK AND OTHER INFORMATION

What Midazolam Injection contains

The active substance is midazolam.

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

What Midazolam Injection looks like and contents of pack

Midazolam Injection 5mg in 1ml is a clear, colourless or slightly yellow, sterile solution contained in clear glass ampoules (small bottles). Each 1ml of this solution contains 5mg of midazolam.

The injection is available in packs of 10 ampoules containing 2ml or 10ml of solution.

Marketing authorization holder

Mercury Pharmaceuticals Ltd, Dashwood House, 69 Old Broad Street, London, EC2M 1QS, United Kingdom

Manufacturer

B. Braun Melsungen AG, Mistelweg 2, 12357 Berlin, Germany.

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