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

Product Identifier

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

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

Intended Use: Pharmaceutical product used as antifungal agent

2. HAZARDS IDENTIFICATION

Classification of the Substance or Mixture

GHS - Classification

Acute Oral Toxicity: Category 4
Reproductive Toxicity: Category 1B Effects on or via lactation
Acute aquatic toxicity: Category 3
Chronic aquatic toxicity: Category 3

EU Classification:

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

EU Risk Phrases:

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.

Label Elements

Signal Word: Danger
2. HAZARDS IDENTIFICATION

Hazard Statements:
- H302 - Harmful if swallowed
- H360D - May damage the unborn child
- H362 - May cause harm to breast-fed children
- H412 - Harmful to aquatic life with long lasting effects

Precautionary Statements:
- P201 - Obtain special instructions before use
- P202 - Do not handle until all safety precautions have been read and understood
- P260 - Do not breathe dust/fume/gas/mist/vapors/spray
- P263 - Avoid contact during pregnancy/while nursing
- P264 - Wash hands thoroughly after handling
- P270 - Do not eat, drink or smoke when using this product
- P273 - Avoid release to the environment
- P281 - Use personal protective equipment as required
- P301+ P312 - IF SWALLOWED: Call a POISON CENTRE or doctor/physician if you feel unwell
- P308 + P313 - IF exposed or concerned: Get medical attention/advice
- P330 - Rinse mouth
- 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 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.

Additional Information:
For a more detailed discussion of potential health hazards and toxicity see Section 11.

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>EU Classification</th>
<th>GHS Classification</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Fosfluconazole</td>
<td>194798-83-9</td>
<td>Not Listed</td>
<td>Xn;R22</td>
<td>Acute Tox. 4(H302)</td>
<td>95-98</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Repr.Cat.2;R61</td>
<td>Repr. 1B (H360D)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>R64</td>
<td>Lact. (H362)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>R52/53</td>
<td>Aquatic Acute 3</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>(H402)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Aquatic Chronic 3</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>(H412)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Sodium hydroxide</td>
<td>1310-73-2</td>
<td>215-185-5</td>
<td>C; R35</td>
<td>Skin Corr. 1A</td>
<td>&lt;1</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>(H314)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Citric acid, anhydrous</td>
<td>77-92-9</td>
<td>201-069-1</td>
<td>Not Listed</td>
<td>Not Listed</td>
<td>**</td>
</tr>
</tbody>
</table>

PZ01600
SAFETY DATA SHEET

Material Name: Fosfluconazole Solution for Injection
Revision date: 18-Mar-2015

### 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 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.

---

**Ingredient** | **CAS Number** | **EU EINECS/ELINCS List** | **EU Classification** | **GHS Classification** | **%**
---|---|---|---|---|---
Water for injection | 7732-18-5 | 231-791-2 | Not Listed | Not Listed | *

**Additional Information:**

**to adjust pH**

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

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.

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
- 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
- Switzerland OEL - TWAs: 2 mg/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).

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
Odor: No data available.
Molecular Formula: Mixture

Solvent Solubility: Highly soluble (>100 mg/mL) in the intravenous formulation (pH 9.0)
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)
Fluconazole
Predicted Log P 5.0
Water for injection
No data available
Fosfluconazole
No data available
Sodium hydroxide
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
Flammability (Solids): No data available
Flash Point (Liquid) (°C): No data available
Upper Explosive Limits (Liquid) (% by Vol.): No data available
Lower Explosive Limits (Liquid) (% by Vol.): No data available

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.
10. STABILITY AND REACTIVITY

Incompatible Materials: As a precautionary measure, keep away from strong oxidizers
Hazardous Decomposition Products: None known

11. TOXICOLOGICAL INFORMATION

Information on Toxicological Effects

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.

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 diarrhoea.

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

**Fluconazole**
- Rat (F) Oral LD50 1575 mg/kg
- Rat (M) Oral LD50 1325mg/kg
- Mouse Oral LD50 1410mg/kg
- Mouse (M) Oral LD50 1520mg/kg
- Dog Intravenous LD50 > 100mg/kg

**Fosfluconazole**
- Rat IV Minimum Lethal Dose > 2000 mg/kg
- Mouse IV Minimum Lethal Dose > 2000mg/kg
- Rat Dermal Minimum Lethal Dose > 2000mg/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)

**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**
11. TOXICOLOGICAL INFORMATION

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

**Fluconazole**

<table>
<thead>
<tr>
<th>Duration</th>
<th>Species</th>
<th>Route</th>
<th>Dose</th>
<th>End Point</th>
<th>Effect(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>3 Month(s)</td>
<td>Rat</td>
<td>Oral 5 mg/kg/day</td>
<td>NOAEL</td>
<td>Liver</td>
<td></td>
</tr>
<tr>
<td>6 Month(s)</td>
<td>Dog</td>
<td>Oral 7.5 mg/kg/day</td>
<td>NOAEL</td>
<td>Liver</td>
<td></td>
</tr>
<tr>
<td>12 Month(s)</td>
<td>Rat</td>
<td>Oral 10 mg/kg/day</td>
<td>LOAEL</td>
<td>Liver</td>
<td></td>
</tr>
<tr>
<td>12 Month(s)</td>
<td>Dog</td>
<td>Oral 2.5 mg/kg/day</td>
<td>NOAEL</td>
<td>Liver</td>
<td></td>
</tr>
</tbody>
</table>

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**

<table>
<thead>
<tr>
<th>Duration</th>
<th>Species</th>
<th>Route</th>
<th>Dose</th>
<th>End Point</th>
<th>Effect(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>24 Month(s)</td>
<td>Rat Female</td>
<td>Oral 10 mg/kg/day</td>
<td>NOAEL</td>
<td>Not carcinogenic</td>
<td></td>
</tr>
<tr>
<td>24 Month(s)</td>
<td>Rat Female</td>
<td>Oral 5 mg/kg/day</td>
<td>LOEL</td>
<td>Benign tumors, Liver</td>
<td></td>
</tr>
<tr>
<td>24 Month(s)</td>
<td>Mouse</td>
<td>Oral 10 mg/kg/day</td>
<td>NOEL</td>
<td>Not carcinogenic</td>
<td></td>
</tr>
</tbody>
</table>

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.

Toxicity:

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

Persistence and Degradability:  
No data available

Bio-accumulative Potential:

Partition Coefficient: (Method, pH, Endpoint, Value)
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:
Class D, Division 2, Subdivision A
Class D, Division 2, Subdivision B

Fosfluconazole
CERCLA/SARA 313 Emission reporting: Not Listed
California Proposition 65: Not Listed
EU EINECS/ELINCS List: Not Listed

Sodium hydroxide
CERCLA/SARA 313 Emission reporting: Not Listed
15. REGULATORY INFORMATION

| CERCLA/SARA Hazardous Substances and their Reportable Quantities: | 1000 lb |
| California Proposition 65 | Not Listed |
| Inventory - United States TSCA - Sect. 8(b) | Present |
| Australia (AICS): | Present |
| EU EINECS/ELINCS List | 215-185-5 |

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

Citric acid, anhydrous
- 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: 201-069-1

16. OTHER INFORMATION

Text of R phrases mentioned in Section 3

- Acute toxicity, oral-Cat.4: H302 - Harmful if swallowed
- Reproductive toxicity-Cat.1B: H360D - May damage the unborn child
- Reproductive toxicity, effects on or via lactation; H362 - May cause harm to breast-fed children
- Hazardous to the aquatic environment, acute toxicity-Cat.3; H402 - Harmful to aquatic life
- Hazardous to the aquatic environment, chronic toxicity-Cat.3; H412 - Harmful to aquatic life with long lasting effects
- Skin corrosion/irritation-Cat.1A; H314 - Causes severe skin burns and eye damage

Xn - Harmful
Toxic to Reproduction: Category 2
C - Corrosive

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.

Reasons for Revision: Updated Section 2 - Hazard Identification. Updated Section 3 - Composition / Information on Ingredients. Updated Section 7 - Handling and Storage. Updated Section 11 - Toxicology Information. Updated Section 1 - Identification of the Substance/Preparation and the Company/Undertaking.
SAFETY DATA SHEET

Material Name:  Fosfluconazole Solution for Injection
Revision date: 18-Mar-2015

Revision date: 18-Mar-2015
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