Midazolam (Palliative Care)

Midazolam

Caution

These guidelines are for use in Palliative Care only.

There is a variable sensitivity to midazolam which is often unpredictable. Intravenous midazolam has a high risk of apnoea and should be avoided in palliative patients.[1]

Presentation

Midazolam 5mg/5ml and Midazolam 15mg/3ml ampoules.
Midazolam nasal spray 5mg/ml (15ml).

Indications (Unlicensed)

For restlessness, anxiety, respiratory distress, terminal agitation, seizures, myoclonic jerks, intractable hiccup, subcutaneous administration.[2]

Dose

Subcutaneous Midazolam[3]

Indication	Stat and initial PRN dose	Initial infusion rate per 24h	Common range
Anxiety/restlessness/ respiratory distress	2.5 – 5mg q2h	10mg	10 – 20 mg
Muscle tension/ spasm	2.5 – 5mg q2h	10mg	10 – 20 mg
Terminal agitation	5 – 10mg q2h	10 – 15mg	10 – 40mg
Seizures	5 – 10mg	30mg	30 – 60mg

There is no maximum dose for midazolam, however the dose should be titrated carefully according to the response.

If the dose exceeds more than 30mg/24 hours advice should be sought from the Palliative Care Team.

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Dose, *cntd*

Midaxolam Nasal Spray
There is no commercial preparation of midazolam nasal spray available in New Zealand, therefore it must be compounded for each patient in the pharmacy. The amount dispensed in each spray is dependant on the spray bottle used.

For WDHB each spray dispenses 0.1ml of solution which provides 0.5mg of midazolam. The dose of intra-nasal midazolam is generally thought to be equivalent to the subcutaneous dose.[4] The dose required is patient and indication dependant.

Advice should be sought from the Palliative Care Team when prescribing midazolam nasal spray.

Diluent

- For subcutaneous bolus administration midazolam does not need to be diluted.
- When added to a syringe driver the recommended diluent is water for injection.[2]

Additional Equipment

- Subcutaneous Safe-T-Intima single lumen [ADM140] (*WDHB policy pending*).
- Subcutaneous infusion pump (Graseby or equivalent) if required.

Compatibility

- Water for injection, 0.9% sodium chloride, morphine sulfate, morphine tartrate, haloperidol, hyoscine hydrobromide, metoclopramide, dexamethasone, ketamine.[5]
- Ranitidine, methadone, fentanyl, oxycodone, cyclizine, levomepromazine, hyoscine N-butylbromide, octreotide.[6]

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Administration

Subcutaneous Administration

- 15mg/3ml formulation should be used to reduce the volume administered.
- Should be injected through a Safe-T-Intima (butterfly) or directly by a subcutaneous needle.
- The Safe-T-Intima should be flushed with 1ml of water after administration of medication.
- Can be administered via a subcutaneous pump (Graseby or equivalent).

Observation and Monitoring

Observe patient for excessive sedation.

Mechanism of Action

Midazolam is a short-acting benzodiazepine with GABA potentiating actions in the central nervous system (CNS).[2]

It relieves anxiety, is a sedative, an anticonvulsant and a muscle relaxant.[1]

Contraindications and Precautions

Contraindications

- Patients with known hypersensitivity to midazolam[1]

Precautions

- Patients with chronic respiratory insufficiency
- Patients with hepatic failure
- Myaesthenia gravis[1]

Possible adverse effects

- Excessive sedation
- Hypotension
- Paradoxical agitation e.g. in elderly/delirium[1]

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Drug Interactions

Cimetidine, erythromycin, diltiazem, verapamil, ketoconazole, fluconazole and itraconazole can inhibit hepatic metabolism of midazolam resulting in a prolonged and more pronounced effect.[1]

References

1	Medsafe Website – Midazolam Datasheet. http://www.medsafe.govt.nz/profs/datasheet/h/Hypnovelinj.htm
2	Twycross R, Wilcock A (eds). Palliative Care Formulary 3rd Edition. Palliativedrugs.com Ltd.
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4	Knoester PD, Jonker DM et al. Pharmacokinetics and Pharmacodynamics of midazolam administered as a concentrated intranasal spray. A study in healthy volunteers. British Journal of Clinical Pharmacology 2002 May 53(5): 501-507.
5	Smith, S. Compatibility of syringe driver admixtures for continuous subcutaneous infusion, Pharmacy Department Auckland Hospital 2002.
6	Back I (eds). Palliative Medicine Handbook (Online Edition). BPM Books, Cardiff, UK. (http://book.pallcare.info/)