



# SAFETY DATA SHEET

Revision date: 18-Mar-2015

Version: 2.0

Page 1 of 10

## 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

### 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

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Sandwich, Kent  
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**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

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

## SAFETY DATA SHEET

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

Page 2 of 10  
Version: 2.0

### 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):**

Hazardous Substance. Non-Dangerous Goods.

**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

**Hazardous**

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

# SAFETY DATA SHEET

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

Page 3 of 10  
Version: 2.0

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

## 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 CO<sub>2</sub>, 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.

## SAFETY DATA SHEET

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

Page 4 of 10  
Version: 2.0

### 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/m<sup>3</sup>

#### Sodium hydroxide

ACGIH Ceiling Threshold Limit:	2 mg/m <sup>3</sup>
Australia PEAK	2 mg/m <sup>3</sup>
Austria OEL - MAKs	2 mg/m <sup>3</sup>
Bulgaria OEL - TWA	2.0 mg/m <sup>3</sup>
Czech Republic OEL - TWA	1 mg/m <sup>3</sup>
Estonia OEL - TWA	1 mg/m <sup>3</sup>
France OEL - TWA	2 mg/m <sup>3</sup>
Greece OEL - TWA	2 mg/m <sup>3</sup>
Hungary OEL - TWA	2 mg/m <sup>3</sup>
Japan - OELs - Ceilings	2 mg/m <sup>3</sup>
Latvia OEL - TWA	0.5 mg/m <sup>3</sup>
OSHA - Final PELs - TWAs:	2 mg/m <sup>3</sup>
Poland OEL - TWA	0.5 mg/m <sup>3</sup>
Slovakia OEL - TWA	2 mg/m <sup>3</sup>
Slovenia OEL - TWA	2 mg/m <sup>3</sup>
Sweden OEL - TWAs	1 mg/m <sup>3</sup>
Switzerland OEL - TWAs	2 mg/m <sup>3</sup>

### 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.

## SAFETY DATA SHEET

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

Page 5 of 10  
Version: 2.0

### 8. EXPOSURE CONTROLS / PERSONAL PROTECTION

<b>Personal Protective Equipment:</b>	Refer to applicable national standards and regulations in the selection and use of personal protective equipment (PPE).
<b>Hands:</b>	Impervious gloves are recommended if skin contact with drug product is possible and for bulk processing operations.
<b>Eyes:</b>	Wear safety glasses or goggles if eye contact is possible.
<b>Skin:</b>	Impervious protective clothing is recommended if skin contact with drug product is possible and for bulk processing operations.
<b>Respiratory protection:</b>	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

<b>Physical State:</b>	Aqueous solution	<b>Color:</b>	No data available.
<b>Odor:</b>	No data available.	<b>Odor Threshold:</b>	No data available.
<b>Molecular Formula:</b>	Mixture	<b>Molecular Weight:</b>	Mixture

<b>Solvent Solubility:</b>	Highly soluble (>100 mg/mL) in the intravenous formulation (pH 9.0)
<b>Water Solubility:</b>	No data available
<b>pH:</b>	No data available.
<b>Melting/Freezing Point (°C):</b>	No data available
<b>Boiling Point (°C):</b>	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.

<b>Evaporation Rate (Gram/s):</b>	No data available
<b>Vapor Pressure (kPa):</b>	No data available
<b>Vapor Density (g/ml):</b>	No data available
<b>Relative Density:</b>	No data available
<b>Viscosity:</b>	No data available

#### Flammability:

<b>Autoignition Temperature (Solid) (°C):</b>	No data available
<b>Flammability (Solids):</b>	No data available
<b>Flash Point (Liquid) (°C):</b>	No data available
<b>Upper Explosive Limits (Liquid) (% by Vol.):</b>	No data available
<b>Lower Explosive Limits (Liquid) (% by Vol.):</b>	No data available

### 10. STABILITY AND REACTIVITY

<b>Reactivity:</b>	No data available
<b>Chemical Stability:</b>	Stable under normal conditions of use.
<b>Possibility of Hazardous Reactions</b>	
<b>Oxidizing Properties:</b>	No data available
<b>Conditions to Avoid:</b>	Fine particles (such as dust and mists) may fuel fires/explosions.

## SAFETY DATA SHEET

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

Page 6 of 10  
Version: 2.0

### 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, parasthesia (tingling or itching), nausea, and diarrhea.

#### 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

## SAFETY DATA SHEET

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

Page 7 of 10  
Version: 2.0

### 11. TOXICOLOGICAL INFORMATION

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

<i>In Vitro</i> Bacterial Mutagenicity (Ames)	<i>Salmonella</i> , <i>E. coli</i>	Negative
<i>In Vivo</i> Cytogenetics	Mouse Bone Marrow	Negative
<i>In Vitro</i> 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

#### 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

<i>Daphnia magna</i> (Water Flea)	LC50	48 Hours	35 mg/L
<i>Pimephales promelas</i> (Fathead Minnow)	LC50	> 50	mg/L
<i>Cyprinodon variegatus</i> (Sheepshead Minnow)	LC50	> 50	mg/L

**Persistence and Degradability:** No data available

#### Bio-accumulative Potential:

**Partition Coefficient: (Method, pH, Endpoint, Value)**

# SAFETY DATA SHEET

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

Page 8 of 10  
Version: 2.0

## Fluconazole

Predicted Log P 5.0

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:

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



## SAFETY DATA SHEET

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

Page 9 of 10  
Version: 2.0

### 15. REGULATORY INFORMATION

CERCLA/SARA Hazardous Substances and their Reportable Quantities:	1000 lb 454 kg
California Proposition 65	Not Listed
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

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

**Page 10 of 10**  
**Version: 2.0**

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**Revision date:** 18-Mar-2015  
Product Stewardship Hazard Communication  
**Prepared by:** 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**