MATERIAL 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
Sandwich, Kent
CT13 9NJ
United Kingdom
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Emergency telephone number:
CHEMTREC (24 hours): 1-800-424-9300

Emergency telephone number:
ChemSafe (24 hours): +44 (0)208 762 8322

Material Name: Voriconazole for IV infusion

Trade Name: Vfend(R)
Chemical Family: Mixture
Intended Use: Pharmaceutical product used as antifungal agent

2. COMPOSITION/INFORMATION ON INGREDIENTS

Hazardous

Ingredient	CAS Number	EU EINECS List	%
Voriconazole	137234-62-9	Not listed	5.88

Ingredient	CAS Number	EU EINECS List	%
Sulfobutylether b-cyclodextrin sodium (SBECD)	7585-39-9	231-493-2	*

Additional Information: * Proprietary
Ingredient(s) indicated as hazardous have been assessed under standards for workplace safety.

3. HAZARDS IDENTIFICATION

Appearance: White lyophilized powder
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.
May cause allergic skin reaction.

Additional Hazard Information:

Short Term: May produce slight eye irritation, Active ingredient is not a skin irritant , 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: Toxic to Reproduction: Category 2
Carcinogenic: Category 3
Irritant

EU Hazard Symbols:

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.

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.

4. FIRST AID MEASURES

Eye Contact: Immediately flush eyes with water for at least 15 minutes. If irritation occurs or persists, get medical attention.

Skin Contact: Wash skin with soap and water. Remove contaminated clothing and shoes. If irritation occurs or persists, get medical attention.

Ingestion: Get medical attention immediately. Do not induce vomiting unless directed by medical personnel. Never give anything by mouth to an unconscious person.

Inhalation: Remove to fresh air. If not breathing, give artificial respiration. Get medical attention immediately.

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: Avoid generating airborne dust. Avoid contact with eyes, skin and clothing. Avoid breathing dust. Wash thoroughly after handling.

Storage Conditions: Store as directed by product packaging.

8. EXPOSURE CONTROLS / PERSONAL PROTECTION

Voriconazole
Pfizer OEL TWA-8 Hr: 0.1 mg/m³

Sulfobutylether b-cyclodextrin sodium (SBECD)
Pfizer OEL TWA-8 Hr: 3.0 mg/m³

Analytical Method: Analytical method available for Voriconazole and Sulfobutylether b-cyclodextrin sodium. Contact Pfizer Inc for further information.

Engineering Controls: Engineering controls should be used as the primary means to control exposures. Local and general ventilation should be used as necessary, when handling this material in bulk.

Personal Protective Equipment:

Hands: Rubber gloves
Eyes: Not required under normal conditions of use. Wear safety glasses or goggles if eye contact is possible.
Skin: Not required for the normal use of this product. Wear protective clothing when working with large quantities.
Respiratory protection: Not required for the normal use of this product. 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: Lyophilized powder **Color:** White
Molecular Formula: Mixture **Molecular Weight:** Mixture

pH: 5.7-7.3 (reconstituted)

10. STABILITY AND REACTIVITY

Stability: Stable at ambient temperatures
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: Thermal decomposition products include oxides of nitrogen, carbon monoxide, carbon dioxide and halogen containing gases.
Polymerization: Will not occur

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

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

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

Sulfobutylether b-cyclodextrin sodium (SBECD)
Eye Irritation Rabbit Non-irritating
Skin Irritation Rabbit Non-irritating
Skin Sensitization - GPMT Guinea Pig Positive

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

Sulfobutylether b-cyclodextrin sodium (SBECD)
6 Month(s) Rat Intravenous 600 mg/kg/day NOAEL Kidney, Liver
1 Month(s) Rat 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

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

Sulfobutylether b-cyclodextrin sodium (SBECD)
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

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

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

Sulfobutylether b-cyclodextrin sodium (SBECD)
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

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.

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

Bioaccumulation and Toxicity: Moderate acute toxicity to aquatic organisms could occur. The active ingredient in this formulation has low potential to bioaccumulate and long-term adverse effects to aquatic organisms are not expected. No toxicity to wastewater treatment microorganisms is expected. See the aquatic toxicity data for the active ingredient in the table, below.

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

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

Sulfobutylether b-cyclodextrin sodium (SBECD)
Rainbow Trout OECD LC50 96 Hours > 220 mg/L
Daphnia magna OECD EC-50 48 Hours > 96 mg/L
Green algae OECD IC50 72 Hours > 100 mg/L

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

Bacterial Inhibition: (Species, Method, End Point, Duration, Result)

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

13. DISPOSAL CONSIDERATIONS

Disposal Procedures: Dispose of waste in accordance with all applicable laws and regulations.

14. TRANSPORT INFORMATION

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
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.

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
Harmful if swallowed.
May damage the unborn child.
Suspected of causing cancer.
May cause damage to liver through prolonged or repeated exposure.
May cause allergic skin reaction.

Canada - WHMIS: Classifications

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

Voriconazole

Standard for the Uniform Scheduling for Drugs and Poisons:	Schedule 4

Sulfobutylether b-cyclodextrin sodium (SBECD)

Inventory - United States TSCA - Sect. 8(b)	Present
Australia (AICS):	Present
EU EINECS List	231-493-2

16. OTHER INFORMATION

Reasons for Revision: Updated Section 3 - Hazard Identification. Updated Section 4 - First Aid Measures. Updated Section 6 - Accidental Release 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: Toxicology and Hazard Communication
Pfizer Global Environment, Health, and Safety

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End of Safety Data Sheet