SAFETY DATA SHEET

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

Pfizer Inc
Pfizer Pharmaceuticals Group
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1-212-573-2222

Pfizer Ltd
Ramsgate Road
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United Kingdom
+00 44 (0)1304 616161

Emergency telephone number:
CHEMTREC (24 hours): 1-800-424-9300
Contact E-Mail: pfizer-MSDS@pfizer.com

Material Name: Vfend (Voriconazole) Powder For Oral Suspension

Trade Name: Vfend®
Chemical Family: Mixture
Intended Use: Pharmaceutical product used as antifungal agent

2. HAZARDS IDENTIFICATION

Appearance: White to off-white powder
Signal Word: DANGER

Statement of Hazard:
May damage the unborn child.
Suspected of causing cancer.

Additional Hazard Information:
Short Term: Harmful if swallowed. May produce slight eye irritation. (based on components). Accidental ingestion may cause effects similar to those seen in clinical use.
Long Term: Adverse reproductive effects seen in repeat-dose animal studies are consistent with the pharmacologic action of this drug and are expected to be relevant to humans. Animal studies indicate that this material may cause adverse effects on the liver, the developing fetus.

Known Clinical Effects:
The most common adverse effects reported with clinical use of voriconazole include visual disturbances, elevations of liver function tests and skin rash. Voriconazole has been associated with photosensitivity skin reactions especially during long term therapy.

EU Classification
EU Indication of danger: Toxic to Reproduction: Category 2
Carcinogenic: Category 3

EU Hazard Symbols:

EU Risk Phrases:
R40 - Limited evidence of a carcinogenic effect.
R61 - May cause harm to the unborn child.
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 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>Ingredient</th>
<th>CAS Number</th>
<th>EU EINECS/ELINCS List</th>
<th>EU Classification</th>
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<td>Xn;R22</td>
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<td>Xn;R48/22</td>
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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: Carbon monoxide, carbon dioxide, nitrogen oxides and fluorine-containing compounds

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 spilled material by a method that controls dust generation. A damp cloth or a filtered vacuum should be used to clean spills of dry solids. 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 dust generation and accumulation. Avoid breathing dust. 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. Refer to Section 12 - Ecological Information, for information on potential effects on the environment. 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.

Voriconazole
- Pfizer OEL TWA-8 Hr: 100µg/m³

Sucrose
- ACGIH Threshold Limit Value (TWA): 10 mg/m³
- Australia TWA: 10 mg/m³
- Belgium OEL - TWA: 10 mg/m³
- Bulgaria OEL - TWA: 10.0 mg/m³
- Estonia OEL - TWA: 10 mg/m³
- France OEL - TWA: 10 mg/m³
- Ireland OEL - TWAs: 10 mg/m³
- Latvia OEL - TWA: 5 mg/m³
8. EXPOSURE CONTROLS / PERSONAL PROTECTION

Material Name: Vfend (Voriconazole) Powder For Oral Suspension

Revision date: 06-Nov-2013

Version: 2.0

<table>
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<th>Country</th>
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<tr>
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<tr>
<td>Slovakia</td>
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Silicon dioxide, colloidal NF

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<tbody>
<tr>
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Titanium dioxide

<table>
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<td>Lithuania OEL - TWA</td>
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<td>OSHA - Final PELS - TWAs:</td>
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<td>Spain OEL - TWA</td>
<td>10 mg/m³</td>
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<tr>
<td>Sweden OEL - TWAs</td>
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</tr>
</tbody>
</table>


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.
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: Powder  Color: White to off-white
Molecular Formula: Mixture  Molecular Weight: Mixture

pH: 3.5-4.5 (reconstituted)
Partition Coefficient (Measured - Log Pow/Log Kow): Log P = 1.75 (Voriconazole)

Polymerization: Will not occur

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)

Voriconazole
- Rat/Mouse Oral LD50 < 300 mg/kg
- Rat/Mouse Oral LDmin. > 100 mg/kg
- Rat IV LD50 > 100 mg/kg
- Rat Dermal LD50 > 2000 mg/kg

Titanium dioxide
- Rat Oral LD50 > 7500 mg/kg
- Rat Subcutaneous LD50 50 mg/kg

Xanthan gum
- Rat Oral LD50 > 5000 mg/kg

Sodium benzoate
11. TOXICOLOGICAL INFORMATION

**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)**

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

**Citric acid, anhydrous**
- Eye Irritation: Rabbit - Severe
- Skin Irritation: Rabbit - Mild

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

**Voriconazole**
- 1 Month(s): Rat Oral 30 mg/kg/day NOAEL Liver
- 6 Month(s): Rat Oral 3 mg/kg/day NOAEL Liver, Kidney
- 12 Month(s): Dog Oral 8 mg/kg/day NOAEL Liver
- 6 Month(s): Rat Intravenous 10 mg/kg/day NOAEL Liver
- 6 Month(s): Dog Oral 6 mg/kg/day NOAEL Liver

**Sucrose**
- 6 Month(s): Rat Oral 29.7 g/kg LD50 Liver
- 10 Day(s): Rat Oral 27370 mg/kg LOAEL Liver, Blood
- 10 Day(s): Mouse Oral 45 g/kg LOAEL Liver, Kidney, Blood, Ureter, Bladder

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

**Voriconazole**
- Reproductive & Fertility: Rat Oral 3 mg/kg/day NOAEL Fetotoxicity
- Embryo / Fetal Development: Rat Oral 10 mg/kg/day LOAEL Teratogenic

**Sodium benzoate**
- Embryo / Fetal Development: Rat Oral 44 g/kg LOEL Developmental toxicity

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

**Voriconazole**
- Bacterial Mutagenicity (Ames): Bacteria Negative
- In Vitro Human Lymphocytes: Equivocal
- In Vivo Micronucleus: Mouse Negative
11. TOXICOLOGICAL INFORMATION

Sucrose
Bacterial Mutagenicity (Ames)  Salmonella  Negative

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

Voriconazole
2 Year(s)  Rat  Oral  18 mg/kg/day  NOEL  Benign tumors, Liver
2 Year(s)  Mouse  Oral  30 mg/kg/day  NOAEL  Malignant tumors, Liver

Carcinogen Status:  See below

Silicon dioxide, colloidal NF
IARC:  Group 3 (Not Classifiable)

Titanium dioxide
IARC:  Group 2B (Possibly Carcinogenic to Humans)
OSHA:  Listed

12. ECOLOGICAL INFORMATION

Environmental Overview:  In the environment, the active ingredient in this formulation is expected to remain in water or migrate through the soil to groundwater and degrade slowly. Harmful effects to aquatic organisms could occur.

Partition Coefficient
(Measured - Log Pow/Log Kow):
Log P = 1.75 (Voriconazole)

Persistence and Degradability:  Ultimate (CO2 Evolution) -0.24% After 28 Day(s) Not readily biodegradable.

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

Voriconazole
Mysidopsis bahia (Mysid Shrimp)  NPDES  LC50  48 Hours  62 mg/L
Red Algae  IC50  73 mg/L
Skeletonema costatum (Marine Diatom)  NPDES  IC-50  48 Hours  74.7 mg/L
Green Algae  OECD  EbC50/72hr (OECD)  EC50  72 Hours  > 97 mg/L
Oncorhynchus mykiss (Rainbow Trout)  OECD  LC50  96 Hours  110 mg/L

Aquatic Toxicity Comments:  A greater than symbol (>) indicates that aquatic toxicity was not observed at the maximum dose tested.

Bacterial Inhibition: (Inoculum, Method, End Point, Result)

Voriconazole
Activated sludge OECD  EC50  3 Hours  > 810 mg/L
Polytox MIC  24 Hours  > 100 mg/L

Voriconazole
Daphnia magna (Water Flea) OECD  21 Day(s)  NOEC  > 1 mg/L
Pimephales promelas (Fathead Minnow) OECD  32 Day(s)  NOEC  1.2 mg/L
Chironomus riparius (Sediment-Dwelling Midges) OECD  28 Day(s)  NOEC  100 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
Carcinogenic: Category 3
EU Risk Phrases:
R40 - Limited evidence of a carcinogenic effect.
R61 - May cause harm to the unborn child.
EU Safety Phrases:
S22 - Do not breathe dust.
S36/37 - Wear suitable protective clothing and gloves.
S53 - Avoid exposure - obtain special instructions before use.

OSHA Label:
DANGER
May damage the unborn child.
Suspected of causing cancer.

Canada - WHMIS: Classifications
WHMIS hazard class:
Class D, Division 2, Subdivision A
### 15. REGULATORY INFORMATION

**Voriconazole**
- California Proposition 65: Not Listed
- Standard for the Uniform Scheduling for Drugs and Poisons: Schedule 4

**Sucrose**
- 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: 200-334-9

**Sodium citrate, dihydrate**
- California Proposition 65: Not Listed
- Australia (AICS): Present

**Sodium benzoate**
- California Proposition 65: Not Listed
- Inventory - United States TSCA - Sect. 8(b): Present
- Australia (AICS): Present
- EU EINECS/ELINCS List: 208-534-8

**Citric acid, anhydrous**
- California Proposition 65: Not Listed
- Inventory - United States TSCA - Sect. 8(b): Present
- Australia (AICS): Present
- EU EINECS/ELINCS List: 201-069-1

**Xanthan gum**
- California Proposition 65: Not Listed
- Inventory - United States TSCA - Sect. 8(b): Present
- Australia (AICS): Present
- EU EINECS/ELINCS List: 234-394-2

**Silicon dioxide, colloidal NF**
- California Proposition 65: Not Listed
- Inventory - United States TSCA - Sect. 8(b): Present
- Australia (AICS): Present
- EU EINECS/ELINCS List: 231-545-4

**Titanium dioxide**
- California Proposition 65: Carcinogen initial date 9/2/11 airborne, unbound particles of respirable size
- Inventory - United States TSCA - Sect. 8(b): Present
- Australia (AICS): Present
- EU EINECS/ELINCS List: 236-675-5

**Natural orange flavor**
- California Proposition 65: Not Listed
15. REGULATORY INFORMATION

16. OTHER INFORMATION

Text of R phrases mentioned in Section 3

R40 - Limited evidence of a carcinogenic effect
R61 - May cause harm to the unborn child.
R22 - Harmful if swallowed.
R48/22 - Harmful: danger of serious damage to health by prolonged exposure if swallowed.

Data Sources:
Pfizer proprietary drug development information. Safety data sheets for individual ingredients.

Reasons for Revision:
Updated Section 2 - Hazard Identification. Updated Section 3 - Composition / Information on Ingredients. Updated Section 4 - First Aid Measures. Updated Section 7 - Handling and Storage. Updated Section 8 - Exposure Controls / Personal Protection. Updated Section 10 - Stability and Reactivity. Updated Section 12 - Ecological Information. Updated Section 15 - Regulatory 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