Generic Name: isavuconazonium sulfate

Applicable Drugs: Cresemba®

Preferred: N/A

Non-preferred: Cresemba® (isavuconazonium sulfate)

Date of Origin: 8/20/2022

Date Last Reviewed / Revised: 9/22/2023

PRIOR AUTHORIZATION CRITERIA

(May be considered medically necessary when criteria I through VI are met)

I. Documented diagnosis of one of the following conditions A, B, or C **AND** must meet criteria listed under applicable diagnosis.

A. Treatment of invasive aspergillosis

i. Clinical and laboratory documentation confirming diagnosis (e.g., computed tomography (CT), serum galactomannan, bronchoalveolar lavage [BAL] galactomannan, Aspergillus polymerase chain reaction (PCR), biopsy, culture).

ii. Documentation of treatment failure, intolerance, or contraindication to voriconazole (e.g., congenital or acquired QT prolongation).

iii. In cases of breakthrough infection during prophylaxis or treatment failure while using a generic oral triazole, documentation of **ALL** the following must also be provided:

1. Adherence to generic triazole therapy.
2. Therapeutic generic triazole blood levels.
3. Fungal culture showing sensitivity to isavuconazole.

B. Treatment of invasive mucormycosis

i. Clinical and laboratory documentation confirming diagnosis (e.g., CT, direct microscopy, culture, histopathology).

ii. Documentation of treatment failure, intolerance, or contraindication to liposomal amphotericin B or amphotericin B lipid complex.

C. Prevention of fungal infections in patients with documented cancer diagnosis treated with allogeneic hematopoietic cell transplant (HCT)

i. Laboratory documentation of neutropenia

ii. Documentation of intolerance, or contraindication to **ALL** the following:

1. Fluconazole
2. Voriconazole

3. Posaconazole

II. Minimum age requirement: 18 years old

III. Documentation of plan for appropriate monitoring and/or dose adjustment when administering with concomitant medications with clinically significant drug interactions per FDA labeling (refer to Table 2).

IV. Request is for a medication with the appropriate FDA labeling, or its use is supported by current clinical practice guidelines.

V. Must be prescribed by or in consultation with a physician specializing in infectious disease, transplant, or oncology.

VI. Refer to plan document for the list of preferred products. If requested agent is not listed as a preferred product, must have a documented failure, intolerance, or contraindication to a preferred product(s).

EXCLUSION CRITERIA

- Coadministration with strong CYP3A4 inhibitors (e.g., ketoconazole or high-dose ritonavir [400 mg every 12 hours]) or strong CYP3A4 inducers (e.g., rifampin, carbamazepine, St. John's wort, or long-acting barbiturates)
- Concomitant familial short QT syndrome
- Administration during pregnancy

OTHER CRITERIA

- Cresemba® oral capsules are preferred over injectable formulation due to bioequivalence between the IV and oral formulations. Please provide clinical justification supporting treatment with Cresemba® injection over oral formulation if injectable is requested.

QUANTITY / DAYS SUPPLY RESTRICTIONS

- Oral capsules
    - Initial authorization
        - 64 capsules for the initial 28 days, then 56 capsules per 28 days (28-day supply limit per fill).
    - Re-authorization
        - 56 capsules per 28 days (28-day supply limit per fill).
- IV injection
    - Initial authorization
        - 32 single-dose vials for the initial 28 days, then 28 single-dose vials per 28 days (28-day supply limit per fill).

- Re-authorization
  - 28 single-dose vials per 28 days (28-day supply limit per fill).

APPROVAL LENGTH

- **Authorization:**
  - Treatment of invasive aspergillosis or invasive mucormycosis: 12 weeks.
  - Prevention of fungal infections in patients with documented cancer diagnosis treated with allogeneic HCT: 12 weeks.
- **Re-Authorization:**
  - Treatment of invasive aspergillosis or invasive mucormycosis: 12 weeks. Renewal may be considered on a case-by-case basis with documentation of continued indicators of active disease, positive response to therapy (e.g., clinical and radiographic improvement), and absence of clinically significant adverse events (e.g., liver toxicity).
  - Prevention of fungal infections in patients with documented cancer diagnosis treated with allogeneic HCT: 12 weeks with documentation of continued neutropenia, positive response to therapy, and absence of clinically significant adverse events (e.g., liver toxicity).

APPENDIX

Table 1. FDA labeled dosage regimen

Dosage Form	How Supplied	Loading Dose	Maintenance Dose
Cresemba® oral	186 mg capsule (equivalent to 100 mg isavuconazole)	2 capsules (372 mg) orally every 8 hours for 6 doses	2 capsules orally once daily 12 to 24 hours after the last loading dose
Cresemba® injectable	372 mg single-dose vial (equivalent to 200 mg isavuconazole)	1 reconstituted vial (372mg) intravenously every 8 hours for 6 doses	1 reconstituted vial (372mg) intravenously once daily 12 to 24 hours after the last loading dose

Table 2. Clinically significant drug-drug interactions with Cresemba® coadministration

Drug	Recommendation	Explanation
Atorvastatin	Use caution	Potential increase in atorvastatin exposure. Monitor for adverse reactions related to atorvastatin.

Bupropion	Use caution	Decrease in bupropion exposure. Dose increase (not to exceed maximum recommended dose) of bupropion may be needed.
Cyclosporine	Use caution	Increase in cyclosporine exposure. Monitor drug levels and adjust cyclosporine dose as needed.
Digoxin	Use caution	Increase in digoxin exposure. Monitor drug levels and adjust digoxin dose as needed.
Lopinavir/ritonavir	Use caution	96% increase in isavuconazole exposure Decreased exposure of lopinavir and ritonavir that may result in loss of efficacy.
Midazolam	Use caution	Increase in midazolam exposure. Consider dose reduction of midazolam.
Mycophenolate Mofetil	Use caution	Increase in mycophenolate mofetil exposure. Monitor for mycophenolate mofetil related toxicities.
Sirolimus	Use caution	Increase in sirolimus exposure. Monitor drug levels and adjust sirolimus dose as needed.
Tacrolimus	Use caution	Increase in tacrolimus exposure. Monitor drug levels and adjust tacrolimus dose as needed.

REFERENCES

1. Cresemba. Prescribing information. Astellas Pharma US, Inc; 2022. Accessed September 19, 2023. https://www.astellas.us/docs/cresemba.pdf.
2. Patterson TF, Thompson GR 3rd, Denning DW, et al. Practice guidelines for the diagnosis and management of aspergillosis: 2016 update by the Infectious Diseases Society of America. *Clin Infect Dis*. 2016;63(4):e1-e60. doi:10.1093/cid/ciw326.
3. Husain S, Camargo JF. Invasive Aspergillosis in solid-organ transplant recipients: guidelines from the American Society of Transplantation Infectious Diseases Community of Practice. *Clin Transplant*. 2019;33(9):e13544. doi:10.1111/ctr.13544.
4. Tissot F, Agrawal S, Pagano L, et al. ECIL-6 guidelines for the treatment of invasive candidiasis, aspergillosis and mucormycosis in leukemia and hematopoietic stem cell transplant patients. *Haematologica*. 2017;102(3):433-444. doi:10.3324/haematol.2016.152900.

5. NCCN Clinical Practice Guidelines in Oncology for prevention and treatment of cancer-related infections V.2.2022. Accessed September 18, 2022. https://www.nccn.org/professionals/physician_gls/pdf/infections.pdf.
6. Cornely OA, Arikan-Akdagli S, Dannaoui E, et al. ESCMID and ECMM joint clinical guidelines for the diagnosis and management of mucormycosis 2013. *Clin Microbiol Infect.* 2014;20 Suppl 3:5-26. doi:10.1111/1469-0691.12371.
7. Stern A, Su Y, Lee YJ, et al. A single-center, open-label trial of isavuconazole prophylaxis against invasive fungal infection in patients undergoing allogeneic hematopoietic cell transplantation. *Biol Blood Marrow Transplant.* 2020;26(6):1195-1202. doi:10.1016/j.bbmt.2020.02.009.