Clonazepam – Palliative Care (Adults)

Contents

1. Overview

Purpose

This protocol outlines the administration, prescribing and monitoring of clonazepam at Te Whatu Ora - Waitematā.

Scope

All medical and nursing staff.

⚠ This guideline is for use in the context of Palliative Care ONLY.

2. Presentation

Clonazepam 0.5mg and 2mg tablets
Clonazepam oral drops 2.5mg/ml (1 drop = 0.1mg of active ingredient)
Clonazepam 1mg/ml ampoules

3. Indications

Licensed:

- Seizures and myoclonus[1, 3]

Unlicensed:

- Anxiety, panic disorder, restless leg syndrome, neuropathic pain, terminal agitation[2, 6]

Unlicensed route of administration:

- Subcutaneous

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4. Mechanism of Action

Clonazepam is a benzodiazepine. It has anti-convulsive, sedative, muscle relaxing and anxiolytic effects. These effects are thought to be mediated mainly by enhancing post-synaptic GABA mediated inhibition.[1] It is a long-acting benzodiazepine with a half-life of 18 to 45 hours.

5. Dose

The conversion ratio for oral (PO) to subcutaneous (SC) clonazepam is 1:1 and therefore the doses are the same for both routes.[4]

Note: Maximum daily dose (including PRN) should not exceed 2-3mg unless advised by the Palliative Care Team. PRN doses may be used more frequently under the advice of the Palliative Care Team.[2]

Indication[1-3]	Route	Stat and Starting PRN doses	Recommended Daily Max dose (including PRN)	Daily Dose Range†
Seizures	PO/Subcut	0.5 – 1mg	4mg	1 – 8mg daily in divided doses
Panic disorder	PO	0.25mg (tablets) or 0.3mg (3 drops) q12hr	2mg	0.5 – 4mg nocte
Restless legs	PO	0.25mg (tablets) or 0.3mg (3 drops) q12hr	2mg	0.5 – 2mg nocte
Neuropathic pain	PO	0.25 – 0.5mg (tablets) or 0.3 – 0.5mg (3 to 5 drops) q12hr	2mg	0.5 – 8mg daily in divided doses
Terminal restlessness	Subcut	0.5mg q2hr	3mg	2 – 8mg over 24 hours
	Syringe driver (CSCI)*	1mg	3mg	2 – 8mg over 24 hours

Note:

- Elderly or debilitated patients may require dose reduction[1]
- Clonazepam is long acting and can be given once daily as a bolus injection, preferably at night (due to its sedative effect)[2]
- Consider starting low doses at bedtime to minimise adverse effects[1]
- †Daily dose range that has been used in palliative care setting – do not exceed maximum daily dose of 2-3mg (including PRN) unless advised by the Palliative Care Team.

⚠ **NEVER** administer clonazepam drops directly into the mouth from the bottle. The medication should be measured into a teaspoon prior to administration. The drops can be mixed with water, tea or fruit juice if required[1].

⚠ *For administration via CSCI, the same dose as oral is recommended, however the prescriber should be on alert for the lower predictable response potentially due to the loss of clonazepam from adsorption onto PVC-containing giving sets.[4]
Therefore, low-sorbing or Non-PVC containing extension set should be used.

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6. Administration

6.1 Diluent

- For subcutaneous bolus administration dilute each 1mg/ml ampoule with 1ml water for injection.[2, 4]
- Inject through a Saf-T-Intima single lumen (butterfly).
- The Saf-T-Intima should be flushed with 0.2ml of water for injection after medication administration.
- Can be administered via a continuous subcutaneous pump (Niki T34).
- When added to a syringe driver the recommended diluent is water for injection or sodium chloride 0.9%.[2, 4]

6.2 Additional equipment

- Subcutaneous Saf-T-Intima single lumen [ADM140]. (*See Te Whatu Ora – Waitematā Policy Palliative Care- Subcutaneous Site Selection, Insertion and Monitoring of BD Saf-T-Intima Cannula*).
- If giving via syringe driver:
    - Continuous subcutaneous infusion pump (Niki T34)
    - Low-sorbing or non-PVC extension set (up to 50% of infused clonazepam is adsorbed onto PVC tubing).

6.3 Compatibility

Compatible with:

Water for injection, 0.9% sodium chloride, methadone, dexamethasone, morphine sulfate, morphine tartrate, oxycodone, haloperidol, hyoscine hydrobromide, hyoscine butylbromide, metoclopramide, octreotide, glycopyrronium, levomepromazine, midazolam, ketamine.[2, 4, 5, 6]

Concentration dependent compatibility with:

Cyclizine[2, 4]

⚠ Do not use if the solution is cloudy or a precipitate is present.

7. Observation and Monitoring

Monitor for excessive drowsiness.

8. Contraindications and Precautions

Contraindications

- Hypersensitivity to clonazepam or other benzodiazepines
- Severe respiratory insufficiency
- Severe hepatic insufficiency.[1]

Precautions

- Respiratory disease
- Hepatic impairment

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- Sleep apnoea syndrome
- Myasthenia gravis
- Avoid sudden withdrawal in patients with seizure activity or history of epilepsy.'[2]

9. Possible Adverse Effects

- Drowsiness
- Fatigue/lassitude
- Muscle weakness
- Dizziness
- Ataxia / Unsteadiness
- Confusional state
- Paradoxical reactions (irritability, aggression, agitation, nightmares)
- Respiratory depression
- Slowed reactions[1,2]

⚠ Adverse effects can be minimised by starting with low doses at bedtime[1]

10. Drug Interactions

- Concurrent use of clonazepam and other centrally acting medications may result in potentiation of their effects e.g. anti-convulsants, hypnotics, opiates, alcohol.[1]
- Phenytoin, carbamazepine and sodium valproate may increase the clearance of clonazepam and hence reduce its therapeutic effect[1] (conversely, clonazepam has unpredictable effects on phenytoin – it may increase, decrease or leave phenytoin plasma concentrations unchanged).[2]
- Effects of clonazepam can be reduced by CYP3A4 inducers (eg carbamazepine, high-dose dexamethasone) and increased by CYP3A4 inhibitors (eg erythromycin, haloperidol, high-dose fluconazole).[4]

11. References

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4	Dickman A, Schneider J. The Syringe Driver – Continuous subcutaneous infusions in palliative care. 3rd ed. New York: Oxford university press; 2011.
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