Ballarat Health Services

Neonatal Drug Guideline

PHENYTOIN

DESCRIPTION AND INDICATION FOR USE

Phenytoin is an anti-convulsant medications used in the management of neonatal seizures. It is generally considered to be a second line therapy for neonatal seizures unresponsive to phenobarbitone. Treatment with phenytoin is complicated by its non-linear pharmacokinetics therefore dosage adjustments and potential drug interactions must be considered carefully.

DOSE

*** Commence maintenance dose:** 12 hours after loading dose

IV:	**Loading Dose**	15mg - 20mg/kg		
IV:	**Maintenance Dose**	CA < 37 weeks	≤ 14 days	2 mg/kg/dose 12 hourly
			> 14 days	5 mg/kg/dose 12 hourly
		CA ≥ 37 weeks	≤ 14 days	4 mg/kg/dose 12 hourly
			> 14 days	5 mg/kg/dose 8 hourly

Beyond the second week of life higher doses are often required to achieve therapeutic levels, especially in young children due to their more rapid metabolism. As toxicity is more difficult to detect in the young, more frequent monitoring may be necessary.

Post neonatal period:
If ex-term and >28 days or corrected gestational age > 44/40 refer to AMH Children's Dosing Companion

RECONSTITUTION/DILUTION

Ampoule = 250 mg in 5 mL (50 mg in 1 mL)

IV:
1. Withdraw 1 mL of 50mg/mL solution
2. Add to 9 mL of 0.9% sodium chloride in a 10mL syringe (total volume = 10 mL) (concentration = 50 mg in 10 mL = **5 mg/ mL**). DO NOT DILUTE FURTHER
3. Discard excess volume to obtain required dose or withdraw dose using another syringe

Once prepared, administer diluted solution within 1 hour.

Not for IM or subcut use

ROUTE AND METHOD OF ADMINISTRATION

Ensure an in-line (0.22 micron) filter is used

IV: LOADING DOSE: give over 60 minutes via continuous infusion via syringe pump

MAINTENANCE DOSES: give over 15 minutes via syringe pump.

NB: Infusion rate must not exceed 1 mg/kg/minute. (Maximum IV rate in an emergency: 3 mg/kg/minute)

Flush with 0.9% sodium chloride before and after administration to avoid injection site irritation
Ensure the post dose flush is infused via the syringe pump at the same rate as the phenytoin to avoid bolus administration.

COMPATIBILITY INFORMATION

Please contact your ward pharmacist for information on drugs or fluids not appearing in the table below. Medications that are not routinely used in the Special Care Nursery have not been included in this table and may be incompatible.

	Compatible	Incompatible
Fluids	Sodium chloride 0.9%	Dextrose 5%, Dextrose 10%
Drugs	**ADMINISTER ALONE**	Aminophylline, Benzylpenicillin, Dobutamine, Fentanyl, Heparin, Morphine, Phenobarbitone, Potassium chloride, Vancomycin

SIDE EFFECTS

- IV dosing can cause hypotension, arrhythmias, bradycardia, cardiovascular collapse or CNS depression therefore cardio-respiratory monitoring is essential
- Vomiting, gastric irritation, liver damage
- Skin rashes – ranging from mild measles-like rash to severe eg: Stevens-Johnson syndrome
- Occasionally haemopoetic complications such as thrombocytopenia, leucopenia, granulocytopenia, macrocytosis and megaloblastic anaemia (responsive to folic acid therapy)
- Local irritation, tenderness and necrosis at injection site
- Hypersensitivity syndrome – may include arthralgias, eosinophilia, fever, liver dysfunction, lymphadenopathy or rash (uncommon in neonates)

SPECIAL PRECAUTIONS

- Caution in patients with hypotension and severe myocardial insufficiency. AVOID in patients with heart block
- Caution in patients with hyperglycaemia (phenytoin has an inhibitory effect on insulin release). AVOID use in hypoglycaemic seizures
- Caution in hypoalbuminaemic and hyperbilirubinaemic patients (results in increased free fraction of phenytoin and may lead to toxicity) and patients with impaired renal and liver function
- Risk of haemolysis at high dose when used in patients with G6PD
- Chronic administration may decrease bone mineral density and increase risk of fractures – vitamin D supplementation may be necessary

DRUG INTERACTIONS

Medication interactions with phenytoin are complex. In general, medications may increase or decrease the effectiveness of phenytoin, and phenytoin may increase or decrease the effectiveness of other medications. When assessing drug interactions for phenytoin, consider the intended duration of treatment, the clinical status of the patient and the serum phenytoin concentration if available.

Medications that may INCREASE phenytoin serum levels:
Amphotericin, Benzodiazepines (diazepam, midazolam), Erythromycin, Omeprazole, Ranitidine, Sulfonamides (eg: cotrimoxazole)

Medications that may DECREASE phenytoin serum levels:
Calcium supplements, Chloral hydrate, Folic acid, Rifampicin, Theopyhlline

Medications that may INCREASE or DECREASE phenytoin serum levels:
Carbamazepine, Phenobarbitone

Medications whose serum levels and/or effects maybe DECREASED by phenytoin:
Corticosteroids, Digoxin, Frusemide, Theophylline, Vitamin D

***Dopamine**:*
Use of IV phenytoin in patients maintained on dopamine may produce sudden hypotension and bradycardia. Use alternative anticonvulsant

NURSING RESPONSIBILITIES

- Observations/Monitoring
  - Therapeutic drug monitoring may be required with this medication. Check if phenytoin serum level results need to be acted upon prior to the administration of the next dose. Check the date and time when the next blood level is required (see below)
  - Cardio-respiratory monitoring is essential during intravenous therapy
  - Observe for arrhythmias, hypotension, bradycardia and respiratory depression during administration
  - Record and report effect of medication on seizure activity
  - Observe infant for signs of toxicity and side effects
  - Observe IV site for signs of extravasation and thrombophlebitis
  - Visually inspect the product for particulate matter and discolouration prior to administration. Do not use if the solution is hazy or contains a precipitate. A faint yellow colour may develop but does not affect potency and these ampoules may be used.
  - Protect from light during storage
  - Phenytoin is highly unstable in any IV solution. Avoid using in central lines because of the risk of precipitation. The use of an in-line filter (0.22 micron) is recommended for IV administration. Flush the line well with sodium chloride 0.9% prior to as well as following administration. Observe the line throughout the infusion; if precipitation occurs stop immediately and notify the doctor. Use within 1 hour of dilution.
  - Oral absorption of phenytoin is unpredictable in neonates and IV administration is preferred. Capsules and injection contain phenytoin sodium and contain 8% less phenytoin than the mixtures and infatabs which contain phenytoin base. Consider dosage adjustment when changing between products.

- Therapeutic drug monitoring:
  Plasma drug concentrations for phenytoin are helpful in guiding therapy due to the non-linear pharmacokinetics of this medication. However, clinical response to treatment is still the mainstay of monitoring rather than achieving plasma concentrations in the target therapeutic range.

	Start Monitoring*	Samples Required		Therapeutic Range	
		Trough	Peak	Trough	Peak
Phenytoin	5 – 7 days	✔ (sample immediately pre-dose)	Not necessary	40 – 80 micromol/L	N/A

* If a loading dose has been given, levels may be sampled earlier to determine if the therapeutic range has been reached or to confirm toxicity. Approximate time to steady state 7 days.