# SAFETY DATA SHEET



## 1. IDENTIFICATION OF THE SUBSTANCE/MIXTURE AND THE COMPANY/UNDERTAKING

**Product Identifier**

**Material Name: Cerebyx® (Fosphenytoin Sodium) Injection**

**Trade Name:** Cerebyx® , PRO-EPANUTIN; PRODILANTIN; CERENEU
**Chemical Family:** Mixture

**Relevant Identified Uses of the Substance or Mixture and Uses Advised Against**

**Intended Use:** Pharmaceutical product used as anticonvulsant

**Details of the Supplier of the Safety Data Sheet**

**Pfizer Inc**
**Pfizer Pharmaceuticals Group**
**235 East 42nd Street**
**New York, New York 10017**
**1-800-879-3477**

**Emergency telephone number:**
**CHEMTREC (24 hours): 1-800-424-9300**
**Contact E-Mail:** pfizer-MSDS@pfizer.com

**Pfizer Ltd**
**Ramsgate Road**
**Sandwich, Kent**
**CT13 9NJ**
**United Kingdom**
**+00 44 (0)1304 616161**
**Emergency telephone number:**
**International CHEMTREC (24 hours): +1-703-527-3887**

## 2. HAZARDS IDENTIFICATION

**Classification of the Substance or Mixture**

**GHS - Classification**

Reproductive Toxicity: Category 2
Carcinogenicity: Category 2

**EU Classification:**

EU Indication of danger: Carcinogenic: Category 3
Toxic to Reproduction: Category 3

EU Risk Phrases:

R40 - Limited evidence of a carcinogenic effect.
R63 - Possible risk of harm to the unborn child.

**Label Elements**

**Signal Word:** Warning
**Hazard Statements:** H361d - Suspected of damaging the unborn child
H351 - Suspected of causing cancer

**Precautionary Statements:** P202 - Do not handle until all safety precautions have been read and understood
P281 - Use personal protective equipment as required
P308 + P313 - IF exposed or concerned: Get medical attention/advice
P405 - Store locked up
P501 - Dispose of contents/container in accordance with all local and national regulations

**Other Hazards** No data available
**Australian Hazard Classification (NOHSC):** Hazardous Substance. Non-Dangerous Goods.

**Note:** This document has been prepared in accordance with standards for workplace safety, which require the inclusion of all known hazards of the product or its ingredients regardless of the potential risk. The precautionary statements and warnings included may not apply in all cases. Your needs may vary depending upon the potential for exposure in your workplace.

## 3. COMPOSITION / INFORMATION ON INGREDIENTS

**Hazardous**

| Ingredient | CAS Number | EU EINECS/ELINCS List | EU Classification | GHS Classification | % |
|---|---|---|---|---|---|
| Fosphenytoin sodium | 92134-98-0 | Not Listed | Repr.Cat.3;R63<br>Carc.Cat.3;R40 | Repr.2 (H361d)<br>Carc.2 (H351) | 5 |

| Ingredient | CAS Number | EU EINECS/ELINCS List | EU Classification | GHS Classification | % |
|---|---|---|---|---|---|
| Tromethamine | 77-86-1 | 201-064-4 | Not Listed | Not Listed | * |
| Water for injection | 7732-18-5 | 231-791-2 | Not Listed | Not Listed | * |

**Additional Information:** * Proprietary
Ingredient(s) indicated as hazardous have been assessed under standards for workplace safety.
In accordance with 29 CFR 1910.1200, the exact percentage composition of this mixture has been withheld as a trade secret.

**For the full text of the R phrases and CLP/GHS abbreviations mentioned in this Section, see Section 16**

## 4. FIRST AID MEASURES

**Description of First Aid Measures**

**Eye Contact:** Flush with water while holding eyelids open for at least 15 minutes. Seek medical attention immediately.

**Skin Contact:** Remove contaminated clothing. Flush area with large amounts of water. Use soap. Seek medical attention.

**Ingestion:** Never give anything by mouth to an unconscious person. Wash out mouth with water. Do not induce vomiting unless directed by medical personnel. Seek medical attention immediately.

**Inhalation:** Remove to fresh air and keep patient at rest. Seek medical attention immediately.

**Most Important Symptoms and Effects, Both Acute and Delayed**

**Symptoms and Effects of Exposure:** For information on potential signs and symptoms of exposure, See Section 2 - Hazards Identification and/or Section 11 - Toxicological Information.
**Medical Conditions Aggravated by Exposure:** None known

**Indication of the Immediate Medical Attention and Special Treatment Needed**
**Notes to Physician:** None

## 5. FIRE FIGHTING MEASURES

**Extinguishing Media:** Extinguish fires with CO2, extinguishing powder, foam, or water.

**Special Hazards Arising from the Substance or Mixture**
**Hazardous Combustion Products:** None known or expected.

**Fire / Explosion Hazards:** Fine particles (such as dust and mists) may fuel fires/explosions.

**Advice for Fire-Fighters**
During all fire fighting activities, wear appropriate protective equipment, including self-contained breathing apparatus.

## 6. ACCIDENTAL RELEASE MEASURES

**Personal Precautions, Protective Equipment and Emergency Procedures**
Personnel involved in clean-up should wear appropriate personal protective equipment (see Section 8). Minimize exposure.

**Environmental Precautions**
Place waste in an appropriately labeled, sealed container for disposal. Care should be taken to avoid environmental release.

**Methods and Material for Containment and Cleaning Up**
**Measures for Cleaning / Collecting:** Contain the source of spill if it is safe to do so. Collect spill with absorbent material. Clean spill area thoroughly.

**Additional Consideration for Large Spills:** Non-essential personnel should be evacuated from affected area. Report emergency situations immediately. Clean up operations should only be undertaken by trained personnel.

## 7. HANDLING AND STORAGE

**Precautions for Safe Handling**
Avoid breathing vapor or mist. Avoid contact with eyes, skin and clothing. When handling, use appropriate personal protective equipment (see Section 8). Wash hands and any exposed skin after removal of PPE. Releases to the environment should be avoided. Review and implement appropriate technical and procedural waste water and waste disposal measures to prevent occupational exposure or environmental releases. Potential points of process emissions of this material to the atmosphere should be controlled with dust collectors, HEPA filtration systems or other equivalent controls.

**Conditions for Safe Storage, Including any Incompatibilities**
**Storage Conditions:** Store as directed by product packaging.
**Specific end use(s):** Pharmaceutical drug product

## 8. EXPOSURE CONTROLS / PERSONAL PROTECTION

**Control Parameters**

**Fosphenytoin sodium**
**Pfizer OEL TWA-8 Hr:** 600µg/$m^3$

**Analytical Method:** Analytical method available for fosphenytoin sodium. Contact Pfizer Inc for further information.

## 8. EXPOSURE CONTROLS / PERSONAL PROTECTION

**Exposure Controls**

**Engineering Controls:** Engineering controls should be used as the primary means to control exposures. General room ventilation is adequate unless the process generates dust, mist or fumes. Keep airborne contamination levels below the exposure limits listed above in this section.

**Personal Protective Equipment:** Refer to applicable national standards and regulations in the selection and use of personal protective equipment (PPE).

**Hands:** Impervious gloves are recommended if skin contact with drug product is possible and for bulk processing operations.

**Eyes:** Wear safety glasses or goggles if eye contact is possible.

**Skin:** Impervious protective clothing is recommended if skin contact with drug product is possible and for bulk processing operations.

**Respiratory protection:** If the applicable Occupational Exposure Limit (OEL) is exceeded, wear an appropriate respirator with a protection factor sufficient to control exposures to below the OEL.

## 9. PHYSICAL AND CHEMICAL PROPERTIES

| | | | |
|---|---|---|---|
| **Physical State:** | Solution | **Color:** | Colorless to pale yellow |
| **Odor:** | No data available. | **Odor Threshold:** | No data available. |
| **Molecular Formula:** | Mixture | **Molecular Weight:** | Mixture |

**Solvent Solubility:** No data available
**Water Solubility:** No data available
**Solubility:** Soluble: Water
**pH:** 8.6-9.0
**Melting/Freezing Point (°C):** No data available
**Boiling Point (°C):** 100
**Partition Coefficient: (Method, pH, Endpoint, Value)**
**Tromethamine**
No data available
**Fosphenytoin sodium**
No data available
**Water for injection**
No data available
**Phenytoin**
Predicted 7.4 Log D 2.47
**Decomposition Temperature (°C):** No data available.

**Evaporation Rate (Gram/s):** No data available
**Vapor Pressure (kPa):** No data available
**Vapor Density (g/ml):** No data available
**Relative Density:** No data available
**Viscosity:** No data available

**Flammablity:**
**Autoignition Temperature (Solid) (°C):** No data available
**Flammability (Solids):** No data available
**Flash Point (Liquid) (°C):** No data available
**Upper Explosive Limits (Liquid) (% by Vol.):** No data available
**Lower Explosive Limits (Liquid) (% by Vol.):** No data available
**Polymerization:** No data available

## 10. STABILITY AND REACTIVITY

**Reactivity:** No data available
**Chemical Stability:** Stable under normal conditions of use.
**Possibility of Hazardous Reactions**
**Oxidizing Properties:** No data available
**Conditions to Avoid:** Fine particles (such as dust and mists) may fuel fires/explosions.
**Incompatible Materials:** As a precautionary measure, keep away from strong oxidizers
**Hazardous Decomposition Products:** No data available

## 11. TOXICOLOGICAL INFORMATION

**Information on Toxicological Effects**
**General Information:** Fosphenytoin sodium is a prodrug of phenytoin and is converted to phenytoin inside the body. The effects seen with fosphenytoin are similar to those of phenytoin.
**Short Term:** Antiepileptic drug: may cause nervous system effects. Accidental ingestion may cause effects similar to those seen in clinical use.
**Long Term:** Increased frequencies of major malformations, minor anomalies, growth abnormalities, mental deficiency, and malignancies have been reported among children born to women who took phenytoin during pregnancy.
**Known Clinical Effects:** The most common adverse effects observed with the clinical use of this drug were rapid eye twitching, dizziness, pruritus, numbness and tingling of the skin, headache, somnolence, and ataxia. Sensory disturbances (severe burning, itching, and/or numbness and tingling of the skin) have been reported following IV administration of fosphenytoin. Other, more serious effects seen with IV use of this drug, particularly when it is administered rapidly, are cardiovascular collapse, central nervous system depression, and/or hypotension.

**Acute Toxicity: (Species, Route, End Point, Dose)**

**Tromethamine**
Rat Oral LD50 5900 mg/kg

**Fosphenytoin sodium**
Mouse IV LD50 234 mg/kg
Rat IV LD50 363mg/kg
Rat IV (bolus) LD50 319.2mg/kg

**Phenytoin**
Mouse Oral LD50 150 mg/kg
Rat Oral LD50 1635mg/kg
Rat Intravenous LD 50 96mg/kg
Rat IM LD 50 >337mg/kg
Rabbit Oral LD 50 >3000mg/kg

**Repeated Dose Toxicity: (Duration, Species, Route, Dose, End Point, Target Organ)**

**Fosphenytoin sodium**
4 Week(s) Rat Intravenous <30 mg/kg/day NOAEL Central nervous system
13 Week(s) Rat Intramuscular 30 mg/kg/day NOAEL Liver
4 Week(s) Dog Intravenous < 15 mg/kg/day NOAEL Central Nervous System
13 Week(s) Dog Intramuscular 15 mg/kg/day NOAEL Central Nervous System, Liver

## 11. TOXICOLOGICAL INFORMATION

**Phenytoin**

| | | | | | |
|---|---|---|---|---|---|
| 2 Week(s) | Rat | Oral | <3125 ppm/day | NOEL | Bone marrow |
| 2 Week(s) | Mouse | Oral | <125 ppm/day | NOEL | Central Nervous System |
| 13 Week(s) | Rat | Oral | 300 ppm/day | NOEL | None identified |
| 13 Week(s) | Mouse | Oral | 150 ppm/day | NOEL | Blood forming organs, Gastrointestinal system, Liver |

**Reproduction & Developmental Toxicity: (Study Type, Species, Route, Dose, End Point, Effect(s))**

**Fosphenytoin sodium**

| | | | | | |
|---|---|---|---|---|---|
| Reproductive & Fertility | Rat | Intramuscular | 25 mg/kg/day | NOEL | Maternal toxicity, Developmental toxicity, Teratogenic |
| Embryo / Fetal Development | Rat | Intravenous | 50 mg/kg/day | NOEL | Maternal Toxicity |
| Embryo / Fetal Development | Rabbit | Intravenous | 50 mg/kg/day | NOEL | Maternal Toxicity |

**Phenytoin**

| | | | | | |
|---|---|---|---|---|---|
| Embryo / Fetal Development | Mouse | Oral | 75 mg/kg/day | NOEL | Maternal toxicity, Fetotoxicity, Teratogenic |
| Embryo / Fetal Development | Mouse | Oral | 45 mg/kg/day | NOEL | Teratogenic |
| Embryo / Fetal Development | Rabbit | Oral | 50 mg/kg/day | NOEL | Fetotoxicity, Teratogenic |
| Embryo / Fetal Development | Monkey | Oral | 10 mg/kg/day | NOEL | Fetotoxicity, Teratogenic |
| Embryo / Fetal Development | Mouse | Subcutaneous | <12.5 mg/kg/day | NOEL | Maternal Toxicity, Fetotoxicity, Teratogenic |

**Genetic Toxicity: (Study Type, Cell Type/Organism, Result)**

**Fosphenytoin sodium**

| | | |
|---|---|---|
| Bacterial Mutagenicity (Ames) | *Salmonella* | Negative |
| *In Vitro* Mammalian Cell Mutagenicity | Hamster Lung Cells | Negative |
| *In Vitro* Chromosome Aberration | Hamster Lung Cells | Negative |
| *In Vivo* Micronucleus Chromosome Aberration | Mouse Bone Marrow | Negative |

**Phenytoin**

| | | |
|---|---|---|
| Bacterial Mutagenicity (Ames) | *Salmonella* | Negative |
| *In Vitro* Chromosome Aberration | Chinese Hamster Ovary (CHO) cells | Negative |
| *In Vitro* Chromosome Aberration | Human Lymphocytes | Negative |
| *In Vivo* Sister Chromatid Exchange | Human Lymphocytes | Positive |
| *In Vivo* Mitotic Spindle Assay | Human Lymphocytes | Negative |

**Carcinogenicity: (Duration, Species, Route, Dose, End Point, Effect(s))**

**Phenytoin**

| | | | | | |
|---|---|---|---|---|---|
| 2 Year(s) | Male Rat | Oral, in feed | 50 mg/kg/day | NOEL | Benign neoplasms, Skin |
| 2 Year(s) | Mouse | Oral, in feed | 25 mg/kg/day | NOEL | Benign tumors, Liver |
| 2 Year(s) | Female Mouse | Oral, in feed | 60 ppm | LOAEL | Liver, neoplasms |
| 2 Year(s) | Female Rat | Oral, in feed | 240 ppm | NOAEL | Not carcinogenic |

**Carcinogen Status:** See below

**Phenytoin**

| | |
|---|---|
| **IARC:** | Group 2B (Possibly Carcinogenic to Humans) |
| **NTP:** | Reasonably Anticipated To Be A Human Carcinogen |

## 12. ECOLOGICAL INFORMATION

**Environmental Overview:** The environmental characteristics of this material have not been fully evaluated. Releases to the environment should be avoided. The information in this section includes the potential hazards of a chemically related material.

**Toxicity:**
**Aquatic Toxicity: (Species, Method, End Point, Duration, Result)**

**Phenytoin**
*Hyallela azteca* (Freshwater Amphipod) OPPTS LC50 96 Hours 18 mg/L
*Daphnia magna* (Water Flea) TAD EC50 48 Hours >39 mg/L
*Pimephales promelas* (Fathead Minnow) OPPTS LC50 96 Hours >23 mg/L

**Persistence and Degradability:** No data available

**Bio-accumulative Potential:**
**Partition Coefficient: (Method, pH, Endpoint, Value)**
**Phenytoin**
Predicted 7.4 Log D 2.47

**Mobility in Soil:** No data available

## 13. DISPOSAL CONSIDERATIONS

**Waste Treatment Methods:** Dispose of waste in accordance with all applicable laws and regulations. Member State specific and Community specific provisions must be considered. Considering the relevant known environmental and human health hazards of the material, review and implement appropriate technical and procedural waste water and waste disposal measures to prevent occupational exposure and environmental release. It is recommended that waste minimization be practiced. The best available technology should be utilized to prevent environmental releases. This may include destructive techniques for waste and wastewater.

## 14. TRANSPORT INFORMATION

**The following refers to all modes of transportation unless specified below.**

Not regulated for transport under USDOT, EUADR, IATA, or IMDG regulations.

## 15. REGULATORY INFORMATION

**Safety, Health and Environmental Regulations/Legislation Specific for the Substance or Mixture**

**Canada - WHMIS: Classifications**

## 15. REGULATORY INFORMATION

**WHMIS hazard class:**
Class D, Division 2, Subdivision A

**Fosphenytoin sodium**

| | |
|---|---|
| **CERCLA/SARA 313 Emission reporting** | Not Listed |
| **California Proposition 65** | Not Listed |
| **EU EINECS/ELINCS List** | Not Listed |

**Tromethamine**

| | |
|---|---|
| **CERCLA/SARA 313 Emission reporting** | Not Listed |
| **California Proposition 65** | Not Listed |
| **Inventory - United States TSCA - Sect. 8(b)** | Present |
| **Australia (AICS):** | Present |
| **Standard for the Uniform Scheduling for Drugs and Poisons:** | Schedule 4 |
| **EU EINECS/ELINCS List** | 201-064-4 |

**Water for injection**

| | |
|---|---|
| **CERCLA/SARA 313 Emission reporting** | Not Listed |
| **California Proposition 65** | Not Listed |
| **Inventory - United States TSCA - Sect. 8(b)** | Present |
| **Australia (AICS):** | Present |
| **REACH - Annex IV - Exemptions from the obligations of Register:** | Present |
| **EU EINECS/ELINCS List** | 231-791-2 |

## 16. OTHER INFORMATION

**Text of R phrases and GHS Classification abbreviations mentioned in Section 3**

Reproductive toxicity-Cat.2; H361d - Suspected of damaging the unborn child
Carcinogenicity-Cat.2; H351 - Suspected of causing cancer

Carcinogenic: Category 3
Toxic to Reproduction: Category 3

R40 - Limited evidence of a carcinogenic effect
R63 - Possible risk of harm to the unborn child.

**Data Sources:** Pfizer proprietary drug development information.

**Reasons for Revision:** Updated Section 1 - Identification of the Substance/Preparation and the Company/Undertaking. Updated Section 11 - Toxicology Information. Updated Section 12 - Ecological Information. Updated Section 16 - Other Information. Updated Section 2 - Hazard Identification. Updated Section 3 - Composition / Information on Ingredients. Updated Section 7 - Handling and Storage.

**Revision date:** 10-Mar-2015

Product Stewardship Hazard Communication
**Prepared by:** Pfizer Global Environment, Health, and Safety Operations

Pfizer Inc believes that the information contained in this Material Safety Data Sheet is accurate, and while it is provided in good faith, it is without warranty of any kind, expressed or implied. If data for a hazard are not included in this document there is no known information at this time.

**End of Safety Data Sheet**