The Use of Subcutaneous Levetiracetam in Palliative Medicine (2018)

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

Preparations
Keppra® 100 mg/ml concentrate for solution for infusion. Each 5 ml vial contains 500 mg of levetiracetam. This preparation is not licensed for subcutaneous administration.

Dose conversion from oral to subcutaneous (SC)
A 1:1 ratio between oral and subcutaneous routes should be used. Therefore, the initial dose by subcutaneous (SC) infusion should be the same as the previously administered total daily dosage of oral levetiracetam.

Doses
The usual starting dose is 500-1000mg over 24 hours via a continuous subcutaneous infusion (CSCI). The maximum licensed dose is 3000mg of levetiracetam in 24 hours. Dose escalation schedules may vary depending on the clinical condition the patient. If higher doses of levetiracetam is to be used subcutaneously, contact pharmacy for advice.

Rate of Infusion
Levetiracetam should be infused via CSCI over 24 hours. However, depending on the volume, two 12 hour drivers may be required.

Hepatic Impairment
No dose adjustment is needed in patients with mild to moderate hepatic impairment. In patients with severe hepatic impairment, the creatinine clearance may underestimate the renal insufficiency. Therefore a 50 % reduction of the daily maintenance dose is recommended when the creatinine clearance is < 60 ml/min/1.73 m²

Renal Impairment

<table>
<thead>
<tr>
<th>Group</th>
<th>Creatinine clearance (ml/min/1.73m²)</th>
<th>Dose and frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>&gt; 80</td>
<td>500 to 1,500 mg twice daily</td>
</tr>
<tr>
<td>Mild</td>
<td>50-79</td>
<td>500 to 1,000 mg twice daily</td>
</tr>
<tr>
<td>Moderate</td>
<td>30-49</td>
<td>250 to 750 mg twice daily</td>
</tr>
<tr>
<td>Severe</td>
<td>&lt; 30</td>
<td>250 to 500 mg twice daily</td>
</tr>
<tr>
<td>End-stage renal disease</td>
<td>-</td>
<td>500 to 1,000 mg once daily</td>
</tr>
</tbody>
</table>

(1) A 750 mg loading dose is recommended on the first day of treatment with levetiracetam.
(2) Following dialysis, a 250 to 500 mg supplemental dose is recommended.

Diluents
Sodium Chloride 0.9% or Water for Injection (WFI) can be used to dilute levetiracetam. Levetiracetam solution for injection should be diluted as much as is practical to avoid irritation at the site of administration.

Compatibility Information
There is limited information to support the combination of levetiracetam with other drugs in CSCI. In OLHCS, we have always administered levetiracetam alone via CSCI and this represents best practice. However, limited clinical experience suggests that levetiracetam may be compatible with morphine sulphate. Please contact pharmacy with any compatibility enquires involving levetiracetam.

Cautions
The administration of levetiracetam to patients with renal impairment may require dose adjustment.
Anecdotally, levetiracetam has caused local irritation including skin blanching/blistering at the administration site. The reason for this is unknown. Site irritation has been reduced by adding 0.5mg of dexamethasone to the syringe pump, or by diluting levetiracetam maximally.

Drug Interactions
There are few known drug interactions between levetiracetam and other medications. Please contact pharmacy for advice.

Issues for Use in the Community
Keppra® 100mg/ml concentration for solution for infusion is not currently reimbursable on the General Medical Services (GMS) card or the Drugs Payment Scheme (DPS) card. Therefore, the patient may have to incur the cost of the medicine.