PHOSPHENYTOIN Sodium Injection, USP

**INDICATIONS AND USAGE**

Fosphenytoin can be used for the control of generalized convulsive status epilepticus in adults and children, ages two years and above. The recommended loading dose is 33 mg PE/kg of fosphenytoin (approximately 50% of the maximum human loading dose) to be administered over 10 minutes. The maximum dose is 1000 mg PE (15 mg/kg or 200 mg/m²) and should not be administered at a rate greater than 150 mg PE/min. In patients with a reduced maximum rate of administration (150 mg PE/min), none experienced severe adverse effects.

**CONTRAINDICATIONS**

Fosphenytoin is contraindicated in patients who have demonstrated hypersensitivity to fosphenytoin or any of its components.

**WARNINGS**

Seizures, angioedema, and/or urticaria were reported in 7 of 16 control patients, who were given placebo or positive controls. These events occurred within 24 hours of drug administration and resolved upon discontinuation of drug. Seizures were not observed in the patients who received fosphenytoin. Firearm accidents, suicide attempts, and self-mutilation have occurred in patients with epilepsy, who were receiving antiepileptic drugs, including phenytoin. Antiepileptic drugs may increase the risk of suicidal thoughts or behavior in all age groups. The use of antiepileptic drugs is accompanied by an increased risk of suicidal thoughts or behavior in patients with epilepsy. Patients should be observed for symptoms of depression, suicidal thoughts or behavior, and any unexplained symptoms or exacerbation of symptoms. Patients with depression should be observed for new or worsening depression. Patients should be observed for symptoms of depression.

**ADVERSE REACTIONS**

Fosphenytoin is completely converted to phenytoin following intramuscular administration, with a mean time to peak plasma concentration of 50 minutes. Maximal plasma concentrations (Cmax) of phenytoin were observed in approximately 3 hours. Phenytoin is highly bound to plasma proteins, primarily albumin, whereas its unbound concentrations are critical in determining its anticonvulsant effects. Phenytoin is highly bound to plasma proteins, primarily albumin, whereas its unbound concentrations are critical in determining its anticonvulsant effects. Contact between convulsing and phenytoin sodium doses. Fosphenytoin is completely converted to phenytoin following intramuscular administration, with a mean time to peak plasma concentration of 50 minutes. Maximal plasma concentrations (Cmax) of phenytoin were observed in approximately 3 hours.

Due to an increased fraction of unbound phenytoin in patients with renal or hepatic disease, plasma concentrations should be measured with caution. (See PRECAUTIONS.)

The Plasma fosphenytoin concentrations following IM administration are lower but more prolonged than those following IV administration. Peak concentrations range from 5 to 15 mg/L and were reached in 1 to 3 hours. The elimination half-life of fosphenytoin is 1 to 2 hours. Absorption/Bioavailability Fosphenytoin is completely bioavailable following IM administration of 150 mg PE/m². No significant differences in plasma fosphenytoin concentrations were observed 1 hour postinfusion when fosphenytoin and phenytoin were administered at similar 3 mg PE/kg or 30 mg/m² dosages.

**Mechanism of Action**

Fosphenytoin is a prodrug of phenytoin and its anticonvulsant effects are due to its conversion to phenytoin. After IV administration to mice, fosphenytoin reached the brain in phase of maximal pharmacological activity. Fosphenytoin is rapidly metabolized to sphenytoin, phenytoin, and other metabolites, which are subsequently excreted in the urine, bile, and feces. The primary route of elimination is renal. The half-life of fosphenytoin is 1 to 2 hours. Absorption/Bioavailability Fosphenytoin is completely bioavailable following IM administration of 150 mg PE/m². No significant differences in plasma fosphenytoin concentrations were observed 1 hour postinfusion when fosphenytoin and phenytoin were administered at similar 3 mg PE/kg or 30 mg/m² dosages.

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The prescriber should be aware that these figures cannot be used to predict the adverse events that patients will experience. All adverse events were recorded during the trials by the clinical investigators using established clinical definitions. For fosphenytoin, the incidence of adverse events was calculated by using the Cochran-Mantel-Haenszel method. Changes in plasma phenytoin concentrations are not predictive of adverse clinical events.

The most commonly occurring drug interactions are listed below:

- Drug interactions may increase plasma phenytoin concentrations include:
  - Valproate
  - Carbamazepine
  - Rifampin
  - Barbiturates
- Drug interactions may decrease plasma phenytoin concentrations include:
  - Phenytoin
  - Soviet
  - Isoniazid
- Drug interactions may not affect plasma phenytoin concentrations include:
  - Oral contraceptives
  - Corticosteroids
  - Cimetidine
  - Probenecid

Corrections, Watertightness, Impairment of Fertility

The effects of fosphenytoin on the male and female rat reproductive systems were assessed. No adverse effects on the reproductive organs or functions of any sex were noted. Male rats given fosphenytoin intravenously at dosage levels up to 1.1 mg/kg/day produced no evidence of testicular suppression or infertility. Female rats given fosphenytoin intravenously at dosage levels up to 1.1 mg/kg/day produced no histopathological alterations or evidence of impaired fertility.

Concentrations not useful in estimating renal function vary with the rate of glomerular filtration. The decline in plasma drug concentrations between dosing is first order.

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