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

Material Name: Fludarabine Phosphate Injection

Trade Name: Not applicable
Chemical Family: Mixture
Intended Use: Pharmaceutical product used as Antineoplastic

2. HAZARDS IDENTIFICATION

Appearance: Liquid
Signal Word: WARNING

Statement of Hazard: Suspected of damaging fertility or the unborn child.
Suspected of causing genetic defects.

Additional Hazard Information:
- Short Term: May cause eye and skin irritation (based on components).
- Long Term: Repeat-dose studies in animals have shown a potential to cause adverse effects on male reproductive system, fetus.

Known Clinical Effects: Bone marrow suppression is the most serious adverse effect seen during clinical use. Adverse effects most commonly reported in clinical use include fever, chills, infection, nausea, vomiting, malaise, fatigue, loss of appetite (anorexia), weakness.

EU Indication of danger: Toxic to reproduction, Category 2
Mutagenic: Category 2

EU Hazard Symbols:

EU Risk Phrases:
- R46 - May cause heritable genetic damage.
- R60 - May impair fertility.
- R61 - May cause harm to the unborn child.

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>Fludarabine phosphate</td>
<td>75607-67-9</td>
<td>Not Listed</td>
<td>Mut. Cat.2;R46 Repr. Cat.2;R60-61</td>
<td>5</td>
</tr>
<tr>
<td>Sodium hydroxide</td>
<td>1310-73-2</td>
<td>215-185-5</td>
<td>C;R35</td>
<td>##</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Ingredient</th>
<th>CAS Number</th>
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<th>EU 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>*</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.

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 spill with absorbent material. 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 generating airborne mists and vapors. Avoid breathing mist or aerosols. Avoid contact with eyes, skin and clothing. When handling, use appropriate personal protective equipment (see Section 8). Wash thoroughly after handling. 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.

Fludarabine phosphate High Reproductive Hazard

Sodium hydroxide

ACGIH Ceiling Threshold Limit: 2 mg/m³
Australia PEAK 2 mg/m³
Austria OEL - MAKs 2 mg/m³
Bulgaria OEL - TWA 2.0 mg/m³
Czech Republic OEL - TWA 1 mg/m³
Estonia OEL - TWA 1 mg/m³
France OEL - TWA 2 mg/m³
Greece OEL - TWA 2 mg/m³
Hungary OEL - TWA 2 mg/m³
Japan - OELs - Ceilings 2 mg/m³
Latvia OEL - TWA 0.5 mg/m³
OSHA - Final PELS - TWAs: 2 mg/m³
Poland OEL - TWA 0.5 mg/m³
Slovakia OEL - TWA 2 mg/m³
Slovenia OEL - TWA 2 mg/m³
Sweden OEL - TWAs 1 mg/m³

Fludarabine phosphate

Pfizer Occupational Exposure Band (OEB): OEB 4 (control exposure to the range of >1ug/m³ to <10ug/m³)
8. EXPOSURE CONTROLS / PERSONAL PROTECTION

Engineering Controls: General room ventilation is adequate unless the process generates dust, mist or fumes. Engineering controls should be used as the primary means to control exposures. 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: Liquid
Molecular Formula: Mixture
Color: No data available.
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)

   Fludarabine phosphate
   Rat   Oral   LD50   > 2000 mg/kg

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

   Sodium hydroxide
   Mouse  IP   LD50  40 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 hydroxide
11. TOXICOLOGICAL INFORMATION

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

- Eye Irritation: Rabbit, Severe
- Skin Irritation: Rabbit, Severe

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

- Fludarabine phosphate
  - Dominant Lethal Assay: Mouse, Negative
  - In Vitro HGPRT Forward Gene Mutation Assay: Chinese Hamster Ovary (CHO) cells, Negative
  - In Vitro Chromosome Aberration: Chinese Hamster Ovary (CHO) cells, Positive
  - Sister Chromatid Exchange: Positive
  - In Vivo Micronucleus: Mouse, Positive

**Carcinogen Status:** None of the components of this formulation are listed as a carcinogen by IARC, NTP or OSHA. See below

12. ECOLOGICAL INFORMATION

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

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
15. REGULATORY INFORMATION

EU Indication of danger: Toxic to reproduction, Category 2
Mutagenic: Category 2

EU Risk Phrases:
R46 - May cause heritable genetic damage.
R60 - May impair fertility.
R61 - May cause harm to the unborn child.

EU Safety Phrases:
S23 - Do not breathe fumes/vapour/spray.
S36/37 - Wear suitable protective clothing and gloves.
S53 - Avoid exposure - obtain special instructions before use.

OSHA Label:
WARNING
Suspected of damaging fertility or the unborn child.
Suspected of causing genetic defects.

Canada - WHMIS: Classifications
WHMIS hazard class:
Class D, Division 2, Subdivision A

Mannitol
- 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

Sodium hydroxide
- CERCLA/SARA Hazardous Substances and their Reportable Quantities: 1000 lb, 454 kg
- Inventory - United States TSCA - Sect. 8(b): Present
- Australia (AICS): Present
- Standard for the Uniform Scheduling for Drugs and Poisons: Schedule 5, Schedule 6
- EU EINECS/ELINCS List: 215-185-5

Water for injection
- 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 mentioned in Section 3
R46 - May cause heritable genetic damage.
R60 - May impair fertility.
R61 - May cause harm to the unborn child.

Data Sources: Publicly available toxicity 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