MIDAZOLAM This drug must be guardrailed

Trade Name	Midazolam (Mylan) Hypnovel® (Roche)
Class	Benzodiazepine
Mechanism of Action	Anxiolytic, sedative, muscle relaxant and anticonvulsant facilitation of GABA (gamma amino butync acids) levels in the brain (inhibitory neurotransmitter)
Indications	Anticonvulsant (3rd line) Sedation / anaesthesia induction Palliative care
Contraindications	Hypersensitivity to Midazolam Shock Caution in extreme preterm (<30 week) or cardiac, renal, or liver failure
Supplied As	1mg/mL in 5mL ampoules for IV use IV midazolam solution can also be used if needed for buccal administration.
Dilution	▪ **Bolus:** No dilution necessary for bolus (if not bolusing from an existing infusion) • **Buccal:** May be mixed with sucrose to mask very bitter flavour ▪ **IV Infusion**: See separate midazolam infusion sheet Take weight (kg) in mL of 1mg/mL midazolam solution and make up to 50mL with sodium chloride 0.9%, or 5% or 10% dextrose **1mL/hr = 20 microgram/kg/hr**. **Maximum concentration = 150 microgram/mL.** If there is a need to fluid restrict then the recipe can be made double strength so that 1mL/hr=40 microgram/kg/hr but it will exceed the maximum concentration if weight >4kg ▪ **Subcutaneous infusion:** See separate infusion sheet
Dosage …. ***Must chart guardrail and use Alaris pump***	**Bolus**: **50 - 100 microgram/kg** Can be given as a bolus from the continuous infusion on the guardrailed pumps or from a separately drawn up 1mg/mL solution If >2 boluses are given either start an infusion or increase the infusion dose Monitor the fluid volume received from the boluses (2.5mL-5mL at standard infusion concentration) **Infusion**: **10 – 100 microgram/kg/hour**. Start low and increase **Buccal** see next page

… Dosage	**Buccal: 200 microgram/kg** If there are neurological/respiratory/swallow concerns, or, to avoid oversedation suggest 50-100mcg/kg dose that can be repeated if required
Guardrails	Conc: Min – 3 microgram/mL Max – 150 microgram/mL Soft Min: 2 microgram/kg/hr Hard Max: 100 microgram/kg/hr Soft Max: 60 microgram/kg/hr Default: 10 microgram/kg/hr
Guardrails Boluses	Default Rate: 50mL/hr – bolus will be given over 3-6 minutes at standard infusion concentration Soft Min: 25 microgram/kg Hard Max: 100microgram/kg Soft Max: 100microgram/kg Default: 50microgram/kg
Interval	**Bolus:** 2-4 hourly **Infusion:** Constant **Buccal:** As required 2-4 hourly but expectation that this is used as a temporising measure whilst starting or increasing a continuous infusion (iv or subcut)
Administration	**Bolus:** Slow IV injection over 3 - 6 minutes **Infusion:** Change bag every 24 hrs **Buccal:** Use a filter needle to withdraw the dose from the glass ampoule into a syringe, then remove the needle and very gently squirt the dose inside the cheek near the gum line.
Compatible With	**Solution:** Dextrose 5% and 10%,Sodium Chloride 0.9% Lactated Ringers **Terminal Y-site:** Adrenaline, alprostadil, amikacin, amiodarone, atropine, benzylpenicillin, calcium gluconate, cefazolin, cefotaxime, clindamycin, digoxin, , dopamine, epinephrine, erythromycin lactobionate, fentanyl, fluconazole, gentamicin, heparin, lidocaine, linezolid, lorazepam, magnesium sulphate, methadone, metoclopramide, metronidazole, milrinone, morphine,naloxone, nitroglycerin, nitroprusside, noradrenaline, pancuronium bromide, paracetamol, piperacillin, potassium chloride, ranitidine, ticarcillin, tobramycin, vancomycin, vasopressin,vecuronium, voriconazole. Evidence in support of compatibility with dopamine, furosemide, insulin, imipenem, and TPN (aminoacid / dextrose/electrolyte) is mixed, use separate lines if at all possible.
Incompatible With	Albumin, aciclovir, amoxicillin, amphotericin, azithromycin, bumetanide, cefepime, ceftazidime, cefuroxime, cotrimoxazole, dexamethasone, diazoxide, epoetin, fosphenytoin, ganciclovir, hydrocortisone succinate, lipid (fat emulsion), meropenem, omeprazole,piperacillin tazobactam, phenytoin, sodium bicarbonate, sulfamethoxazole/trimethoprim.
Monitoring	Continuous cardio-respiratory monitoring Monitor BP and oxygen saturation Assess for pain. (Midazolam has NO analgesic properties)

Stability	Single use vial Discard vial immediately after use. Continuous infusions need to be changed after 24 hours
Storage	Store unopened vials at room temperature <25^{o}C. Do not freeze, Protect from light. Midazolam is a recorded drug kept in the controlled drug safe.
Adverse Reactions	Hypotension, Respiratory depression and apnoea Extravasation pH 3.0
Metabolism	Highly protein bound, major hepatic metabolism with slow elimination by kidneys. T½ 6 – 7 hrs. Rapid onset (<3 mins) with peak sedation 20-30 mins after IV. Bioavailability following buccal administration is approximately 50% versus 36% following oral administration.
Comments	Consider initially low dose with increasing dose as required. May need increased dose with prolonged use, due to tolerance developing. Midazolam injection is suitable for oral administration.
References	1. Burtin P, Jacqz-Aigrain E, Girard P et al. Populations pharmacokinetics of Midazolam in neonates. Clinical Pharmacol Ther 1994;56:615-25 2. Neofax ® www.micromedexsolutions.com 3. NZHPA Notes on Injectable Drugs 5th Edition 4. NZF for Children www.nzf.org.nz 5. Taketomo et al Paediatric and Neonatal Dosage Handbook 19th edition. Lexicomp 2012 6. Trissel IV medication compatibilities in www.micromedexsolutions.com
Updated By	P Schmidt & B Robertshawe December 2004 A Lynn, B Robertshawe July 2009, Sept 2009, March 2010 A Lynn, B Robertshawe Nov 2012 (re-order profile, discard vial) A Lynn May 2013 / Aug 2015 (guardrail boluses) A Lynn, B Robertshawe June 2017 (update of compatibility data) A Lynn, B Robertshawe, M Meeks Aug 2017 (add in buccal administration) N Austin, M Wallenstein, B Robertshawe Aug 2019 (update rate and compatibilities) A Lynn, M Wallenstein, B Robertshawe Oct 2021 (routine update) A Lynn, N Austin , B Robertshawe June 2022 (review buccal dosing)