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

Product Identifier

Material Name: Estramustine Phosphate Powder for Injection

Trade Name: EMCYT; ESTRACYT

Chemical Family: Nitrogen Mustard

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

Intended Use: Pharmaceutical product used as Antineoplastic

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

Pfizer Ltd
Ramsgate Road
Sandwich, Kent
CT13 9NJ
United Kingdom
+00 44 (0)1304 616161

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

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 1B
Carcinogenicity: Category 2

US OSHA Specific - Classification

Physical Hazard: Combustible Dust

EU Classification:

EU Indication of danger: Toxic to reproduction, Category 2
Carcinogenic: Category 3

EU Risk Phrases:

R40 - Limited evidence of a carcinogenic effect
R61 - May cause harm to the unborn child.
R62 - Possible risk of impaired fertility.

Label Elements

Signal Word: Danger

Hazard Statements:

H351 - Suspected of causing cancer
H360Df - May damage the unborn child. Suspected of damaging fertility
May form combustible dust concentrations in air
Precautionary Statements:
P202 - Do not handle until all safety precautions have been read and understood
P280 - Wear protective gloves/protective clothing/eye protection/face protection
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
Australian Hazard Classification (NOHSC):

Note:
This document has been prepared in accordance with standards for workplace safety, which requires the inclusion of all known hazards of the product or its ingredients regardless of the potential risk. The precautionary statements and warning 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>Ingredient</th>
<th>CAS Number</th>
<th>EU EINECS/ELINCS List</th>
<th>EU Classification</th>
<th>GHS Classification</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Estramustine Phosphate</td>
<td>4891-15-0</td>
<td>225-512-3</td>
<td>Repr.Cat.2;R61</td>
<td>Carc. 2 (H351)</td>
<td>60</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Repr.Cat. 3:R62</td>
<td></td>
<td></td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>Cat.3:R40</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Ingredient</th>
<th>CAS Number</th>
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<th>EU Classification</th>
<th>GHS Classification</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mannitol</td>
<td>69-65-8</td>
<td>200-711-8</td>
<td>Not Listed</td>
<td>Not Listed</td>
<td>*</td>
</tr>
<tr>
<td>Meglumine</td>
<td>6284-40-8</td>
<td>228-506-9</td>
<td>Not Listed</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 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.
SAFETY DATA SHEET

Material Name: Estramustine Phosphate Powder for Injection
Revision date: 23-Mar-2015

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: Formation of toxic gases is possible during heating or fire.

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 spilled material by a method that controls dust generation. A damp cloth or a filtered vacuum should be used to clean spills of dry solids. 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
Minimize dust generation and accumulation. Avoid breathing dust. 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**
Refer to available public information for specific member state Occupational Exposure Limits.

**Estramustine Phosphate**
**Pfizer OEL TWA-8 Hr:** 2 µg/m³

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

**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:** Powder
**Color:** White
**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
**pH:** No data available
**Melting/Freezing Point (°C):** No data available
**Boiling Point (°C):** No data available
**Partition Coefficient: (Method, pH, Endpoint, Value)**
**Mannitol**
No data available
**Meclumine**
No data available
**Estramustine Phosphate Sodium**
No data available
**Estramustine Phosphate**
No data available
**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

**Flammability:**
**Autoignition Temperature (Solid) (°C):** No data available
SAFETY DATA SHEET

Material Name: Estramustine Phosphate Powder for Injection
Revision date: 23-Mar-2015

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: The information in this section describes the hazards of various forms of the active ingredient. The toxicities of the two materials can be expected to be similar. The remaining information describes the potential hazards of the individual ingredients.

Long Term: Animal studies have shown a potential to cause adverse effects on the fetus. Repeat-dose studies in animals have shown a potential to cause adverse effects on reproductive system.

Known Clinical Effects: Clinical use of estrogens has resulted in breast changes (enlargement, tenderness, and secretion), along with effects on the genitourinary (changes in vaginal bleeding), and GI systems. Effects on the skin, eyes, and CNS have also been reported.

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

- **Mannitol**
  - Rat Oral LD 50 13500 mg/kg
  - Mouse Oral LD 50 22 g/kg

- **Estramustine Phosphate Sodium**
  - Rat Oral LD50 > 2000 mg/kg
  - Rat Para-periosteal LD50 225mg/kg
  - Rat Intraperitoneal LD50 337-550mg/kg
  - Mouse Oral LD50 > 2000mg/kg
  - Mouse Intravenous LD50 440mg/kg

Acute Toxicity Comments: A greater than symbol (>) indicates that the toxicity endpoint being tested was not achievable at the highest dose used in the test.

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

- **Estramustine Phosphate Sodium**
  - 4 Week(s) Rat Intraperitoneal 40 mg/kg/day LOAEL Male reproductive system, Female reproductive system
  - 4 Week(s) Rat Oral 100 mg/kg/day LOAEL Male reproductive system, Female reproductive system
  - 6 Week(s) Rat Oral 30 mg/kg/day LOAEL Male reproductive system, Female reproductive system
  - 8 Week(s) Dog Intravenous 0.1 mg/kg/day LOAEL
  - 6 Month(s) Non-human Primate Oral 30 mg/kg/day LOAEL Male reproductive system, Female reproductive system
11. TOXICOLOGICAL INFORMATION

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

Estramustine Phosphate Sodium
Embryo / Fetal Development  Rat  Oral  2 mg/kg/day  LOAEL  Fetotoxicity

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

Estramustine Phosphate Sodium
Bacterial Mutagenicity (Ames)  Salmonella , E. coli  Negative
In Vitro Chromosome Aberration  Human Lymphocytes  Negative
In Vitro Micronucleus  Mouse Bone Marrow  Negative

Carcinogen Status:  See below

Estramustine Phosphate Sodium
IARC:  Estrogen use in post-menopausal women - Group 1
Nitrogen Mustard - Group 2A

12. ECOLOGICAL INFORMATION

Environmental Overview:  Environmental properties have not been thoroughly investigated. Releases to the environment should be avoided.

Toxicity:  No data available

Persistence and Degradability:  No data available

Bio-accumulative Potential:  No data available

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
WHMIS hazard class:
D2a  very toxic materials

Mannitol
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  200-711-8

Meglumine
CERCLA/SARA 313 Emission reporting  Not Listed
California Proposition 65  Not Listed
Inventory - United States TSCA - Sect. 8(b)  Present
Australia (AICS):  Present
EU EINECS/ELINCS List  228-506-9

Estramustine Phosphate
CERCLA/SARA 313 Emission reporting  Not Listed
California Proposition 65  Not Listed
Australia (AICS):  Present
EU EINECS/ELINCS List  225-512-3

16. OTHER INFORMATION

Text of R phrases and GHS Classification abbreviations mentioned in Section 3
Carcinogenicity-Cat.2; H351 - Suspected of causing cancer
Reproductive toxicity-Cat.1B; H360Df - May damage the unborn child. Suspected of damaging fertility
Carcinogenic: Category 3
Toxic to Reproduction: Category 2
R40 - Limited evidence of a carcinogenic effect
R61 - May cause harm to the unborn child.
R62 - Possible risk of impaired fertility.

Data Sources: Pfizer proprietary drug development information. Publicly available toxicity information.

Reasons for Revision: Updated Section 2 - Hazard Identification. Updated Section 3 - Composition / Information on Ingredients. Updated Section 11 - Toxicology Information. Updated Section 7 - Handling and Storage. Updated Section 16 - Other Information.

Revision date: 23-Mar-2015

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