Applicable Drugs: Cresemba (isavuconazonium sulfate)

Preferred: N/A

Non-preferred: Cresemba (isavuconazonium sulfate)

Date of Origin: 8/20/2022

Date Last Reviewed / Revised: 5/19/2026

PRIOR AUTHORIZATION CRITERIA

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

I. Documented diagnosis of one of the following conditions A or B **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 (e.g., congenital or acquired QT prolongation) to at least one of the following triazoles: voriconazole, itraconazole or posaconazole delayed release

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.

II. Minimum age requirements:

A. Capsules: 6 years of age or older AND weight at least 16 kg

B. Vials: 1 year of age or older

III. If administering via NG tube, patient must be 6 years of age or older AND weigh at least 16kg

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

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

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

VII. 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. For injection requests, clinical justification supporting treatment with Cresemba injection over oral formulation is required.

QUANTITY / DAYS SUPPLY RESTRICTIONS

- Capsules
    - Initial authorization
        - **186 mg capsule:** 64 capsules for the initial 28 days, then 56 capsules per 28 days (28-day supply limit per fill).
        - **74.5 mg capsule (for pediatrics aged 6 to <18 years old AND <32kg ONLY):** 136 capsules for the initial 28 days, then 112 capsules per 28 days (28-day supply limit per fill).
    - Re-authorization
        - **186 mg capsule**: 56 capsules per 28 days (28-day supply limit per fill).
        - **74.5 mg capsule (for pediatrics aged 6 to <18 years old AND <32kg ONLY):** 112 capsules per 28 days (28-day supply limit per fill).
- Vials

- 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.
- **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).

APPENDIX

Table 1. Adult 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 (48 hours)	2 capsules orally once daily 12 to 24 hours after the last loading dose
	74.5 mg capsule (equivalent to 40mg isavuconazole)	5 capsules (375mg) orally every 8 hours for 6 doses (48 hours)	5 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. Pediatric FDA labeled dosing regimen

Dosage Form	How Supplied	Age & Weight	Loading Dose	Maintenance Dose
Cresemba oral	74.5 mg capsule (equivalent to 40mg isavuconazole)	6 to <18 years 16kg to <18kg	2 capsules (149 mg) orally every 8 hours for 6 doses (48 hours)	2 capsules orally (149 mg) once daily 12 to 24 hours after the last loading dose
		6 to <18 years 18 kg to <25kg	3 capsules (223.5 mg) orally every 8 hours for 6 doses (48 hours)	3 capsules (223.5 mg) orally once daily 12 to 24 hours after the last loading dose.
		6 to <18 years 25 kg to <32 kg	4 capsules (298 mg) orally every 8 hours for 6 doses (48 hours)	4 capsules (298 mg) orally once daily 12 to 24 hours after the last loading dose.
		6 to <18 years 18 kg to <25kg	5 capsules (372 mg) orally every 8 hours for 6 doses (48 hours)	5 capsules (372mg) 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 to <3 years old <18 kg	15mg/kg IV every 8 hours for 6 doses (48 hours)	15mg/kg IV once daily
		3 to <18 years old AND <37 kg	10mg/kg IV every 8 hours for 6 doses (48 hours)	10mg/kg IV once daily
		3 to <18 years old AND ≥ 37 kg	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

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DISCLAIMER: Medication Policies are developed to help ensure safe, effective and appropriate use of selected medications. They offer a guide to coverage and are not intended to dictate to providers how to practice medicine. Refer to Plan for individual adoption of specific Medication Policies. Providers are expected to exercise their medical judgement in providing the most appropriate care for their patients.