

SECTION 1: IDENTIFICATION

1.1. Product Identifier

Dosage Form: Capsule

Product Name: CRESEMBA® (Isavuconazonium Sulfate) Capsules

1.2. Intended Use of the Product

Use of the substance/mixture: Pharmaceutical research, manufacture of clinical drug product, and clinical use.

1.3. Name, Address, and Telephone of the Responsible Party

Company

Astellas US LLC

1 Astellas Way

Northbrook, IL 60062

Tel.: 800-888-7704

www.us.astellas.com

1.4. Emergency Telephone Number

Emergency Number : 800-727-7003 Medical Communications

SECTION 2: HAZARDS IDENTIFICATION

This product is a drug, as defined by the US Food, Drug, and Cosmetic Act (21 U.S.C. 301 et seq.) It is in solid, final form for direct administration to the patient. Therefore, is it exempt from the US 2012 Hazard Communication Standard, as defined in the 29 CFR 1910.1200(b)(5)(iii).

SECTION 3: COMPOSITION/INFORMATION ON INGREDIENTS

This product is a drug, as defined by the US Food, Drug, and Cosmetic Act (21 U.S.C. 301 et seq.) It is in solid, final form for direct administration to the patient. Therefore, is it exempt from the US 2012 Hazard Communication Standard, as defined in the 29 CFR 1910.1200(b)(5)(iii).

SECTION 4: FIRST AID MEASURES

4.1. Description of First Aid Measures

First-aid Measures General: Never give anything by mouth to an unconscious person. If you feel unwell, seek medical advice (show the label if possible).

First-aid Measures After Inhalation: Remove to fresh air and keep at rest in a position comfortable for breathing. Obtain medical attention if breathing difficulty persists.

First-aid Measures After Skin Contact: Rinse immediately with plenty of water. Obtain medical attention if irritation develops or persists.

First-aid Measures After Eye Contact: Rinse cautiously with water for at least 15 minutes. Remove contact lenses, if present and easy to do. Continue rinsing. Obtain medical attention.

First-aid Measures After Ingestion: Do not induce vomiting. Rinse mouth. Immediately call a POISON CENTER or doctor/physician.

4.2. Most important symptoms and effects, both acute and delayed

Symptoms/Injuries: Harmful if swallowed. Suspected of damaging the unborn child. Causes damage to organs (liver, adrenals, thyroid) through prolonged or repeated exposure.

Symptoms/Injuries After Inhalation: Exposure to capsule contents: May cause respiratory irritation.

Symptoms/Injuries After Skin Contact: Exposure to capsule contents: May cause skin irritation.

Symptoms/Injuries After Eye Contact: Exposure to capsule contents: May cause eye irritation.

Symptoms/Injuries After Ingestion: Harmful if swallowed.

Chronic Symptoms: Suspected of damaging the unborn child. Prolonged or repeated exposure may cause damage to the liver, thyroid, and adrenals.

4.3. Indication of Any Immediate Medical Attention and Special Treatment Needed

If you feel unwell, seek medical advice (show the label where possible).

SECTION 5: FIRE-FIGHTING MEASURES

5.1. Extinguishing Media

Suitable Extinguishing Media: Water spray, fog, carbon dioxide (CO₂), alcohol-resistant foam, or dry chemical.

Unsuitable Extinguishing Media: Do not use a heavy water stream. Use of heavy stream of water may spread fire.

5.2. Special Hazards Arising From the Substance or Mixture

Fire Hazard: Not considered flammable but may burn at high temperatures.

Explosion Hazard: Product is not explosive.

Reactivity: Hazardous reactions will not occur under normal conditions.

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5.3. Advice for Firefighters

Precautionary Measures Fire: Exercise caution when fighting any chemical fire.

Firefighting Instructions: Use water spray or fog for cooling exposed containers. Do not allow run-off from fire fighting to enter drains or water courses.

Protection During Firefighting: Do not enter fire area without proper protective equipment, including respiratory protection.

Other Information: Refer to Section 9 for flammability properties.

SECTION 6: ACCIDENTAL RELEASE MEASURES

6.1. Personal Precautions, Protective Equipment and Emergency Procedures

General Measures: Avoid all contact with skin, eyes, or clothing. Avoid breathing (dust).

6.1.1. For Non-emergency Personnel

Protective Equipment: Use appropriate personal protection equipment (PPE).

Emergency Procedures: Evacuate unnecessary personnel.

6.1.2. For Emergency Responders

Protective Equipment: Equip cleanup crew with proper protection.

Emergency Procedures: Ventilate area.

6.2. Environmental Precautions

Prevent entry to sewers and public waters. Notify authorities if product enters sewers or public waters.

6.3. Methods and Material for Containment and Cleaning Up

For Containment: Contain any spills with dikes or absorbents to prevent migration and entry into sewers or streams.

Methods for Cleaning Up: Clear up spills immediately and dispose of waste safely. Sweep spilled substance into containers; if appropriate, moisten first to prevent dusting. Contact competent authorities after a spill.

6.4. Reference to Other Sections

See Heading 8. Exposure controls and personal protection.

SECTION 7: HANDLING AND STORAGE

7.1. Precautions for Safe Handling

Hygiene Measures: Handle in accordance with good industrial hygiene and safety procedures. Wash hands and other exposed areas with mild soap and water before eating, drinking or smoking and when leaving work.

7.2. Conditions for Safe Storage, Including Any Incompatibilities

Technical Measures: Comply with applicable regulations.

Storage Conditions: Store in a dry, cool and well-ventilated place. Keep container closed when not in use. Keep/Store away from ignition sources, direct sunlight, extremely high or low temperatures and incompatible materials.

Incompatible Products: Strong oxidizers.

7.3. Specific End Use(s)

Pharmaceutical research, manufacture of clinical drug product, and clinical use of drug product.

SECTION 8: EXPOSURE CONTROLS/PERSONAL PROTECTION

8.1. Control Parameters

For substances listed in section 3 that are not listed here, there are no established exposure limits from the manufacturer, supplier, importer, or the appropriate advisory agency including: ACGIH (TLV), NIOSH (REL), or OSHA (PEL).

8.2. Exposure Controls

Appropriate Engineering Controls

: Ensure adequate ventilation, especially in confined areas. Emergency eye wash fountains and safety showers should be available in the immediate vicinity of any potential exposure. Ensure all national/local regulations are observed.

Personal Protective Equipment

: Protective goggles. Gloves. Protective clothing.



Materials for Protective Clothing

: Chemically resistant materials and fabrics.

Hand Protection

: Wear chemically resistant protective gloves.

Eye Protection

: Chemical goggles or safety glasses.

Skin and Body Protection

: Wear suitable protective clothing. Air hood, lab coat, apron, boots or other impermeable clothing may be worn when handling large amounts.

Respiratory Protection

: None required under normal product handling conditions.

Environmental Exposure Controls

: Do not allow the product to be released into the environment.

Consumer Exposure Controls

: Do not eat, drink or smoke during use.

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SECTION 9: PHYSICAL AND CHEMICAL PROPERTIES

9.1. Information on Basic Physical and Chemical Properties

Physical State	: Capsule
Appearance	: Swedish orange (reddish-brown color) body marked with the Astellas logo in black ink, white cap overprinted with "766" in black ink, (opaque)
Odor	: Odorless
Odor Threshold	: No data available
pH	: 1.9 - 2.6 (based on drug substance)
Evaporation Rate	: No data available
Melting Point	: No data available
Freezing Point	: No data available
Boiling Point	: No data available
Flash Point	: No data available
Auto-ignition Temperature	: No data available
Decomposition Temperature	: No data available
Flammability (solid, gas)	: No data available
Vapor Pressure	: No data available
Relative Vapor Density at 20 °C	: No data available
Relative Density	: No data available
Solubility	: In water: > 1 g/mL
Partition Coefficient: N-Octanol/Water	: No data available
Viscosity	: No data available
Molecular Weight	: 814.84 g/mol (Isavuconazonium sulfate)

9.2. Other Information

No additional information available

SECTION 10: STABILITY AND REACTIVITY

- 10.1. Reactivity:** Hazardous reactions will not occur under normal conditions.
- 10.2. Chemical Stability:** Stable under recommended handling and storage conditions (see section 7).
- 10.3. Possibility of Hazardous Reactions:** Hazardous polymerization will not occur.
- 10.4. Conditions to Avoid:** Direct sunlight. Extremely high or low temperatures. Ignition sources. Incompatible materials.
- 10.5. Incompatible Materials:** Strong oxidizers.
- 10.6. Hazardous Decomposition Products:** Carbon oxides (CO, CO₂). Nitrogen oxides. Sulfur oxides. Hydrogen fluoride.

SECTION 11: TOXICOLOGICAL INFORMATION

11.1. Information On Toxicological Effects

Acute Toxicity: Not classified

Isavuconazonium Sulfate Capsules	
LD50 Oral Rat	708 - 1024 mg/kg

Skin Corrosion/Irritation: Not classified. Capsule content is a slight irritant at high concentrations, no irritation at ≤ 1 mg/mL. (pH: 1.9 - 2.6)

Serious Eye Damage/Irritation: Not classified. Capsule content is a slight irritant at high concentrations, no irritation at ≤ 1 mg/mL. (pH: 1.9 - 2.6)

Respiratory or Skin Sensitization: Not classified

Germ Cell Mutagenicity: Not classified

Isavuconazonium sulfate (946075-13-4)	
Ames test	Negative
ML/TK	Borderline positive at cytotoxic concentrations
MNT in vivo	Negative
Assessment	Not mutagenic

Carcinogenicity: Not classified. Isavuconazonium sulfate is not listed by NTP, OSHA, or IARC as a carcinogen.

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Reproductive Toxicity: Suspected of damaging the unborn child. Based on animal data, isavuconazonium is predicted to have the potential teratogenic risk. Skeletal anomalies consistent with azole anti-fungal agents were reported in both rats and rabbits at systemic exposures below that observed for the clinical maintenance dose of 200 mg/day.

Specific Target Organ Toxicity (Single Exposure): Not classified

Specific Target Organ Toxicity (Repeated Exposure): Causes damage to organs (liver, adrenals, thyroid) through prolonged or repeated exposure.

Isavuconazonium sulfate (946075-13-4)	
Liver	Increased liver weight, hypertrophy
Adrenals	Increased adrenal weight, cortical hypertrophy
Thyroid	Increased thyroid weight, increased activity

Aspiration Hazard: Not classified

Symptoms/Injuries After Inhalation: Exposure to capsule contents: May cause respiratory irritation.

Symptoms/Injuries After Skin Contact: Exposure to capsule contents: May cause skin irritation.

Symptoms/Injuries After Eye Contact: Exposure to capsule contents: May cause eye irritation.

Symptoms/Injuries After Ingestion: Harmful if swallowed.

Chronic Symptoms: Suspected of damaging the unborn child. Prolonged or repeated exposure may cause damage to the liver, thyroid, and adrenals.

SECTION 12: ECOLOGICAL INFORMATION

12.1. Toxicity

Ecology - General : Very toxic to aquatic life with long lasting effects.

Isavuconazonium sulfate (946075-13-4)	
NOEC chronic fish	0.1 mg/l (Pimephales promelas)
NOEC chronic crustacea	0.1 mg/l (Daphnia magna)
EC ₁₀ algae	0.02 mg/l (Pseudokirchneriella subcapitata)
EC ₅₀ microorganisms	> 100

12.2. Persistence and Degradability

Isavuconazonium sulfate (946075-13-4)	
Persistence and Degradability	Not readily biodegradable.
DT ₅₀ water	3.3/4.4 d
DT ₉₀ water	11/15 d
DT ₅₀ sediment	222/33 d
DT ₉₀ sediment	737/109 d
DT ₅₀ system	204/13 d
DT ₉₀ system	842/107 d
Additional information	The drug substance shifted from the water phase to the sediment phase with a maximum of 71% and 47% after 30 days and 7 days in system 1 and 2, respectively. Two relevant metabolites (> 10% of applied radioactivity) were present in the sediment layer of one water/sediment system.

12.3. Bioaccumulative Potential

Isavuconazonium sulfate (946075-13-4)	
Log Kow	3.86

12.4. Mobility in Soil

Isavuconazonium sulfate (946075-13-4)	
Log Koc	2180 - 2660 L/kg (sludge); 2,020 - 2,830 L/kg (soil)

12.5. Other Adverse Effects

Other Information : Avoid release to the environment.

SECTION 13: DISPOSAL CONSIDERATIONS

13.1. Waste treatment methods

Waste Disposal Recommendations: Dispose of contents and container according to local, regional, national, and international regulations.

Ecology – Waste Materials: This material is hazardous to the aquatic environment. Keep out of sewers and waterways. Avoid release to the environment.

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SECTION 14: TRANSPORT INFORMATION

14.1. In Accordance with DOT Not regulated for transport.

14.2. In Accordance with IMDG Not regulated for transport.

14.3. In Accordance with IATA Not regulated for transport.

SECTION 15: REGULATORY INFORMATION

15.1 US Federal Regulations Not applicable

15.2 US State Regulations Not applicable

SECTION 16: OTHER INFORMATION, INCLUDING DATE OF PREPARATION OR LAST REVISION

Revision Date : 09/16/2016

Other Information : This document has been prepared in accordance with the SDS requirements of the OSHA Hazard Communication Standard 29 CFR 1910.1200.

This information is based on our current knowledge and is intended to describe the product for the purposes of health, safety and environmental requirements only. It should not therefore be construed as guaranteeing any specific property of the product.