

Subcutaneous Levetiracetam ('Keppra') in Palliative and End of Life Care

Background

Benzodiazepines are the first line management for prolonged seizures or status epilepticus in palliative and end of life care.

It is common practice to stop established oral antiepileptic drugs once the oral route is lost and switch to an alternative antiepileptic drug via the subcutaneous (SC) route. An example from clinical practice might be stopping oral levetiracetam and commencing a syringe driver with starting doses of midazolam from 20 to 30 mg, with the dose escalated if seizures are witnessed. While benzodiazepines generally achieve effective seizure control, they also cause sedation. This sedative effect may be desirable in agitated patients. However, the sole use of sedating medications risks ongoing sedation of a patient who might otherwise have regained consciousness following a postictal period. Use of off-label subcutaneous levetiracetam offers the possibility of maintaining seizure control when the oral route is lost without increasing the level of sedation. (The use of medicinal products off-label is widespread. Surveys say that up to one quarter of all prescriptions in palliative care come into this category. This includes the use of two or more medications in a syringe driver. The British Pain Society and Association for Palliative Medicine have produced recommendations for this practice).

It is recommended to initiate SC levetiracetam only following advice from the Palliative Care Team or Hospice.

Indications

The treatment of epileptic seizures and status epilepticus in palliative and end of life care for patients who are unable to take their medications orally and when IV access is not possible or not desired.

Generally SC levetiracetam would be used for patients who have had good seizure control on oral levetiracetam and who are unable to swallow this and in whom a switch to SC midazolam is not appropriate due to sedation.

Pharmacology

Levetiracetam is effective for a broad range of seizure types. Its efficacy and tolerability compare favourably to other antiepileptic drugs in both cancer-related and non-cancer related seizures. Unlike carbamazepine and phenytoin, it does not interact with dexamethasone or induce cytochrome P450.

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Cautions (from BNF)

Dose should be reduced in patients with renal impairment. In adults maximum 2g daily if eGFR 50-80ml/min/1.73m². Maximum 1.5g daily if eGFR 30-50ml/min/1.73m². Maximum 1g daily if eGFR less than 30ml/min/1.73m²

Side effects (from BNF)

Common or very common:

Anxiety, appetite decreased, asthenia, behaviour abnormal, cough, depression, diarrhoea, dizziness, drowsiness, gastrointestinal discomfort, headache, increased risk of infection, insomnia, mood altered, movement disorders, nausea, skin reactions, vertigo and vomiting

Uncommon:

Alopecia, concentration impaired, confusion, hallucination, leucopenia, muscle weakness, myalgia, paraesthesia, psychotic disorder, suicidal behaviours, thrombocytopenia, vision disorders, weight changes

Rare or very rare:

Acute kidney injury, agranulocytosis, hepatic disorders, hyponatraemia, neutropenia, pancreatitis, pancytopenia, personality disorder, rhabdomyolysis, severe cutaneous adverse reactions (SCAR), thinking abnormal

Subcutaneous administration

Use of off-label subcutaneous levetiracetam offers the possibility of maintaining seizure control when the oral route is lost and there is no IV access, without increasing the level of sedation.

Levetiracetam injection (100mg/ml) can be given via a syringe driver using a PO:SC dose ratio of 1:1, diluted with either water for injection or sodium chloride 0.9%. **Therefore, the initial dose by SC infusion should be the same as the previously administered total daily dosage taken orally. SC levetiracetam is generally not commenced if the patient has not already been taking the drug orally.** Usual oral dose is to start levetiracetam 250-500mg bd. Maximum oral dose is 1.5mg bd.

There is limited clinical experience that suggests that levetiracetam is compatible with diamorphine, haloperidol, hyoscine butylbromide, levomepromazine, methadone,

metoclopramide, midazolam, morphine sulfate, oxycodone and ranitidine using sodium chloride 0.9% as diluent but it is generally administered alone in a separate syringe driver.

Do not exceed 2g due to volume capacity in the 30ml syringe driver and monitor for site reaction and seizure activity.

Please contact a Pharmacist, the Palliative Care Team (tel. 01423 553464) or Hospice (01423 872658) for advice.

References

Use of medications beyond (off-label) and without (unlicensed) Marketing Authorisation (MA) in palliative care and pain medicine (2012):

https://www.britishpainsociety.org/static/uploads/resources/files/useofmeds_professional_final.pdf

British National Formulary <https://bnf.nice.org.uk/drug/levetiracetam.html>

Levetiracetam Summary of Product Characteristics

<https://www.medicines.org.uk/emc/product/2296/smpc#gref>

Palliative Care Formulary 7th Edition (2020)

Sutherland AE, Curtin J, Bradley V *et al* Subcutaneous levetiracetam for the management of seizures at the end of life. *BMJ Supportive and Palliative Care* 2018; 8: 129-135