

MIDAZOLAM 5MG/ML AMP, 1ML AMP:

Class: Benzodiazepine

Indications: Preoperative sedation; moderate sedation prior to diagnostic or radiographic procedures; ICU sedation (continuous infusion); induction and maintenance of general anesthesia, anxiety, status epilepticus, conscious sedation (intranasal route)

Available dosage form in the hospital: AMP (5MG/ML, 15MG/3ML)

Trade Names:

Dosage:

The dose of midazolam needs to be individualized based on the patient's age, underlying diseases, and concurrent medications. Consider reducing dose by 20% to 50% in elderly, chronically ill, or debilitated patients and those receiving opioids or other CNS depressants.

-Preoperative/preprocedural sedation: Healthy adults <60 years:

-*I.M.*: 0.07-0.08 mg/kg 30-60 minutes prior to surgery/procedure; usual dose: 5 mg

-*I.V.*: 0.02-0.04 mg/kg; repeat every 5 minutes as needed to desired effect or up to 0.1-0.2 mg/kg

-*Intranasal (unlabeled route)*: 0.1 mg/kg; administer 10-20 minutes prior to surgery/procedure (Uygun-Bayramiçli, 2002). **Note:** Use 5 mg/mL injectable concentrated solution to deliver dose. Due to the low pH of the solution, burning upon administration is likely to occur.

-Conscious sedation: I.V.:

-*Manufacturer's labeling:*

-Healthy adults <60 years:

- Initial: Some patients respond to doses as low as 1 mg; no more than 2.5 mg should be administered over a period of 2 minutes. Additional doses of midazolam may be administered after a 2-minute waiting period and evaluation of sedation after each dose increment. A total dose >5 mg is generally not needed.
- Maintenance: 25% of dose used to reach sedative effect

-Adults ≥60 years, debilitated, or chronically ill: Refer to geriatric dosing.

-*Alternate recommendations:* American Society for Gastrointestinal Endoscopy: Initial: 0.5-2 mg slow I.V. over at least 2 minutes; slowly titrate to effect by repeating doses every 2-3 minutes if needed; usual total dose: 2.5-5 mg (Waring, 2003)

-Anesthesia: I.V.:

-*Induction:* Adults <55 years:

- Unpremedicated patients: 0.3-0.35 mg/kg over 20-30 seconds; after 2 minutes, may repeat if necessary at 25% of initial dose every 2 minutes, up to a total dose of 0.6 mg/kg in resistant cases
- Premedicated patients: Usual dosage range: 0.05-0.2 mg/kg (Barash, 2009; Miller, 2010). Use of 0.2 mg/kg administered over 5-10 seconds has been shown to safely produce anesthesia within 30 seconds (Samuelson, 1981) and is recommended for ASA physical status P1 and P2 patients. When used with other anesthetic drugs (ie, co-induction), the dose is <0.1 mg/kg (Miller, 2010).
-ASA physical status >P3 or debilitation: Reduce dose by at least 20% (Miller, 2010).

-*Maintenance:* 0.05 mg/kg as needed (Miller, 2010), or continuous infusion 0.015-0.06 mg/kg/hour (0.25-1 mcg/kg/minute) (Barash, 2009; Miller, 2010)

-Sedation in mechanically-ventilated patients: I.V.: Initial dose: 0.01-0.05 mg/kg (~0.5-4 mg); may repeat at 5- to 15-minute intervals until adequate sedation achieved; maintenance infusion: 0.02-0.1 mg/kg/hour (0.3-1.7 mcg/kg/minute). Titrate to reach desired level of sedation. Titration to maintain a light rather than a deep level of sedation is recommended unless clinically contraindicated (Barr, 2013). May consider a trial of daily awakening; if agitated after discontinuation of drip, then restart at 50% of the previous dose (Kress, 2000).

-Status epilepticus refractory to standard therapy (unlabeled use): I.V.: **Note:** Intubation required; adjust dose based on hemodynamics, seizure activity, and EEG. 0.15-0.3 mg/kg (usual dose: 5-15 mg); may repeat every 10-15 minutes as needed **or** 0.2 mg/kg bolus followed by a continuous infusion of 0.05-0.6 mg/kg/hour (0.83-10 mcg/kg/minute) (Lowenstein, 2005; Meierkord, 2010)

-Status epilepticus, prehospital treatment (unlabeled use): I.V.: **Note:** Administered by paramedics when convulsions last >5 minutes **or** if convulsions are occurring after having intermittent seizures without regaining consciousness for >5 minutes: 10 mg once (Silbergleit, 2012)

Geriatric

The dose of midazolam needs to be individualized based on the patient's age, underlying diseases, and concurrent medications. Consider reducing dose by 20% to 50% in elderly, chronically ill, or debilitated patients and those receiving opioids or other CNS depressants.

-Anesthesia: I.V.:

- Induction: Adults >55 years:
- Unpremedicated patients: Initial dose: 0.3 mg/kg
- Premedicated patients: Reduce dose by at least 20% (Miller, 2010).
- Maintenance: Refer to adult dosing.

-Conscious sedation: I.V.: Initial: 0.5 mg slow I.V.; give no more than 1.5 mg in a 2-minute period; if additional titration is needed, give no more than 1 mg over 2 minutes, waiting another 2 or more minutes to evaluate sedative effect; a total dose of >3.5 mg is rarely necessary

-Preoperative/preprocedural sedation: Adults >60 years (without concomitant opioid administration): I.M.: 2-3 mg (or 0.02-0.05 mg/kg) 30-60 minutes prior to surgery/procedure; some may only require 1 mg (or 0.01 mg/kg) if anticipated intensity and duration of sedation is less critical.

Renal Impairment:

There are no dosage adjustments provided in manufacturer's labeling; however, patients with renal failure receiving a continuous infusion cannot adequately eliminate the active hydroxylated metabolites (eg, 1-hydroxymidazolam) contributing to prolonged sedation sometimes for days after discontinuation (Spina, 2007).

-Intermittent hemodialysis: Supplemental dose is not necessary.

-Continuous venovenous hemofiltration (CVVH): Unconjugated 1-hydroxymidazolam not effectively removed; 1-hydroxymidazolamglucuronide effectively removed; sieving coefficient = 0.45 (Swart, 2005).

-Peritoneal dialysis: Significant drug removal is unlikely based on physiochemical characteristics.

Hepatic Impairment:

-Severe hepatic impairment (eg, cirrhosis): **Note:** Use with caution in patients with any degree of hepatic impairment; patients with hepatic encephalopathy likely to be more sensitive to midazolam.

-Single dose (eg, induction): No dosage adjustment recommended; patients with hepatic impairment may be more sensitive compared to patients without hepatic impairment; anticipate longer duration of action (MacGilchrist, 1986; Trouvin, 1988).

-Multiple dosing or continuous infusion: Expect longer duration of action and accumulation; based on patient response, dosage reduction likely to be necessary (Trouvin, 1988).

Common side effect:

Respiratory: Decreased tidal volume and/or respiratory rate decrease, apnea (3% children)

Pregnancy Risk Factor: D