Levetiracetam (Subcutaneous Infusion)1 *

Introduction

Description: Levetiracetam is a pyrrolidone derivative with anti-epileptic properties, chemically unrelated to existing anti-epileptic active substances. Specialist palliative care involvement is essential.

Preparations

<table>
<thead>
<tr>
<th>Strength</th>
<th>Preparation</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Injection</td>
<td></td>
<td></td>
</tr>
<tr>
<td>500mg/5ml</td>
<td>ampoules</td>
<td>Generic preparations are available as well as Keppra®</td>
</tr>
</tbody>
</table>

Indications

<table>
<thead>
<tr>
<th>Licensed</th>
<th>Unlicensed</th>
</tr>
</thead>
<tbody>
<tr>
<td>Levetiracetam solution for infusion is licensed for intravenous use only.</td>
<td>Unlicensed use when administered by CSCI.</td>
</tr>
<tr>
<td>Mono or adjunctive treatment of partial onset seizures, adjunctive treatment of myoclonic and generalised tonic-clonic seizures.</td>
<td>Monotherapy of generalised seizures. Refer to seizures guideline.</td>
</tr>
</tbody>
</table>

In palliative care CSCI Levetiracetam may be considered by specialist palliative care practitioners as an alternative for patients when oral administration of Levetiracetam is not feasible or when a benzodiazepine (midazolam/clonazepam) is inappropriate, for example if sedation proves troublesome.

Cautions

- Contra-indicated in people with hypersensitivity to other pyrrolidine derivatives, for example procyclidine
- Use with caution in patients with renal or hepatic impairment or with a psychiatric disorder. See below for dose adjustments according to renal function.
- Avoid abrupt withdrawal.
Important drug interactions

- None.

Side effects

- Very common: somnolence, headache, nasopharyngitis.
- Common: depression, hostility/aggression, anxiety, insomnia, nervousness/irritability, convulsion, dizziness, balance disorders, vertigo, lethargy, tremor, anorexia, cough, abdominal pain, diarrhoea, dyspepsia, vomiting, nausea, rash, asthenia/fatigue. Less common but serious reactions include depression, psychosis, suicidality, leukopenia, neutropenia, Stevens-Johnson syndrome, toxic epidermal necrolysis, erythema multiforme, hyponatremia.
- May rarely exacerbate seizure frequency or severity
- Refer to full Summaries of Product Characteristics (SPCs) for complete tabulated list of adverse effects.

Dose and administration

The initial starting dose for monotherapy is 500mg/24 hours, and titrated/increased if needed at fortnightly intervals. If the patient has been taking oral levetiracetam use a PO:SC dose ratio of 1:1.

The subcutaneous (SC) administration of levetiracetam is unlicensed, but published reports and case studies suggest administration by either SC or continuous subcutaneous infusion (CSCI) at concentrations of up to 100mg/ml is well tolerated.

- Given over 24 hours via a syringe pump (CSCI) using water for injection as diluent. Maximal dilution with WFI is recommended in order to preserve the infusion site.
- Two syringe pumps may be required for doses above 2g/day or the use of a 50ml syringe.

In situations where the patient has not previously received levetiracetam there is limited information on how to proceed. The licensed dose titration can take at least 2 weeks to reach a therapeutic dose. Off-label approach is to start at 1g by CSCI over 24 hours and increase as necessary over 2-4 days to 3g by CSCI over 24 hours.

Use in impaired renal function

<table>
<thead>
<tr>
<th>Creatinine clearance (ml/min/1.73m²)</th>
<th>Total daily dose /24 hours</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt; 80</td>
<td>1g to 3g</td>
</tr>
<tr>
<td>50-80</td>
<td>1g to 2g</td>
</tr>
<tr>
<td>30-49</td>
<td>500mg to 1.5g</td>
</tr>
<tr>
<td>&lt;30</td>
<td>500mg to 1g</td>
</tr>
</tbody>
</table>
Practice points

- Unlike other anti-epileptics, levetiracetam has a low potential for pharmacokinetic drug interactions.
- Consider administering levetiracetam using two CME T34 syringe pumps if daily doses are above 2g/day or with the appearance of skin reactions.

Resources and references


Levetiracetam Monographs. Summary of Product Characteristics (SPC)
http://www.medicines.org.uk/emc/