

Alert	High risk of causing significant patient harm when used in error.																
Indication	Sedation during ventilation or procedure. Treatment of refractory seizure.																
Action	The sedative and anticonvulsant properties of midazolam are related to GABA accumulation and occupation of benzodiazepine receptors. Anti-anxiety properties are related to increasing the glycine inhibitory neurotransmitter.																
Drug Type	Short acting benzodiazepine.																
Trade Name	Hypnovel, Midazolam Alphapharm, Midazolam DBL, Midazolam Pfizer, Midazolam Sandoz.																
Presentation	5 mg/mL ampoule 5mg/5mL ampoule																
Dosage / Interval	<table border="1"> <thead> <tr> <th>Method</th> <th>Dose</th> </tr> </thead> <tbody> <tr> <td>IV infusion for sedation</td> <td>0.2–1 microgram/kg/minute</td> </tr> <tr> <td>IV infusion for seizures</td> <td>Loading dose: 150–200 microgram/kg over 3–5 minutes Maintenance dose: 1–7 microgram/kg/minute</td> </tr> <tr> <td>IV bolus</td> <td>50 microgram/kg/dose every 2 hours when required (Dose range: 50–150 microgram/kg/dose)</td> </tr> <tr> <td>IM injection</td> <td>50 microgram/kg/dose every 4 hours when required (Dose range: 50–150 microgram/kg/dose)</td> </tr> <tr> <td>Oral</td> <td>250 microgram/kg as a single dose</td> </tr> <tr> <td>Sublingual</td> <td>200 microgram/kg as a single dose</td> </tr> <tr> <td>Intranasal</td> <td>200 microgram/kg per dose as a single dose (Dose range: 200–300 microgram/kg/dose)</td> </tr> </tbody> </table>	Method	Dose	IV infusion for sedation	0.2–1 microgram/kg/minute	IV infusion for seizures	Loading dose: 150–200 microgram/kg over 3–5 minutes Maintenance dose: 1–7 microgram/kg/minute	IV bolus	50 microgram/kg/dose every 2 hours when required (Dose range: 50–150 microgram/kg/dose)	IM injection	50 microgram/kg/dose every 4 hours when required (Dose range: 50–150 microgram/kg/dose)	Oral	250 microgram/kg as a single dose	Sublingual	200 microgram/kg as a single dose	Intranasal	200 microgram/kg per dose as a single dose (Dose range: 200–300 microgram/kg/dose)
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Route	IV, IM, Oral, Sublingual, Intranasal.																
Preparation/Dilution	<p>IV infusion for sedation. Using 5 mg/mL injection, draw up 0.6 mL/kg (3 mg/kg of midazolam) and add glucose 5%, glucose 10% or sodium chloride 0.9% to make final volume 50 mL. Infuse at a rate of 1 mL/ hour = 1 microgram/kg/minute.</p> <p>Using 5mg/5mL injection, draw up 3 mL/kg (3 mg/kg of midazolam) and add glucose 5%, glucose 10% or sodium chloride 0.9% to make final volume 50 mL. Infuse at a rate of 1 mL/ hour = 1 microgram/kg/minute.</p> <p>IV infusion for seizures. Using 5 mg/mL injection, draw up 3 mL/kg (15 mg/kg of midazolam) and add glucose 5%, glucose 10% or sodium chloride 0.9% to make final volume 50 mL. Infuse at a rate of 1 mL/hour = 5 microgram/kg/minute.</p> <p>Using 5 mg/5mL injection, draw up 15 mL/kg (15 mg/kg of midazolam) and add glucose 5%, glucose 10% or sodium chloride 0.9% to make final volume 50 mL. Infuse at a rate of 1 mL/hour = 5 microgram/kg/minute.</p> <p>IV bolus, IM injection, oral, sublingual and intranasal Using 5 mg/mL injection, draw up 0.4 mL (2000 microgram of midazolam) and add 9.6 mL of sodium chloride 0.9% to make final volume of 10 mL with a concentration of 200 microgram/mL. Using 5 mg/5mL injection, draw up 1 mL (1000 microgram of midazolam) and add 4 mL of sodium chloride 0.9% to make final volume of 5 mL with a concentration of 200 microgram/mL.</p>																
Administration	<p>IV infusion: As a continuous infusion via a syringe pump.</p> <p>IV bolus: Give as a slow push over 10 minutes.⁹</p> <p>Oral: IV ampoules may be used for oral administration.</p> <p>Intranasal: IV ampoules may be used for intranasal administration. Drop dose into alternating nostrils over 15 seconds. Absorption is rapid; maximum effect in 10 minutes and duration up to 2 hours. May be irritating to nasal mucosa.</p> <p>IM: Inject deep into a large muscle.</p>																

Monitoring	Observe for apnoea, respiratory depression, blood pressure and level of sedation.
Contraindications	Known hypersensitivity to midazolam.
Precautions	In preterm infants, especially in extreme preterm, midazolam half-life is increased from 4–6 hours in term neonates up to 22 hours in premature infants. It is longer with impaired liver function. Caution when concurrently used with opioids – midazolam interacts with other central nervous system depressants and may increase the risk of drowsiness, respiratory depression and hypotension. Withdraw slowly after chronic administration. Abrupt discontinuation may precipitate withdrawal seizures. Caution in neonates with renal and hepatic impairment – increased sensitivity to central nervous system (CNS) effects; use doses at lower end of the range. Rapid IV infusion may result in hypotension, respiratory depression or seizure.
Drug Interactions	Concurrent administration with erythromycin promotes accumulation. Xanthines may decrease the anaesthetic/sedative effect of benzodiazepines. Care needs to be taken with adding or withdrawing caffeine or aminophylline.
Adverse Reactions	Hypotension and reduced cardiac output, particularly when used in combination with fentanyl. Respiratory depression and apnoea. Hypersalivation. Nasal discomfort (with intranasal route). Seizure-like myoclonus (more common in premature neonates receiving via intravenous route).
Compatibility	Fluids: Glucose 5%, glucose 10%, sodium chloride 0.9%. Y-site: Amino acid solutions. Abciximab, amikacin, amiodarone, anidulafungin, atracurium, bivalirudin, calcium gluconate, caspofungin, cefotaxime cephazolin, ciprofloxacin, cisatracurium, clindamycin, digoxin, dopamine, doripenem, eptifibatide, erythromycin, esmolol, fentanyl, fluconazole, gentamicin, glyceryl trinitrate, haloperidol lactate, hydromorphone, labetalol, linezolid, methadone, methylprednisolone, metronidazole, milrinone, morphine sulfate, noradrenaline (norepinephrine), palonosetron, pancuronium, potassium chloride, ranitidine, remifentanyl, sodium nitroprusside, tirofiban, tobramycin, vancomycin, vecuronium.
Incompatibility	Fluids: No information. Y-site: Fat emulsion. Aciclovir, albumin, aminophylline, amoxicillin, ampicillin, azathioprine, azithromycin, cefepime, ceftazidime, chloramphenicol, clonidine, dexamethasone, ertapenem, esomeprazole, flucloxacillin, foscarnet, furosemide (frusemide), ganciclovir, hydrocortisone sodium succinate, imipenem-cilastatin, indomethacin, omeprazole, phenobarbital (phenobarbitone), piperacillin-tazobactam (EDTA-free), potassium acetate, sodium bicarbonate, thiopental (thiopentone), tramadol, trimethoprim-sulfamethoxazole.
Stability	Diluted solution: Store at 2–8°C and use within 24 hours.
Storage	Ampoule: Store below 25°C. Protect from light. Schedule 4D (S4D) medication therefore store in dangerous drug safe and record use in S4D register.
Special comments	Flumazenil is a specific benzodiazepine antagonist and may be used (very limited experience in the neonate) to rapidly reverse respiratory depression – 10 microgram/kg/dose IV push. May repeat every minute for up to 4 more doses.
Evidence summary	Refer to Full version
References	Refer to Full version

Original version Date: 23/03/2016	Author: NMF Consensus Group
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Risk Rating: Medium	Due for Review: 23/02/2020
Approved by: JHCH CQ&PCC	Approval Date: 27/09/2016