Clonazepam (Injection) (Red)*

*** Colour code:**
Red – For medicines normally initiated and used under specialist guidance

Introduction

Description: Benzodiazepine with anti-epileptic properties.

Specialist palliative care involvement is essential.

Preparations

Route	Preparation	Licence type[1]
Oral	500 microgram tablets 2mg tablets 500micrograms/5ml and 2mg/5ml oral solution 2.5mg/ml oral drops	**Oral drops are unlicensed** †
Injection	1mg/1ml with water for injection 1ml diluent	**Unlicensed in the UK** † **-** needs to be imported

Indications and uses

Licensed	Unlicensed †
Epilepsy	Neuropathic pain
Myoclonus	Restless legs syndrome
	Terminal restlessness
	Anxiety and panic attacks

Cautions

- Chronic respiratory disease.
- Moderate hepatic impairment.
- Renal impairment (not dialysed). Start at low doses and increase according to response.

[1] † Indicates this use is off licence

- Consider gradual reduction if treatment has to be stopped and patient has a history of epilepsy.

Contra-indications

Clonazepam is contra-indicated for use in patients with:

- acute pulmonary insufficiency
- myasthenia gravis
- severe hepatic impairment
- severe respiratory insufficiency
- sleep apnoea syndrome.

If the patient is in the last days of life, these are not absolute contra-indications. Careful titration is however necessary.

- Drug interactions:
  - clonazepam is extensively metabolised by CYP3A4 to inactive metabolites
  - reduced effect - clonazepam effect may be REDUCED by co-administration of CYP3A4 inducers, such as carbamazepine, high dose dexamethasone and phenobarbital
  - increased effect: inhibitors of CYP3A4, such as bicalutamide, erythromycin, high dose fluconazole and haloperidol MAY ENHANCE the effect of clonazepam
  - clonazepam and phenytoin have unpredictable effects on each other's plasma concentrations - clonazepam may or may not alter phenytoin plasma concentration, whereas phenytoin may decrease the plasma concentration of clonazepam. Monitor the phenytoin plasma level if given concurrently with clonazepam and adjust dose if necessary
  - effect on clonazepam's metabolism by other drugs may persist for several days after discontinuation of the causative drug - be aware of the potential for interaction: doses may need to be adjusted.
- Side effects:
  - drowsiness (dose dependent), impaired psychomotor skills, fatigue, cognitive impairment and hypotonia
  - start with a low dose and titrate up to minimise unwanted effects.

Note: use of benzodiazepines in elderly patients increases the risk of falls and fractures.

Dose and administration

- Dose recommendations depend on the indication.
- For continuous subcutaneous infusion (CSCI) administration the same dose as oral therapy is recommended.

- In elderly patients, the initial dose should not exceed 500 micrograms/24 hours if newly prescribed.

Route	Dosage
Oral	500 micrograms at night (250 micrograms if concerned about drowsiness), up to 4mg/day.
Subcutaneous	Common dose range in palliative care: • 1mg to 4mg over 24 hours • doses up to 8mg in 24 hours have been used. The dose of clonazepam should be carefully adjusted to individual requirements, and used with caution in patients with chronic respiratory disease, renal or moderate hepatic impairment. Manufacturers also state the stability of the diluted clonazepam is maintained for up to 12 hours, although there are reports of CSCI administration over 24 hours without apparent unexpected effect.

Diluent

- Use the diluent ampoule (Water for Injection) supplied with the clonazepam ampoules if administering the clonazepam as a bolus injection. The clonazepam ampoule must be diluted prior to a bolus administration.
- **If administering clonazepam via a syringe pump** over 24 hours (CSCI), there is no need to use the diluent ampoule supplied in the box as the clonazepam will be administered diluted in the syringe pump. Use sodium chloride 0.9% as the diluent if clonazepam is to be administered on its own.

Compatibility

- It has been shown that sorption into PVC infusion sets occurs with clonazepam injection. The clinical significance of this effect is yet to be determined, although another study has shown that significant loss of clonazepam (up to 50%) does occur when infused through PVC tubing over 24 hours. Use of non-PVC tubing solved this problem.
- Please check with specialist palliative care pharmacists for further information/compatibilities.

Practice points

- As there is now no commercially available clonazepam injection in the UK, ampoules have to be imported. To check local availability contact your local specialist palliative care pharmacist. There may be a delay in obtaining and costs can be significant.

- The community pharmacist, GP and community nurse should be informed.
- The unscheduled care service should be informed that the patient is receiving this medicine.
- Clonazepam can be prescribed by the patient's GP for the indications listed in liaison with local palliative care specialists.

Resources and references

- Twycross R, Wilcock A, Howard P. Palliative Care Formulary PCF6. 6th ed. England: Pharmaceutical Press; 2017.
- Dickman A, Schneider J. The Syringe Driver. 4th ed: Oxford University Press; 2016.
- Summary of Product Characteristics (SPC) http://www.medicines.org.uk/emc/search