SAFETY DATA SHEET

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

Product Identifier

Material Name: Voriconazole for IV infusion

Trade Name:
Vfend: SPIONIC; VIMERO; Voriconazole pfizer

Chemical Family:
Mixture

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

Pfizer Ltd
Ramsgate Road
Sandwich, Kent
CT13 9NJ
United Kingdom
+00 44 (0)1304 616161

Emergency telephone number:
CHEMTREC (24 hours): 1-800-424-9300
International CHEMTREC (24 hours): +1-703-527-3887

Contact E-Mail: pfizer-MSDS@pfizer.com

2. HAZARDS IDENTIFICATION

Classification of the Substance or Mixture

GHS - Classification

Skin Sensitization: Category 1
Reproductive Toxicity: Category 1B
Carcinogenicity: Category 2
Specific target organ systemic toxicity (repeated exposure): Category 2

US OSHA Specific - Classification

Physical Hazard: Combustible Dust

EU Classification:

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

EU Risk Phrases:

R40 - Limited evidence of a carcinogenic effect.
R43 - May cause sensitization by skin contact.
R61 - May cause harm to the unborn child.

Label Elements

Signal Word: Danger
2. HAZARDS IDENTIFICATION

Hazard Statements:
- H317 - May cause an allergic skin reaction
- H351 - Suspected of causing cancer
- H360D - May damage the unborn child
- H373 - May cause damage to organs through prolonged or repeated exposure
- May form combustible dust concentrations in air

Precautionary Statements:
- P202 - Do not handle until all safety precautions have been read and understood
- P260 - Do not breathe dust/fume/gas/mist/vapors/spray
- P272 - Contaminated work clothing should not be allowed out of the workplace
- P280 - Wear protective gloves/protective clothing/eye protection/face protection
- P308 + P313 - IF exposed or concerned: Get medical attention/advice
- P302+ P352 - IF ON SKIN: Wash with plenty of soap and water
- P333 + P313 - If skin irritation or rash occurs: Get medical advice/attention
- P363 - Wash contaminated clothing before reuse
- 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.

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>GHS Classification</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Voriconazole</td>
<td>137234-62-9</td>
<td>Not Listed</td>
<td>Carc. Cat.3;R40</td>
<td>Acute Tox.3 (H301)</td>
<td>5-7</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Repr. Cat.2;R61</td>
<td>Carc. 2 (H351)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Xn;R22</td>
<td>Repr. 1B (H360D)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Xn;R48/22</td>
<td>STOT RE 2 (H373)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Aquatic Acute 3</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>(H402)</td>
<td></td>
</tr>
<tr>
<td>Sulfobutylether b-cyclodextrin sodium (SBEC)</td>
<td>7585-39-9</td>
<td>231-493-2</td>
<td>Xi;43</td>
<td>Skin Sens. 1</td>
<td>*</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>(H317)</td>
<td></td>
</tr>
</tbody>
</table>

Additional Information:
* 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.
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: Use carbon dioxide, dry chemical, or water spray.

Special Hazards Arising from the Substance or Mixture
Hazardous Combustion Products: Carbon monoxide, carbon dioxide, nitrogen oxides and fluorine-containing compounds
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.

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 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.

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 generating airborne dust. 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. 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

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

Sulfobutylether b-cyclodextrin sodium (SBECD)
Pfizer OEL TWA-8 Hr: 3000µg/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.
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

<table>
<thead>
<tr>
<th>Physical State:</th>
<th>Lyophilized powder</th>
<th>Color:</th>
<th>White</th>
</tr>
</thead>
<tbody>
<tr>
<td>Odor:</td>
<td>No data available.</td>
<td>Odor Threshold:</td>
<td>No data available.</td>
</tr>
<tr>
<td>Molecular Formula:</td>
<td>Mixture</td>
<td>Molecular Weight:</td>
<td>Mixture</td>
</tr>
</tbody>
</table>

| Solvent Solubility: | No data available |
| Water Solubility:   | No data available |
| pH:                 | 5.7-7.3 (reconstituted) |
| Melting/Freezing Point (°C): | No data available |
| Boiling Point (°C):  | No data available. |

Sulfobutylether b-cyclodextrin sodium (SBECD)
No data available
9. PHYSICAL AND CHEMICAL PROPERTIES

Voriconazole

<table>
<thead>
<tr>
<th>Property</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Decomposition Temperature (°C)</td>
<td>No data available</td>
</tr>
<tr>
<td>Evaporation Rate (Gram/s)</td>
<td>No data available</td>
</tr>
<tr>
<td>Vapor Pressure (kPa)</td>
<td>No data available</td>
</tr>
<tr>
<td>Vapor Density (g/ml)</td>
<td>No data available</td>
</tr>
<tr>
<td>Relative Density</td>
<td>No data available</td>
</tr>
<tr>
<td>Viscosity</td>
<td>No data available</td>
</tr>
<tr>
<td>Flammability</td>
<td></td>
</tr>
<tr>
<td>Autoignition Temperature (Solid) (°C)</td>
<td>No data available</td>
</tr>
<tr>
<td>Flammability (Solids)</td>
<td>No data available</td>
</tr>
<tr>
<td>Flash Point (Liquid) (°C)</td>
<td>No data available</td>
</tr>
<tr>
<td>Upper Explosive Limits (Liquid) (% by Vol.)</td>
<td>No data available</td>
</tr>
<tr>
<td>Lower Explosive Limits (Liquid) (% by Vol.)</td>
<td>No data available</td>
</tr>
<tr>
<td>Polymerization</td>
<td>Will not occur</td>
</tr>
</tbody>
</table>

10. STABILITY AND REACTIVITY

<table>
<thead>
<tr>
<th>Property</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reactivity</td>
<td>No data available</td>
</tr>
<tr>
<td>Chemical Stability</td>
<td>Stable under normal conditions of use.</td>
</tr>
<tr>
<td>Possibility of Hazardous Reactions</td>
<td></td>
</tr>
<tr>
<td>Oxidizing Properties</td>
<td>No data available</td>
</tr>
<tr>
<td>Conditions to Avoid</td>
<td>Fine particles (such as dust and mists) may fuel fires/explosions.</td>
</tr>
<tr>
<td>Incompatible Materials</td>
<td>As a precautionary measure, keep away from strong oxidizers</td>
</tr>
<tr>
<td>Hazardous Decomposition Products</td>
<td>No data available</td>
</tr>
</tbody>
</table>

11. TOXICOLOGICAL INFORMATION

**Information on Toxicological Effects**

**General Information:**
The information included in this section describes the potential hazards of the individual ingredients.

**Short Term:**
May produce slight eye irritation., May be harmful if swallowed. (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.

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

**Sulfobutylether b-cyclodextrin sodium (SBECD)**
- Rat Oral LD50 > 2000 mg/kg
- Rat/Mouse IV LD50 > 2000 mg/kg

**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
**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)**

**Sulfobutylether b-cyclodextrin sodium (SBEDC)**
- Eye Irritation: Rabbit, Non-irritating
- Skin Irritation: Rabbit, Non-irritating
- Skin Sensitization: GPMT, Guinea Pig, Positive

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

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

**Sulfobutylether b-cyclodextrin sodium (SBEDC)**
- 6 Month(s) Rate Intravenous: 600 mg/kg/day NOAEL Kidney, Liver
- 1 Month(s) Rate Intravenous: 160 mg/kg/day NOAEL Kidney
- 6 Month(s) Dog Intravenous: 600 mg/kg/day NOAEL Kidney
- 1 Month(s) Dog Intravenous: 120 mg/kg/day NOAEL Kidney

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

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

**Sulfobutylether b-cyclodextrin sodium (SBEDC)**
- Fertility and Embryonic Development: Rat Intravenous: 1500 mg/kg/day NOAEL No effects at maximum dose
- Embryo / Fetal Development: Rabbit Intravenous: 1500 mg/kg/day NOAEL Not Teratogenic
- Prenatal & Postnatal Development: Rat Intravenous: 600 mg/kg/day NOAEL Maternal Toxicity

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

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

**Sulfobutylether b-cyclodextrin sodium (SBEDC)**
- Bacterial Mutagenicity (Ames) Salmonella, E. coli Negative
- In Vitro Chromosome Aberration: Human Lymphocytes Negative
- Mammalian Cell Mutagenicity: Chinese Hamster Ovary (CHO) cells HGPRT Negative
- In Vivo Micronucleus: Mouse Bone Marrow Negative

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

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

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.

Toxicity:

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

Sulfobutylether b-cyclodextrin sodium (SBEDC)

Onchorhynchus mykiss (Rainbow Trout) OECD LC50 96 Hours > 220 mg/L
Daphnia magna (Water Flea) OECD EC50 48 Hours > 96 mg/L
Green algae OECD IC50 72 Hours > 100 mg/L

Voriconazole
Mysisidopsis bahia (Mysid Shrimp) NPDES LC50 48 Hours 62 mg/L
Red Algae IC50 73 mg/L
Skeletonema costatum (Marine Diatom) NPDES IC50 48 Hours 74.7 mg/L
Green Algae OECD EbC50/72hr (OECD) EC50 72 Hours > 97 mg/L
Onchorhynchus 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 > 810 mg/L
Polytox MIC > 100 mg/L

Chronic Aquatic Toxicity: (Species, Method, Duration, Endpoint, Result, Adverse Endpoint)

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

Persistence and Degradability:

Biodegradation: (Method, Inoculum, Biodeg Study, Result, Endpoint, Duration, Classification)

Voriconazole
OECD Activated sludge Ultimate (CO2 Evolution) -0.24% After 28 Day(s) Not Ready

Bio-accumulative Potential:
SAFETY DATA SHEET

Material Name: Voriconazole for IV infusion
Revision date: 04-Apr-2015

Partition Coefficient: (Method, pH, Endpoint, Value)
Voriconazole
Measured  7  Log P  1.75

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

Voriconazole
CERCLA/SARA 313 Emission reporting  Not Listed
California Proposition 65  Not Listed
Standard for the Uniform Scheduling for Drugs and Poisons: Schedule 4
EU EINECS/ELINCS List  Not Listed
15. REGULATORY INFORMATION

Sulfobutylether b-cyclodextrin sodium (SBECD)

- 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: 231-493-2

16. OTHER INFORMATION

Text of R phrases and GHS Classification abbreviations mentioned in Section 3

Acute toxicity, oral-Cat.3; H301 - Toxic if swallowed
Carcinogenicity-Cat.2; H351 - Suspected of causing cancer
Reproductive toxicity-Cat.1B; H360D - May damage the unborn child
Specific target organ toxicity, repeated exposure-Cat.2; H373 - May cause damage to organs through prolonged or repeated exposure
Sensitization, skin-Cat.1; H317 - May cause an allergic skin reaction
Hazardous to the aquatic environment, acute toxicity-Cat.3; H402 - Harmful to aquatic life

Carcinogenic: Category 3
Toxic to Reproduction: Category 2
Xn - Harmful
Xi - Irritant

R22 - Harmful if swallowed.
R40 - Limited evidence of a carcinogenic effect
R61 - May cause harm to the unborn child.
R43 - May cause sensitization by skin contact.
R48/22 - Harmful: danger of serious damage to health by prolonged exposure if swallowed.

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 12 - Ecological Information. Updated Section 1 - Identification of the Substance/Preparation and the Company/Undertaking. Updated Section 16 - Other Information.

Revision date: 04-Apr-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