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

Material Name: Voriconazole Film Coated Tablets

<table>
<thead>
<tr>
<th>Trade Name:</th>
<th>Vfend</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chemical Family:</td>
<td>Mixture</td>
</tr>
<tr>
<td>Intended Use:</td>
<td>Pharmaceutical product used as antifungal agent</td>
</tr>
</tbody>
</table>

2. HAZARDS IDENTIFICATION

Appearance: White tablets
Signal Word: DANGER

Statement of Hazard:
Harmful if swallowed.
May damage the unborn child.
Suspected of causing cancer.
May cause damage to liver through prolonged or repeated exposure.

Additional Hazard Information:

**Short Term:**
May produce slight eye irritation. 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 Indication of danger:**
Harmful
Toxic to Reproduction: Category 2
Carcinogenic: Category 3

EU Hazard Symbols:

EU Risk Phrases:
2. HAZARDS IDENTIFICATION

R22 - Harmful if swallowed.
R40 - Limited evidence of a carcinogenic effect.
R48/22 - Harmful: danger of serious damage to health by prolonged exposure if swallowed.
R52/53 - Harmful to aquatic organisms, may cause long-term adverse effects in the aquatic environment.
R61 - May cause harm to the unborn child.

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>Ingredient</th>
<th>CAS Number</th>
<th>EU EINECS/ELINCS List</th>
<th>EU 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>33.3</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>R52/53</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Repr. Cat.2;R61</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Xn;R22</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Xn;R48/22</td>
<td></td>
</tr>
<tr>
<td>Titanium dioxide</td>
<td>13463-67-7</td>
<td>236-675-5</td>
<td>Not Listed</td>
<td></td>
</tr>
<tr>
<td>Croscarmellose sodium</td>
<td>74811-65-7</td>
<td>Not Listed</td>
<td>Not Listed</td>
<td></td>
</tr>
<tr>
<td>Magnesium stearate</td>
<td>557-04-0</td>
<td>209-150-3</td>
<td>Not Listed</td>
<td>*</td>
</tr>
<tr>
<td>Starch, pregelatinized</td>
<td>9005-25-8</td>
<td>232-679-6</td>
<td>Not Listed</td>
<td></td>
</tr>
</tbody>
</table>

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: Not applicable

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. If tablets or capsules are crushed and/or broken, avoid breathing dust and avoid contact with eyes, skin, and clothing. When handling, use appropriate personal protective equipment (see Section 8). Wash hands and any exposed skin after removal of PPE. 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.

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

Titanium dioxide
ACGIH Threshold Limit Value (TWA) 10 mg/m³ TWA
Australia TWA 10 mg/m³
Austria OEL - MAKs Listed
8. EXPOSURE CONTROLS / PERSONAL PROTECTION

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.
8. EXPOSURE CONTROLS / PERSONAL PROTECTION

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>Tablets</th>
<th>Color:</th>
<th>White</th>
</tr>
</thead>
<tbody>
<tr>
<td>Molecular Formula:</td>
<td>Mixture</td>
<td>Molecular Weight:</td>
<td>Mixture</td>
</tr>
</tbody>
</table>

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)

**Magnesium stearate**
- Rat Oral LD50 > 2000 mg/kg
- Rat Inhalation LC50 > 2000 mg/m³

**Povidone**
- Rat Oral LD50 100 g/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

**Hydroxypropyl methylcellulose**
- Rat Oral LD50 > 10,000 mg/kg

**Triacetin**
- Rat Oral LD 5 3000 mg/kg
- Mouse Oral LD 50 1100 mg/kg

**Titanium dioxide**
- Rat Oral LD50 > 7500 mg/kg
- Rat Subcutaneous LD 50 50 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.
11. TOXICOLOGICAL INFORMATION

Irritation / Sensitization: (Study Type, Species, Severity)

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)

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

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
Liver  Reproductive system

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

Voriconazole
Bacterial Mutagenicity (Ames)  Bacteria  Negative
In Vitro  Human Lymphocytes  Equivocal
In Vivo  Micronucleus  Mouse  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

Povidone
IARC: Group 3

Titanium dioxide
IARC: Group 3 (Not Classifiable)

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.

Mobility, Persistence and Degradability: The active ingredient in this formulation is water soluble and is expected to remain primarily in water and degrade slowly.
12. ECOLOGICAL INFORMATION

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

Voriconazole
Mysisopsis 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

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: Harmful
Toxic to Reproduction: Category 2
Carcinogenic: Category 3

EU Risk Phrases:
R22 - Harmful if swallowed.
R40 - Limited evidence of a carcinogenic effect.
R48/22 - Harmful: danger of serious damage to health by prolonged exposure if swallowed.
R52/53 - Harmful to aquatic organisms, may cause long-term adverse effects in the aquatic environment.
R61 - May cause harm to the unborn child.

EU Safety Phrases:
### 15. REGULATORY INFORMATION

<table>
<thead>
<tr>
<th>OSHA Label:</th>
</tr>
</thead>
<tbody>
<tr>
<td>DANGER</td>
</tr>
<tr>
<td>Harmful if swallowed.</td>
</tr>
<tr>
<td>May damage the unborn child.</td>
</tr>
<tr>
<td>Suspected of causing cancer.</td>
</tr>
<tr>
<td>May cause damage to liver through prolonged or repeated exposure.</td>
</tr>
</tbody>
</table>

**WHMIS hazard class:**
Class D, Division 2, Subdivision A

**Voriconazole**
- Standard for the Uniform Scheduling for Drugs and Poisons: Schedule 4

**Hydroxypropyl methylcellulose**
- Inventory - United States TSCA - Sect. 8(b): Listed
- Australia (AICS): Listed
- Standard for the Uniform Scheduling for Drugs and Poisons: Schedule 4

**Titanium dioxide**
- Inventory - United States TSCA - Sect. 8(b): Listed
- Australia (AICS): Listed
- EU EINECS/ELINCS List: 236-675-5

**Triacetin**
- Inventory - United States TSCA - Sect. 8(b): Listed
- Australia (AICS): Listed
- EU EINECS/ELINCS List: 203-051-9

**Water, purified**
- Inventory - United States TSCA - Sect. 8(b): Listed
- Australia (AICS): Listed
- REACH - Annex IV - Exemptions from the obligations of Register: Present
- EU EINECS/ELINCS List: 231-791-2
15. REGULATORY INFORMATION

<table>
<thead>
<tr>
<th>Material Name</th>
<th>Australia (AICS)</th>
<th>EU EINECS/ELINCS List</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lactose NF, monohydrate</td>
<td>Listed</td>
<td>209-150-3</td>
</tr>
<tr>
<td>Croscarmellose sodium</td>
<td>Listed</td>
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</tr>
<tr>
<td>Magnesium stearate</td>
<td>Listed</td>
<td></td>
</tr>
<tr>
<td>Inventory - United States TSCA - Sect. 8(b)</td>
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<tr>
<td>REACH - Annex IV - Exemptions from the obligations of Register:</td>
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<tr>
<td>EU EINECS/ELINCS List</td>
<td>232-679-6</td>
<td></td>
</tr>
</tbody>
</table>

16. OTHER INFORMATION

Text of R phrases mentioned in Section 3

R22 - Harmful if swallowed.
R40 - Limited evidence of a carcinogenic effect
R61 - May cause harm to the unborn child.
R48/22 - Harmful: danger of serious damage to health by prolonged exposure if swallowed.
R52/53 - Harmful to aquatic organisms, may cause long-term adverse effects in the aquatic environment.

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

Reasons for Revision: Updated Section 2 - Hazard Identification. 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 11 - Toxicology Information. Updated Section 12 - Ecological Information. Updated Section 13 - Disposal Considerations. Updated Section 15 - Regulatory Information.

Prepared by: Product Stewardship Hazard Communications
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