Milam

(Midazolam) Injection BP

5mg/5ml

میلام انجکشن 5 ملی گرام/5 ملی لیٹر

(میڈازولام) انجکشن بی پی

COMPOSITION:
Each 5ml ampoule contains:
Midazolam……5mg
(As Midazolam hydrochloride)
Finished Product Specs.: BP

MECHANISM OF ACTION:
It is thought that the actions of benzodiazepines such as midazolam are mediated through the inhibitory neurotransmitter gamma-aminobutyric acid (GABA), which is one of the major inhibitory neurotransmitters in the brain. Benzodiazepines increase the activity of GABA, thereby producing a calming effect, relaxing skeletal muscles, and inducing sleep. Benzodiazepines bind to the benzodiazepine site on GABA-α receptors, which potentiates the effects of GABA by increasing the frequency of chloride channel opening.

INDICATIONS:
Midazolam 1mg/ml is a short-acting sleep-inducing drug that is indicated:

In adults
- Conscious sedation before and during diagnostic or therapeutic procedures with or without local anesthesia.
- Anesthesia.
  - Premedication before induction of anesthesia.
  - Induction of anesthesia.
  - As a sedative component in combined anesthesia.
- Sedation in intensive care units.

In children
- Conscious sedation before and during diagnostic or therapeutic procedures with or without local anesthesia.
- Anesthesia.
  - Premedication before induction of anesthesia.
- Sedation in intensive care units.

DOSAGE AND ADMINISTRATION:
STANDARD DOSAGE:
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 pediatric 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.

Indication	Adults < 60 years	Adults ≥ 60y / debilitated or chronically ill	Children
conscious sedation	**IV** Initial dise: 2 -2.5mg Titration doses: 1mg Total dose: 3.5 - 7.5mg	**IV** Initial dise: 0.5 -1mg Titration doses: 0.5-1mg Total dose: <3.5mg	**IV in patients 6 months-5 years** Initial dise: 0.05 -0.1mg/kg Total dose: < 6mg **IV in patients 6-12 years** Initial dise: 0.025 -0.05mg/kg Total dose: < 10mg **rectal > 6 months** 0.3-0.5mg/kg I.M 1-15 years **IM 1-15 years** 0.05-0.15mg/kg
Anesthesia 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
Anesthesia Induction	**IV** 0.15-0.2mg/kg (0,3-0.35 without premedication)	**IV** 0.05-0.15mg/kg (0.15-0.3 without premedication)	
Sedative component in combined anesthesia	**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: 0.03-0.3 mg/kg in increments of 1-2.5mg Maintance dose: 0.03-0.2 mg/kg/h		**IV in pre-term new-born infants < 32 weeks gestational age** 0.03mg/kg **IV in new-born infants > 32 weeks 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 dosage: 0,06-0.12mg/kg/h

Maintenance of anesthesia:
Intravenous administration
For maintenance of the desired level of unconsciousness further small doses should be injected IV. The dose and the intervals between doses vary according to the individual reaction of the patient.

PRECAUTIONS:
Midazolam should be administered only by experienced physicians or specifically trained personnel in a setting fully equipped for the monitoring and support of respiratory and cardiovascular function and by persons specifically trained in the recognition and management of expected adverse events including respiratory and cardiac resuscitation.

Special caution should be exercised when administering midazolam to high-risk patients:
- Adults over 60 years of age.
- Chronically ill or debilitated patients.
- Patients with chronic respiratory insufficiency.
- Patients with chronic renal failure, impaired hepatic function or with impaired cardiac function.
- Pediatric patients especially those with cardiovascular instability.

These high-risk patients require lower dosages and should be continuously monitored for early signs of alterations of vital functions.

As with any substance with CNS depressant and/or muscle-relaxant properties, particular care should be taken when administering midazolam to a patient with myasthenia gravis.
Tolerance: Some loss of efficacy has been reported when midazolam was used as long-term sedation in intensive care units (ICU).
Dependence: When midazolam is used in long-term sedation in ICU, it should be borne in mind that physical dependence on midazolam may develop. The risk of dependence increases with dose and duration of treatment; it is also greater in patients with a medical history of alcohol and/or medicinal product abuse.
Withdrawal symptoms: Abrupt termination of the treatment will be accompanied by withdrawal symptoms. The following symptoms may occur: headaches, muscle pain, anxiety, tension, restlessness, confusion, irritability, rebound insomnia, mood changes, hallucinations and convulsions. Since the risk of withdrawal symptoms is greater after abrupt discontinuation of treatment, it is recommended to decrease doses gradually.
Amnesia: Midazolam causes anterograde amnesia, the duration of which is directly related to the administered dose. Prolonged amnesia can present problems in outpatients, who are scheduled for discharge following intervention.
Paradoxical reactions: Paradoxical reactions such as agitation, involuntary movements (including tonic/clonic convulsions and muscle tremor), hyperactivity, hostility, rage reaction, aggressiveness, paroxysmal excitement and assault, have been reported to occur with midazolam. These reactions may occur with high doses and/or when the injection is given rapidly. The highest incidence to such reactions has been reported among children and the elderly.
Altered elimination of midazolam: Midazolam elimination may be altered in patients receiving compounds that inhibit or induce CYP3A4 and the dose of midazolam may need to be adjusted accordingly.
Midazolam elimination may also be delayed in patients with liver dysfunction, low cardiac output and in new-born infants.
Pediatric Population
Preterm new-born and new-born infants: Due to an increased risk of apnea, extreme caution is advised when sedating preterm and former preterm non intubated patients. Careful monitoring of respiratory rate and oxygen saturation is required.
Adverse hemodynamic events have been reported in pediatric patients with cardiovascular instability; rapid intravenous administration should be avoided in this population.
Pediatric patients less than 6 months: Pediatric patients less than 6 months of age are particularly vulnerable to airway obstruction and hypoventilation, therefore titration with small increments to clinical effect and careful respiratory rate and oxygen saturation monitoring are essential.
Concomitant use of alcohol / CNS depressants: The concomitant use of midazolam with alcohol or/and CNS depressants should be avoided. Such concomitant use has the potential to increase the clinical effects of midazolam possibly including severe sedation or clinically relevant respiratory depression.
Risk from concomitant use of opioids: Concomitant use of Midazolam and opioids may result in sedation, respiratory depression, coma and death. Because of these risks, concomitant prescribing of sedative medicines such as benzodiazepines or related drugs such as Midazolam with opioids should be reserved for patients for whom alternative treatment options are not possible. If a decision is made to prescribe Midazolam concomitantly with opioids, the lowest effective dose should be used, and the duration of treatment should be as short as possible. The patients should be followed closely for signs and symptoms of respiratory depression and sedation. In this respect, it is strongly recommended to inform patients and their caregivers (where applicable) to be aware of these symptoms.
Medical history of alcohol or medicinal product abuse: Midazolam as other benzodiazepines should be avoided in patients with a medical history of alcohol or drug abuse.
Discharging criteria: After receiving midazolam, patients should be discharged from hospital or consulting room only when recommended by treating physician and if accompanied by an attendant. It is recommended that the patient is accompanied when returning home after discharge.

SIDE EFFECTS:
Like all medicines midazolam can cause side effects, although not everybody gets them.
The following undesirable effects have been reported (frequency not known). Stop midazolam if the following side effects are noted. They can be life-threatening and may need urgent medical treatment. Anaphylactic shock, and may also have shortness of breath, wheezing or trouble breathing. Heart attack (cardiac arrest). Signs may include chest pain which may spread to neck and shoulders and down your left arm. Breathing problems or complications, 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.

INTERACTIONS:
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, care should be taken with the following medicines there are tranquilizers, hypnotics, sedatives, antidepressants, narcotic analgesics, antihistamines, medicines to treat fungal infections (ketoconazole, voriconazole, fluconazole, itraconazole, posaconzole), macrolide antibiotics (such as erythromycin or clarithromycin), diltiazem (used to treat high blood pressure), medicines for HIV called protease inhibitors (such as saquinavir), atorvastatin, rifampicin and The herbal medicine St. John's Wort.

OVERDOSAGE:
Symptoms
Like other benzodiazepines, midazolam commonly cause drowsiness, ataxia, dysarthria and nystagmus. Overdose of midazolam is seldom life-threatening if the drug is taken alone, but may lead to areflexia, apnoea, hypotension, cardiorespiratory depression and in rare cases to coma, Coma, if it occurs, usually lasts a few hours but it may be more protracted and cyclical, particularly in elderly patients. Benzodiazepine respiratory depressant effects are more serious in patients with respiratory disease.
Benzodiazepines increase the effects of other central nervous system depressants, including alcohol.
Treatment
Monitor the patient's vital signs and institute supportive measures as indicated by the patient's clinical state. In particular, patients may require symptomatic treatment for cardiorespiratory effects or central nervous system effects.
If CNS depression is severe consider the use of flumazenil, a benzodiazepine antagonist under closely monitored conditions.

AVAILABILITY:
Milam Injection 5mg/5ml: 10 x 5ml Ampoules.

DOSAGE:
As directed by the registered medical practitioner.

INSTRUCTIONS:
- Protect from heat and light.
- Store below 30°C.
- To be sold on the prescription of a registered medical practitioner only.

Keep all medicines out of the reach of children.

Manufactured by :
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