



## Fosphenytoin

Updated: November 8, 2020.

## OVERVIEW

### Introduction

Fosphenytoin is a prodrug of phenytoin available in parenteral forms only. While not specifically associated with cases of drug induced liver injury, fosphenytoin is converted to phenytoin which is a well known cause of acute idiosyncratic drug induced liver disease.

### Background

Fosphenytoin (fos' fen i toyn") is a hydantoin derivative that is a prodrug of phenytoin that is rapidly converted to phenytoin and is likely to have the same mechanisms of activity, efficacy and side effects as phenytoin. Phenytoin acts by stabilization of neuronal membranes through increasing the efflux and decreasing the influx of sodium ions across GABA regulated Na<sup>+</sup> channels in neuron cell membranes. Fosphenytoin was approved for use in the United States in 1996. Current indications are for the short term treatment of tonic-clonic seizures and status epilepticus, for prevention and treatment of seizures during neurosurgery and for temporary replacement of phenytoin when oral administration is not possible. Fosphenytoin is available in parenteral formulations in 2 and 10 mL vials in concentrations of 50 mg/mL generically and under the brand name Cerebyx. The recommended dose in adults is a loading dose of 10 to 20 phenytoin sodium equivalents per kilogram intravenously initially, and then a maintenance dose of 4 to 6 equivalents per kilogram each day in divided doses. Once oral therapy can be introduced, phenytoin is usually substituted. Common adverse events include pruritus, nystagmus, dizziness, somnolence, nausea and vomiting. Rare but potentially severe adverse reactions include cardiac arrhythmias, hypotension and bradycardia with rapid infusions for which reason the infusion rate should not exceed 50 phenytoin mg equivalents per minute in adults and 2 equivalents per kilogram per minute in children. Other uncommon severe adverse reactions include hypersensitivity reactions, angioedema, DRESS and Stevens Johnson syndrome.

### Hepatotoxicity

Hepatic injury has not been specifically ascribed to use of fosphenytoin, but because it is metabolized to phenytoin, it is likely to cause similar hepatic injury. Cases of typical immunoallergic hepatitis and DRESS syndrome have been reported in patients initially treated with fosphenytoin and then converted to the oral form.

Likelihood score: A (well known cause of clinically apparent liver injury).

## Mechanism of Injury

The mechanism of fosphenytoin and phenytoin hepatotoxicity is not known, but is thought to be immunoallergic.

## Outcome and Management

The course and outcome of hepatotoxicity from fosphenytoin should be similar to that of phenytoin.

References on the safety and hepatotoxicity of fosphenytoin are included in the Annotated Bibliography of Phenytoin, last updated in July 2020.

Drug Class: [Anticonvulsants](#); see also [Phenytoin](#)

## PRODUCT INFORMATION

### REPRESENTATIVE TRADE NAMES

Fosphenytoin – Generic, Cerebyx®

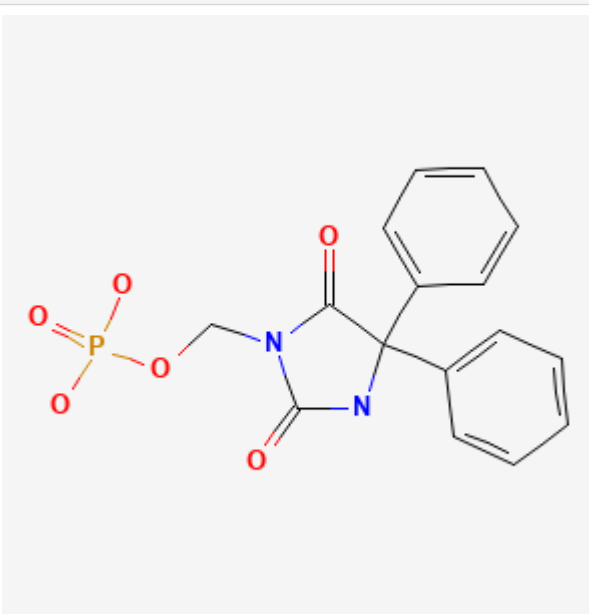
### DRUG CLASS

Anticonvulsants

### COMPLETE LABELING

Product labeling at [DailyMed](#), National Library of Medicine, NIH

## CHEMICAL FORMULA AND STRUCTURE

DRUG	CAS REGISTRY NUMBER	MOLECULAR FORMULA	STRUCTURE
Fosphenytoin	93390-81-9	C <sub>16</sub> -H <sub>15</sub> -N <sub>2</sub> -O <sub>6</sub> -P	 <p>The chemical structure of Fosphenytoin is shown. It consists of a central five-membered imidazolidinone ring. One nitrogen atom of the ring is substituted with a benzyl group (a methylene group attached to a phenyl ring). The other nitrogen atom is substituted with a (2-phenylphenyl)methyl group (a methylene group attached to a biphenyl system). A phosphate group (a phosphorus atom bonded to four oxygen atoms) is attached to the methylene group of the benzyl substituent.</p>