BRIEF ADMINISTRATION GUIDE

For detailed information refer to The Australasian Neonatal Medicines Formulary **phenytoin** guideline

Critical Note: there are minor variations between the ANMF and Waikato DHB best practice within this drug guideline – see yellow shaded text

Indications: Treatment of neonatal seizures (second line after phenobarbitone)

Route: Intravenous (preferably central line), oral (maintenance dosing only)
Note: Oral absorption can be reduced or erratic in neonates

- Injection supplied as phenytoin sodium 100 mg/2 ml ampoule
  Note: Excipients include ethanol and propylene glycol
- Oral supplied as phenytoin 30 mg/5 ml oral suspension
  - pH of phenytoin is 12

Dose:

Loading Dose
20 mg/kg

Maintenance Dose

- Initially 2.5 mg/kg (by IV infusion or orally), commencing 12 hours after the loading dose
- Dose should be individualised according to clinical response and plasma phenytoin concentration
- Dose interval as per table below:

Age (days)	Term infants	Preterm infants
0-7	12 hourly	24 hourly
8-30	8 hourly	12 hourly
>30	6 hourly	8 hourly

Notes:

- Phenytoin does not follow linear kinetics so an increase in dose may be disproportionate to the increase in serum concentration. If a dose increase is required, do so gradually, no more than 10% of the daily dose at any one time.
- Phenytoin sodium (injection) 100 mg is approximately equivalent in therapeutic effect to phenytoin base (oral suspension) 92 mg. Care is needed when switching between formulations and additional therapeutic drug monitoring and dose adjustment may be required
- Phenytoin has numerous drug interactions – please check e.g. using NZ formulary https://www.nzfchildren.org.nz/interactions/stockleys/of/10244361000116102

Preparation and administration

Compatible fluids: sodium chloride 0.9%

Intravenous

- Dilute 2mL (100mg) of phenytoin with 18mL of sodium chloride 0.9% to make a concentration of **5 mg/ml OR** use undiluted (**50mg/mL**) in high volume loading dose or fluid restricted infant
- Draw up prescribed dose and administer diluted phenytoin through a 0.22 micron in-line filter. Inspect the solution carefully and do not use if precipitation or haziness occur
- Infuse **loading dose over 30 minutes**
- Infuse **maintenance dose over 5 minutes** (maximum rate 60 mg/kg/hour)
- Administer via a central line or into a large vein. Flush well with sodium chloride 0.9% before and after administration (after at the same rate of infusion)

Oral (maintenance dosing only)

- Shake the bottle well prior to use and draw up the prescribed dose
- May be administered with or without feeds, but should remain consistent

Monitoring

- Blood pressure, pulse, respiratory rate, and ECG continuously during infusion and every 15 minutes for 1 hour after administration
- CBC, liver function, renal function and blood glucose levels
- Observe for injection site reactions and extravasation
- Observe for signs and symptoms of rapid administration and hypersensitivity
- Phenytoin serum trough levels should be taken 24 hours after IV loading dose, then at least weekly if therapy continued (more frequently in very preterm or extreme low birth weight, or after any dose adjustment or drug formulation change)
    - Therapeutic total phenytoin level (trough): 40 – 80 micromol/L
    - Caution interpreting levels in infants with hypo- or hyper-bilirubinaemia, renal impairment, uraemia, or concomitant use of sodium valproate
    - Adjust for hypoalbuminaemia - approximate therapeutic intervals for hypoalbuminemic patients**:**
        - Plasma albumin 30 g/L: 30 - 60 micromol/L
        - Plasma albumin 20 g/L: 20 - 40 micromol/L
- If on long term therapy consider thyroid function, calcium, phosphate, vitamin D and alkaline phosphatase

Storage and Stability

- Prepare diluted phenytoin immediately before use and discard any remaining ampoule contents. Complete administration of diluted solution within four hours of dilution (preferably one hour).
- Store oral solution at room temperature and discard according to expiry date on bottle

Guardrails Information

Phenytoin will be Guardrail profiled on the CC pump for NICU. Following are the guardrail limits:

Guardrails Drug Name	**Phenytoin***
Concentration (mg/ml)	
Minimum	5
Maximum	50
Dose rate (mg/kg/hour)	
Default	40
Soft minimum	39
Soft maximum	60
Hard max	61

References

- Australian Neonatal Medicines Formulary. Phenytoin Drug Guideline. 2021. Available from https://www.seslhd.health.nsw.gov.au/sites/default/files/groups/Royal_Hospital_for_Women/Neonatal/Neomed/neomed21phenytoin.pdf
- Truven Health Analytics Inc. Pediatrics and Neofax®. Phenytoin monograph. Accessed 21st February 2022. Available from: http://www.micromedexsolutions.com.
- Auckland DHB Phenytoin Sodium Drug Guideline. April 2020. Available from: https://starship.org.nz/guidelines/phenytoin-sodium/
- Canterbury DHB Neonatal Services. Phenytoin Drug Information Sheet. July 2021. Available from: http://www.cdhb.health.nz/Hospitals-Services/Health-Professionals/Neonatal-Clinical-Resources/Neonatal-Drug-Information-Sheets.
- New Zealand Formulary for Children (NZFc) v116. Phenytoin. Accessed 21st February 2022. Available from: https://www.nzfchildren.org.nz/nzf_2726.
- Phelps SJ, Hagemann TM, Lee KR, Thompson AJ. The Teddy Bear Book: Pediatric Injectable Drugs. 11th edition. American Society of Health-System Pharmacists; 2018.
- The Royal Children's Hospital Melbourne. Paediatric Injectable Guidelines. Accessed 21st February 2022. Available from: https://pig.rch.org.au.
- New Zealand Hospital Pharmacists Assoc. Inc. Notes on Injectable Drugs 8th ed. Available from https://www.noids.nz/wp-content/uploads/2020/11/Phenytoin-S.pdf .

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