

SECTION 1: IDENTIFICATION

1.1. Product Identifier

Dosage Form: Powder for injection

Product Name: CRESEMBA® (isavuconazonium sulfate) for Injection

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

2.1. Classification of the Substance or Mixture

Classification (GHS-US)

Comb. Dust
Acute Tox. 4 (Oral) H302
Skin Irrit. 2 H315
Eye Irrit. 2A H319
Repr. 2 H361
STOT RE 1 H372
Aquatic Chronic 1 H410

2.2. Label Elements

GHS-US Labeling

Hazard Pictograms (GHS-US)



Signal Word (GHS-US)

: Warning

Hazard Statements (GHS-US)

: May form combustible dust concentrations in air.
H302 - Harmful if swallowed.
H315 - Causes skin irritation.
H319 - Causes serious eye irritation.
H361 - Suspected of damaging the unborn child.
H372 - Causes damage to organs (liver, adrenals, thyroid) through prolonged or repeated exposure.
H410 - Very toxic to aquatic life with long lasting effects.

Precautionary Statements (GHS-US)

: P201 - Obtain special instructions before use.
P202 - Do not handle until all safety precautions have been read and understood.
P260 - Do not breathe dust.
P264 - Wash hands, forearms and face thoroughly after handling.
P270 - Do not eat, drink or smoke when using this product.
P273 - Avoid release to the environment.
P280 - Wear eye protection, protective clothing, protective gloves.
P301+P312 - If swallowed: Call a doctor, a POISON CENTER if you feel unwell.
P302+P352 - If on skin: Wash with plenty of water.
P305+P351+P338 - If in eyes: Rinse cautiously with water for several minutes. Remove contact lenses, if present and easy to do. Continue rinsing.
P308+P313 - If exposed or concerned: Get medical advice/attention.
P314 - Get medical advice/attention if you feel unwell.

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P321 - Specific treatment (see Section 4 on this SDS).
P330 - Rinse mouth.
P332+P313 - If skin irritation occurs: Get medical advice/attention.
P337+P313 - If eye irritation persists: Get medical advice/attention.
P362+P364 - Take off contaminated clothing and wash it before reuse.
P391 - Collect spillage.
P405 - Store locked up.
P501 - Dispose of contents/container in accordance with local, regional, national, and international regulations.

2.3. Other Hazards

Exposure may aggravate those with pre-existing eye, skin, or respiratory conditions.

2.4. Unknown Acute Toxicity (GHS-US)

No data available

SECTION 3: COMPOSITION/INFORMATION ON INGREDIENTS

3.1. Substance

Not applicable

3.2. Mixture

Name	Product Identifier	%	Classification (GHS-US)
Isavuconazonium sulfate	(CAS No) 946075-13-4	80	Acute Tox. 4 (Oral), H302 Skin Irrit. 2, H315 Eye Irrit. 2A, H319 Repr. 2, H361 STOT RE 1, H372 Aquatic Chronic 1, H410
D-Mannitol	(CAS No) 69-65-8	<= 20	Comb. Dust
Mannitol	(CAS No) 87-78-5	<= 20	Comb. Dust

Full text of H-phrases: see section 16

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: Remove contaminated clothing. Gently wash with plenty of soap and water followed by rinsing with water for at least 15 minutes. Call a POISON CENTER or doctor/physician if you feel unwell. Wash contaminated clothing before reuse.

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 serious eye irritation. Causes skin irritation. Causes damage to organs (liver, adrenals, thyroid) through prolonged or repeated exposure.

Symptoms/Injuries After Inhalation: May cause respiratory irritation.

Symptoms/Injuries After Skin Contact: Causes skin irritation.

Symptoms/Injuries After Eye Contact: Causes serious 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, or 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.

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5.2. Special Hazards Arising From the Substance or Mixture

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

Explosion Hazard: Combustible dust. Fine dust clouds may form explosive mixtures with air.

Reactivity: Hazardous reactions will not occur under normal conditions.

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). Avoid generating 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: Stop leak if safe to do so. Eliminate ignition sources. Ventilate area.

6.2. Environmental Precautions

Prevent entry to sewers and public waters. Notify authorities if liquid 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. Take up large spills with vacuum. Contact competent authorities after a spill. Avoid generation of dust during clean-up of spills.

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

Additional Hazards When Processed: Local exhaust is recommended where dust may occur.

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. Proper grounding procedures to avoid static electricity should be followed. Use explosion-proof electrical, ventilating, and lighting equipment.

Storage Conditions: Store in a dry, cool and well-ventilated place at 2 - 8 °C (35.6 - 46.4 °F). Keep container closed when not in use. Keep/Store away from direct sunlight, extremely high or low temperatures and incompatible materials.

Incompatible Products: Strong oxidizers.

Storage Temperature: 2 - 8 °C (35.6 - 46.4 °F)

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. Proper grounding procedures to avoid static electricity should be followed. Use explosion-proof equipment.

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Personal Protective Equipment : Protective goggles. Gloves. Protective clothing. Dust formation: dust mask.



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.
Respiratory Protection : In case of inadequate ventilation wear respiratory protection.
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.

SECTION 9: PHYSICAL AND CHEMICAL PROPERTIES

9.1. Information on Basic Physical and Chemical Properties

Physical State : Solid
Appearance : White to yellow cake
Odor : Odorless
Odor Threshold : No data available
pH : 1.9 - 2.6
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: Harmful if swallowed.

CRESEMBA® (isavuconazonium sulfate) for Injection	
ATE (Oral)	885.00 mg/kg body weight
LD50 Intravenous Rat	≈ 10 mg/kg (i.v. bolus)
LD50 Intravenous Rat	> 20 mg/kg (i.v. slow bolus)
LD50 Intravenous Monkey	64 mg/kg (i.v. bolus)
LD50 Intravenous Monkey	120 mg/kg (i.v. infusion)

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Isavuconazonium sulfate (946075-13-4)	
LD50 Oral Rat	708 - 1024 mg/kg
D-Mannitol (69-65-8)	
LD50 Oral Rat	13500 mg/kg

Skin Corrosion/Irritation: Causes skin irritation. Slight irritant at high concentrations, no irritation at ≤ 1 mg/mL. (pH: 1.9 - 2.6)

Serious Eye Damage/Irritation: Causes serious eye irritation. 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.

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: May cause respiratory irritation.

Symptoms/Injuries After Skin Contact: Causes skin irritation.

Symptoms/Injuries After Eye Contact: Causes serious 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)
EC₁₀ algae	0.02 mg/l (Pseudokirchneriella subcapitata)
EC₅₀ microorganisms	> 100

12.2. Persistence and Degradability

Isavuconazonium sulfate (946075-13-4)	
Persistence and Degradability	Not readily biodegradable.
DT₅₀ water	3.3/4.4 d
DT₉₀ water	11/15 d
DT₅₀ sediment	222/33 d
DT₉₀ sediment	737/109 d
DT₅₀ system	204/13 d
DT₉₀ 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.

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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.

SECTION 14: TRANSPORT INFORMATION

14.1. In Accordance with DOT

Proper Shipping Name : ENVIRONMENTALLY HAZARDOUS SUBSTANCES, SOLID, N.O.S. (Isavuconazonium sulfate)
Hazard Class : 9
Identification Number : UN3077
Label Codes : 9
Packing Group : III
Marine Pollutant : Marine pollutant
ERG Number : 171



14.2. In Accordance with IMDG

Proper Shipping Name : ENVIRONMENTALLY HAZARDOUS SUBSTANCE, SOLID, N.O.S. (Isavuconazonium sulfate)
Hazard Class : 9
Identification Number : UN3077
Packing Group : III
Label Codes : 9
EmS-No. (Fire) : F-A
EmS-No. (Spillage) : S-F



Marine Pollutant : Marine pollutant

14.3. In Accordance with IATA

Proper Shipping Name : ENVIRONMENTALLY HAZARDOUS SUBSTANCE, SOLID, N.O.S. (Isavuconazonium sulfate)
Packing Group : III
Identification Number : UN3077
Hazard Class : 9
Label Codes : 9
ERG Code (IATA) : 9L



SECTION 15: REGULATORY INFORMATION

15.1 US Federal Regulations

CRESEMBA® (isavuconazonium sulfate) for Injection	
SARA Section 311/312 Hazard Classes	Delayed (chronic) health hazard Immediate (acute) health hazard
D-Mannitol (69-65-8)	
Listed on the United States TSCA (Toxic Substances Control Act) inventory	
Mannitol (87-78-5)	
Listed on the United States TSCA (Toxic Substances Control Act) inventory	

15.2 US State Regulations

Neither this product nor its chemical components appear on any US state lists.

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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.

GHS Full Text Phrases:

Acute Tox. 4 (Oral)	Acute toxicity (oral) Category 4
Aquatic Chronic 1	Hazardous to the aquatic environment - Chronic Hazard Category 1
Eye Irrit. 2A	Serious eye damage/eye irritation Category 2A
Repr. 2	Reproductive toxicity Category 2
Skin Irrit. 2	Skin corrosion/irritation Category 2
STOT RE 1	Specific target organ toxicity (repeated exposure) Category 1
H302	Harmful if swallowed
H315	Causes skin irritation
H319	Causes serious eye irritation
H361	Suspected of damaging the unborn child
H372	Causes damage to organs through prolonged or repeated exposure
H410	Very toxic to aquatic life with long lasting effects

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.