**Alert**
The safety and efficacy of levetiracetam therapy in neonatal seizures has not been evaluated by randomised controlled trials. Consult a paediatric neurologist for further advice on dose recommendations.

**Indication**
Treatment of neonatal seizures.

**Action**
The exact mechanism of action of levetiracetam is unclear. Levetiracetam appears to act by modulation of synaptic neurotransmitter release (GABA, glutamic acid) through binding to the synaptic vesicle glycoprotein 2A and by effects on calcium entry and release pathways in the brain.

**Drug Type**
Anticonvulsant

**Trade Name**
Hospira Levetiracetam, Keppra IV, Levetiracetam IV APOTEX, Levetiracetam Juno, Levetiracetam Sandoz
Keppra Oral, Kerron Oral, Levetiracetam-AFT Oral

**Presentation**
500 mg/5 mL vial
100 mg/mL oral solution

**Dosage / Interval**
**Acute onset seizures refractory to first-line therapy (e.g. hypoxic ischaemic encephalopathy)**

<table>
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<tr>
<th>Maintenance Dose 10 mg/kg/dose</th>
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<tr>
<td>Start 12 hours after loading dose</td>
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<tr>
<td>Postnatal Age</td>
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<td>0–7 days</td>
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<tr>
<td>8+ days</td>
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<td>Dose can be increased to 30 mg/kg/dose (maximum 60 mg/kg/day)</td>
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**Add-on therapy for recurrent seizures**
IV or PO – 10 mg/kg/dose every 12 hours day 0-7 of life and 8-12 hourly from day 8 of life (maximum dose 60 mg/kg/day)

**Route**
IV and Oral

**Preparation/Dilution**
**IV**
Draw up 3 mL (300 mg) and add 17 mL of sodium chloride 0.9% or glucose 5% to make a final volume of 20 mL with a concentration of 15 mg/mL. Infuse dose over 15 minutes.

**Oral**
Give undiluted. If volume is too small, take 1 mL (100 mg) and add 9 mL of water for injection to make a final volume of 10 mL with a concentration of 10 mg/mL.

**Administration**
IV infusion: Infuse over 15 minutes.

Oral: May be given with or without feed (although feed delays the absorption of levetiracetam - this is not a problem if the infant is on maintenance doses). May be given at the same time as other medications.

**Monitoring**
The goal is to achieve clinical control of seizures. Monitor side effects clinically (see adverse reactions). There is a paucity of evidence on target serum concentrations in neonates. Therapeutic concentrations are not routinely measured but may be useful to optimise dose and interval. Target trough concentration > 20 mg/L when seizure frequency is high and 10–40 mg/L subsequently titrated to seizure control. [1, 2, 16] Trough concentration may be useful to determine dosing adjustments in renal impairment. Consult paediatric neurologist for further advice.

**Contraindications**
Hypersensitivity to levetiracetam or any of the ingredients.

**Precautions**
Do not stop levetiracetam therapy abruptly in infants on prolonged therapy (refer to special comments section). Use with caution in renal impairment. Although similar dosing has been used in premature infants, there are minimal pharmacokinetic data
in this population.

**Drug Interactions**
Clearance may be increased by 30% with co-administration of phenobarbital (phenobarbitone), carbamazepine and phenytoin.

**Adverse Reactions**
Adverse reactions are very rare. Sedation and irritability have been reported in neonates. In children, commonly reported problems include behavioural problems and somnolence, loss of appetite, vomiting, dizziness, rash and insomnia. These are more common with polytherapy. [3] Other rare adverse effects that have been reported in older children and adults (but not observed in neonates so far): thrombocytopenia, leukopenia, neutropenia, toxic epidermal necrolysis, Stevens-Johnson syndrome, erythema multiforme, hepatitis, hepatic failure, weight loss, pancreatitis.

**Compatibility**
Fluids: Glucose 5% (10% not tested), sodium chloride 0.9%.
Y-site: No information available.

**Incompatibility**
Fluids: No information available.
Y-site: Amino acid and lipid solutions.

**Stability**
Diluted solution: Stable for 24 hours at 2–8°C or 6 hours at 25°C. Vials are single use only.
For oral solution: Once opened, discard after 7 months.

**Storage**
Store below 25°C.

**Special comments**
In children, oral bioavailability is 100% and no dose adjustment necessary when changing from IV to oral or vice versa. If therapy is to be stopped, levetiracetam should be withdrawn slowly in consultation with a paediatric neurologist. A general weaning regimen is 20–25% reduction per week over 4–5 weeks.[4]

**Evidence summary**
As per NMF Consensus Group. Refer to reference manual or electronic version.

**References**
As per NMF Consensus Group. Refer to reference manual or electronic version.