

## Subcutaneous Levetiracetam in Palliative and End of Life Care (Adults)

### 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 no longer are able to swallow this. It 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 that would be seen if switched to SC midazolam.

SC levetiracetam is generally not commenced unless the patient has been taking the drug orally, but there may be exceptions to this. Usual oral dose is to start levetiracetam 250-500mg bd. Maximum licensed oral dose is 1.5g bd.

## 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.

## Cautions (from BNF)

Dose should be reduced in patients with renal impairment. In adults if:

eGFR (ml/min/1.73m <sup>2</sup> )	Maximum dose per day
50-79	2g per day
30-49	1.5g per day
<30	1g per day

## 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 tendencies, thrombocytopenia, vision disorders, weight changes

Rare or very rare: Acute kidney injury, agranulocytosis, bone marrow disorders, delirium, encephalopathy, gait abnormal, hepatic disorders, hyponatraemia, neutropenia, pancreatitis, personality disorder, QT interval prolongation, rhabdomyolysis, seizures exacerbated, severe cutaneous adverse reactions, thinking abnormal.

Frequency not known: Neuroleptic malignant syndrome

## Subcutaneous Dose

PO:SC dose ratio of 1:1

Therefore, the initial dose by SC infusion should be the same as the previously administered total daily dosage taken orally.

Note however because of practicalities **the maximum dose of levetiracetam in a single syringe driver is 2g** as higher doses exceed the volume capacity of a 30ml syringe driver.

For higher doses discuss options with the palliative care team. A second syringe driver may be an option if considered practical.

**Traffic light status:** Amber specialist recommendation (palliative care)

### Subcutaneous Administration

Drug	Dilution	Administration
Levetiracetam injection 100mg/ml (licensed for iv use)	Diluted to maximum volume with either water for injection or more usually sodium chloride 0.9%.  Usually require a 30mL syringe	Subcutaneous infusion over 24 hours

**Monitor the patient for site reaction and seizure activity.**

### Compatibility with other drugs:

Limited clinical experience suggests that levetiracetam is compatible with the following drugs and these are listed in the current online version of the Palliative Care Formulary.

It may be necessary to consider mixing with other drugs if there is a need to limit the number of syringe drivers, particularly if patient would otherwise require more than 2 drivers.

Clonidine, diamorphine, fentanyl, glycopyrronium, haloperidol, hyoscine butylbromide, levomepromazine, methadone, metoclopramide, midazolam, morphine sulphate and oxycodone.

Generally, sodium chloride 0.9% is used as diluent and local skin reactions occur in about 5% of patients.

The Palliative Care Formulary also publishes a database of clinical practice reports for continuous subcutaneous infusion use via a syringe driver in palliative care. This 'Syringe Driver Database' may have additional information available on multi drug combinations. Medicines Information can be contacted to access this additional information.

Because of practicalities of fitting the solution into a 30mL syringe (max volume approx. 23mL) mixing with other drugs will potentially further limit the dose of levetiracetam.

## Contact details for more information.

<b>Harrogate Area</b>	
Harrogate District Hospital NHS Foundation Trust Palliative Care Team	01423 553464
Saint Michael's Hospice, Harrogate	01423 879687
Harrogate Trust Medicines Information-pharmacy	0113 2065377 or <a href="mailto:medicines.information@nhs.uk">medicines.information@nhs.uk</a>
<b>York Area</b>	
York Hospital Palliative Care Team	01904 725835
York Community Palliative Care Team	01904 777770
St Leonards Hospice, York	01904 708553
York Trust Medicines Information – pharmacy	01904 725960 or <a href="mailto:yhs-tr.medicines.information@nhs.net">yhs-tr.medicines.information@nhs.net</a>
<b>Scarborough Area</b>	
Scarborough Hospital Palliative Care Team	01723 342446
Scarborough Community Palliative Care team	This provided by St Catherine's Hospice, Scarborough. Community Palliative Care Team Tel: (01723) 356043
St Catherine's Hospice, Scarborough	01723 351421
<b>Primary care Medicines Advice Contact (SPS support)</b>	0300 770 8564 or <a href="mailto:asksps.nhs@sps.direct">asksps.nhs@sps.direct</a>

## 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](https://www.britishpainsociety.org/static/uploads/resources/files/useofmeds_professional_final.pdf)

British National Formulary <https://bnf.nice.org.uk/drug/levetiracetam.html> (accessed 16.2.2024)

Levetiracetam Summary of Product Characteristics

<https://www.medicines.org.uk/emc/product/2296/smpc> (text revised 07/2023)

Palliative Care Formulary – online (accessed 16.2.2024)

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

Sutherland A, Meldon C, Harrison T, Miller M Subcutaneous Levetiracetam for the Management of Seizures at the End of Life: An Audit and Updated Literature Review. *J Palliat Med* 2021 24(7) : 976-981