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

Material Name: Fosfluconazole Solution for Injection

| Trade Name: | PRODIF |
| Synonyms: | 2-(2,4-Difluorophenyl)-1,3-bis(1H-1,2,4-triazol-1-yl)-2-propyl dihydrogen phosphate |
| Chemical Family: | Prodrug of fluconazole; Synthetic class of compounds known as bis-triazoles |
| Intended Use: | Pharmaceutical product used as antifungal agent |

2. HAZARDS IDENTIFICATION

Appearance: Aqueous solution
Signal Word: CAUTION

Statement of Hazard: Harmful if swallowed.
May cause harm to the unborn child.
May cause harm to breastfed babies.

Additional Hazard Information:

- **Long Term:** Rare cases of serious liver damage and allergic reactions have been reported. Repeat-dose studies in animals have shown a potential to cause adverse effects on the developing fetus.
- **Known Clinical Effects:** There have been reports of multiple congenital abnormalities in infants whose mothers were being treated for 3 or more months with high dose (400-800mg/day) fluconazole. Fluconazole is found in human breast milk at concentrations similar to plasma. Therefore, nursing mothers should limit exposure. Adverse effects reported in clinical trials include headache, paraesthesia (tingling or itching), nausea, and diarrhea.

**EU Indication of danger:** Toxic to Reproduction: Category 2
Harmful
Dangerous for the Environment

EU Hazard Symbols:

- T

EU Risk Phrases:
2. HAZARDS IDENTIFICATION

R22 - Harmful if swallowed.
R61 - May cause harm to the unborn child.
R64 - May cause harm to breastfed babies.
R52/53 - Harmful to aquatic organisms, may cause long-term adverse effects in the aquatic environment.

Australian Hazard Classification (NOHSC):

Additional Information:
For a more detailed discussion of potential health hazards and toxicity see Section 11.
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 Ingredient</th>
<th>CAS Number</th>
<th>EU EINECS/ELINCS List</th>
<th>EU Classification</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fosfluconazole</td>
<td>194798-83-9</td>
<td>Not Listed</td>
<td>Xn;R22</td>
<td>95-98</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Repr.Cat.2;R61</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>R64;R52/53</td>
<td></td>
</tr>
<tr>
<td>Sodium hydroxide</td>
<td>1310-73-2</td>
<td>215-185-5</td>
<td>C,R35</td>
<td>&lt;1</td>
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<tr>
<td>Citric acid, anhydrous</td>
<td>77-92-9</td>
<td>201-069-1</td>
<td>Not Listed</td>
<td>**</td>
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</tbody>
</table>

<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>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:
** to adjust pH
* 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 the spill if it is safe to do so. Absorb spills with non-combustible absorbent material and transfer into a labeled container for disposal.

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: Avoid breathing vapor or mist. Avoid contact with eyes, skin and clothing. When handling, use appropriate personal protective equipment (see Section 8). Wash thoroughly after handling. Refer to Section 12 - Ecological Information, for information on potential effects on the environment. 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.

Fosfluconazole
  Pfizer OEL TWA-8 Hr: 600µg/m³

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
8. EXPOSURE CONTROLS / PERSONAL PROTECTION

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: Aqueous solution
Molecular Formula: Mixture
Color: No data available.
Molecular Weight: Mixture
Solvent Solubility: Highly soluble (>100 mg/mL) in the intravenous formulation (pH 9.0)

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
Hazardous Decomposition Products: None known

11. TOXICOLOGICAL INFORMATION

General Information: Fosfluconazole is quickly and efficiently converted (hydrolyzed) in the body (and by all tested animal species) to fluconazole. The toxicities of the two materials can be expected to be similar. The remaining information describes the potential hazards of the individual ingredients.

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

<table>
<thead>
<tr>
<th>Fluconazole</th>
<th>Rat (F) Oral LD50</th>
<th>1575 mg/kg</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rat (M) Oral LD50</td>
<td>1325 mg/kg</td>
<td></td>
</tr>
</tbody>
</table>

PZ01600
11. TOXICOLOGICAL INFORMATION

Fosfluconazole

Eye Irritation: Rabbit, Minimal
Skin Irritation: Rabbit, Non-irritating
Skin Sensitization - GPMT: Guinea Pig, Negative

Sodium hydroxide

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

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

Fluconazole

3 Month(s) Rat Oral 5 mg/kg/day NOAEL Liver
6 Month(s) Dog Oral 7.5 mg/kg/day NOAEL Liver
12 Month(s) Rat Oral 10 mg/kg/day LOAEL Liver
12 Month(s) Dog Oral 2.5 mg/kg/day NOAEL Liver

Reproduction & Development Toxicity: (Duration, Species, Route, Dose, End Point, Effect(s))

Fluconazole

Reproductive & Fertility: Rat Oral 20 mg/kg/day NOAEL Negative
Embryo / Fetal Development: Rabbit Oral 20 mg/kg/day NOAEL Maternal Toxicity, Not Teratogenic
Embryo / Fetal Development: Rat Oral 5 mg/kg/day NOAEL Fetotoxicity, Maternal Toxicity
Embryo / Fetal Development: Rat Oral 80 mg/kg/day LOAEL Maternal Toxicity, Developmental toxicity

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

Fluconazole

In Vitro: Bacterial Mutagenicity (Ames): Salmonella, E. coli, Negative
In Vivo: Cytogenetics: Mouse Bone Marrow, Negative
In Vitro: Cytogenetics: Human Lymphocytes, Negative

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

Fluconazole

24 Month(s) Rat Female Oral 10 mg/kg/day NOAEL Not carcinogenic
24 Month(s) Rat Female Oral 5 mg/kg/day LOEL Benign tumors, Liver
24 Month(s) Mouse Oral 10 mg/kg/day NOEL Not carcinogenic
11. TOXICOLOGICAL INFORMATION

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

12. ECOLOGICAL INFORMATION

Environmental Overview: The environmental characteristics of this material have not been fully evaluated. The aquatic toxicity studies below were conducted with fluconazole (100.88 mg fosfluconazole is chemically equivalent to 80 mg fluconazole). In the environment, this substance is expected to remain in water or migrate through the soil to groundwater. Harmful effects to aquatic organisms could occur. Releases to the environment should be avoided.

Bioaccumulation and Toxicity: Moderate acute toxicity to aquatic organisms could occur. This material has potential to bioaccumulate and long-term adverse effects to aquatic organisms are possible.

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

Fluconazole

*Daphnia magna* (Water Flea) LC50 48 Hours 35 mg/L
*Pimephales promelas* (Fathead Minnow) LC50 > 50 mg/L
*Cyprinodon variegatus* (Sheepshead Minnow) LC50 > 50 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
Harmful
Dangerous for the Environment

EU Risk Phrases:
15. REGULATORY INFORMATION

R22 - Harmful if swallowed.
R61 - May cause harm to the unborn child.
R64 - May cause harm to breastfed babies.
R52/53 - Harmful to aquatic organisms, may cause long-term adverse effects in the aquatic environment.

EU Safety Phrases:

S36 - Wear suitable protective clothing.
S53 - Avoid exposure - obtain special instructions before use.
S57 - Use appropriate containment to avoid environmental contamination.

OSHA Label:

CAUTION
Harmful if swallowed.
May cause harm to the unborn child.
May cause harm to breastfed babies.

Canada - WHMIS: Classifications

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

Sodium hydroxide

CERCLA/SARA Hazardous Substances and their Reportable Quantities:
Inventory - United States TSCA - Sect. 8(b) Present
Australia (AICS): Present
Standard for the Uniform Scheduling for Drugs and Poisons: Schedule 5
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

Citric acid, anhydrous

Inventory - United States TSCA - Sect. 8(b) Present
Australia (AICS): Present
EU EINECS/ELINCS List 201-069-1
16. OTHER INFORMATION

Text of R phrases mentioned in Section 3

R22 - Harmful if swallowed.
R35 - Causes severe burns.
R61 - May cause harm to the unborn child.
R64 - May cause harm to breastfed babies.
R52/53 - Harmful to aquatic organisms, may cause long-term adverse effects in the aquatic environment.

Data Sources: Pfizer proprietary drug development 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