



# MATERIAL SAFETY DATA SHEET

Revision date: 03-Oct-2011

Version: 1.0

Page 1 of 8

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

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### 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:

Known Clinical Effects:

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. 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.

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

EU Hazard Symbols:



EU Risk Phrases:

## MATERIAL SAFETY DATA SHEET

Material Name: Fosfluconazole Solution for Injection  
Revision date: 03-Oct-2011

Page 2 of 8  
Version: 1.0

### 2. HAZARDS IDENTIFICATION

**Australian Hazard Classification (NOHSC):**

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.  
Hazardous Substance. Non-Dangerous Goods.

**Additional Information:  
Note:**

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

**Hazardous**

Ingredient	CAS Number	EU EINECS/ELINCS List	EU Classification	%
Fosfluconazole	194798-83-9	Not Listed	Xn;R22 Repr.Cat.2;R61 R64 R52/53	95-98
Sodium hydroxide	1310-73-2	215-185-5	C;R35	<1
Citric acid, anhydrous	77-92-9	201-069-1	Not Listed	**

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

**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.

## MATERIAL SAFETY DATA SHEET

Material Name: Fosfluconazole Solution for Injection  
Revision date: 03-Oct-2011

Page 3 of 8  
Version: 1.0

### 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/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>

## MATERIAL SAFETY DATA SHEET

Material Name: Fosfluconazole Solution for Injection  
Revision date: 03-Oct-2011

Page 4 of 8  
Version: 1.0

### 8. EXPOSURE CONTROLS / PERSONAL PROTECTION

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>

**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

<b>Physical State:</b>	Aqueous solution	<b>Color:</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)		

### 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)

##### Fluconazole

Rat (F)	Oral	LD50	1575 mg/kg
Rat (M)	Oral	LD50	1325 mg/kg

## MATERIAL SAFETY DATA SHEET

Material Name: Fosfluconazole Solution for Injection  
Revision date: 03-Oct-2011

Page 5 of 8  
Version: 1.0

### 11. TOXICOLOGICAL INFORMATION

Mouse Oral LD50 1410 mg/kg  
Mouse (M) Oral LD50 1520 mg/kg  
Dog Intravenous LD50 > 100 mg/kg

#### Fosfluconazole

Rat IV Minimum Lethal Dose > 2000 mg/kg  
Mouse IV Minimum Lethal Dose > 2000 mg/kg  
Rat Dermal Minimum Lethal Dose > 2000 mg/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

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

## MATERIAL SAFETY DATA SHEET

Material Name: Fosfluconazole Solution for Injection  
Revision date: 03-Oct-2011

Page 6 of 8  
Version: 1.0

### 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:**

## MATERIAL SAFETY DATA SHEET

Material Name: Fosfluconazole Solution for Injection  
Revision date: 03-Oct-2011

Page 7 of 8  
Version: 1.0

### 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:	1000 lb
Inventory - United States TSCA - Sect. 8(b)	454 kg
Australia (AICS):	Present
Standard for the Uniform Scheduling for Drugs and Poisons:	Present
EU EINECS/ELINCS List	Schedule 5
	Schedule 6
	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

## MATERIAL SAFETY DATA SHEET

Material Name: Fosfluconazole Solution for Injection  
Revision date: 03-Oct-2011

Page 8 of 8  
Version: 1.0

### 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

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**End of Safety Data Sheet**