

## PHENOBARBITAL (previously known as Phenobarbitone\*)

<b>Trade Name</b>	Phenobarbital Sodium (injection) Martindale Pharmaceuticals Oral mixture alcohol free made up by Pharmacy										
<b>Class</b>	Anticonvulsant										
<b>Mechanism of Action</b>	Limits the spread of seizure activity, by enhancement of GABA binding to neuro-inhibitory receptors										
<b>Indications</b>	<b>Indication 1:</b> Seizures <b>Indication 2:</b> Sedation <b>Indication 3:</b> Non-narcotic drug withdrawal <b>Indication 4:</b> Enzyme induction prior to HIDA scan										
<b>Contraindications</b>	Caution when used in renal and hepatic disease										
<b>Supplied As</b>	<b>IV:</b> 200 mg/mL phenobarbital sodium (20 mg/0.5 mL occasionally supplied when stock short) <b>Must be diluted to 20 mg/mL prior to administration</b> <b>Oral:</b> 10mg/mL										
<b>Dilution</b> <b>Dec 2020:</b> <b>Due to a worldwide shortage of phenobarbital, draw up the required dose and then store the remainder of the solution in a labelled syringe in the fridge to be used if needed for subsequent doses. Discard syringe after 24 hours.</b>	<table border="1"> <thead> <tr> <th>Drug</th> <th>0.9% Sodium Chloride Added</th> <th>Final Volume</th> <th>Concentration</th> </tr> </thead> <tbody> <tr> <td>200 mg (1 mL)</td> <td>9 mL</td> <td>10 mL</td> <td><b>20 mg/mL</b></td> </tr> </tbody> </table>			Drug	0.9% Sodium Chloride Added	Final Volume	Concentration	200 mg (1 mL)	9 mL	10 mL	<b>20 mg/mL</b>
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200 mg (1 mL)	9 mL	10 mL	<b>20 mg/mL</b>								
<b>Maximum Single dose = 100 mg (5mL) unless documented by two Drs/CNS-ANP</b> <b>If the dose volume is &lt;0.5mL then will need to further dilute before infusing via the T34 pump (see T34 protocol)</b>											
<b>Dosage</b>	<b>Indications 1,2: Loading dose</b> 20 mg/kg/dose Further doses of 10 mg/kg/dose may be given up to a total of 40 mg/kg for seizures. <b>Indications 1,2,3: Maintenance dose</b> 3 – 4 mg/kg/dose May need to increase to 5mg/kg/day after 1-2 weeks as phenobarbital clearance is expected to increase by this time. <b>Indication 4:</b> 5 mg/kg/day orally for 5 days prior to a HIDA scan										

<b>Interval</b>	<p><b>Loading dose:</b> Single dose with repeat doses as above when clinically required for seizure control</p> <p><b>Maintenance:</b> Once a day, if given a loading dose then start maintenance 12-24 hours afterwards</p>
<b>Administration</b>	<p><b>Loading dose:</b> Give IV over 20 minutes (<b>max 1 mg/kg/minute</b>)</p> <p><b>Maintenance:</b> Oral or IV slow push</p>
<b>Compatible With</b>	<p>5% dextrose water, 10% dextrose water, normal saline</p> <p>At terminal injection site above filter: amikacin, aminophylline, calcium gluconate, fentanyl, heparin, meropenem, sodium bicarbonate, vancomycin, TPN (not lipid)</p>
<b>Incompatible With</b>	<p>Do not mix in syringe or administer with any other drugs as many incompatibilities have been reported including but not limited to;</p> <p>Clindamycin, gentamicin, insulin, midazolam, morphine, phenytoin, ranitidine, pancuronium, suxamethonium, lipid</p>
<b>Interactions</b>	<p>Increased levels (usually) with phenytoin, valproate; Paracetamol: possible decrease in effect due to induction of hepatic enzymes by phenobarbitone – prolonged use of both may lead to liver damage</p>
<b>Monitoring</b>	<p>If checking maintenance treatment take trough level 5-7 days (or five half-lives) after loading dose or dose change; if concerned about toxicity or effectiveness of load, take level 6-8 hrs after dose.</p> <p>Serum levels reference range: 65-130 micromol/L (15-30 mcg/ml). If levels too high omit at least one dose before reducing maintenance dose.</p>
<b>Stability</b>	<p><b>IV:</b> (2020 COVID update) After dilution with 0.9% sodium chloride draw up the required dose and then store the remainder in a syringe in the fridge for up to <b>24</b> hours for use of the same patient if subsequent doses are needed.</p> <p><b>Oral:</b> 30 days at room temperature</p>
<b>Storage</b>	<p><b>IV:</b> Store unopened vials in the Controlled Drugs Safe</p> <p><b>Oral:</b> Store at room temperature</p>
<b>Adverse Reactions</b>	<p>Sedation - levels above 170 micromol/L (40mcg/mL)</p> <p>Respiratory depression – esp. with doses &gt; 30 mg/kg and serum levels above 260 micromol/L (60mcg/mL)</p> <p>Hypothermia, arrhythmias, hypotension, necrosis at injection site, rash, megaloblastic anaemia</p>

<b>Metabolism</b>	Onset of action after IV administration is within 5 min, peak effect within 30 min. Oral absorption 70-90%. Metabolised mostly in the liver with 20-50% excreted unchanged in urine; clearance can be increased by alkalinisation of urine. Protein binding decreased in neonates. Serum half-life 40-200 hrs (drops after first few wks).
<b>Comments</b>	Controlled drug (C5) In emergency situations out of normal pharmacy hours, the IV preparation can be diluted with water and given orally *In line with the (NZULM) nomenclature the official generic name of phenobarbitone is now phenobarbital. Community Pharmacy can charge a compounding fee. Prices vary so suggest calling community pharmacy to warn patient of costs.
<b>References</b>	<ol style="list-style-type: none"> <li>1. Neofax, 1999 &amp; 2000</li> <li>2. Medicines for Children, RCPCH, 1999</li> <li>3. J Clin Pharm 1994;34(4) 312</li> <li>4. NEJM 1999; 341(7) 485-9</li> <li>5. Neurology 1981; 31:1107</li> <li>6. Trissel LA, Handbook on Injectable Drugs, 12<sup>th</sup> Ed, 2003</li> <li>7. Milap et al. Stability of phenobarbital sodium diluted in 0.9% sodium chloride injection. AJHP 1986; <a href="https://doi.org/10.1093/ajhp/43.2.384">https://doi.org/10.1093/ajhp/43.2.384</a></li> </ol>
<b>Updated By</b>	<p>A Lynn, B Robertshawe June 2007  A Lynn, B Robertshawe September 2007  A Lynn, B Robertshawe, F Robertson May 2009 (new pumps)  A Lynn, B Robertshawe September 2009, June 2010 guardrail  A Lynn, B Robertshawe Dec 2012 (re-order profile)  A Lynn B Robertshawe May 2018 (update name to phenobarbital as per NZULM)  A Lynn, M Wallenstein, B Robertshawe, October 2020 (update, oral solution no longer needs refrigeration)  A Lynn, N Austin, M Wallenstein, B Robertshawe Jan 2021  (extended storage of injection due to worldwide shortage.)</p>