

# phenytoin

## 100mg/2mL injection, 30mg/5mL oral mixture

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**Note:**

This guideline provides advice of a general nature. This statewide guideline has been prepared to promote and facilitate standardisation and consistency of practice, using a multidisciplinary approach. The guideline is based on a review of published evidence and expert opinion.

Information in this statewide guideline is current at the time of publication.

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Health practitioners in the South Australian public health sector are expected to review specific details of each patient and professionally assess the applicability of the relevant guideline to that clinical situation.

If for good clinical reasons, a decision is made to depart from the guideline, the responsible clinician must document in the patient's medical record, the decision made, by whom, and detailed reasons for the departure from the guideline.

This statewide guideline does not address all the elements of clinical practice and assumes that the individual clinicians are responsible for discussing care with consumers in an environment that is culturally appropriate and which enables respectful confidential discussion. This includes:

- The use of interpreter services where necessary,
- Advising consumers of their choice and ensuring informed consent is obtained,
- Providing care within scope of practice, meeting all legislative requirements and maintaining standards of professional conduct, and
- Documenting all care in accordance with mandatory and local requirements

**This is a High Risk Medication** 

An overdose can be rapidly fatal.

Increases in dose must be in small increments (10%) because metabolism of phenytoin is saturable and rate-limited. Small dosage adjustments may result in large changes in free serum phenytoin levels.

### Dose and Indications

#### Anticonvulsant

##### Intravenous Loading Infusion

20 mg/kg as a single dose

##### Intravenous or Oral Maintenance Dose

2 to 4 mg/kg every 12 hrs, commencing 12 hours after the loading dose

Adjust dose according to response and phenytoin concentrations.

### Preparation and Administration

#### Intravenous

Dilute 1mL (50mg) of phenytoin injection with 9mL of 0.9% sodium chloride (to a total of 10mL). The solution now contains 5mg/mL phenytoin.

Example Table:

Dose	10mg	20mg	30mg	40mg	50mg
Volume	2mL	4mL	6mL	8mL	10mL

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Discard remaining solution.

Administer over 30 minutes. Where the phenytoin must be administered more rapidly, the administration rate must not exceed 3mg/kg/min.

Intravenous phenytoin can precipitate in solution: consider the following to lower the risk:

- > **Dilute** to 5mg/mL in 0.9% sodium chloride to facilitate infusion of dose and to reduce local irritation of vein. Do not dilute further than this.
- > **Administer** via an in-line filter.
- > **Flush** the line well with 0.9% sodium chloride prior to, as well as following, drug administration.
- > **Observe** the line throughout the infusion; if precipitation occurs, stop immediately and notify the doctor.
- > **Use** within one hour of dilution.

**Oral**

Shake the bottle well prior to drawing up a dose as the phenytoin has a tendency to precipitate out of solution. The solution contains 6mg/mL phenytoin.

Dose	3mg	6mg	9mg	12mg	15mg
Volume	0.5mL	1mL	1.5mL	2mL	2.5mL

Nasogastric feeds may decrease absorption of nasogastric phenytoin; separate administration where possible by 2 hours or change to IV phenytoin.

**Compatible Fluids**

Sodium chloride 0.9%

Phenytoin may precipitate if reconstituted in any other solution or mixed in the line with any other solution including parenteral nutrition.

**Adverse Effects****Common**

Vomiting, agitation, neurological adverse events (sedation, nystagmus), irritation at IV injection site (thrombophlebitis and skin necrosis)

Hirsutism and gingival hypertrophy with long term use

Rapid IV injection may cause hypotension, arrhythmias, bradycardia, cardiovascular collapse, CNS depression and respiratory depression.

**Rare**

Choreiform movements, hyperglycaemia, osteomalacia and rickets, Stevens-Johnson syndrome, toxic epidermal necrolysis, cerebellar atrophy, haematologic abnormalities, hepatitis, nephritis, interstitial pneumonitis



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Hypersensitivity reactions (skin rash, fever, abnormal liver function, eosinophilia, blood dyscrasias, albuminuria) are extremely unlikely in this population.

**Monitoring****Monitoring Phenytoin by Trough Levels**

Age (days)	Therapeutic range:
	Total serum phenytoin (protein-bound plus free drug)
≤ 28	25 to 60 micromol/L
> 28	40 to 80 micromol/L

- > Close Therapeutic Drug Monitoring is required using trough levels.
- > A lower therapeutic range is recommended in neonates due to reduced protein binding of phenytoin in the first month of life.
- > It takes approximately one week of maintenance dosing if no loading dose has been administered to attain steady state. If loading dose has been given trough levels may be taken after 48 hours.
- > Blood levels can be unpredictable because of variable absorption, saturation pharmacokinetics, and enhancement or inhibition of metabolism by drugs that share the same hepatic enzyme metabolic pathway. In particular, phenobarbitone can cause both competitive inhibition of phenytoin metabolism and with prolonged use induces phenytoin metabolism.
- > Rapid intravenous dosing can cause cardiovascular side effects. Cardiac, respiratory and BP monitoring is recommended, particularly for intravenous loading doses.
- > Hypoalbuminaemia or displacement of phenytoin from albumin by bilirubin can increase the percentage of unbound (free, active) phenytoin and this may complicate the interpretation of serum levels. Toxicity may occur even though the total serum phenytoin level may seem within the normal therapeutic range. In such a scenario free phenytoin levels should be measured.
- > Phenytoin interacts with a range of medications; please check with your local pharmacy department for specific advice.

**Practice Points**

- > Rapid bolus injection should be avoided, as this is associated with hypotension, arrhythmias, bradycardia, cardiovascular collapse, CNS depression and/or respiratory depression.
- > Use cautiously in patients on medication with cardiac effects (ie digoxin, lignocaine, dopamine and beta-blockers).
- > Phenytoin is contraindicated with hypoglycaemic seizures as well as severe sinus bradycardia, sinoatrial block, second or third degree AV block, Stokes-Adams syndrome and acute porphyrias.



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- > Therapeutic hypothermia prolongs the already variable half-life of phenytoin and levels in cooled infants are likely to be higher than in normothermic infants.
- > Phenytoin must not be mixed with glucose solutions.
- > Ampoule also contains propylene glycol, ethanol and sodium hydroxide or hydrochloric acid.
- > Intramuscular and subcutaneous route are not recommended due to local tissue reactions. Continuous intravenous infusion is generally not recommended due to low solubility and resultant precipitation.

**Document Ownership & History**

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