Safety Data Sheet

Voriconazole for Injection

Section 1: Chemical Product and Company Identification

Product Name: Voriconazole for Injection
Chemical Name(s): (2R,3S)-2-(2,4-difluorophenyl)-3-(5-fluoro-4 pyrimidinyl)-1-(1H-1,2,4-triazol-1-yl)-2-butanol and 2-Hydroxypropy-.beta.-cyclodextrin
Synonym: Voriconazole
CAS Number: Voriconazole: 137234-62-9; Hydroxypropyl beta cyclodextrin: 128446-35-5
RTECS #: N/F
Trade Name: VFEND®, Voriconazole
Chemical Formula: $C_{16}H_{14}F_3N_5O$ and $C_{54}H_{102}O_{39}$

Contact Information:
X-GEN Pharmaceuticals, Inc.
PO Box 445, Big Flats, NY 14814
Technical Assistance: 607-562-2700
Online Assistance: www.x-gen.us

Emergency phone number:
National Poison Control
1-800-222-1222

**For information regarding recommended uses and restrictions on usage refer to the product package insert.

Section 2: Hazard Identification

Hazard pictograms (GHS-US):

Potential Acute Health Effects: This is a medicinal product that may affect body functions. When inside vials the hazard is considered negligible. May produce slight eye irritation.

Potential Chronic Health Effects: Voriconazole may produce slight eye irritation

Carcinogenic Effects: Not available

Mutagenic Effects: Not available

Teratogenic Effects: Animal studies indicate that this material may cause adverse effects on the liver, the developing fetus.

Developmental Toxicity: Classified development toxin (possible). The substance may be toxic to the liver. Repeated or prolonged exposure to the substance can produce target organ damage.

Adverse effects: The substance is possibly harmful for the aquatic environment, due to its antibiotic properties. The most common adverse effects reported with clinical use of voriconazole include visual disturbance, elevations of liver function tests and skin rash. Voriconazole has been associated with photosensitivity skin reactions especially during long term therapy.

Section 3: Composition and Information on Ingredients

Principle Components:

Name	CAS #	Qty per unit (mg/vial)
Voriconazole	137234-62-9	200
Hydroxypropyl beta cyclodextrin	128446-35-5	3,200

Section 4: First Aid Measures

General: Remove from exposure. Remove contaminated clothing. For treatment advice, seek guidance from an occupational health physician or other licensed health-care provider familiar with workplace chemical exposure. If person is not breathing give artificial respiration. If breathing is difficult give oxygen. Persons developing serious hypersensitivity (anaphylactic) reactions must receive immediate medical attention. Obtain medical attention.

Inhalation: If inhaled remove to fresh air. If not breathing, give artificial respiration or give oxygen by trained personnel. Get immediate medical attention.

Skin contact: In case of skin contact, immediately wash skin with soap and plenty of water. Remove and wash / dispose of contaminated clothing promptly. Get medical attention if symptoms occur.

Eye contact: In case of contact with eyes, hold eyelids apart and flush eyes with plenty of water. After initial flushing, remove any contact lenses and continue flushing for at least 15 minutes. Have eyes examined and tested by medical personnel.

Ingestion: If swallowed, wash out mouth with water provided person is conscious. Never give anything by mouth to an unconscious person. Get medical attention. DO NOT induce vomiting unless directed to do so by medical personnel.

Notes to physician: See product package insert for complete information.

Medical Attention: Seek emergency medical attention if you think you have used too much of this medicine.

Section 5: Fire Fighting Measures

Flammability of the product: No applicable information found.

Combustion Products: Carbon monoxide, carbon dioxide, nitrogen oxide and fluorine-containing compounds also emits toxic fumes under fire conditions.

Unusual Fire and Explosion Hazards: No applicable information found. Fine particles (such as dust and mist) may fuel fires/explosions.

Extinguishing Media and instruction: Use water spray, DRY chemical powder or appropriate foam, carbon dioxide.

Protective equipment & precautions for firefighters: As in any fire, evacuate personnel to a safe area. Firefighters should wear self-contained breathing apparatus pressure-demand, MSHA/NIOSH (approved or equivalent) and full protective gear to prevent contact with eye and skin.

Special remarks on fire hazard: No applicable information found.

Special remarks on explosion hazard: No applicable information found.

Section 6: Accidental Release Measures

Release to land:
Land spill: Vacuum material with appropriate dust collection in place. If a vacuum is not available, lightly mist material and remove by sweeping or wet wiping. Wear appropriate equipment including eye protection, to avoid exposure. Ventilate area and wash spill site after pick-up complete.

Small Spill: Contain the source of spill when it is safe to do so. Use appropriate tools to put the spilled solid in a convenient waste disposal container, taking care NOT to generate dust. Finish cleaning by using a filtered vacuum to clean dry solids and use a damp cloth on the contaminated surface to clean spill area thoroughly. Place waste in appropriately labeled, sealed container for disposal in accordance with local, state, and federal regulations.

Large Spill: Non-Essential personnel should be evacuated from the affected area. Vacuum material with appropriate dust collection in place. If a vacuum is not available, lightly mist material and remove by sweeping or wet wiping. Wear appropriate equipment including eye protection, to avoid exposure. For proper waste disposal, see section 13 of the SDS.

Release to air: Avoid raising and breathing dust. If dust is generated, wear a disposable dust respirator (N95), and reduce exposures by ventilating area. Clean up spill immediately.

Release to Water: Do not empty into drains. If the spill could potentially enter any waterway, including intermittent dry creeks, contact the local authorities.
In the USA, contact: **USA Coast Guard National Response Center** 1-800-424-8802.
In case of accident or spill, notify: **National Poison Control** 1-800-222-1222
Refer to local water authority; drain disposal is not recommended.

Protective equipment: Reference section 8 for Personal Protection, and section 13 for proper disposal information.

Section 7: Handling and Storage

Handling: As a general rule, when handling Voriconazole for Injection, wash thoroughly after handling. Wash hands before eating. Use with adequate ventilation. Avoid breath dust, vapor, mist or gas. Avoid contact with skin, eyes. Avoid ingestion and inhalation. Avoid prolonged or repeated exposure. When handling, use appropriate personal protective equipment (See section 8).

Storage: Keep container tightly closed. Keep container in a cool, dry, well ventilated area. Protect from light and store at controlled room temperature 20° - 25°C (68° - 77°F). Refer to product packaging.

Incompatibilities: Keep away from strong oxidizing agents.

Section 8: Exposure Controls / Personal Protection

Engineering Controls: Use process enclosure, local exhaust ventilation, or other engineering controls to keep airborne levels below recommended exposure limits. If user operation generates dust, fume or mist, use ventilation to keep exposure to airborne contaminants below the exposure limit. When inside vials the hazard is considered negligible. If opened for some purpose, then follow below advices.

Personal Protection: Safety glasses. Lab coat. Chemical-resistant gloves. Dust respirator. Be sure to use an approved/ certified respirator or equivalent. Wear safety glasses or goggles if eye contact is possible. Full suit. Dust respirator. Boots. Gloves. A self-contained breathing apparatus should be used to avoid inhalation of the product. Suggested protective clothing might not be sufficient; consult a specialist BEFORE handling this product.

Respiratory Protection: Under normal use, respirators are not required. Use NIOH/MSHA approved respirator if exposure limits are exceeded or when dust generated. Personnel wearing respirators should be fit tested and approved for respirator use, under OSHA Respiratory Protection Standard 29 CFR 1910.134.

Exposure limit: This product is not specifically listed by OSHA as hazardous. However, this material may cause sensitization or an allergic response with minimal exposure. Under conditions of overexposure, the material may be hazardous.

Section 9: Physical and Chemical Properties

Physical appearance: A lyophilized powder or cake
Color: White to off white
Molecular Weight: Not available
Taste: Not available
Odor: Not available
Odor Threshold: Not Established
pH: 4.5-8.0

Melting Point: Not Established
Freezing Point: Not Established
Boiling Point: Not Established
Flash Point: Not Established
Evaporation rate: Not Established
Flammability: Not Established
Upper Flammable Limit: Not Established
Lower Flammable Limit: Not Established

Vapor Pressure: Not Established
Vapor Density: Not Established
Relative density: Not Established
Partition Coefficient: Not Established
Auto-Ignition Temperature: Not Established

Decomposition Temperature: Not Established
Viscosity: Not Established
Dispersion Properties: Not Established
Solubility: Not Established

Section 10: Stability and Reactivity

Reactivity: No applicable information found.

Chemical stability: Stable at normal temperatures and pressures.

Possibility of hazardous reaction: No applicable information found.

Conditions to avoid: Moisture, heat.

Incompatible materials: Acids, strong oxidizer.

Hazardous decomposition products: CO_x, NO_x and emits toxic fumes under fire conditions.

Corrosion: No Data Available.

Polymerization: Not known to occur.

Section 11: Toxicological Information

Routes of exposure: Absorbed through skin, eye contact, inhalation and ingestion.

Symptoms:
Short term: May produce slight eye irritation/ May be harmful if swallowed. 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 and developing fetus.

Reproductive toxicity: If this drug is used during pregnancy, or if the patient becomes pregnant while taking this drug, the patient should be apprised of the potential risk to the fetus. Women of childbearing potential should use effective contraception during therapy.

FDA Pregnancy Category: D

Toxicity to animals:
Oral Rat/Mouse: LD50: 300 mg/kg
Oral Rat/Mouse: LDmin: 100mg/kg

Rat IV: LD50: 100 mg/kg
Rat Dermal: LD50: 2000mg/kg

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

1 Month(s) Rat: Oral30 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

Reproductive & Fertility Rat: Oral3 mg/kg/day NOAEL Fetotoxicity
Embryo/Fetal Development Rat: Oral 10 mg/kg/day LOAEL Teratogenic

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

2 Year(s) Rat: Oral 19 mg/kg/day NOEL Benign tumors, Liver
2 Year(s) Mouse: Oral 30 mg/kg/day NOAEL Malignant tumor, Liver

Measures of toxicity: Not available

Additional reproductive health and toxicity data is available from the National Institute for Occupational Safety and Health (NIOSH) and/or Registry of Toxic Effects of Chemical Substance (RTECS).

Section 12: Ecological Information

Ecotoxicity: No applicable information found

Bioaccumulation potential: No applicable information found

Products of biodegradation: No applicable information found

Toxicity of the products of biodegradation: No applicable information found

Section 13: Disposal Information

Waste classification: Non-Hazardous (This product is not specifically listed by OSHA as hazardous. However, this material may cause sensitization or an allergic response with minimal exposure. Under conditions of overexposure, the material may be hazardous.)
Waste from residues/unused products: Dissolve or mix material with a suitable combustible solvent and incinerate in a chemical incinerator equipped with an afterburner and scrubber. Material should be

disposed of in accordance with all local and national legislation. Packaging should be disposed of in line with all local and national legislation. Handle contaminated vials as product.
Waste Disposal: Disposal includes medicine, empty vials. Dispose of waste in accordance with all applicable federal, state and local laws.

Section 14: Transport Information

DOT Classification: Not a DOT controlled material (United States)

USA DOT **Proper Shipping Name:** Not regulated
CANADA **Proper Shipping Name:** Not regulated.
AIR (ICAO/IATA) **Proper Shipping Name:** Not regulated.
VESSEL (IMO/IMDG) **Proper Shipping Name:** Not regulated.
EUROPEAN Transportation: **ADR/RID Hazard Classification:** Not regulated.
U.S. Customs Harmonization Number: Not regulated.

UN Number: Not regulated
UN Shipping name: Not relevant
Transport hazard class: Not relevant
Packing Group: Not relevant
Environmental hazard: None
Transport in bulk: Not relevant
Special precautions needed with transport: None

Section 15: Regulatory Information

EUROPEAN COMMUNITY

Council Directive 94/33/EC of 22 June 1994 on the protection of young people at work: Must not be used by persons under 18 years of age.

Council Directive 92/85/EEC of 19 October 1992 on the introduction of measures to encourage improvements in the safety and health at work of pregnant workers and workers who have recently given birth or are breastfeeding: Not regulated. However, it is recommended, that the employer assess the working conditions and, if there is any risk to the safety or health and any effects on the pregnancy or breastfeeding of workers, take the necessary measures to adjust the working conditions.

Implementation of directive 2001/82/EC of the European Parliament and of the council of 6 November 2001 in the Community code relating to veterinary medical products: Denmark: The Danish Medicines Agency must be notified that this substance is produced, imported, exported, stored, sold, delivered, packed, possessed or in other ways handled in Denmark. For other countries: Please contact national authorities regarding notification of the substance.

Federal and State Regulations:
UNITED STATES FEDERAL REGULATIONS

Superfund Amendments and Reauthorization Act (SARA) Title III 311/312 hazard categories:

Fire: No **Pressure generating:** No **Reactivity:** No **Acute:** Yes **Chronic:** No

313 Reportable Ingredients: Not listed.
Title III notes:
Comprehensive Response, Compensation, and Liability Act (CERCLA) CERCLA RQ: Not listed **Toxic Substances Control Act (TSCA) TSCA Regulatory:** Not listed.
National Response Center: US Coast Guard National Center Response Telephone number is 800-424-8802.

UNITED STATES STATE REGULATIONS

California Proposition 65: Not listed.

CANADA

Workplace Hazardous Material Information System (WHMIS) hazard symbol and classification WHMIS Controlled: Not regulated.
Canadian Environmental Protection Act: Not listed.

CHEMICAL SAFETY ASSESSMENT: No CSR.

HMIS (U.S.A.):
Health Hazard: ND
Fire Hazard: ND
Reactivity: ND
Personal Protection: ND

National Fire Protection Association (U.S.A.):
Health: ND
Flammability: ND
Reactivity: ND

Protective Equipment: Gloves. Lab coat. Safety glasses. Dust Respirator. Be sure to use an approved/certified respirator or equivalent.

Section 16: Other Information

References: Not available
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Prepared & Approved by: X-GEN Pharmaceuticals, Inc. Quality Department & Safety Committee

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