1. Purpose and scope

To facilitate the safe and effective use of phenobarbitone in the Neonatal Intensive Care Unit (NICU) at Waikato Hospital.

2. Drug

Drug	**Phenobarbitone sodium, phenobarbital**
Drug action	Phenobarbitone limits the spread of seizure activity, possibly by increasing inhibitory neurotransmission via enhancement of GABAergic systems.[1,2] It also appears to elevate the seizure threshold.[2] Half life is 40 to 200 hours (very variable).[1,2] It is primarily (50-70%) metabolized in the liver to an inactive metabolite then excreted in the urine. Renal clearance is enhanced by alkaline urine and diminished by acidic urine.[2] Low protein binding (approx 30%)[1] and widely distributed (Volume of distribution 0.6-1.0L/kg).[2] The brain/plasma phenobarbitone ratio is approximately 0.7 and decreases with decreasing gestational age.[2]
Indications	• Seizures
Presentation	• Phenobarbitone sodium 200mg / 1ml ampoules • Phenobarbitone solution 10mg/ml (manufactured by Waikato Hospital Pharmacy on an individual patient basis) Note: the contents of the ampoule can be diluted to 10mg/ml and administered orally[1], but contains excipients e.g. propylene glycol • Clear, colourless to pale yellow solution[3] • pH of undiluted phenobarbitone sodium is 8.5 to 10.5 [3]
Route	• slow IV infusion over 15 to 30 minutes1 (usual is 20 minutes4) Note: Maximum rate of administration is 1mg/kg/min5 • Oral • IM, but can cause tissue irritation / necrosis. Administer undiluted.
Dose	**Loading dose:** 20mg/kg[1,2,6,] Note: additional doses of 5mg/kg can be administered if no response, up to a total of 40mg/kg.[1] **Maintenance dose**: 2.5 - 5mg/kg, adjusted according to response. Use lower dose (2.5mg/kg) in the presence of significant asphyxia or renal failure. Administer once daily starting 24 hours after the loading dose.[1,2,3]
Contraindications	• Known hypersensitivity to barbiturates, or any component of the formulation • Acute porphyria • Severe respiratory depression or pulmonary insufficiency
Precautions	• Respiratory depression • Hepatic or renal impairment • Avoid extravasation (alkaline solution) • Avoid rapid administration (increases risk of serious side effects e.g. respiratory depression, change in blood pressure)

Compatibilities and Incompatibilities	• Compatible with sodium chloride 0.9%, glucose 5% or 10%, glucose and sodium chloride solutions, Ringers and Compound sodium lactate3 • Do not mix with any other medicines, unless approved by Pharmacy (solution is highly alkaline and therefore likely to be incompatible with many drugs)3
Adverse effects	• Hypotension, respiratory depression, apnoea, laryngospasm, bronchospasm (especially if given too fast) • Sedation, confusion, CNS depression or excitement • Vasodilation • Syncope, ataxia, coma • Nausea • Hypersensitivity reactions (skin rashes) • Phlebitis, tissue necrosis at injection site • Hepatitis, cholestasis

3. Administration

Competency for administration	This procedure is carried out by, or under, the direct supervision of a registered nurse/ registered midwife who holds generic IV certification **and** Neonatal specific certifications NCV/NAC and NIC2, as well as Guardrails competency.
Preparation & Administration	**Dilute** as per 'NICU Drugs' computer software available on all desktops in the NICU. If this resource is not available, dilute as per the default dilution below: • Draw up contents of ampoule 200mg (1ml) and dilute to 10mL with compatible fluid. Resulting solution is 20mg/mL. • From this solution, draw up prescribed dose and further dilute if required to make minimum infusion volume of 1.6ml • Administer by slow IV injection, preferably via CVAD if possible (as solution is irritant) using a Guardrails profiled syringe driver • Filter prior to administration through a PALL 0.2 micron filter • Flush before and after administration with sodium chloride 0.9%
Observations and management	• Observe IV site for signs of irritation / thrombophlebitis • Document vital signs hourly and when required3 • Continuous cardiorespiratory monitoring during infusion **Plasma phenobarbitone levels**: Monitor serum phenobarbitone levels after the loading dose and once patient has reached steady state – after approx. 10 to 14 days (or earlier if indicated), then as required. Measure trough level just prior to next dose. Therapeutic plasma levels: 65-170micromol/L.
Storage	• Store at room temperature (below 25oC).3 • Protect from light3 • Prepare immediately before use as no information is available regarding stability.[3] Discard ampoule after opening.
Special Considerations	• **Unregistered medicine** available under section 29.7 Names of patient and doctor prescribing must be sent to Pharmacy when ordering. • Phenobarbitone is a substrate and also induces many CYP enzymes so is associated with numerous drug interactions. Monitor and measure levels if other known interacting medications are initiated or ceased.2 • Tolerance, psychological and physical dependence may occur with long-term use. If discontinuing decrease the daily phenobarbitone dose by 10%, if tolerated, and monitor closely.1 • Do not use if more than slightly discoloured or contains a precipitate • Do not administer intra-arterially via a peripheral line or subcutaneously

Rescue medication	No known antidote Oxygen, vasopressors and assisted ventilation may be required. Consider elimination of phenobarbitone by alkalinising the urine, with diuretics and/or dialysis.[2,4]

4. Guardrails Information[8]

Guardrails Drug Name **Phenobarbitone(load***
Pump CC

	0.4-1kg	1-2kg	2-3kg & 3-5kg
Concentration (mg/mL)			
Minimum	5	12.5	20
Maximum	20	20	20
Default			
Administration Rate (mg/kg/hr)			
Soft minimum	30	30	30
Default	60	60	60
Soft maximum	120	120	120
Hard maximum	120	120	120

Guardrails Drug Name **Phenobarbitone(main***
Pump CC

	0.4-1kg	1-2kg	2-3kg	3-5kg
Concentration (mg/mL)				
Minimum	0.25	0.62	1.25	1.87
Maximum	5	10	15	20
Default				
Administration Rate (mg/kg/hr)				
Soft minimum	7.5	7.5	7.5	7.5
Default	15	15	15	15
Soft maximum	15	15	15	15
Hard maximum	24	24	24	24

5. Associated Documents

- Waikato DHB NICU "to give slow infusion / intermittent infusion" procedure. Document reference 4360.

6. References

1 Micromedex® 1.0 (Healthcare Series), (electronic version). Paediatrics and Neofax – Phenobarbitone sodium. Truven Health Analytics, Greenwood Village, Colorado, USA. Last accessed 15 February 2016. Available from : http://www.micromedexsolutions.com/

2 Auckland NICU Drug Protocols – Phenobarbitone, November 2011. Available from: http://www.adhb.govt.nz/newborn/DrugProtocols/Default.htm Last accessed 15 February 2016.

3 New Zealand Hospital Pharmacists Association: Notes on Injectable Drugs, 7th Edition, Phenobarbital sodium. Published 2015, Wellington NZ.

4 Phenobarbitone sodium (NICU unofficial guideline). David Bouchier. Aug 2013. Waikato DHB.

5 The Royal Children's Hospital Melbourne: Paediatric Injectable Guidelines 4th Edition, Adrenaline. Published July 2011, Melbourne Australia.

6 BNF for children 2011-2012.

7 The New Zealand Formulary Editorial Team. New Zealand Formulary for Children. Phenobarbital. NZ. Last accessed 15 February 2016. Available from http://nzfchildren.org.nz/nzf_2646

8 Guardrails Data Sheets, Waikato Hospital, Hamilton, NZ, May 2015.