Gabapentin
Newborn use only

2022

<table>
<tr><td>Alert</td><td>There are no prospective studies on the dosing, efficacy and safety in neonates.
Gabapentin is a potential drug of abuse and dependence in adults.[1]
The effects of both gabapentin and pain on the neonatal neurodevelopment are unknown.[2]
Indiscreet use of gabapentin carries a significant risk of masking of symptoms of a serious underlying disease causing pain and irritability (e.g. sepsis, cardiac failure or raised intracranial pressure).
Gabapentin should not be started without a full and thorough review by a senior neonatologist.
In New South Wales, it is recommended to notify the Pain Management team at Sydney Children's Hospital Network on the commencement of gabapentin.</td></tr>
<tr><td>Indication</td><td>Chronic pain and irritability*
Visceral hyperalgesia*
*Both these conditions are diagnoses of exclusion and any underlying aetiology should be treated appropriately before commencing gabapentin.</td></tr>
<tr><td>Action</td><td>Gabapentin is structurally related to the neurotransmitter GABA (gamma-aminobutyric acid); however, gabapentin and its metabolites do not bind to GABA receptors or influence the degradation or uptake of GABA. The mechanism by which gabapentin exerts its analgesic and anticonvulsant effects is unknown.[3] In vitro studies showed that gabapentin selectively inhibit the alpha-2 delta-1 (α2δ−1) subunit of calcium channels thereby alleviating neuropathic pain. Further investigation is warranted to determine whether treatment in neonates causes increased GABA levels or α2δ−1 inhibition.[2, 4]</td></tr>
<tr><td>Drug type</td><td>Analgesic and anticonvulsant</td></tr>
<tr><td>Trade name</td><td>Neurotin, Gabacor and other multiple brands available</td></tr>
<tr><td>Presentation</td><td>100 mg capsule</td></tr>
<tr><td>Dose</td><td>NOTE: Gabapentin should not be started without a full and thorough review by a senior neonatologist.
In New South Wales, it is recommended to notify the Pain Management team at Sydney Children's Hospital Network on the commencement of gabapentin.

Suggested dosing (ANMF consensus)[5, 6]
Initial dose:
<table>
<tr><th>Age</th><th>Dose</th><th>Interval</th></tr>
<tr><td>Term infants</td><td>5 mg/kg/dose</td><td>8 hourly</td></tr>
<tr><td>Preterm infants < 40 weeks CGA</td><td>2.5 mg/kg/dose</td><td>8 hourly</td></tr>
<tr><td>Preterm infants ≥ 40 weeks CGA</td><td>5 mg/kg/dose</td><td>8 hourly</td></tr>
<tr><td>Renal Impairment*</td><td>Dose*</td><td>Interval*</td></tr>
<tr><td>Mild</td><td>2.5 mg/kg/dose</td><td>8 hourly</td></tr>
<tr><td>Moderate</td><td>1.25 mg/kg/dose</td><td>8 hourly</td></tr>
<tr><td>Severe</td><td>0.625 mg/kg/dose</td><td>8 hourly</td></tr>
</table>
*OR refer to the following table - modified from Renal Paediatric doses (ANMF consensus):
<table>
<tr><th>Renal Impairment</th><th>Dose</th><th>Interval</th></tr>
<tr><td>Mild</td><td>3.75 mg/kg/dose</td><td>12 hourly</td></tr>
<tr><td>Moderate</td><td>3.75 mg/kg/dose</td><td>24 hourly</td></tr>
<tr><td>Severe</td><td>3.75 mg/kg/dose</td><td>48 hourly</td></tr>
</table>
Maintenance dose
If no response after 4 days of initial therapy, increase the dose by 50-100% to a maximum of 10 mg/kg/dose 8 hourly.**
If no response after 4 days with maximal therapy, discontinue therapy.
**In renal impairment – use 50%, 25% and 12.5% of the original dose 8 hourly for mild, moderate and severe impairment, respectively.

Weaning
If used for > 8 days, wean the dose over 2-4 weeks (e.g. wean by 5-10 mg/kg/day weekly) (ANMF consensus)</td></tr>
</table>

Dose adjustment	Therapeutic hypothermia – Not applicable. ECMO – Not applicable. Renal impairment – Refer to dose section Hepatic impairment – No information.
Maximum dose	35 mg/kg/day.[5]
Total cumulative dose	
Route	Oral or via gastric tube
Preparation	Mix the contents of one capsule (= 100 mg) in 5 mL of water to make concentration of 20 mg/mL. (Modified from MIMS online) (ANMF consensus)
Administration	
Monitoring	Sleepiness Bradycardia Nystagmus Gabapentin withdrawal upon abrupt cessation (tachycardia, emesis, increased irritability).[7] Renal function
Contraindications	Hypersensitivity to gabapentin or the inactive ingredients
Precautions	Severe renal impairment
Drug interactions	
Adverse reactions	Somnolence Bradycardia Nystagmus Gabapentin withdrawal upon abrupt cessation (tachycardia, emesis, increased irritability).[4]
Compatibility	Not applicable
Incompatibility	Not applicable
Stability	Capsule contents dispersed in water: Make a fresh solution for each dose and use immediately. Discard unused portion.
Storage	Neurontin: Store below 30°C. Gabacor: Store below 25°C.
Excipients	Neurontin: Lactose monohydrate, purified talc, maize starch, gelatin, titanium dioxide, Opacode Blue S-1-4118 (ARTG ID: 2703) (Shellac, titanium dioxide, indigo carmine aluminium lake, butan-1-ol, ethanol, methanol). Gabacor: Maize starch, lactose, purified talc, gelatin, sodium lauryl sulfate, titanium dioxide. For other brands: Refer to individual product information.
Special comments	
Evidence	**Background** Gabapentin is used for neurologic pain in adult and children. Gabapentin is thought to decrease central sensitisation, therefore reducing pain recognition.[8] Gabapentin usage in neonates is increasing despite no prospective studies evaluating the dosing, efficacy and safety in neonatal period.[2, 5, 9] Gabapentin is being used in neonatal intensive care units for management of chronic pain and irritability, visceral hyperalgesia, and neonatal abstinence syndrome. Visceral hyperalgesia is a type of neuropathic pain caused by up-regulation of gastrointestinal sensory input leading to pain, irritability and feeding intolerance in infants with neurologic impairment and other co-morbidities. In the gastrointestinal tract, non-painful stimuli such as abdominal distention from feeding or gas may result in irritability, hypertonicity, poor oral feeding and/or feeding intolerance.[6, 7] In adults, gabapentin is commonly used to help alleviate cancer and chemotherapy-related pain, spinal cord injury-related pain, and peripheral neuropathic pain. In children, additional uses include postoperative and visceral pain management, dystonia, and management of irritability in medically and neurologically complex patients.[10-12] **Efficacy**

	Pain and irritability: Abdi et al reported gabapentin usage in US NICUs between 2005-2016. A total of 374 infants received gabapentin during their hospitalisation in the NICU. Of those, 12% had severe BPD, 12% had congenital brain abnormalities, 11.2% with seizures, 10.7% with chromosomal abnormalities and 6.7% with NAS. About 20% received gabapentin within the first 30 days of life.[2] Burnsed et al reported a retrospective study on neonates and infants treated with gabapentin. Median corrected gestational age at initiation was 44 weeks (range 36.2–75 weeks). The most common indications for starting therapy were agitation and pain. Gabapentin was initiated at doses 2.5 to 5 mg/kg/day. Doses were increased every 3 to 5 days to effect, to a maximum documented dose of 35 mg/kg/day. Infants reached their goal dose on average 26 days (range 0–116 days) after initiation. Gabapentin was well tolerated and was associated with lower pain scores and decreased need for multiple sedative medications. There was only one adverse event (oversedation) noted.[5] Sacha et al, in a retrospective case series reported gabapentin usage in 22 neonates and infants in neonatal ICU with chronic pain and agitation. The average starting dosage was 10.2 mg/kg/day (range 4.6 to 16.3 mg/kg/day), and most regimens were divided 3 times daily. The average maximum gabapentin dose after dose titration was 16.4 mg/kg/day (range 9 to 25.5 mg/kg/day). Twenty patients had a median N-PASS score of 3 charted at baseline. After gabapentin therapy, the median last evaluable NPASS score was 0.[13] Behm et al treated a neonate with chronic refractory pain due to severe contractures and dislocated hips resulting from amyoplasia congenita.[14] Gabapentin was used to treat a neonate with hypotonicity, functional short gut, microduplication of chromosome 22 to control pain and irritability refractory to sedatives and analgesics. Infant was started with 5 mg/kg/day and increased to 15 mg/kg/day.[15] **Visceral hyperalgesia**: A retrospective case series reported 11 medically complex infants with neurologic and gastrointestinal co-morbidities in whom gabapentin was used after failed therapy with multiple sedatives and analgesics. Starting dose was 5 mg/kg/dose 2-3 times a day in majority of them. In 8/11 of them, there was decreased irritability and/or improved feed intolerance and oral feeding.[7] A case series reported 3 neurologically intact infants with enteral feeding intolerance and gastrointestinal morbidity alone (congenital diaphragmatic hernia, gastroschisis). Initiation of gabapentin in these infants resolved retching associated with enteral feedings within 3 days. The infants began with minimal or no oral feeding and advanced to full oral feedings within 120 days of gabapentin initiation.[16] Another case series reported 15 infants with complex congenital heart disease who experienced feeding difficulty after cardiac surgery. Their mean age was 2.4 months. Children were treated with gabapentin 10 mg/kg/dose twice daily initially and if no sedation after the first doses, frequency was increased to 3 times daily. Majority experienced improved oral intake after initiation of gabapentin. Prior to gabapentin initiation, infants averaged 401 ± 451 mL/day voluntary oral intake; after gabapentin infants averaged 781 ± 586 mL/day. There were no acute safety issues or sedation effects.[17] **Neonatal Abstinence Syndrome:** Gabapentin usage for NAS is limited to a single case report. After failure to therapy with methadone and clonidine, gabapentin was initiated at 10 mg/kg/day divided every 8 hours and titrated over 1 week to a maximum dose of 20 mg/kg/day. After 48 hours at the maximum dose, Finnegan scores fell below 3 and the infant was successfully weaned from methadone and clonidine over the next 8 weeks. Gabapentin was then weaned off over 2 weeks with no recurrence of symptoms.[18] **Safety** Gabapentin was well tolerated with a very few short term side effects reported.[2, 5, 7] Abrupt cessation (for example, nil by mouth status due to feed intolerance) may lead to withdrawal symptoms including tachycardia, emesis and increased irritability.[7] No data exist on the long-term developmental impact of gabapentin therapy.[6] **Pharmacokinetics** Gabapentin is not metabolised in the body and excreted unchanged in urine.[3] Therefore dose adjustment is necessary in renal impairment.
Practice points	
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VERSION/NUMBER	DATE
Original 1.0	9/06/2022
REVIEW	9/06/2027

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