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

Material Name: Estramustine Phosphate Sodium Capsules

Trade Name: EMCYT; ESTRACYT
Chemical Family: Nitrogen Mustard
Intended Use: Pharmaceutical product used as Antineoplastic

2. HAZARDS IDENTIFICATION

Appearance: White Capsules
Signal Word: DANGER

Statement of Hazard:
Suspected of causing cancer.
May damage the unborn child.
Suspected of damaging fertility.

Additional Hazard Information:
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.

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.

Australian Hazard Classification (NOHSC):
2. HAZARDS IDENTIFICATION

Note: This document has been prepared in accordance with standards for workplace safety, which require the inclusion of all known hazards of the active substance or its intermediates 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>Ingredient</th>
<th>CAS Number</th>
<th>EU EINECS/ELINCS List</th>
<th>EU Classification</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Estramustine Phosphate Sodium</td>
<td>52205-73-9</td>
<td>257-735-7</td>
<td>Repr. Cat. 2; R61</td>
<td>140mg***</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Repr. Cat. 3; R62</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Cat. 3; R40</td>
<td></td>
</tr>
<tr>
<td>Silicon dioxide, colloidal NF</td>
<td>7631-86-9</td>
<td>231-545-4</td>
<td>Not Listed</td>
<td>*</td>
</tr>
<tr>
<td></td>
<td></td>
<td>418-260-2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Talc (non-asbestiform)</td>
<td>14807-96-6</td>
<td>238-877-9</td>
<td>Not Listed</td>
<td>*</td>
</tr>
<tr>
<td>Magnesium stearate</td>
<td>557-04-0</td>
<td>209-150-3</td>
<td>Not Listed</td>
<td>*</td>
</tr>
<tr>
<td>Sodium lauryl sulfate</td>
<td>151-21-3</td>
<td>205-788-1</td>
<td>Not Listed</td>
<td>*</td>
</tr>
<tr>
<td>Hard gelatin capsules</td>
<td>MIXTURE</td>
<td>Not Listed</td>
<td>Not Listed</td>
<td>*</td>
</tr>
</tbody>
</table>

Additional Information: Ingredient(s) indicated as hazardous have been assessed under standards for workplace safety.

For the full text of the R phrases mentioned in this Section, see Section 16

4. 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.

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.

5. FIRE FIGHTING MEASURES

Extinguishing Media: Use carbon dioxide, dry chemical, or water spray.

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

Fire Fighting Procedures: During all fire fighting activities, wear appropriate protective equipment, including self-contained breathing apparatus.

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

Health and Safety Precautions: Personnel involved in clean-up should wear appropriate personal protective equipment (see Section 8). Minimize exposure.

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.

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

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

General Handling: Minimize dust generation and accumulation. If tablets or capsules are crushed and/or broken, avoid breathing dust and 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.

Storage Conditions: Store as directed by product packaging.

8. EXPOSURE CONTROLS / PERSONAL PROTECTION

Refer to available public information for specific member state Occupational Exposure Limits.

Estramustine Phosphate Sodium

Pfizer OEL TWA-8 Hr: 2 µg/m³

Silicon dioxide, colloidal NF

Australia TWA 2 mg/m³
Austria OEL - MAKs 4 mg/m³
Czech Republic OEL - TWA 0.1 mg/m³
4.0 mg/m³

Estonia OEL - TWA 2 mg/m³
Germany - TRGS 900 - TWAs 4 mg/m³
Germany (DFG) - MAK 4 mg/m³ inhalable fraction

Ireland OEL - TWAs 6 mg/m³
2.4 mg/m³

Latvia OEL - TWA 1 mg/m³

OSHA - Final PELs - Table Z-3 Mineral D: 20 mppcf
Listed

Slovakia OEL - TWA 4.0 mg/m³
Slovenia OEL - TWA 4 mg/m³

Talc (non-asbestiform)

ACGIH Threshold Limit Value (TWA) 2 µg/m³
Australia TWA 2.5 mg/m³
Austria OEL - MAKs 2 mg/m³
### 8. EXPOSURE CONTROLS / PERSONAL PROTECTION

<table>
<thead>
<tr>
<th>Country</th>
<th>OEL - TWA</th>
<th>OEL - TWAs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Belgium</td>
<td>2 mg/m³</td>
<td>10 mg/m³</td>
</tr>
<tr>
<td>Bulgaria</td>
<td>1.0 fiber/cm³</td>
<td>6.0 mg/m³</td>
</tr>
<tr>
<td>Czech Republic</td>
<td>2.0 mg/m³</td>
<td></td>
</tr>
<tr>
<td>Denmark</td>
<td>0.3 fiber/cm³</td>
<td>10 mg/m³</td>
</tr>
<tr>
<td>Finland</td>
<td>0.5 fiber/cm³</td>
<td>5 mg/m³</td>
</tr>
<tr>
<td>Greece</td>
<td>10 mg/m³</td>
<td>2 mg/m³</td>
</tr>
<tr>
<td>Hungary</td>
<td>2 mg/m³</td>
<td></td>
</tr>
<tr>
<td>Ireland</td>
<td>10 mg/m³</td>
<td>0.8 mg/m³</td>
</tr>
<tr>
<td>Lithuania</td>
<td>2 mg/m³</td>
<td>1 mg/m³</td>
</tr>
<tr>
<td>Netherlands</td>
<td>0.25 mg/m³</td>
<td></td>
</tr>
<tr>
<td>OSHA - Final PELs -</td>
<td>20 mppcf</td>
<td></td>
</tr>
<tr>
<td>Table Z-3 Mineral D:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Poland</td>
<td>4.0 mg/m³</td>
<td>1.0 mg/m³</td>
</tr>
<tr>
<td>Portugal</td>
<td>2 mg/m³</td>
<td></td>
</tr>
<tr>
<td>Romania</td>
<td>2 mg/m³</td>
<td></td>
</tr>
<tr>
<td>Slovakia</td>
<td>2 mg/m³</td>
<td>10 mg/m³</td>
</tr>
<tr>
<td>Slovenia</td>
<td>2 mg/m³</td>
<td></td>
</tr>
<tr>
<td>Spain</td>
<td>2 mg/m³</td>
<td></td>
</tr>
<tr>
<td>Sweden</td>
<td>2 mg/m³</td>
<td>1 mg/m³</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Magnesium stearate</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ACGIH Threshold</td>
<td>10 mg/m³</td>
<td></td>
</tr>
<tr>
<td>Lithuania OEL - TWA</td>
<td>5 mg/m³</td>
<td></td>
</tr>
<tr>
<td>Sweden OEL - TWAs</td>
<td>5 mg/m³</td>
<td></td>
</tr>
<tr>
<td>Sodium lauryl sulfate</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pfizer OEL TWA-8 Hr:</td>
<td>0.3 mg/m³</td>
<td></td>
</tr>
</tbody>
</table>

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

**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.

**Environmental Exposure Controls:**
Refer to specific Member State legislation for requirements under Community environmental legislation.

**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: Capsule
Molecular Formula: Mixture
Color: White
Molecular Weight: Mixture

10. STABILITY AND REACTIVITY

Chemical Stability: Stable under normal conditions of use.
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

11. TOXICOLOGICAL INFORMATION

General Information: The information included in this section describes the potential hazards of the individual ingredients.

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

Magnesium stearate
Rat Oral LD50 > 2000 mg/kg
Rat Inhalation LC50 > 2000 mg/m³

Sodium lauryl sulfate
Rat Oral LD50 1288 mg/kg

Talc (non-asbestiform)
Rat Oral LD50 > 1600 mg/kg

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

Irritation / Sensitization: (Study Type, Species, Severity)

Sodium lauryl sulfate
Eye Irritation Rabbit Moderate
Skin Irritation Rabbit Mild Moderate
Skin Sensitization - GPMT Guinea Pig Negative
Skin Sensitization - LLNA Mouse Negative

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
11. TOXICOLOGICAL INFORMATION

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

<table>
<thead>
<tr>
<th>Study Duration</th>
<th>Species</th>
<th>Route</th>
<th>Dose</th>
<th>End Point</th>
<th>Effect(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>8 Week(s)</td>
<td>Dog</td>
<td>Intravenous</td>
<td>0.1 mg/kg/day</td>
<td>LOAEL</td>
<td></td>
</tr>
<tr>
<td>6 Week(s)</td>
<td>Rat</td>
<td>Oral</td>
<td>30 mg/kg/day</td>
<td>LOAEL</td>
<td></td>
</tr>
<tr>
<td>6 Month(s)</td>
<td>Non-human Primate</td>
<td>Oral</td>
<td>30 mg/kg/day</td>
<td>LOAEL</td>
<td></td>
</tr>
</tbody>
</table>

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

- **Sodium lauryl sulfate**: Bacterial Mutagenicity (Ames): *Salmonella* Negative
- **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

- **Silicon dioxide, colloidal NF**: IARC: Group 3 (Not Classifiable)
- **Talc (non-asbestiform)**: IARC: Group 3 (Not Classifiable)
- **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.

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

- **Sodium lauryl sulfate**: *Oncorhynchus mykiss* (Rainbow Trout) LC50 96 Hours 3.6 mg/L

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

EU Symbol: T
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.

EU Safety Phrases:
S22 - Do not breathe dust.
S36/37 - Wear suitable protective clothing and gloves.
S53 - Avoid exposure - obtain special instructions before use.

OSHA Label:
DANGER
Suspected of causing cancer.
May damage the unborn child.
Suspected of damaging fertility.

Canada - WHMIS: Classifications
WHMIS hazard class:
D2a very toxic materials

Estramustine Phosphate Sodium
EU EINECS/ELINCS List 257-735-7

Silicon dioxide, colloidal NF
Inventory - United States TSCA - Sect. 8(b) Present
Australia (AICS): Present
EU EINECS/ELINCS List 231-545-4 418-260-2
15. REGULATORY INFORMATION

Talc (non-asbestiform)
- Inventory - United States TSCA - Sect. 8(b) Present
- Australia (AICS): Present
- EU EINECS/ELINCS List: 238-877-9

Magnesium stearate
- Inventory - United States TSCA - Sect. 8(b) Present
- Australia (AICS): Present
- EU EINECS/ELINCS List: 209-150-3

Sodium lauryl sulfate
- Inventory - United States TSCA - Sect. 8(b) Present
- Australia (AICS): Present
- Standard for the Uniform Scheduling for Drugs and Poisons: Schedule 6
- EU EINECS/ELINCS List: 205-788-1

16. OTHER INFORMATION

Text of R phrases mentioned in Section 3
- 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 12 - Ecological Information. Updated Section 15 - Regulatory Information.

Prepared by:
- Product Stewardship Hazard Communication
- 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