phenytoin (fen-i-toyn)

Dilantin, Phenytek, Tremytoine

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Classification
Therapeutic: antiarrhythmics (group IB), anticonvulsants
Pharmacologic: hydantoins

Pregnancy Category D

Indications
Treatment/prevention of tonic-clonic (grand mal) seizures and complex partial seizures. Unlabeled Use: As an antiarrhythmic, particularly for ventricular arrhythmias associated with digoxin toxicity, prolonged QT interval, and surgical repair of congenital heart diseases in children. Management of neuropathic pain, including trigeminal neuralgia.

Action
Limits seizure propagation by altering ion transport. May also decrease synaptic transmission. Antiarrhythmic properties as a result of shortening the action potential and decreasing automaticity. Therapeutic Effects: Diminished seizure activity. Termination of ventricular arrhythmias.

Pharmacokinetics
Absorption:
Absorbed slowly from the GI tract. Bioavailability differs among products; the Dilantin and Phenytek preparations are considered to be "extended" products. Other products are considered to be prompt release.

Distribution:
Distributes into CSF and other body tissues and fluids. Enters breast milk; crosses the placenta, achieving similar maternal/fetal levels. Preferentially distributes into fatty tissue.

Protein Binding:
Adults 90–95%; protein binding in neonates (up to 20% free fraction available), infants (up to 15% free), and patients with hyperbilirubinemia, hypoalbuminemia, severe renal dysfunction or uremia.

Metabolism and Excretion:
Mostly metabolized by the liver; minimal amounts excreted in the urine.

Half-life: 22 hr (range 7–42 hr).

TIME/ACTION PROFILE (anticonvulsant effect)

ROUTE ONSET PEAK DURATION
PO 2–24hr (1wk)* 1.5–3hr 6–12hr
PO-ER 2–24hr (1wk) 4–12hr 12–36hr
IV 0.5–1 hr (1 wk) rapid 12–24 hr

(*time required for onset of action without a loading dose)

Contraindications/Precautions
Contraindicated in: Hypersensitivity; Hypersensitivity to propylene glycol (phenytoin injection only); Alcohol intolerance (phenytoin injection and liquid only); Atrial fibrillation, atrial flutter, 1st-degree heart block, or abnormal conduction (phenytoin injection only). Concurrent use of delavirdine.

Use Cautiously in:
All patients (may increase risk of suicidal thoughts/behaviors); Hepatic or renal disease (may increase risk of adverse reactions; dose reduction recommended for hepatic impairment); Patients with severe cardiac or respiratory disease (may be fatal if phenytoin use results in an increase in the risk of adverse reactions).

OB: Safety not established; may result in fetal hydantoin syndrome if used chronically or hemorrhage in the newborn if used at term; use with extreme caution.

Lactation:
Safety not established.

Pedi:
Suspension contains sodium benzoate, a metabolite of benzyl alcohol that can cause potentially fatal gasping syndrome in neonates. Use with caution.

Geri:
Use of IV phenytoin may result in an increased risk of serious adverse reactions.

Exercise Extreme Caution in:
Patients positive for HLA-B*1502 allele (unauthorized use). Patients on maintenance doses when a loading dose is not required should be closely monitored for signs of toxicity.

Adverse Reactions/Side Effects
Most listed are for chronic use of phenytoin

CNS: SUICIDAL THOUGHTS, ataxia, agitation, confusion, dizziness, drowsiness, dysarthria, dyskinesia, extrapyramidal syndrome, headache, insomnia, weakness.

EENT: diplopia, nystagmus.

CV: hypotension, tachycardia.

GI: gingival hyperplasia, nausea, constipation, drug-induced hepatitis, vomiting.

Derm: STEVENS-JOHNSON SYNDROME, TOXIC EPIDERMAL NECROLYSIS, hypertrichosis, rash, exfoliative dermatitis, pruritus, purple glove syndrome.

Hemat: AGRANULOCYTOSIS, APLASTIC ANEMIA, leukopenia, megaloblastic anemia, thrombocytopenia.

MS: osteomalacia, osteoporosis.

Misc: fever, lymphadenopathy.

Interactions
Drug-Drug: May increase the effects of delavirdine, resulting in loss of virologic response and potential resistant (concurrent use contraindicated). Acute ingestion of

Dose-Related: None known.

Toxicity and Management:
Antidotes: None known.

Supportive/Lifesaving Measures: Include management of convulsions, cardiorespiratory support, and treatment of specific adverse reactions. Consult中毒管理手册 for further information.
Phenytoin may lower the anticoagulant effect of warfarin. May also reduce the effect of mazepine. May increase the effects of amides like carbamazepine and nortriptyline.

**Phenytoin**

**PO (Neonates up to 6 mo):** Loading dose 15–20 mg/kg at 1–3 mg/kg/divided doses, usually dosing range 50–100 mg q 10–15 min until arrhythmia is abolished, or a total of 15 mg/kg has been given, or toxicity occurs.

**PO (Children 6–6 yr):** Loading dose 7.5–9 mg/kg/day in 2–3 divided doses.

**PO (Children 6–16 yr):** 8–10 mg/kg/day in 2–3 divided doses.

**PO (Neonates up to 6 mo):** 5–8 mg/kg/day in divided doses, may require q 8 hr dosing.

**IV (Adults):** Intravenous bolus loading dose—15–20 mg. Rate not to exceed 25–50 mg/min. Maintenance dose—same as PO dosing above.

**IV (Children):** Intravenous bolus loading dose—15–20 mg/kg at 1–3 mg/kg/min. Maintenance dose—same as PO dosing above.

**Antiarhythmic**

**PO (Children 6–16 yr):** 0.5–1.25 mg/kg q 6–8 hr for 2 days, then maintenance at 0.5–1 mg/kg/day in divided doses 1–4 times/day.

**PO (Children):** 1.25 mg/kg q 12 hr; may taper up to total loading dose of 15 mg/kg. Maintenance dose—5–10 mg/kg/day in 2–3 divided doses IV or PO.

**NURSING IMPLICATIONS**

Assessment

- **Monitor closely for notable changes in behavior that could indicate the emergence or worsening of suicidal thoughts or behavior on depression.**

- **Assess oral hygiene.** Vomitus clearing beginning within 10 days of initiation of phenytoin therapy may help control gingival hyperplasia.

- **Assess patient for phenytoin hypersensitivity syndrome (fever, skin rash, lymphadenopathy).** Rash usually occurs within the first 2 wk of therapy. Hypersensitivity syndrome usually occurs at 3–8 wk but may occur up to 12 wk after initiation of therapy. May lead to renal failure, rhabdomyolysis, or hepatic necrosis, may be fatal.

- **Observe patient for development of rash. Discontinue phenytoin at the first sign of skin reactions. Serious adverse reactions such as exfoliative, paraproteic, or bullous rashes or the development of lupus erythematosus, Stevens-Johnson syndrome and toxic epidermal necrolysis are significantly more common in patients with a particular human leukocyte antigen (HLA) allele, HLA-B*1502 (occurs almost exclusively in patients with Asian ancestry, including Han Chinese, Filipinos, Malaysians, South Asian Indians, and some other Asians).**
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phenytoin

Thais). Avoid using phenytoin or fosphenytoin as alternatives to carbamazepine for patients who test positive. If less serious skin eruptions (measles-like or scarlatiniform) occur, phenytoin may be resumed after complete clearing of the rash. If rash progresses, further use of fosphenytoin or phenytoin should be avoided.

● Assess mental status (orientation, mood, behavior) before and periodically during therapy. Monitor closely for notable changes in behavior that could indicate the emergence or worsening of suicidal thoughts or behavior or depression.

● Seizures: Assess location, duration, frequency, and characteristics of seizure activity. EEG may be monitored periodically throughout therapy.

● Monitor IV, ECG, and respiratory function continuously during administration of IV phenytoin and throughout period when peak serum phenytoin levels occur (15–30 min after administration).

● Arthralgias: Monitor ECG continuously during treatment of arthralgias.

● Lab Test Considerations: Monitor CBC, serum calcium, albumin, and hepatic function tests prior to and monthly for the first several months, then periodically during therapy.

● May cause serum alkaline phosphatase, GGT, and glucose levels.

● Monitor serum folate concentrations periodically during prolonged therapy.

● Toxicity and Overdose: Monitor serum phenytoin levels routinely. Therapeutic blood levels are 10–20 mcg/mL (8–15 mcg/mL in neonates) in patients with normal serum albumin and renal function. In patients with altered protein binding (neonates, patients with renal failure, hypoalbuminemia, acute trauma), free phenytoin serum concentrations should be monitored. Therapeutic serum free phenytoin levels are 1–2 mcg/mL.

● Progressive signs and symptoms of phenytoin toxicity include nystagmus, ataxia, confusion, nausea, slurred speech, and dizziness.

Potential Nursing Diagnoses

Risk for injury (Indications)

Impaired oral mucous membrane (Side Effects)

Implementation

● Implement seizure precautions.

● When transferring from phenytoin to another anticonvulsant, dosage adjustments are made gradually over several weeks.

● When substituting fosphenytoin for oral phenytoin therapy, the same total daily dose may be given as a single dose. Unlike parenteral phenytoin, fosphenytoin may be given safely by the IM route.

● PO: Administer with or immediately after meals to minimize GI irritation. Shake liquid preparations well before pouring. Use a calibrated measuring device for accurate dose. Capsules may be opened and mixed with food or fluids for patients with difficulty swallowing. To prevent direct contact of alkaline drug with mucosa, have patient swallow a liquid first. Follow with mixture of medication, then follow with a full glass of water or milk or soft food.

● If patient is receiving enteral tube feedings, 2 hr should elapse between feeding and phenytoin administration. If phenytoin is administered via nasogastric tube, flush tube with 2–4 oz water before and after administration.

● Do not substitute compound phenytoin capsules with phenytoin sodium capsules, because they are not bioequivalent.

● Capsules labeled “extended” may be used for once-a-day dose; those labeled “prompt” may result in toxic serum levels if used for once-a-day dose.

IV Administration

● IV: Slight yellow color will not alter solution potency. If refrigerated, may form precipitate, which dissolves after warming to room temperature. Discard solution that is not clear.

● To prevent precipitation and minimize local venous irritation, follow infusion with 0.9% NaCl through the same needle or catheter. Avoid extravasation; phenytoin is caustic to tissues; may lead to purple glove syndrome. Monitor infusion site closely.

● Direct IV: Administer at a rate not to exceed 50 mg over 1 min in adults or 1–3 mg/kg/min in neonates. Rapid administration may result in severe hypotension, cardiovascular collapse, or CNS depression.

● Intravenous Infusion: Diluent: Administer at a rate not to exceed 50 mg over 1 min in adults or 1–3 mg/kg/min in neonates. Rapid administration may result in severe hypotension, cardiovascular collapse, or CNS depression.

● Intramuscular Infusion: Diluent: Administer by mixing with no more than 50 ml of 0%. NaCl. Concentration: 1–10 mg/mL. Administer immediately following admixture. Use tubing with a 0.45- to 0.22-micron in-line filter. Rate: Complete infusion within 1 hr at a rate not to exceed 50 mg/min. In patients who
Y-Site Incompatibility: 

Y-Site Compatibility:

- pranolol, protamine, pyridoxime, quinupristin/dalfopristin, ranitidine, rocuronium, ritodrine, sodium acetate, sodium bicarbonate, streptokinase, streptodornase, sucralfate, sucralfate, succinylcholine, suxamethonium, tacrolimus, teniposide, theophylline, thiamine, thiotepa, ticarcillin/clavulanate, tigecycline, tirofiban, tolazoline, trimethoprim/sulfamethoxazole, vancomycin, vasopressin, vecuronium, verapamil, vinblastine, vincristine, vinorelbine, vitamin B complex with C, voriconazole, zoledronic acid.

Additive Incompatibility: Do not admix with other solutions or medications, especially dopamine, because precipitation will occur.

Patient/Family Teaching

- Instruct patient to take medication as directed, at the same time each day. If a dose is missed from a once-a-day schedule, take as soon as possible. Maximum rate of 25 mg/min [may be as low as 5–10 mg/min]. Maximum daily dose is 10 mg/kg/day.

- Advise patient to carry identification describing disease process and medication regimen at all times.

- Advise patient not to take phenytoin within 2–3 hr of antacids.

- Instruct patient to monitor cardiac function and BP throughout treatment or surgery.

- Advise patient to notify health care professional of medication regimen prior to treatment or surgery.

- Advise diabetic patients to monitor blood glucose carefully and to notify health care professional of significant changes.

- Instruct patient to notify health care professional of all Rx or OTC medications, vitamins, or herbal products being taken and to consult with health care professional before taking other medications and alcohol.

- Advise patient on importance of maintaining good dental hygiene and seeing dentist frequently for teeth cleaning to prevent tenderness, bleeding, and gingival hyperplasia. Institution of oral hygiene program within 10 days of initiation of phenytoin therapy may minimize growth rate and severity of gingival enlargement. Patients under 23 yr of age and those taking doses 500 mg/day are at increased risk for gingival hyperplasia.

- Advise patient to carry identification describing disease process and medication regimen at all times.
Phenytoin

- Instruct patients that behavioral changes, skin rash, fever, sore throat, mouth ulcers, easy bruising, petechiae, unusual bleeding, abdominal pain, chills, pale stools, dark urine, jaundice, severe nausea or vomiting, drowsiness, shared speech, unsteady gait, swollen glands, or persistent headache should be reported to health care professionals immediately. Advise patient and family to notify health care professionals if thoughts about suicide or dying, attempts to commit suicide, new or worse depression, new or worse anxiety, feeling very agitated or restless; panic attacks; trouble sleeping; new or worse irritability; acting aggressive, being angry or violent; acting on dangerous impulses; an extreme increase in activity and talking, other unusual changes in behavior or mood occur.

- Advise female patients to use an additional nonhormonal method of contraception during therapy and until next menstrual period. Instruct patient to notify health care professional if pregnancy is planned or suspected. Encourage patients who become pregnant to enroll in the North American Antiepileptic Drug (NAAED) Pregnancy Registry by calling 1-888-233-2334 or on the web at www.aedpregnancyregistry.org. Enrollment must be done by patients themselves.

- Emphasize the importance of routine exams to monitor progress. Patient should have routine physical exams, especially monitoring skin and lymph nodes, and EEG testing.

Evaluation/Desired Outcomes

- Decrease or cessation of seizures without excessive sedation.
- Suppression of status epilepticus.
- Relief of intractable pain.

Why was this drug prescribed for your patient?