Baxter

Package leaflet: Information for the patient
Midazolam 1 mg/ml solution for injection/infusion
Midazolam (as Midazolam hydrochloride)

The name of your medicine is Midazolam 1 mg/ml solution for injection/infusion, which will be referred to as Midazolam throughout this leaflet.

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 pharmacist 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 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 is and what it is used for**
2. **What you need to know before you take Midazolam**
3. **How to take Midazolam**
4. **Possible side effects**
5. **How to store Midazolam**
6. **Contents of the pack and other information**

1. What Midazolam is and what it is used for
Midazolam 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.

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 take Midazolam
Do not take Midazolam if:
- You are allergic (hypersensitive) to midazolam or any of the other ingredients of this 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 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 pharmacist or nurse before you are given this medicine.

Warnings and precautions for use
Take special care with Midazolam
Children and babies
If your child is going to be given this medicine:
- It is particularly important to tell your doctor or pharmacist 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 this will include monitoring of breathing and oxygen levels

Adults
Before Midazolam is given, let your doctor or pharmacist or nurse know 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 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.
- 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').

If any of the above apply to you, or if you are not sure, talk to your doctor or pharmacist or nurse before you are given Midazolam.

Interactions with other medicines
Other medicines and Midazolam
Please tell your doctor or pharmacist or nurse if you are taking or have recently taken any other medicines, including 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 pharmacist or nurse if you are taking any of the following medicines:
- Antidepressants (Medicines for depression)
- Hypnotics (medicines to make you sleep)
- Sedatives (to make you feel calm or sleepy)
- Tranquilisers (for anxiety or to help you sleep)
- Carbamazepine or phenytoin (these may be used for fits or seizures)
- Rifampicin (used to treat mycobacterial infections such as 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 (used to treat high cholesterol)
- Anti-histamines (used to treat allergies)
- 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 if you are not sure, talk to your doctor or pharmacist 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

Drinking alcohol
Do not drink alcohol if you have been given Midazolam. This is because alcohol can increase the sedative effect of Midazolam and may cause problems with your breathing.
Pregnancy, breast-feeding and fertility
Talk to your doctor if you are pregnant, or think you are pregnant. Your doctor will decide if this medicine is suitable for you.
Do not breast-feed for 24 hours after being given Midazolam. This is because Midazolam may pass into your breast milk.

Driving and using machines
- Do not drive or use machinery until you are completely recovered. Your doctor should advise you when you can start these again.
- Midazolam 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.

Midazolam contains sodium
This medicinal product contains less than 1 mmol sodium (23 mg) per ampoule, i.e. essentially "sodium-free".

3. How to take Midazolam
Midazolam should be given only by experienced healthcare professionals (doctor or pharmacist 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.

Dosage, Mode and / or route (s) of administration, Frequency of administration and Duration of treatment

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. 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.

Midazolam may be given to you in one of four different 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).

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

How much Midazolam will be given to you
The dose of Midazolam varies from one patient to another. Your doctor will decide on a suitable dose for you. It depends on your age, weight and general health. It also depends on:
- why are you being treated and the type of sedation needed, what you need the medicine for,
- how you respond to treatment,
- whether you are going to be given other medicines at the same time.

After being given Midazolam
After your treatment, you should always be accompanied to your home by an adult who can take care of 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.

The following information is intended for medical or healthcare professionals only.
The tear-off portion above is intended for the patient

INFORMATION FOR HEALTHCARE PROFESSIONALS
Midazolam 1 mg/ml solution for injection/infusion
Midazolam (as Midazolam hydrochloride)

Please refer to the Summary of Product Characteristics for full prescribing information
Presentation
Each ml contains midazolam (as hydrochloride) 1 mg.
Each 5 ml ampoule contains midazolam (as hydrochloride) 5 mg. Each 5 ml Clear glass (type I) ampoule packed in cartons of 5, 10 & 25 ampoules. Not all pack sizes may be marketed.
This medicine contains sodium.The sodium content is less than 1 mmol (23 mg) per ampoule i.e sodium-free.

Posology and method of administration
Midazolam is a potent sedative agent that requires titration and slow administration. Titration is strongly recommended to safely obtain the desired level of sedation according to the clinical need, physical status, age and concomitant medication. In adults over 60 years, debilitated or chronically ill patients and paediatric patients, dose should be determined with caution and risk factors related to each patient should be taken into account. Standard dosages are provided in the table below. Additional details are provided in the text following the table.

Indication	**Adults <60 years**	**Adults ≥60 years / debilitated or chronically ill**	**Children**
Conscious sedation	**IV** Initial dose: 2-2.5mg Titration doses: 1mg Total dose : 3.5-7.5mg	**IV** Initial dose : 0.5-1mg Titration doses : 0.5-1mg Total dose : <3.5mg	**IVin patients 6 months-5 years** Initial dose: 0.05-0.1mg/kg Total dose: <6mg **IVin patients 6-12 years** **Initial dose:** 0.025-0.05mg/kg Total dose:<10mg **rectal >6 months** 0.3-0.5mg/kg **IM 1-15 years** 0.05-0.15mg/kg
Anaesthesia premedication	**IV** 1-2mg repeated **IM** 0.07-0.1mg/kg	**IV** Initial dose: 0.5mg Slow up titration as needed **IM** 0.025-0.05mg/kg	**rectal >6 months** 0.3-0.5mg/kg **IM 1-15 years** 0.08-0.2mg/kg
Anaesthesia induction	**IV** 0.15-0.2mg/kg (0.3-0.35 without premedication)	**IV** 0.05-0.15 mg/kg (0.15-0.3 without premedication)	
Sedative component in combined anaesthesia	**IV** intermittent doses of 0.03-0.1mg/kg or continuous infusion of 0.03-0.1mg/kg/h	**IV** lower doses than recommended for adults <60 years	
Sedation in ICU	**IV** Loading dose: 0.03-0.3mg/kg in increments of 1-2.5mg Maintenance dose: 0.03-0.2mg/kg/h		**IV in neonates <32 weeks gestational** age 0.03mg/kg/h **IV in neonates >32weeks and children up to 6 months** 0.06mg/kg/h **IV in patients >6 months of age** Loading dose: 0.05-0.2mg/kg Maintenance dose: 0.06-0.12mg/kg/h

CONSCIOUS SEDATION DOSAGE
For conscious sedation prior to diagnostic or surgical intervention, midazolam is administered IV. The dose must be individualised and titrated, and should not be administered by rapid or single bolus injection.
The onset of sedation may vary individually depending on the physical status of the patient and the detailed circumstances of dosing (e.g. speed of administration, amount of dose). If necessary, subsequent doses may be administered according to the individual need. The onset of action is about 2 minutes after the injection. Maximum effect is obtained in about 5 to 10 minutes.

Adults
The IV injection of midazolam should be given slowly at a rate of approximately 1mg in 30 seconds.
- *In adults below the age of 60,* the initial dose is 2 to 2.5 mg given 5 to 10 minutes before the beginning of the procedure. Further doses of 1mg may be given as necessary. Mean total doses have been found to range from 3.5 to 7.5 mg. A total dose greater than 5mg is usually not necessary.
- *In adults over 60 years of age*, debilitated or chronically ill patients, the initial dose must be reduced to 0.5-1.0mg and given 5-10 minutes before the beginning of the procedure. Further doses of 0.5 to 1mg may be given as necessary. Since in these patients the peak effect may be reached less rapidly, additional midazolam should be titrated very slowly and carefully. A total dose greater than 3.5mg is usually not necessary.

Children
IV administration: Midazolam should be titrated slowly to the desired clinical effect. The initial dose of midazolam should be administered over 2 to 3 minutes. One must wait an additional 2 to 5 minutes to fully evaluate the sedative effect before initiating a procedure or repeating a dose. If further sedation is necessary, continue to titrate with small increments until the appropriate level of sedation is achieved. Infants and young children less than 5 years of age may require substantially higher doses (mg/kg) than older children and adolescents.

- *Paediatric patients less than 6 months of age*: paediatric patients less than 6 month of age are particularly vulnerable to airway obstruction and hypoventilation. For this reason, the use in conscious sedation in children less than 6 months of age is not recommended.
- *Paediatric patients 6 months to 5 years of age*: initial dose 0.05 to 0.1mg/kg. A total dose up to 0.6mg/kg may be necessary to reach the desired endpoint, but the total dose should not exceed 6mg. Prolonged sedation and risk of hypoventilation may be associated with the higher doses.
- *Paediatric patients 6 to 12 years of age*: initial dose 0.025 to 0.05mg/kg. A total dose of up to 0.4mg/kg to a maximum of 10mg may be necessary. Prolonged sedation and risk of hypoventilation may be associated with the higher doses.
- *Paediatric patients 12 to 16 years of age:* should be dosed as adults.

Rectal administration**:**
The product may be used rectally if required.
The total dose of midazolam usually ranges from 0.3 to 0.5mg/kg. Rectal administration of the ampoule solution is performed by means of a plastic applicator fixed on the end of the syringe. If the volume to be administered is too small, water may be added up to a total volume of 10ml. Total dose should be administered at once and repeated rectal administration avoided.
The use in children less than 6 months of age is not recommended, as available data in this population are limited.

IM administration: the doses used range between 0.05 and 0.15mg/kg. A total dose greater than 10.0mg is usually not necessary. This route should only be used in exceptional cases. Rectal administration should be preferred as IM injection is painful.
In children less than 15kg of body weight, midazolam solutions with concentrations higher than 1mg/ml are not recommended. Higher concentrations should be diluted to 1mg/ml.

ANAESTHESIA DOSAGE
PREMEDICATION
Premedication with midazolam given shortly before a procedure produces sedation (induction of sleepiness or drowsiness and relief of apprehension) and preoperative impairment of memory. Midazolam can also be administered in combination with anticholinergics. For this indication midazolam should be administered IV or IM, deep into a large muscle mass 20 to 60 minutes before induction of anaesthesia), or preferably via the rectal route in children (see below).
Close and continuous monitoring of the patients after administration of premedication is mandatory as interindividual sensitivity varies and symptoms of overdose may occur.
Adults
For preoperative sedation and to impair memory of preoperative events, the recommended dose for adults of ASA Physical Status I & II and below 60 years is 1-2mg IV repeated as needed, or 0.07 to 0.1mg/kg administered IM. The dose must be reduced and individualised when

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Baxter Pharmaceuticals India Private Limited

Artwork Code : 1400007592
Quality of Paper/Board : Super Sun Shine
Quality of Gum :
Colour Code : BLACK
Barcode Information:
Barcode Scan Report:
Packing: 5ml Amp
Country: United Kingdom, Ireland
Ref. Code Creation/Blockage Note:
"Controlled Copy" Holder (1) (2) (3) (4) (5)

Artwork Req. No: 25857
Size of Artwork (In mm) : 600x175
GSM of Paper/Board : 60 GSM
Pantone Pantone Pantone Pantone Pantone Pantone Pantone Pantone Pantone Pantone
Plant Location : Injectable
Language : English
Artwork Control Key No.:

Date: 28/08/19

If you receive more Midazolam than you should
Your medicine will be given to you by a doctor or nurse. If you are accidentally given too much Midazolam you may:
- Feel drowsy and lose your co-ordination (ataxia) and reflexes.
- Have problems with speech (dysarthria) and unusual eye movements (nystagmus).
- Develop low blood pressure (hypotension). This may make you feel dizzy or light-headed.
- Stop breathing (apnoea) and suffer cardiorespiratory depression (slowed or stopped breathing and heart beat) and coma.

If you receive Midazolam in intensive care unit for sedation, for a long time If you receive long term treatment with Midazolam (are given the medicine for a long time) you may:
- Become tolerant to Midazolam. The medicine becomes less effective and does not work as well for you.
- Become dependent upon this medicine and get withdrawal symptoms (see "If you stop using Midazolam").

If you stop using Midazolam
Risk of Withdrawal symptoms:
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.
These include:
- Mood changes
- Fits (convulsions)
- Headache
- Muscle pain
- Problems with sleeping (insomnia)
- Feeling very worried (anxious), tense, restless, confused or bad tempered (irritable).
- Hallucinations (Seeing and possibly hearing things that do not really exist)

Your doctor will gradually reduce the dose to avoid withdrawal symptoms.
If you have any further questions on the use of this medicine, ask your doctor, pharmacist or nurse.

4. Possible side effects
Like all medicines, Midazolam can cause side effects, although not everybody will get them.
The following undesirable effects may occur during the administration of midazolam 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:

- 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.
- Heart attack (cardiac arrest). signs may include chest pain.
- Breathing problems or complications (sometimes causing the breathing to stop).
- Muscle spasm around the throat, causing choking.

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
Mental and Nervous system problems:
- Being less alert
- Feeling confused
- Feeling very happy or excited (euphoria).
- 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. You may experience this after your treatment. In isolated cases this has been prolonged (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.
- Withdrawal symptoms (see 'Stopping Midazolam' in Section 3 above)
- Falls and fractures. The risk increases if you take other medicines known to cause drowsiness (for example, sedatives or sleeping pills), or alcohol.

Elderly patients
- Use of Midazolam may increase the 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 pharmacist or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via (See details below). By reporting side effects you can help provide more information on the safety of this medicine.

United Kingdom
Yellow Card Scheme Website: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the
Google Play or Apple App Store.

Ireland
HPRA Pharmacovigilance Earlsfort, Terrace IRL - Dublin 2
Tel: +353 1 6764971, Fax: +353 1 6762517
Website: www.hpra.ie,e-mail: medsafety@hpra.ie

5. How to store Midazolam
Your doctor or pharmacist or nurse 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.
Keep the ampoules in the outer carton in order to protect from light.
Do not use this medicine after the expiry date which is stated on the ampoule label and carton after "EXP". The expiry date refers to the last day of that month.
Do not use this medicine if you notice visible particles.
Do not dispose of any medication in the sewage system or in the household waste. Ask your pharmacist to eliminate medications that you no longer use. These measures will help protect the environment.

6. Contents of the pack and other information

What Midazolam contains: The active substance is:
Midazolam……..…..1 mg (as midazolam hydrochloride).
Each ml contains 1 mg of midazolam (as hydrochloride).Each 5 ml ampoule contains 5 mg of midazolam (as hydrochloride).
The other ingredients are: Sodium chloride, Sodium hydroxide, Hydrochloric acid and Water for Injections.

What Midazolam looks like and contents of the pack
Midazolam comes in a clear glass ampoule. It is a clear, colourless to pale yellow solution.
The following packs are available:
5 ml glass ampoule: packs of 5, 10 and 25.
Not all pack sizes may be marketed.

Marketing Authorisation Holder
Ireland:
Baxter Holding B.V.
Kobaltweg 49,
3542CE Utrecht, Netherlands

United Kingdom:
Baxter Healthcare Limited
Caxton Way
Thetford, Norfolk IP24 3SE, United Kingdom

Manufacturer
UAB Norameda,
Meistru 8a, 02189, Vilnius, Lithuania

Bieffe Medital S.P.A
Via Nuova Provinciale, 23034- Grosotto (SO), Italy

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

Czech Republic	Midazolam BAXTER
Estonia	Midazolam BAXTER
France	Midazolam Baxter 1mg/ml Solution pour Injection/Perfusion
Hungary	Midazolam Baxter 1mg/ml oldatos injekció/infúzió
Ireland	Midazolam 1mg/ml solution for injection/infusion
Latvia	Midazolam Baxter 1mg/mL šķīdums injekcijām/infūzijām
Lithuania	Midazolam Baxter 1mg/ml injekcinis ar infuzinis tirpalas
Poland	Midazolam BAXTER
Portugal	Midazolam BAXTER
Romania	Midazolam Baxter 1 mg/ml soluție injectabilă/perfuzabilă
Slovakia	Midazolam Baxter 1 mg/ml
The Netherlands	Midazolam Baxter 1mg/ml oplossing voor injectie/infusie
UK	Midazolam 1mg/ml solution for injection/infusion

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midazolam is administered to adults over 60 years of age, debilitated, or chronically ill patients.
The recommended initial IV dose is 0.5mg and should be slowly uptitrated as needed. A dose of 0.025 to 0.05mg/kg administered IM is recommended. In case of concomitant administration of narcotics the midazolam dose should be reduced. The usual dose is 2 to 3mg.
Paediatric Patients
Neonates and children up to 6 months of age:
The use in children less than 6 months of age is not recommended as available data are limited.
Children over 6 months of age:
Rectal administration:
The product may be used rectally if required.
The total dose of midazolam, usually ranging from 0.3 to 0.5mg/kg should be administered 15 to 30 minutes before induction of anaesthesia.
Rectal administration of the ampoule solution is performed by means of a plastic applicator fixed on the end of the syringe. If the volume to be administered is too small, water may be added up to a total volume of 10ml.
IM administration: As IM injection is painful, this route should only be used in exceptional cases. Rectal administration should be preferred. However, a dose range from 0.08 to 0.2mg/kg of midazolam administered IM has been shown to be effective and safe. In children between ages 1 and 15 years, proportionally higher doses are required than in adults in relation to body- weight.
In children less than 15kg of body weight, midazolam solutions with concentrations higher than 1mg/ml are not recommended. Higher concentrations should be diluted to 1mg/ml.

INDUCTION
Adults
If midazolam is used for induction of anaesthesia before other anaesthetic agents have been administered, the individual response is variable. The dose should be titrated to the desired effect according to the patient's age and clinical status. When midazolam is used before or in combination with other IV or inhalation agents for induction of anaesthesia, the initial dose of each agent should be significantly reduced, at times to as low as 25% of the usual initial dose of the individual agents. The desired level of anaesthesia is reached by stepwise titration. The IV induction dose of midazolam should be given slowly in increments. Each increment of not more than 5mg should be injected over 20 to 30 seconds allowing 2 minutes between successive increments.
- *In premedicated adults below the age of 60 years*, an IV dose of 0.15 to 0.2mg/kg will usually suffice.
- *In non-premedicated adults below the age of 60* the dose may be higher (0.3 to 0.35mg/kg IV). If needed to complete induction, increments of approximately 25% of the patient's initial dose may be used. Induction may instead be completed with inhalational anaesthetics. In resistant cases, a total dose of up to 0.6mg/kg may be used for induction, but such larger doses may prolong recovery.
- *In premedicated adults over 60 years of age,* debilitated or chronically ill patients, the dose should be significantly reduced, e.g., down to 0.05-0.15mg/kg administered IV over 20- 30 seconds and allowing 2 minutes for effect.
- *Non-premedicated adults over 60 years* of age usually require more midazolam for induction; an initial dose of 0.15 to 0.3mg/kg is recommended. Non-premedicated patients with severe systemic disease or other debilitation usually require less midazolam for induction. An initial dose of 0.15 to 0.25mg/kg will usually suffice.

SEDATIVE COMPONENT IN COMBINED ANAESTHESIA
Adults
Midazolam can be given as a sedative component in combined anaesthesia by either further intermittent small IV doses (range between 0.03 and 0.1mg/kg) or continuous infusion of IV midazolam (range between 0.03 and 0.1mg/kg/h) typically in combination with analgesics. The dose and the intervals between doses vary according to the patient's individual reaction.
In adults over 60 years of age, debilitated or chronically ill patients, lower maintenance doses will be required.

SEDATION IN INTENSIVE CARE UNITS
The desired level of sedation is reached by stepwise titration of midazolam followed by either continuous infusion or intermittent bolus, according to the clinical need, physical status, age and concomitant medication (see section 4.5).
Adults
IV loading dose: 0.03 to 0.3 mg/kg should be given slowly in increments. Each increment of 1 to 2.5 mg should be injected over 20 to 30 seconds allowing 2 minutes between successive increments. In hypovolaemic, vasoconstricted, or hypothermic patients the loading dose should be reduced or omitted.
When midazolam is given with potent analgesics, the latter should be administered first so that the sedative effects of midazolam can be safely titrated on top of any sedation caused by the analgesic.
IV maintenance dose: doses can range from 0.03 to 0.2 mg/kg/h. In hypovolaemic, vasoconstricted, or hypothermic patients the maintenance dose should be reduced. The level of sedation should be assessed regularly. With long-term sedation, tolerance may develop and the dose may have to be increased.

Neonates and children up to 6 months of age:
Midazolam should be given as a continuous IV infusion, starting at 0.03mg/kg/h (0.5 µg/kg/min) in neonates with a gestational age <32 weeks, or 0.06 mg/kg/h (1 µg/kg/min) in neonates with a gestational age > 32 weeks and children up to 6 months.
Intravenous loading doses are not recommended in premature infants, neonates and children up to 6 months, rather the infusion may be run more rapidly for the first several hours to establish therapeutic plasma levels. The rate of infusion should be carefully and frequently reassessed, particularly after the first 24 hours so as to administer the lowest possible effective dose and reduce the potential for drug accumulation.
Careful monitoring of respiratory rate and oxygen saturation is required.

Children over 6 months of age:
In intubated and ventilated paediatric patients, a loading dose of 0.05 to 0.2 mg/kg IV should be administered slowly over at least 2 to 3 minutes to establish the desired clinical effect. Midazolam should not be administered as a rapid intravenous dose. The loading dose is followed by a continuous IV infusion at 0.06 to 0.12 mg/kg/h (1 to 2 µg/kg/min).The rate of infusion can be increased or decreased (generally by 25% of the initial or subsequent infusion rate) as required or supplemental IV doses of midazolam can be administered to increase or maintain the desired effect.
When initiating an infusion with midazolam in haemodynamically compromised patients, the usual loading dose should be titrated in small increments and the patient monitored for haemodynamic instability, e.g. hypotension. These patients are also vulnerable to the respiratory depressant effects of midazolam and require careful monitoring of respiratory rate and oxygen saturation.
In premature infants, neonates and children less than 15 kg of bodyweight, midazolam solutions with concentrations higher than 1mg/ml are not recommended. Higher concentrations should be diluted to 1mg/ml.

Special populations
Renal Impairment
In patients with renal impairment (creatinine clearance <10ml/min) the pharmacokinetics of unbound midazolam following a single IV dose is similar to that reported in healthy volunteers. However, after prolonged infusion in intensive care unit (ICU) patients, the mean duration of the sedative effect in the renal failure population (shown after prolonged infusion in intensive care unit (ICU) patients) was considerably increased most likely due to accumulation of α-hydroxymidazolam glucuronide. There is no specific data in patients with severe renal impairment (creatinine clearance below 30ml/min) receiving midazolam for induction of anaesthesia.
Hepatic Impairment
Hepatic impairment reduces the clearance of IV midazolam with a subsequent increase in terminal half-life. Therefore the clinical effects may be stronger and prolonged. The required dose of midazolam may be reduced and proper monitoring of vital signs should be established. (See section 4.4).
Paediatric population
See above and section 4.4.

Incompatibilities
Do not dilute Midazolam ampoules with dextran glucose 6%.
Midazolam should not be mixed with alkaline solutions.Midazolam precipitates with sodium bicarbonate.
Midazolam must not be mixed with other medicinal products except those mentioned in section 6.6.
Shelf life
3 years
Chemical and physical in-use stability of the dilutions has been demonstrated for 24 hours at room temperature and for 3 days at 5°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 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. (for dilution, see also section 6.6)

Special precautions for storage
Keep the ampoules in the original outer carton in order to protect from light.
For storage conditions after dilution of the medicinal product, see section 6.3.
This healthcare professional leaflet was last approved in **04/2019**.

Baxter Pharmaceuticals India Private Limited

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