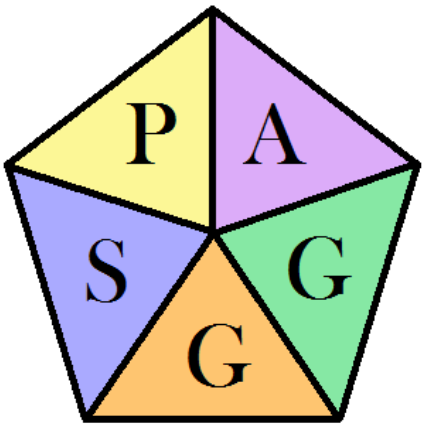

Specialist Palliative Care
Audit and Guidelines Group

Specialist Palliative Care Audit and Guidelines Group (SPAGG)

Clinical Guideline for Commencing Levetiracetam via Syringe Driver

Version 2.0

Date Issued:	March 2021
Review Date:	March 2025

Document Title	Clinical Guideline for Commencing Levetiracetam via Syringe Driver
Document Date	March 2021
Document Purpose and Intended Audience	This guideline has been produced to support the conversion or commencement of levetiracetam via continuous subcutaneous syringe driver in adult patients with a palliative diagnosis. For use by palliative medicine specialists
Authors	Dr Kate Holyhead Dr Sharon Twigger
References	1. Freiherr von Hornstein W et al. Levetiracetam continuous subcutaneous infusion in the management of seizures. First experience. (Poster IAPC Education & Research Seminar 2014) 2. Rémi C et al. Continuous subcutaneous use of levetiracetam: A retrospective review of tolerability and clinical effects. Journal of Pain & Palliative Care Pharmacotherapy 2014; 28(4): 371-377 3. Beatty et al. The use of subcutaneous levetiracetam for the control of seizures in adults at the end of life. (Poster EAPC 2015) 4. Bollig G, Sauer F, Leonhardt AK. Subcutaneous use of levetiracetam in palliative care – a case report and review of the literature. (Poster EAPC 2015) 5. Murray-Brown FL, Stewart A. Remember Keppra: seizure control with subcutaneous levetiracetam infusion. BMJ Supportive & Palliative Care 2016; 6 (1): 12–13 6. Wells GH et al. Continuous subcutaneous levetiracetam in the management of seizures at the end of life: a case report. Wells GH, et al. Age Ageing. 2016; 45(2): 321-2 7. Doré M et al. Exploration into the use of continuous subcutaneous levetiracetam within Palliative Care. BMJ Supportive & Palliative Care 2017; 7(suppl 1) A36 P-97 (Poster ASP 2017) 8. Twigger S et al. The use of subcutaneous levetiracetam in the west midlands' palliative care population: a retrospective audit. BMJ Supportive & Palliative Care 2018; 8(suppl 1) A71-A72 (Poster ASP 2018) 9. Sutherland AE et al. Subcutaneous levetiracetam for the management of seizures at the end of life. BMJ Supportive & Palliative Care 2018; 8(2): 129-135

Consultation Process	Endorsed and approved by SPAGG
Review Date (must be within three years)	March 2025
Approval Signatures: SPAGG chair SPAGG secretary	 Dr J. Tomas Dr A Gray
Date Approved by SPAGG: March 2018	
Date submitted to Area Prescribing Committee:	

Version	Date	Summary of change/ process
1	March 2018	Endorsed and approved by SPAGG
2	March 2021	Endorsed and approved by SPAGG
3		

Table of Contents

1 Scope of the guideline

This guidance has been produced to support the use of subcutaneous levetiracetam in palliative care patients who require treatment for seizure control but are unable to take levetiracetam orally and when IV access is not an appropriate intervention.

2 General information

This guidance has been developed to establish a degree of consensus and uniformity in clinical practice that is likely to be beneficial to patient care despite a low quality evidence base.

3 Background information

The management of seizures in patients approaching the end of life has previously relied on the use of benzodiazepines and phenobarbitone administered via a syringe driver. The transition from oral anti-epileptic medications to these agents, whilst standard accepted practice, has no established, widely used conversion. There is a small but growing body of evidence to suggest that using the injectable form of levetiracetam subcutaneously is a safe and effective alternative way to administer anti-epileptic medication towards the end of life.

In the UK the drug leviteracetam is increasingly used in patients with secondary epilepsy caused by brain tumours as well as being used prophylactically in patients post-neurosurgery to remove or debulk tumours. In addition, NICE guidance recommends levetiracetam as first line treatment for myoclonic and focal seizures and as an adjunct for generalised tonic-clonic and absence seizures.

Its mechanism of action is presumed to be an interference of neurotransmitter release from the synaptic vesicle via binding to synaptic vesicle protein SV2A. Unlike many other anti-epileptic medications levetiracetam does not require the CYP450 enzymes for metabolism. A third is metabolised predominantly by non-hepatic hydrolysis, and the remainder is excreted by the kidneys unchanged. It therefore has fewer drug interactions than other anti-epileptics, which is particularly advantageous in palliative care.

4 Guideline statements

4.1 Indication

- Subcutaneous levetiracetam has a potential role in the treatment of epileptic seizures in palliative care patients who are unable to take their medications orally and when IV access is not an appropriate intervention to maintain good seizure control.

- Use of subcutaneous levetiracetam is 'off licence' and this should be discussed with the patient as with any other off licence medication.

4.2 Dosing

- Oral bioavailability of levetiracetam is 95-100% therefore it is recommended that subcutaneous dosing should mirror standard oral dose.

- For a patient already receiving oral levetiracetam the ratio for conversion from oral to subcutaneous use is 1:1 (level D evidence).

- The usual starting dose, in a patient not previously using oral levetiracetam, is 500-1000mg over 24 hours via continuous subcutaneous infusion (CSCI).

- The oral formulation states a dose increase of 500mg at two week intervals is advised. Patient condition should be considered when deciding on a titration schedule in this patient group.

- The maximum licensed dose is 3000mg over 24 hours. Higher doses (up to 4000mg) have been stated in the literature (level D evidence).

4.3 Volumes and Diluent

- Both 0.9% saline and water for injection have been used as a diluent (level D evidence).

- Levetiracetam is available as a 100mg/ml IV formulation (5ml ampoules). Its use subcutaneously is off licence and when used via CSCI the recommended dilution for IV use cannot be achieved. The osmolarity of levetiracetam has been reported as high and this may add to the risk of inflammatory site reactions. To reduce the likelihood of site reactions as with all syringe drivers, it is recommended to use the highest dilution possible (level D evidence).

- Levetiracetam can be infused in a 30ml syringe over 24 hours, however there may be limitations to the dose that can delivered due to volume capacity (i.e. typically the maximum dose of levetiracetam that can be delivered through a BD T34 syringe driver using a 30ml syringe will be 2grams due to the volume – please refer local policies on delivery of CSCI).

- When higher doses are required the volumes can be problematic to administer. Alternative options (depending on local policies on delivery of CSCI) may include running the levetiracetam in either a 50ml syringe or to use two 12 hourly 30ml

syringe drivers (level D evidence). There is also a T60 syringe driver pump available which some hospice in-patient units keep for this purpose.

4.4 Compatibility

- There is limited evidence available regarding the compatibility of subcutaneous levetiracetam with other medications and no data on drug stability when mixed with other agents. It is advisable to run levetiracetam in a separate syringe driver where possible.

- It has been combined successfully in individual case reports with

    - Morphine sulfate,
    - Oxycodone,
    - Midazolam,
    - Metoclopramide,
    - haloperidol,
    - hyoscine butylbromide
    - levomepromazine,
    - dexamethasone
    - methadone,
    - rantidine,
    - diamorphine
    - (level D evidence). Please contact pharmacy for further advice.

Generally sodium chloride 0.9% is used as the diluent for combincations and local skin reactions occur in 5% of patients (PCF7)

5 Patient information and counselling

No patient information leaflet available at date of guideline publication. It's use off licence should be discussed with patients prior to use.

6 Other issues

6.1 Adverse events

There have been cases of mild erythema to the infusion site (level D evidence). For information regarding the general side effects of levetiracetam please consult the manufacturer's Summary of Product Characteristics (SPC).

6.2 Prescribing considerations

Dose adjustment is required in renal failure (see table below). Dose reduction is not required in mild to moderate hepatic impairment.

Group	Creatinine clearance (ml/min/1.73m2)	Dose and frequency
Normal	>80	500 to 1500mg twice daily
Mild	50-79	500 to 1000mg twice daily
Moderate	30-49	250 to 750mg twice daily

Severe Dialysis	<30	250 to 500mg twice daily 500 to 1000mg once daily

6.3 In the event of a seizure

Benzodiazepines remain the first line treatment for a prolonged seizure or status epilepticus.

7 Monitoring of the guideline

Adherence to the guideline may from time to time be formally monitored.

8 Authors

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