

<b>Alert</b>	As part of the Australian national harmonisation program, as of May 2016, all therapeutic drugs except lithium are now reported in mass units: microgram/L, mg /L etc. Phenobarbital is now reported in mg/L. To convert to micromol/L, multiply by 4.306.															
<b>Indication</b>	<ol style="list-style-type: none"> <li>1. Treatment of neonatal seizures.</li> <li>2. Initial treatment of non-opioid neonatal abstinence syndrome (NAS).</li> <li>3. Add-on treatment of opioid NAS uncontrolled by morphine at maximum dose (if 3 consecutive NAS scores average <math>\geq 8</math> or 2 consecutive NAS scores average <math>\geq 12</math>).</li> <li>4. Treatment of hyperbilirubinaemia (unclear role).</li> <li>5. Treatment of cholestasis (unclear role).</li> <li>6. Preparation for liver scintigraphy (unclear role).</li> </ol>															
<b>Action</b>	Phenobarbital enhances inhibitory neurotransmission via activation of GABA receptor.															
<b>Drug Type</b>	Anticonvulsant. Sedative.															
<b>Trade Name</b>	Fawns & McAllan Phenobarbitone Sodium Solution for injection; Phenobarbitone (Aspen) Solution for injection; Phenobarbitone Aspen Tablets; Phenobarbitone Elixir															
<b>Presentation</b>	IV: 200 mg/mL ampoule (contains 10% alcohol and 67.8% propylene glycol) PO: 15 mg/5 mL oral liquid (contains 9.6% alcohol); 10 mg/mL alcohol free liquid can be manufactured by the pharmacy department; 30 mg tablets.															
<b>Dosage / Interval</b>	<p><b>IV dosing:</b> Loading dose: 20 mg/kg/dose infuse over 20 minutes (maximum infusion rate 1 mg/kg/minute). Additional loading doses (10 mg/kg) may be administered at 30 minute intervals if necessary (maximum cumulative loading dose = 40 mg/kg).</p> <p>Maintenance dose: 4 mg/kg/dose (3–5 mg/kg/dose) every 24 hours as a slow IV push over 5 minutes. Start maintenance dose 24 hours after loading dose.</p> <p><b>Oral dosing:</b></p> <table border="1"> <thead> <tr> <th>Indication</th> <th>Loading dose</th> <th>Maintenance dose</th> </tr> </thead> <tbody> <tr> <td>Anticonvulsant</td> <td>IV only- refer to IV dosing</td> <td>3–5mg/kg every 24 hours and titrate as per seizure control and therapeutic concentrations.</td> </tr> <tr> <td>NAS</td> <td>15 mg/kg</td> <td>5 mg/kg/day in 1–2 divided doses and titrate to NAS score.</td> </tr> <tr> <td>Jaundice</td> <td>-</td> <td>5 mg/kg every 24 hours</td> </tr> <tr> <td>Liver scintigraphy<sup>7</sup></td> <td>-</td> <td>5 mg/kg/day in 2 divided doses for 5 days prior to scan</td> </tr> </tbody> </table>	Indication	Loading dose	Maintenance dose	Anticonvulsant	IV only- refer to IV dosing	3–5mg/kg every 24 hours and titrate as per seizure control and therapeutic concentrations.	NAS	15 mg/kg	5 mg/kg/day in 1–2 divided doses and titrate to NAS score.	Jaundice	-	5 mg/kg every 24 hours	Liver scintigraphy <sup>7</sup>	-	5 mg/kg/day in 2 divided doses for 5 days prior to scan
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Liver scintigraphy <sup>7</sup>	-	5 mg/kg/day in 2 divided doses for 5 days prior to scan														
<b>Route</b>	IV and oral															
<b>Preparation/Dilution</b>	IV: Draw up 1 mL (200 mg) of phenobarbital and add 9 mL water for injection to make final volume of 10 mL with a concentration of 20 mg/mL. Oral: Liquid does not require preparation.															
<b>Administration</b>	IV: Loading dose: Infuse over 20 minutes (maximum infusion rate 1 mg/kg/minute). Maintenance dose: Slow IV push over 5 minutes. Oral: Give immediately before or with feeds to minimise GI irritation.															
<b>Monitoring</b>	Serum concentration monitoring is not routinely required except for seizure control. Measure serum concentrations 24 hours after starting phenobarbital. Serum target: 15–40 mg/L (65–172 micromol/L). Consider repeating concentrations 1 week after the commencement and subsequent concentrations as per clinical need. Consider monitoring liver function tests.															

<b>Contraindications</b>	Hypersensitivity to phenobarbital or any ingredients. Any forms of acute porphyria.
<b>Precautions</b>	Use with caution in renal or hepatic impairment. Dependence may develop with prolonged use – consider weaning instead of abrupt withdrawal (Refer to special comments section). Therapeutic hypothermia may increase the serum concentrations of phenobarbital – monitor serum concentrations closely.
<b>Drug Interactions</b>	Morphine, fentanyl, midazolam and other CNS depressants may have an additive effect with phenobarbital in causing respiratory depression. Consider starting phenobarbital at the lower end of the dose range in these patients. Blood concentrations of digoxin, metronidazole, corticosteroids (e.g. betamethasone, dexamethasone), vitamin D, and beta-blockers (e.g. propranolol, sotalol) may be reduced if administered concurrently with phenobarbital. Concurrent administration of phenytoin with phenobarbital has variable effects on serum concentrations of either drug. Serum concentrations should be monitored for both drugs.
<b>Adverse Reactions</b>	Drowsiness, lethargy - sucking reflex may be impaired and feeding may be poor. Respiratory depression, apnoea. Hypotension, laryngospasm, bronchospasm, apnoea - if IV administration is too rapid. Phlebitis, tissue necrosis if extravasation occurs. GI intolerance. Physical dependence and tolerance. May occur with prolonged use: Folate deficiency, hepatitis, hypocalcaemia.
<b>Compatibility</b>	Fluids: Sodium chloride 0.45%, sodium chloride 0.9%, glucose 5%, glucose 10%.  Y-site: Amino acid solutions. Amikacin, atropine, calcium chloride, fentanyl, furosemide, magnesium sulfate, milrinone, phenytoin, piperacillin/tazobactam.
<b>Incompatibility</b>	Fluids: Lipid emulsions.  Y-site: Adrenaline (epinephrine) hydrochloride, aminophylline, atracurium, benzylpenicillin, buprenorphine, caspofungin, cefotaxime, ceftazidime, chlorpromazine, ciclosporin, dobutamine, dolasetron, ephedrine, erythromycin, esmolol, haloperidol lactate, hydralazine, hydrocortisone sodium succinate, hydromorphone, ketamine, lidocaine (lignocaine), midazolam, mycophenolate mofetil, noradrenaline (norepinephrine), ondansetron, pentamidine, pethidine, phentolamine, prochlorperazine mesilate, promethazine, protamine, ranitidine, suxamethonium, verapamil.
<b>Stability</b>	Use diluted/opened solution as soon as possible. Ampoules are for single use only.
<b>Storage</b>	Protect from light. Store below 25°C. Phenobarbital is a Schedule 4 Appendix D (S4D) medication.
<b>Special comments</b>	Elimination half-life: In infants 28-41 weeks gestation: Half-life of the drug was estimated (mean±SD) to be 114-2 ± 43.0 h, 73.19 ± 24.17 h and 41.23 ± 13.95 h in patients 1 - 10, 11 - 30 and 31 - 70 days old, respectively; neonates with perinatal asphyxia undergoing hypothermia 173.9±62.5 hours. Converting from mass units to SI units: 1 mg/L = 4.306 micromol/L. The general taper recommended for phenobarbital is 10-25% of the original dose every month. A faster taper is recommended for patients on therapy for less than 1 month <sup>18</sup>
<b>Evidence summary</b>	As per NeoMed Consensus Group. Refer to reference manual or electronic version.
<b>References</b>	As per NeoMed Consensus Group. Refer to reference manual or electronic version.

<b>Original version Date: 21/06/2016</b>	<b>Author: Neonatal Medicines Formulary Consensus Group</b>
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