

PACKAGE LEAFLET: INFORMATION FOR THE PATIENT
Midazolam 2mg/ml Solution for Injection/Infusion
Midazolam 5mg/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.
- This medicine has been prescribed for you. 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 name of your medicine is Midazolam 2mg/ml Solution for Injection/Infusion, Midazolam 5mg/ml Solution for Injection/Infusion; it will be called Midazolam Injection for ease here after

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 2 mg/ml & 5 mg/ml Solution for injection or infusion contains Midazolam. Midazolam belongs to a group of medicines called benzodiazepines. It can cause you to fall asleep and it can also relieve anxiety .

Midazolam is used to:

- sedate patients before and during minor medical, dental and surgical procedures (such as passing a tube into the stomach, intestine, bladder, lungs or heart)
- provide sedation for patients in intensive care
- bring about anaesthesia in high risk and elderly patients, especially where it is important to keep the heart and blood vessels in a stable state. This works best when heavy opiate (narcotic) premedication has been given, or when midazolam is given with a narcotic pain relieving drug such as fentanyl.

2. What you need to know before you are given Midazolam Injection

You should 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 applies to you. If you are not sure, talk to your doctor or nurse before you are given Midazolam Injection.

Warnings and precautions

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

Children

If your child is going to be given this medicine:

It is very important to tell your doctor or nurse if your child has cardiovascular disease (heart problems). Your child will be 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

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

- You suffer from a lung or breathing disorder
- You have a problem with your kidneys or liver
- You are over 60 years old .
- You have a long-term illness or are debilitated (have an illness that makes you feel very weak, run down and short of energy)
- 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 a problem 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 have a personality disorder
- You suffer from heart disease or have abnormally low volume of blood in the circulation (for example, due to heavy and abnormal bleeding, dehydration or severe burns).
- If 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, 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:

- Drugs that act on the brain and spinal cord (such as strong pain relievers)
- Diltiazem or verapamil (for angina or hypertension; verapamil may also be used to control irregular heartbeats)
- medicines to treat high blood pressure (methyldopa)
- Fluconazole, ketoconazole, voriconazole, posaconazole or itraconazole (anti-fungal medicines)
- Erythromycin , roxithromycin or clarithromycin (macrolide antibiotics)
- Any other benzodiazepine drug, hypnotic, sedative or tranquiliser (for anxiety or to help you sleep)
- medicines for epilepsy (fits) such as phenytoin and carbamazepine
- medicines used in HIV infections called protease inhibitors (such as saquinavir as a protease inhibitors) and efavirenz
- medicines for Hepatitis C (protease inhibitors such as boceprevir and telaprevir)
- Antidepressants or antipsychotics (medicines to treat depression or schizophrenia)

- Antihistamine (used to treat allergies)
- Atorvastatin (used to treat high cholesterol)
- Rifampicin (used to treat mycobacterial infections such as tuberculosis)
- St John's Wort (the herbal medicine).
- Ticagrelor (used to prevent heart attack)
- Aprepitant (used to stop you feeling or being sick)

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.

If you are already taking one of these medicines, speak to your doctor before you are 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 can cause problems with your breathing.

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.

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.

Pregnancy

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.

Breast- feeding

As midazolam may be found in breast milk you should not breast-feed for 24 hours after being given Midazolam Injection.

Driving and using machines:

- Do not drive or operate machinery until you are completely recovered, your doctor should advise you when you can start these again.
- If Midazolam Injection is used along with other drugs that can affect the brain or spinal cord (such as strong pain relievers), you may take longer to recover from the combined effects; in this case, you should ask your doctor for advice about when you may return home or resume normal activities.

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 machinery.

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

Midazolam Injection contains Sodium

Midazolam 10 mg/5 ml Solution for Injection or Infusion is essentially 'sodium free' as it contains less than 1 mmol sodium (23 mg) per ampoule.

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 given by intravenous injection (injection into a vein) or by intravenous infusion (given by a drip into the vein).

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

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 is used for premedication (to cause relaxation, calm and drowsiness before an anesthetic) it may be given into the back passage (rectum).

If you are given more Midazolam Injection than you should

This is unlikely as your injection will be administered by a doctor or nurse. If you are concerned about the dose, discuss this 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 have any further questions on the use of this product ask your doctor or nurse.

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.

The following effects have been seen with Midazolam Injection 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
- 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 taking Midazolam Injection and see a doctor straight away if you notice any of the following side effects:

- Any sudden wheeziness, difficulty in breathing, swelling of the eye lids, face or lips, rash or itching (especially of your whole body) this is called Anaphylactic shock and is life-threatening
- 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).

Effect on behavior:

- Agitation
- Restlessness
- Irritability
- Hostility, rage or aggression or assault
- Excitement.
- Hyperactivity
- Changes in libido
- Inappropriate behavior

Mental and Nervous system problems:

- Confusion, disorientation
- Involuntary movements
- Nightmares, abnormal dreams
- Psychoses (losing contact with reality)
- Drowsiness and prolonged sedation• 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
- Difficulty coordinating 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).
- Potential 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.

General:

- Tiredness (fatigue).

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).

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.

Elderly patients:

- Older patients taking benzodiazepine medicines have a higher risk of falling and breaking bones

Patients with severe kidney disease:

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

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

HPRA Pharmacovigilance

Earlsfort Terrace

IRL - Dublin 2

Tel: +353 1 6764971

Fax: +353 1 6762517

Website: www.hpra.ie

e-mail: medsafety@hpra.ie

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 ampoule in the outer carton in order to protect from light. Do not store above 25°C.

For single use only.

Once the ampoule has been opened it should be used immediately. If only part used, discard the remaining 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 Injection contains

The active substance is Midazolam.

Midazolam 5mg/ml: Each 2ml ampoule contains 10mg of midazolam.

Midazolam 2mg/ml: Each 5ml ampoule contains 10mg of midazolam.

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

What Midazolam Injection looks like and contents of pack

Midazolam 2mg/ml Solution for Injection/Infusion is a clear, colourless or slightly yellow, sterile solution for injection or infusion. Each 5ml glass ampoule contains 10mg of active ingredient, Midazolam.

Midazolam 5mg/ml Solution for Injection/Infusion is a clear, colourless or slightly yellow, sterile solution for injection or infusion. Each 2ml glass ampoule contains 10mg of active ingredient, Midazolam.

Pack size: 5 or 10 ampoules may be packaged together in cartons.

Not all pack sizes may be marketed.

Marketing Authorisation Holder

Mercury Pharmaceuticals (Ireland) Ltd.,

4045, Kingswood Road, City West Business Park, Co Dublin, Ireland

Manufacturer

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

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