PHENOBARBITAL

Read in conjunction with Disclaimer

Formulary: Restricted Requires Neonatologist or Neurologist review within 24 hours of initiation.	
Presentation	**Oral Solution:** 10 mg/mL **Ampoule:** 200 mg/mL
Classification	Barbiturate

Indication	• Neonatal seizures
	• Neonatal jaundice
	• Neonatal abstinence syndrome (NAS)
	  ○ Adjunct to morphine
	  ○ Non-opiate withdrawal

Special Considerations	**Contraindications** • Acute porphyrias • Severe respiratory depression **Precautions** • Use with caution in renal or hepatic impairment. • Dependence may develop with prolonged use – consider weaning instead of abrupt withdrawal. • Therapeutic hypothermia may increase the serum concentrations of phenobarbital.
Monitoring	• Observe for signs of extravasation – can lead to tissue necrosis. • Monitor for hypotension. • Monitor for changes in respiration. • **With prolonged therapy:** full blood count, renal and liver function, vitamin D levels. **Therapeutic Drug Monitoring:** • **Sampling time:** Immediately prior to next dose. • **Therapeutic range:** 15 to 40 mg/L. • *Note: In infants with NAS, serum concentrations of 20 to 30 mg/L are associated with adequate symptom control.* • **Time to reach steady state:** 2 to 4 weeks.
Compatibility	**Fluids:** Sodium chloride 0.9%, sodium chloride 0.45%, water for injection, glucose 5%, glucose 10%.
Incompatibility	**Y-site:** Adrenaline (epinephrine), amiodarone, benzylpenicillin, caspofungin, cefotaxime, clindamycin, dobutamine, erythromycin, ketamine, lidocaine, midazolam, noradrenaline, paracetamol, pyridoxine, suxamethonium, total parentral nutrition (TPN). *This list is not exhaustive, contact pharmacy.*
Interactions	• Morphine and other CNS depressants may have an additive effect with phenobarbital in causing respiratory depression. Consider using lower doses of phenobarbital. • Blood concentrations of amiodarone, amlodipine, clindamycin, clonazepam, colecalciferol, dexamethasone, diazepam, digoxin, hydrocortisone, levetiracetam, metronidazole, midazolam, propranolol, sotalol, sildenafil, sirolimus, and voriconazole may be reduced if

	administered concurrently with phenobarbital. *This list is not exhaustive, contact pharmacy.* • Concurrent administration of phenytoin with phenobarbital has variable effects on serum concentrations of either medication. Serum concentrations should be monitored for both medication.
Side Effects	**Common:** Hypotension, respiratory depression/insufficiency, sedation, feeding disorder, extravasation and irritation to veins.
	Infrequent/Rare: Bradycardia, hyponatremia, paradoxical hyperactivity and irritability may occur.
Storage & Stability	**Oral Solution:** Store at room temperature, below 25°C. Protect from light. **Ampoule:** Store at room temperature, below 25°C.
Comments	Also known as phenobarbitone. Oral solution contains 10.8% v/v ethanol.

ORAL

Presentation (for oral use)

Oral Solution: 10 mg/mL

Dosage

<u>Neonatal seizures</u>

Loading dose: Loading dose given IV, see Intravenous Infusion section below.

Maintenance dose: 3 to 5 mg/kg**/day** in 1 or 2 divided doses, commencing 12 to 24 hours after the loading dose.

<u>Neonatal jaundice</u>

5 mg/kg once daily.

<u>NAS – Adjunct to morphine</u>

Loading dose: 10mg/kg

Medical staff are to review the infant within 12 to 24 hours of the loading dose to determine whether a maintenance dose is required.

Maintenance dose: 1.5 to 2.5 mg/kg/dose every 12 hours.

<u>NAS – Non-opiate withdrawal</u>

	NAS Score	Dose/Action
Step 1 (Starting dose)	Score averages greater than 8 for 3 consecutive scores.	**Loading dose:** 15 mg/kg. *Medical staff are to review the infant within 12 to 24 hours of the loading dose to determine whether a maintenance dose is required.* **Maintenance dose:** 3 mg/kg/dose every 12 hours.
Step 2	If score persists greater 8 despite Step 1 dose.	**Maintenance dose:** 4 mg/kg/dose every 12 hours.
Step 3	If score persists greater than 8 despite Step 2 dose.	**Maintenance dose:** 5 mg/kg/dose every 12 hours.

ORAL

Dose adjustment	• Adjust dose according to response and concentration monitoring. • **Renal impairment:** Use with caution. Dosage adjustment may be required in severe renal impairment. Some references suggest a dose reduction of 50% and/or 24 hourly administration in severe renal impairment. • **Hepatic impairment:** Use with caution, phenobarbital exposure is increased with hepatic impairment. Dosage adjustment may be required in severe hepatic impairment.
Weaning	• Weaning should be led by NAS scores and the infant's clinical condition. • A suggested weaning regimen is to reduce the dose by 20% of the original dose every 48 hours.
Administration	• Draw prescribed dose into oral/enteral syringe. • Can be given Oral/OGT/NGT. • Mixture is bitter and may be poorly tolerated. Consider administering a loading dose via the OGT/NGT if the infant has poor suck. • Give with or soon after a feed to minimise GI irritation.

INTRAVENOUS INFUSION

Presentation (for IV use)	**Ampoule:** 200 mg/mL ***Available from CIVAS (KEMH Only):*** *20 mg/mL*
Dosage	**<u>Neonatal seizures</u>** **Loading dose:** 20 mg/kg If no response, a further 10 to 20 mg/kg may be given if seizure persist or recur at least 15 minutes after the completion of the initial loading dose. **Maximum total loading dose:** 40 mg/kg **Maintenance dose:** 3 to 5 mg/kg**/day** in 1 or 2 divided doses, commencing 12 to 24 hours after the loading dose.
Dose Adjustment	Very low birth weight (less than 1500 g) preterm infants, may require lower loading doses of less than 15 mg/kg IV followed by single injection of less than 3 mg/kg/day 24 hours later.
Preparation	**Ampoule**: 200 mg/mL **Dilution:** • Draw up 1 mL (200 mg) of phenobarbital and make up to 10 mL total volume with a compatible fluid. • *Concentration now equal to* **20 mg/mL**. ***Note:*** *Due to high viscosity of phenobarbital, ensure thorough mixing of medication and diluent.*
Administration	**IV infusion:** • Infuse via syringe driver pump over 20 to 30 minutes. • Maximum infusion rate: 1 mg/kg/minute.

INTRAMUSCULAR INJECTION			
	Presentation (for IM use)	**Ampoule:** 200 mg/mL	
	Dosage	**Neonatal seizures** *Only to be administered IM when IV and PO not available/suitable.* **Loading dose:** 20 mg/kg If no response, a further 10 to 20 mg/kg may be given if seizure persist or recur at least 15 minutes after the completion of the initial loading dose. **Maximum total loading dose:** 40 mg/kg **Maintenance dose:** 3 to 5 mg/kg**/day** in 1 or 2 divided doses, commencing 12 to 24 hours after the loading dose.	
	Preparation	Use undiluted.	
	Administration	*Only to be administered IM when IV and PO not available/suitable.* • Draw up the prescribed dose. • Inject as per the Medication Administration Guideline.	

Related Policies, Procedures, and Guidelines

CAHS Clinical Practice Guidelines:

End of Life Care

Hypoxic Ischaemic Encephalopathy (HIE) and Therapeutic Hypothermia

Neonatal Abstinence Syndrome

Seizures: Neonatal

Jaundice

Pharmaceutical and Medicines Management Guidelines:

CAHS Neonatology – Medication Administration Guideline

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Document history

Keywords	Phenobarbitone, phenobarbital, seizures, epilepsy, neonatal abstinence syndrome				
Abbreviations	NAS: neonatal abstinence syndrome, IM: intramuscular, IV: intravenous, PO: oral				
Document Owner:	Chief Pharmacist				
Author/ Reviewer	KEMH & PCH Pharmacy/Neonatology Directorate				
Version Info:	V4.0 – full review, new template, added NAS dosing, routes of administration updated to align with use.				
Date First Issued:	03/2008	Last Reviewed:	27/10/2025	Review Date:	27/10/2030
Endorsed by:	Neonatal Directorate Management Group			Date:	24/02/2026
NSQHS Standards Applicable:	☒ Std 1: Clinical Governance		☒ Std 4: Medication Safety		
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