10 x 10 mL Single Dose Vials
FOR INTRAMUSCULAR OR INTRAVENOUS USE
NDC 60505-0765-4

Fosphenytoin Sodium Injection USP
500 mg PE in 10 mL (PE = phenytoin sodium equivalents)
(50 mg PE in mL)
FOR INTRAMUSCULAR OR INTRAVENOUS USE
Rx Only

For IM or IV Use.
Each 10 mL contains fosphenytoin sodium 750 mg equivalent to 500 mg phenytoin sodium,
tromethamine as a buffer, hydrochloric acid and water for injection. Additional hydrochloric acid
and/or sodium hydroxide may be added to adjust pH to 8.3 to 9.3.

Usual Dosage:
See prescribing information.

Note:
Administration differs from parenteral
phenytoin. See Dosage and Administration.

Store under refrigeration at
2\°C to 8\°C (36\°F to 46\°F). The
product should not be stored at room
temperature for more than 48 hours.
Vials that develop particulate matter
should not be used.

DOSES OF FOSPHENYTOIN SODIUM INJECTION
ARE EXPRESSED AS THEIR PHENYTOIN SODIUM
EQUIVALENTS (PE = phenytoin sodium equivalents).

Manufactured by:
Apotex Inc.
Toronto, Ontario
Canada M9L 1T9

Manufactured for:
Apotex Corp.
Weston, FL
33326

UNVARNISHED AREA FOR
Lot & Exp.
40 mm x 48 mm
NDC 60505-0765-4
10 mL Single Dose Vial

Only
Fosphenytoin Sodium Injection USP
500 mg PE* in 10 mL
(50 mg PE in mL)
For IM or IV Use

* PE = phenytoin sodium equivalents.
Each vial contains fosphenytoin sodium 750 mg equivalent to 500 mg phenytoin sodium.
Usual Dosage: See prescribing information.

Store under refrigeration at 2°C to 8°C (36°F to 46°F).

Mfg. by: Apotex Inc.
Toronto, Ontario, Canada M9L 1T9

UNVARNISHED AREA: 12 mm x 20.63 mm

Enlarged 200%
Fosphenytoin Sodium Injection USP

100 mg PE in 2 mL (PE = phenytoin sodium equivalents)

For IM or IV Use.

Usual Dosage:
See prescribing information.

Note:
Administration differs from parenteral phenytoin. See Dosage and Administration.

Store under refrigeration at 2°C to 8°C (36°F to 46°F). The product should not be stored at room temperature for more than 48 hours.

Vials that develop particulate matter should not be used.

Doses of fosphenytoin sodium injection are expressed as their phenytoin sodium equivalents (PE = phenytoin sodium equivalents).

For more information, please refer to the prescribing information.
Fosphenytoin Sodium Injection USP

MECHANISM OF ACTION
Phenytoin acts on the nervous system by modulating sodium currents at neuronal synapses. This property may also be responsible for anticonvulsant effects. The sodium channel modulating effect is shared with structurally similar compounds (eg, barbiturates, succinimides, oxazolidinediones, and other related anticonvulsants). The interaction with sodium channels also appears to be responsible for the antiseizure properties of phenytoin and its prodrug fosphenytoin.

Phenylhydantoins are derivatives of phthalimide, which is a heterocyclic compound that contains a phthalimide ring and a phenyl ring. Phenytoins exhibit anticonvulsant properties in animal models and in clinical settings.

Absorption/Bioavailability
Fosphenytoin is a prodrug of phenytoin. When fosphenytoin sodium injection is administered by IV infusion, maximum plasma fosphenytoin concentrations are achieved within 0.5 to 2 hours, depending on the rate of administration. The volume of distribution of fosphenytoin at steady state is approximately 13 L/kg. Intramuscular administration of fosphenytoin sodium injection results in rapid absorption and achieving maximum plasma fosphenytoin concentrations within 0.5 to 2 hours, depending on the rate of administration.

Intravenous Administration
The dose for parenteral administration is based on a patient's weight in kilograms (see DOSAGE AND ADMINISTRATION). The dose is calculated as a loading dose followed by a maintenance dose. The loading dose is calculated as 15 to 20 mg PE/kg. The maintenance dose is calculated as 5 to 10 mg PE/kg administered over 24 hours. The dosage requirements are highly variable and must be individualized. The serum glucose concentration should be measured prior to administration of fosphenytoin sodium injection and monitored during therapy. Hypoglycemia has been reported in patients with diabetes mellitus who are begun on fosphenytoin sodium injection therapy. The patient's serum glucose concentration should be monitored at least weekly during therapy. The maintenance dose should be adjusted as necessary based on the serum glucose concentration. Fosphenytoin sodium injection may cause a decrease in serum glucose concentrations in diabetic patients. The decrease occurs as a result of the decrease in insulin release and the increase in glucose utilization by the brain.

Intramuscular Administration
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Drugs that may decrease plasma phenytoin concentrations include: carbamazepine, chronic alcohol abuse, reserpine.

Tests

micronucleus test.

or higher on a mg/m2 basis).

The carcinogenic potential of fosphenytoin has not been studied.  Assessment of the carcinogenic potential of phenytoin in

allergic process were not seen (see

Approximately 2% of the 859 individuals who received fosphenytoin sodium injection in premarketing clinical trials discontinued

TABLE 2

Incidence in Controlled Clinical Trials - IV Administration To Patients With Epilepsy or Neurosurgical Patients:

The most significant drug interactions following administration of fosphenytoin sodium injection are expected to occur with

Drug Interactions

metabolizing enzymes.

Displacement.  Phenytoin is metabolized by hepatic cytochrome P450 enzymes and is particularly susceptible to inhibitory

effects, caution is advised when administering fosphenytoin sodium injection with other drugs that significantly bind to serum

TABLE 3

Incidence in Controlled Trials - IM Administration to Patients With Epilepsy

The median lethal dose of fosphenytoin given intravenously in mice and rats was 156 mg PE/kg and approximately 250 mg PE/kg, or

Tissue Toxicity Following Fosphenytoin Sodium Injection Overdose

The most common adverse event noted was nausea (11.1%).  The following adverse events were noted in less than 2% of the patients:

Central Nervous System:

Because fosphenytoin sodium injection is a prodrug of phenytoin, the following information may be helpful. Initial symptoms of acute

extrapyramidal symptoms, extrapyramidal syndromes, and extrapyramidal syndrome.

Other idiosyncratic reactions, side effects, and adverse events that have been reported with the use of fosphenytoin sodium injection or

Urogenital:

Confused state, delirium, dysphoria, depression, convulsion, flat affect, headache, hypoglycemia, hyperreflexia, hypertension, jaundice, paresthesia, fever, psychiatric disorder, psychomotor retardation, psychosis, psychoses, psychotic disorder, pyrexia.

TABLE 4

Incidence in Controlled Clinical Trials - IV Fosphenytoin and/or Fusphenytoin

The initial daily maintenance dose of fosphenytoin sodium injection is 4 to 6 mg PE/kg/day.

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Pruritis

2.2

0.0

4.4

The initial daily maintenance dose of fosphenytoin sodium injection is 4 to 6 mg PE/kg/day.

injection administration to patients with renal and/or hepatic disease, or in those with hypoalbuminemia, fosphenytoin clearance to

TABLE 5

Incidence in Controlled Clinical Trials - IM Fosphenytoin

The use of fosphenytoin sodium injection in patients with severe hepatic dysfunction is unwarranted.  Although fosphenytoin sodium injection

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TABLE 6

Incidence in Controlled Clinical Trials - IV Administration To Patients With Epilepsy or Neurosurgical Patients:

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**NDC 60505-0746-5**

2 mL Vial

Fosphenytoin Sodium Injection USP

100 mg PE (PE = phenytoin sodium equivalents) in 2 mL

For IM or IV Use

Mfg. by Apotex Corp.

Toronto, Ontario, Canada M9L 1T9

Phone: (905) 884-2050
Fax: (905) 884-9876

For position of Lot & Exp

Unvarnised Area 0.472" (12 mm)

Non Printing Dieline

0.1273" (3.175 mm) CR

Enlarged 200 %