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

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Emergency telephone number:
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International CHEMTREC (24 hours): +1-703-527-3887

Contact E-Mail: pfizer-MSDS@pfizer.com

2. HAZARDS IDENTIFICATION

Classification of the Substance or Mixture
GHS - Classification
Reproductive Toxicity: Category 2
Carcinogenicity: Category 2

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

An Occupational Exposure Value has been established for one or more of the ingredients (see Section 8).

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

<table>
<thead>
<tr>
<th>Hazardous</th>
<th>Ingredient</th>
<th>CAS Number</th>
<th>EU EINECS/ELINCS List</th>
<th>GHS Classification</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fosphenytoin sodium</td>
<td>92134-98-0</td>
<td>Not Listed</td>
<td>Repr.2 (H361d) Carc.2 (H351)</td>
<td>5</td>
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</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Ingredient</th>
<th>CAS Number</th>
<th>EU EINECS/ELINCS List</th>
<th>GHS Classification</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tromethamine</td>
<td>77-86-1</td>
<td>201-064-4</td>
<td>Not Listed</td>
<td>*</td>
</tr>
<tr>
<td>Water for injection</td>
<td>7732-18-5</td>
<td>231-791-2</td>
<td>Not Listed</td>
<td>*</td>
</tr>
</tbody>
</table>

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 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: None known or expected.

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

Advice for Fire-Fighters
During all firefighting 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. Cleanup 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/m³

Tromethamine
Pfizer Occupational Exposure Band (OEB): OEB 1 (control exposure to the range of 1000ug/m³ to 3000ug/m³)

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.
8. EXPOSURE CONTROLS / PERSONAL PROTECTION

Personal Protective Equipment:
Refer to applicable national standards and regulations in the selection and use of personal protective equipment (PPE). Contact your safety and health professional or safety equipment supplier for assistance in selecting the correct protective clothing/equipment based on an assessment of the workplace conditions, other chemicals used or present in the workplace and specific operational processes.

Hands: Impervious gloves (e.g. Nitrile, etc.) are recommended if skin contact with drug product is possible and for bulk processing operations. (Protective gloves must meet the standards in accordance with EN374, ASTM F1001 or international equivalent.)

Eyes: Wear safety glasses or goggles if eye contact is possible. (Eye protection must meet the standards in accordance with EN166, ANSI Z87.1 or international equivalent.)

Skin: Impervious protective clothing is recommended if skin contact with drug product is possible and for bulk processing operations. (Protective clothing must meet the standards in accordance with EN13982, ANSI 103 or international equivalent.)

Respiratory protection: Under normal conditions of use, 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 (e.g. particulate respirator with a half mask, P3 filter). (Respirators must meet the standards in accordance with EN140, EN143, ASTM F2704-10 or international equivalent.)

9. PHYSICAL AND CHEMICAL PROPERTIES

<table>
<thead>
<tr>
<th>Property</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Physical State:</td>
<td>Solution</td>
</tr>
<tr>
<td>Odor:</td>
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</tr>
<tr>
<td>Molecular Formula:</td>
<td>Mixture</td>
</tr>
<tr>
<td>Solvent Solubility:</td>
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</tr>
<tr>
<td>Water Solubility:</td>
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</tr>
<tr>
<td>Solubility:</td>
<td>Soluble: Water</td>
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<tr>
<td>pH:</td>
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<tr>
<td>Melting/Freezing Point (°C):</td>
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</tr>
<tr>
<td>Boiling Point (°C):</td>
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</tr>
<tr>
<td>Partition Coefficient: (Method, pH, Endpoint, Value)</td>
<td>Tromethamine Predicted 7.4 log D -4.668</td>
</tr>
<tr>
<td></td>
<td>Fosphenytoin sodium Predicted 7.4 log D 2.47</td>
</tr>
<tr>
<td></td>
<td>Color: Colorless to pale yellow</td>
</tr>
<tr>
<td></td>
<td>Odor Threshold: No data available.</td>
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<tr>
<td></td>
<td>Molecular Weight: Mixture</td>
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<tr>
<td>Decomposition Temperature (°C):</td>
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<tr>
<td>Evaporation Rate (Gram/s):</td>
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<td>Vapor Pressure (kPa):</td>
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<tr>
<td>Vapor Density (g/ml):</td>
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<tr>
<td>Relative Density:</td>
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</tr>
<tr>
<td>Viscosity:</td>
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<tr>
<td>Flammability:</td>
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<tr>
<td>Autoignition Temperature (Solid) (°C):</td>
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<tr>
<td>Flammability (Solids):</td>
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<td>Flash Point (Liquid) (°C):</td>
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<td>Upper Explosive Limits (Liquid) (% by Vol.):</td>
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</tr>
<tr>
<td>Lower Explosive Limits (Liquid) (% by Vol.):</td>
<td>No data available</td>
</tr>
</tbody>
</table>
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
- Rat Dermal LD50 > 5000mg/kg

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

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

Tromethamine
- Eye Irritation Rabbit Slight
- Skin Irritation Rabbit Slight

Repeated Dose Toxicity: (Duration, Species, Route, Dose, End Point, Target Organ)
### 11. TOXICOLOGICAL INFORMATION

**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

**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  \(\text{<12.5 mg/kg/day}\)  NOEL  Maternal Toxicity, Fetotoxicity, Teratogenic

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

**Tromethamine**
- Bacterial Mutagenicity (Ames)  \(E.\ coli\)  Negative

**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
11. TOXICOLOGICAL INFORMATION

Carcinogen Status: See below

Phenotin
- **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, Endpoint, Duration, Result)
  - **Tromethamine**
    - *Daphnia magna* (Water Flea) OECD EC50 48 Hours >980 mg/L
    - *Pseudokirchneriella subcapitata* (Green Alga) OECD EC50 48 Hours 473 mg/L
  - **Phenotin**
    - *Hyalella 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
  - **Tromethamine**
    - Activated sludge OECD EC50 >1000 mg/L

Persistence and Degradability: No data available

Bio-accumulative Potential:
- **Partition Coefficient:** (Method, pH, Endpoint, Value)
  - **Tromethamine**
    - Predicted 7.4 Log D -4.668
  - **Phenotin**
    - 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

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 CLP/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

Data Sources: Pfizer proprietary drug development information.
SAFETY DATA SHEET

Material Name: Cerebyx® (Fosphenytoin Sodium) Injection
Revision date: 27-Mar-2018

Reasons for Revision: Updated Section 1 - Identification of the Substance/Preparation and the Company/Undertaking. Updated Section 2 - Hazard Identification. Updated Section 8 - Exposure Controls / Personal Protection.

Revision date: 27-Mar-2018
Prepared by: Product Stewardship Hazard Communication

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