Phenytoin Sodium

Brand names	Dilantin, Phenytek, generics
Medication error potential	Look-alike, sound-alike drug names. Confusion has been noted between Feldene, fluconazole, fosphenytoin, nystatin, phenazopyridine, PHENobarbital, and phytonadione.[1] Dilantin has been mistaken for Diflucan, Dilaudid, dilTIAZem, Neutrontin, and Nystatin.[1] Confusion with fosphenytoin and PHENobarbital has resulted in patient harm, and confusion with PHENobarbital has resulted in death.[1]
Contraindications and warnings	**Contraindications:** Phenytoin is contraindicated in patients with a history of hypersensitivity to hydantoin products.[2] Parenteral phenytoin affects ventricular automaticity and is contraindicated in patients with sinus bradycardia, sinoatrial block, second- and third-degree atrioventricular block, and Adams-Stokes syndrome.[2] **Warnings:** IV rate of administration should not exceed 50 mg/min in *adults* and 1–3 mg/kg/min in pediatric patients.[2] Abrupt discontinuation of phenytoin may increase seizure frequency and/or precipitate status epilepticus. If an allergic or hypersensitivity reaction or a life-threatening adverse event occurs, rapid substitution of an alternative anticonvulsant may be necessary. If phenytoin is discontinued due to development of a rash, an anticonvulsant *not* belonging to the hydantoin family and one structurally dissimilar should be used.[26-28] Phenytoin should be used cautiously in patients with hypotension and severe myocardial insufficiency. The FDA is investigating the possibility of an increased risk of phenytoin-associated serious skin reactions (e.g., Stevens-Johnson syndrome and toxic epidermal necrolysis) in patients who have the human leukocyte antigen allele HLA-B*1502.[3] This allele may be present in individuals with ancestry across broad areas of Asia, including Han Chinese, Filipinos, Malaysians, South Asian Indians, and Thais.[3] At this time, phenytoin should be avoided as an alternative for carbamazepine in patients who test positive for HLA-B*1502.[3] (See Monitoring in the Comments section.) A relationship between phenytoin and the development of localized or generalized lymphadenopathy including benign lymph node hyperplasia, pseudolymphoma, lymphoma, and Hodgkin disease has been noted.[2] Lymph node involvement may occur with or without symptoms and signs resembling anticonvulsant hypersensitivity syndrome. (See the Comments section.)
Infusion-related cautions	Rapid administration has resulted in hypotension and cardiovascular collapse.[2] Purple glove syndrome is the development of progressive distal limb edema, discoloration, and pain after peripheral administration of IV phenytoin.[4,5] Although this may occur from a reaction of the interstitial tissue to extravasation of phenytoin, it can occur in the absence of infiltration. Resolution of signs/symptoms may spontaneously occur, but extensive skin necrosis, limb ischemia, and compartmental syndrome with fasciotomies may require skin grafting, or limb amputation. (See Appendix E for management.) Because of the high risk of extravasation and local tissue irritation with peripheral administration of phenytoin, especially in neonates with peripheral scalp IV lines, fosphenytoin should be considered *in lieu* of phenytoin. (See the Fosphenytoin monograph.)
Dosage	In obese patients with active seizures the loading doses should be calculated on adjusted body weight using the following equation[5] (see Appendix B): Dosing weight (kg) = Ideal Body Weight (IBW) + 1.33 (measured weight – IBW) **Arrhythmias (Class 1B) (digoxin-induced tachyarrhythmias):** 1.25 mg over 5 minutes. May repeat every 5 minutes titrated to a total of 15 mg/kg. This should be followed by maintenance dosing that ranges from 5–10 mg/kg/day divided into 2–3 doses.[6]

Dosage *(cont.)*

Post-traumatic epilepsy (see status epilepticus for dosing): Although prophylactic phenytoin has been used for the prevention of epilepsy following head trauma, its use is controversial.[7-9,31,32] There are no compelling data in the pediatric literature to show that such treatment reduces the long-term risk of posttraumatic epilepsy or improves long-term neurologic outcome. Several recent reports have suggested that levetiracetam should replace phenytoin/fosphenytoin.[36-38] It should *not* be used for the prevention of late epilepsy. Children with severe, acute neurotrauma have markedly altered protein binding and phenytoin metabolism and may require larger doses and more frequent dosing.[9,11] Free serum phenytoin concentration should be monitored.[10]

Status epilepticus (generalized convulsive)

Loading dose (assumes no previous phenytoin)

Neonates: 8–20 mg/kg[2,12,13] (may prefer phenobarbital or a benzodiazepine)

Infants and children: 15–20 mg/kg[2,14-16]

Adolescents and *adults*: 10–15 mg/kg not to exceed 1 g[2]

Maintenance dose

Neonates: 4–8 mg/kg/day divided q 12–24 hr.[13,17] Some suggest smaller doses of 3–5 mg/kg/day.[12] Extremely difficult to obtain serum concentrations following conversion to oral therapy; therefore, consider an alternative anticonvulsant for oral dosing.[10,12,18]

Infants and children: For 4 weeks to <1 years, 4–8 mg/kg/day.[12] For 1–12 years, 8–10 mg/kg/day divided q 8 hr.[12,14,16]

Adolescents and *adults*: If ≥12 years, 4–8 mg/kg/day divided q 8–12 hr.[12] The manufacturer recommends 100 mg q 6–8 hr.[2]

Dosage adjustment in organ dysfunction

Dosage adjustment may be required in patients with hepatic[2] or renal dysfunction.[19,20] Due to an increased fraction of unbound phenytoin in neonates, patients with renal or hepatic disease, or in those with hypoalbuminemia, the interpretation of total phenytoin plasma concentrations should be made with caution.[18] Free phenytoin serum concentrations should be measured in patients with renal dysfunction, or in those who are hypoalbuminemic because of decreases in protein binding, increases in volume of distribution, and altered clearance.[10,18] Although several equations have been used to predict free phenytoin serum concentrations in those with low albumin or renal failure, they may over predict concentrations and are not recommended for use in children.[33]

Maximum dosage

20 mg/kg as a single dose, not to exceed 1 g.[22] Doses as large as 25 mg/kg/day divided q 6 hr were used to achieve total serum phenytoin concentrations within the "therapeutic range" in a neonate.[22] If large doses are used, free phenytoin concentrations should be monitored. Because of age-dependent variation in phenytoin elimination, individualize dosage based on total and/or free serum concentrations.

Additives

Undiluted injection contains 0.2 mEq sodium/mL of phenytoin.[23] Contains 40% propylene glycol. (See Appendix C for specific information about propylene glycol and potential for toxicity.)

Suitable diluents

Phenytoin is highly unstable in any IV solution; therefore, it should only be diluted in NS and should not be mixed with other medications.[23] An inline 0.22–5 micron filter is recommended due to the high potential for precipitation of the solution.[23]

Maximum concentration

50 mg/mL (commercially available)[2]