MONOGRAPH

MIDAZOLAM

Scope (Staff):	Medical, Pharmacy, Nursing, Anaesthetic Technicians
Scope (Area):	All Clinical Areas

Child Safe Organisation Statement of Commitment

CAHS commits to being a child safe organisation by applying the National Principles for Child Safe Organisations. This is a commitment to a strong culture supported by robust policies and procedures to reduce the likelihood of harm to children and young people.

This document should be read in conjunction with this DISCLAIMER

⚠ HIGH RISK MEDICINE ⚠

QUICKLINKS

Dosage/Dosage Adjustments	Administration	Compatibility	Monitoring

DRUG CLASS

Midazolam is a short acting benzodiazepine medication which potentiates the inhibitory effects of GABA throughout the Central Nervous System (CNS), resulting in anxiolytic, sedative, hypnotic, muscle relaxant and antiepileptic effects.[1]

Midazolam is a High Risk Medicine.

INDICATIONS AND RESTRICTIONS[1, 3, 5]

Midazolam is used at PCH for the following indications:

- Emergency treatment of seizures
- Preoperative or procedural sedation
- Premedication
- Sedation during ventilation – must only be administered in the Emergency Department (ED), Paediatric Critical Care (PCC) or Theatre with continuous cardio-respiratory monitoring
- Induction and maintenance of anaesthesia
- Acute arousal and agitation – Arousal and Agitation Drug Management Guideline

- Palliative care – seizure management, sedation and management of anxiety and agitation associated with dyspnoea

CONTRAINDICATIONS[2]

- Hypersensitivity to midazolam or any component of the formulation
- Hypersensitivity to benzodiazepines
- Myasthenia gravis
- Acute narrow angle glaucoma
- Patients in shock or coma, or in acute alcoholic intoxication with depression of vital signs

PRECAUTIONS[1, 3, 5]

- Respiratory disease, sleep apnoea
- Muscle weakness
- Renal/hepatic impairment
- Cardiac disease
- Co-administration with opioids and/or other CNS depressants

FORMULATIONS

Listed below are products available at PCH, other formulations may be available, check with pharmacy if required.

- Midazolam (Pfizer®) **5** mg/**1** mL Plastic Ampoule
- Midazolam **5** mg/**5** mL Glass Ampoule
- Midazolam **15** mg/**3** mL Glass Ampoule
- Midazolam **50** mg/**10** mL Glass Ampoule

For Continuous Midazolam Infusion – ED / PCC / Theatre ONLY

STANDARD FIXED CONCENTRATION

- Midazolam **15** mg (in sodium chloride 0.9%) in **30** mL (Baxter®) Pre-filled Syringe
- Midazolam **50** mg (in sodium chloride 0.9%) in **50** mL (Baxter®) Pre-filled Syringe

Imprest location: Formulary One

DOSAGE & DOSAGE ADJUSTMENTS

Neonates: Refer to Neonatal Medication Protocols

GENERAL

- Calculate dose using Ideal Body Weight (IBW) in obese children.[4, 5] Refer to Guidelines for Drug Dosing in Overweight and Obese Children 2 to 18 Years of Age.
- Use only in clinical areas with facilities for resuscitation and cardio-respiratory monitoring.
- The doses below are within the standard reference range for each indication, however, the dose of midazolam may need to be titrated to the patient's clinical needs and response.

SEIZURES[4, 5]

Buccal / intranasal – For seizures lasting longer than 5 minutes**:**

- ≥ 4 weeks of age – 18 years: buccal / intranasal 0.2–0.3 mg/kg (maximum 10 mg).

  Repeat once after 5–10 minutes if required.

Intermittent intravenous injection

- ≥ 4 weeks of age – 18 years: IV 0.15–0.2 mg/kg (maximum 10 mg) over 2–5 minutes.

  Repeat once after 5–10 minutes if required.

Intravenous infusion for status epilepticus – in ED / PCC / Theatre ONLY with continuous monitoring

- If seizures are still not controlled, a **continuous IV infusion** may then be required.
- Advanced airway assessment / management and assisted ventilation may be required.[4]
- Commence at 50 microg/kg/hr and titrate to effect. Infusion rate of up to 1000 microg/kg/hr may be necessary.[5, 6]
- Bolus dose for breakthrough seizures: 150 microg/kg/**dose** as required.[5]
- Depending on the dose, not all patients will necessarily be intubated and ventilated.

PREOPERATIVE or PROCEDURAL SEDATION

Cumulative sedation and timing of administration must be considered when midazolam is prescribed to patients already receiving sedating medications.

Oral

Use lower dose with opioids or other CNS depressants or for high-risk children (e.g. with cardiac or respiratory compromise).

- 6 months – 18 years: oral 0.25 – 0.5 mg/kg (maximum 20 mg) given 20 to 30 minutes before procedure.[4, 5, 7]

- Doses up to 1 mg/kg (maximum 20 mg) may **RARELY** be required for children 6 months to less than 6 years or uncooperative children.[3, 4, 7]

SEDATION DURING VENTILATION[8]
To be administered ONLY in ED / PCC / Theatre with continuous monitoring.

Refer to Analgesia and Sedation in Paediatric Critical Care Guideline for detailed guidance on sedation management with midazolam.

Intravenous (IV) infusion

All patients under 50 kg:

- Loading dose: 50 – 100 microg/kg/dose stat, if required.
- Continuous infusion rate range: 0 – 250 microg/**kg**/hr (max 10 mg/hr) – (usual starting rate 50 microg/kg/hr), titrated to target sedation score. Higher infusion rates may be necessary if patient develops tolerance.
- Bolus dose: 50 microg/**kg** every 5 – 10 minutes as required.

All patients 50 kg and above:

- Loading dose: 2.5 – 5 mg/dose stat, if required.
- Continuous infusion rate range: 0 – 10 **mg/hr** (usual starting rate 2.5 **mg/hr**), titrated to target sedation score. Higher infusion rates may be necessary if patient develops tolerance.
- Bolus dose: 2.5 mg/dose every 5 – 10 minutes as required.

Depending on the dose, not all patients will necessarily be intubated and ventilated.

AROUSAL AND AGITATION

Intramuscular

- ≥ 6 years: IM 2.5 – 5 mg/dose (50 – 150 microg/kg)
- Repeat dose after 30 – 60 minutes if necessary.
    - < 16 years: Maximum 10 mg/24 hours
    - ≥ 16 years: Maximum 20 mg/24 hours

Refer to Arousal and Agitation Drug Management Guideline for further details.

PALLIATIVE CARE – please consult palliative care team for specialist advice.

Seizure control at end of life – subcutaneous / intravenous infusion

- ≥ 4 weeks of age – 18 years: continuous subcut / IV initial dose 1 mg/kg/24 hours increasing gradually to a maximum of 7 mg/kg/24 hours (usual maximum 60 mg/24 hours; up to 150 mg/24 hours may be used at the discretion of a palliative care consultant for patients with refractory epilepsy)[9]

Anxiety, agitation at end of life – Subcutaneous/intravenous infusion[9]

Refer to The Association of Paediatric Palliative Medicine Master Formulary.

DOSAGE ADJUSTMENTS

Dosage adjustment is recommended in severe renal impairment, liver failure, congestive heart failure, limited pulmonary reserve.[2, 4, 5]

Lower doses may be appropriate if the patient is receiving other sedative agents (e.g. an opioid); adjust dose according to response.[5]

Careful use of bolus doses in patients with haemodynamic instability, hypotension, post-cardiac surgery.[8]

Renal impairment: eGFR calculator

- eGFR ≥ 30 mL/min/1.73 m^2: No dosage adjustment[3]
- eGFR 10–29 mL/min/1.73 m^2: Reduce initial dose by 25%[3]
- eGFR < 10 mL/min/1.73 m^2: Reduce initial dose by 50%[3]

Hepatic impairment:

- Impairment increases sensitivity to CNS effects; avoid in severe impairment as can precipitate coma.[1]

ADMINISTRATION

CHECK AND RECHECK ROUTE OF ADMINISTRATION

The route of administration may vary depending on the indication.

Buccal

- Use plastic ampoule containing midazolam 5 mg/1 mL
- 1 mL contains approximately 20 drops
- Administer to the buccal mucosa between the gums and the cheek. Dose may be divided to both sides of the mouth.[5]
- For more information on administration of buccal midazolam refer to the PCH Pharmacy Buccal Midazolam Information Leaflet

Intranasal – For seizures lasting longer than 5 minutes, as per Dosage.

- Intranasal midazolam is used less often due to nasal irritation and a burning sensation, although it has a rapid onset of action (5–15 minutes).[4, 5]
- Administer using a mucosal atomiser (MAD nasal drug delivery device) or via needleless syringe; divide dose between both nostrils. Maximum volume: 1 mL per nostril. See Appendix 1 for detailed instructions.
- If necessary, dose can be administered (dripping it slowly) directly from plastic ampoule into nostrils .[5]

Oral

Midazolam 5 mg/1 mL plastic ampoule solution may be given orally.

- Tastes bitter and acidic when given orally; dilute with a small volume of clear liquid (e.g. apple juice, undiluted cordial or lemonade) to disguise taste.[4]

Intravenous

Intravenous push – *must only be administered by medical staff (or under the direct supervision of medical staff in ED/PCC/Theatre)*

- Give neat as a slow push over at least 2 minutes.[5, 10]
- In practice it may be given in less than 2 minutes at the discretion of medical staff.

Intravenous infusion – ED & PCC & Theatre ONLY

Use the following standardised concentrations:

Patient's Weight	Concentration** (in Sodium Chloride 0.9%)	Notes
10 kg or less	15 mg in 30 mL (0.5 mg/1 mL)	In a 3 kg patient, 50 microg/kg/hr = 0.3 mL/hr
Above 10 kg	50 mg in 50 mL (1 mg/1 mL)	In a 20kg patient, 50 microg/kg/hr = 1 mL/hr

Patients 10 kg or less may be prescribed the higher strength (50 mg in 50 mL) preparation to manage fluid overload if clinically indicated, at the treating consultant's discretion.

****Deviation from the above concentrations must be approved by a consultant.**
Consider risks associated with deviation from the above weight-band recommendation.

Intramuscular administration

- Inject (undiluted) deeply into a large muscle mass, generally the anterior-lateral aspect of the thigh.[5] Use a Luer lock syringe if patient is agitated to avoid inadvertent disconnection.

Subcutaneous administration

- Give as a continuous subcutaneous infusion.[8, 10]

COMPATIBILITY *(LIST IS NOT EXHASTIVE)*

Compatible fluids:[10]
Sodium chloride 0.9%, glucose 5%, glucose 10%, Hartmann's, Ringer's

Compatible at Y-site:[10]
Amiodarone, calcium chloride, calcium gluconate, cefazolin, cefotaxime, ceftriaxone, ciclosporin, ciprofloxacin, clindamycin, digoxin, erythromycin, fentanyl, fluconazole, gentamicin, heparin

sodium, hydromorphone, metoclopramide, metronidazole, morphine sulfate, palonosetron, paracetamol, tobramycin, vancomycin

Only commonly used drugs are listed below. This is not a complete list of incompatible drugs. Compatibilities of IV drugs must be checked when two or more drugs are given concurrently.

INCOMPATIBLE drugs:[3, 10]

Aciclovir, amoxicillin, azithromycin, dexamethasone, flucloxacillin, furosemide, phenobarbital, piperacillin-tazobactam, trimethoprim-sulfamethoxazole

MONITORING

The level of patient observation and nursing supervision will be influenced by the dose and combination of medications being administered and the patient's clinical history/co-morbidities. This should be anticipated and a monitoring plan documented in the patients records by the prescriber/treating medical team in each area.

Observations during sedation period – Procedural Sedation Guideline

At a minimum, 15 minutely observations will be recorded on the age-appropriate Observation and Response Tool (or more frequently as directed by the prescriber):

- Heart rate, respiratory rate, oxygen saturation measured by pulse oximetry,
- Blood pressure (if clinically indicated)
- University of Michigan Sedation Scale (UMSS) during the sedation period
- Pain intensity score (if indicated)

Note: post procedure sedation can become more pronounced following cessation of a painful stimulus.

Monitoring should commence with administration of midazolam and until patient returns to pre-sedation conscious level.

Increased nursing supervision and frequency of observation should be initiated for:

- Patients with increased risk factors
- Patients who have received multiple sedating agents
- Patients with UMSS ≥ 2

Monitor for signs of withdrawal in prolonged use (if infusion is ≥ 3 days). Symptoms include convulsions, hallucinations, tremor, abdominal and muscle cramps, vomiting and sweating.[1, 5] Refer to Withdrawal Assessment Tool – Version 1 (WAT–1) MR859.80 and Withdrawal Syndrome Management Guideline.

ADVERSE EFFECTS[1, 3, 5, 11]

Common: drowsiness, oversedation, light-headedness, hypotension (can be severe with IV injection), ataxia, hypersalivation, slurred speech, blurred vision

Infrequent: headache, vertigo, confusion, paradoxical excitation or aggression, euphoria, anterograde amnesia, skin rash, laryngospasm, bronchospasm, nausea, vomiting, restlessness, hallucination, disinhibition, respiratory depression (particularly with high doses or on rapid injection), acidic taste, nasal irritation (intranasal)

Rare: arrhythmias, bradycardia, cardio-respiratory arrest, anaphylactic reactions, dry mouth, dysponea, urinary retention, jaundice, coma (particularly with high doses or on rapid injection), convulsions (more common in neonates), incontinence, wheezing, tachycardia, nystagmus, delirium, transient elevated liver function tests, cough, hiccup, increased appetite, hyperventilation, movement disorders

STORAGE

- Ampoule: store below 25°C. Protect from light.[2, 10]
- Midazolam is a Schedule 4 Recordable medication (S4R) and legally must be stored and recorded as such. Refer to Schedule 8 and Restricted Schedule 4 Medication Policy.

INTERACTIONS

Midazolam may interact with other medications; please consult PCH approved references (e.g. Clinical Pharmacology), your ward pharmacist or PCH Medicines Information Service on extension 63546 for more information.

REVERSAL OF BENZODIAZEPINE OVERDOSE/OVERSEDATION

Flumazenil can be used to reverse the effects of midazolam. Clinical areas must ensure they have access to flumazenil injection before administering midazolam.

- **IV injection**: 5 – 10 microg/kg (maximum 200 microg) administered over 15 seconds.
    - If response is inadequate, repeat dose every 60 seconds to a maximum of 50 microg/kg (usual maximum 1 mg; children >12 years old in Paediatric Critical Care may use maximum 2 mg). [3, 4]

A continuous IV infusion may be commenced if drowsiness recurs after IV injection.

- **Continuous IV infusion**: 2 – 10 microg/kg/hour (maximum 400 microg/hour), adjust dose to response.[3, 11]

Please note: The information contained in this guideline is to assist with the preparation and administration of **Midazolam**. Any variations to the doses recommended should be clarified with the prescriber prior to administration

Related CAHS internal policies, procedures, and guidelines
Analgesia and Sedation in Paediatric Critical Care
Arousal and Agitation Drug Management Guideline

Drug Dosing in Overweight and Obese Children 2 to 18 Years of Age Guideline
Flumazenil
High Risk Medicines
Intramuscular (IM) injections
PCH Pharmacy Buccal Midazolam Information Leaflet
Procedural Sedation
Schedule 8 and Restricted Schedule 4 Medication Policy
Withdrawal Syndrome Management Guideline

Manufacturer Safety Data Sheet (SDS)

To access the Manufacturer SDS for this product, use the following link to ChemAlert.

References

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11. Royal Pharmaceutical Society of Great Britain, Royal College of Paediatrics and Child Health, British Medical Association, Neonatal and Paediatric Pharmacists Group. BNF for children; 2024 [cited 2024 Feb 29]. Available from: BNF

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Appendix 1: Preparation and Administration guide for Intranasal Midazolam

Midazolam can be administered using an intranasal Mucosal Atomisation Device (MAD Nasal™).

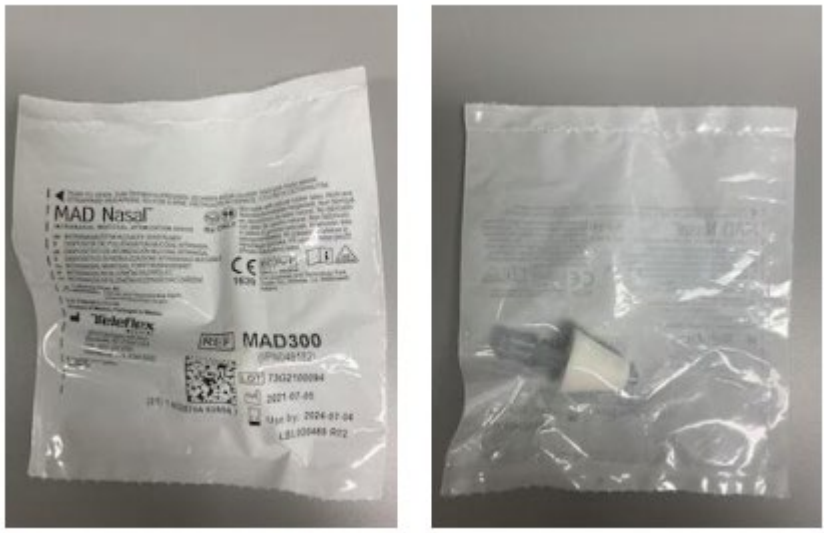

Image 1: MAD Nasal™.

Instructions:

1. Draw up the desired dose of midazolam solution in a syringe, plus an additional 0.1 mL to account for the dead space in the MAD nasal™.

2. Attach the MAD nasal™ and push the plunger to the desired dose to prime the MAD nasal™. Note: Not priming the MAD may result in underdosing.

3. Ensure the patient is positioned safely on the bed or on the parent or caregiver's lap.

4. Using the free hand to hold the occiput of the child's head stable, place the MAD Nasal™ against the nostril of the child aiming slightly up and outward (toward the top of the ear).

5. Administer the dose as a rapid push and avoid spillage from the nose by ensuring an adequate seal.

6. The dose can be divided over both nostrils to increase the absorptive area. Doses greater than 1 mL should be divided between both nostrils.