

Clinical Policy: Isavuconazonium (Cresemba)

Reference Number: HIM.PA.108

Effective Date: 08.17

Last Review Date: 08.19

Line of Business: HIM*

[Revision Log](#)

See [Important Reminder](#) at the end of this policy for important regulatory and legal information.

Description

Isavuconazonium (Cresemba[®]) is an azole antifungal.

**For Health Insurance Marketplace (HIM), if request is through pharmacy benefit, Cresemba intravenous is non-formulary and cannot be approved using these criteria; refer to the formulary exception policy, HIM.PA.103.*

FDA Approved Indication(s)

Cresemba is indicated for the treatment of:

- Invasive aspergillosis in patients 18 years of age and older.
- Invasive mucormycosis in patients 18 years of age and older.

Policy/Criteria

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

It is the policy of health plans affiliated with Centene Corporation[®] that Cresemba is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Aspergillosis (must meet all):

1. Diagnosis of aspergillosis;
2. Age \geq 18 years;
3. Prescribed by or in consultation with an infectious disease specialist;
4. Failure of voriconazole at up to maximally indicated doses, unless contraindicated or clinically significant adverse effects are experienced;
5. Dose does not exceed the following:
 - a. Loading dose: 372 mg (2 capsules) every 8 hours for 48 hours (12 capsules or 6 doses);
 - b. Maintenance dose: 372 mg (2 capsules) per day.

Approval duration: 3 months for capsules (refer to HIM.PA.103 for intravenous)

B. Mucormycosis (must meet all):

1. Diagnosis of mucormycosis;
2. Age \geq 18 years;
3. Prescribed by or in consultation with an infectious disease specialist;
4. Failure of amphotericin B at up to maximally indicated doses, unless contraindicated or clinically significant adverse effects are experienced;
5. Dose does not exceed the following:

- a. Loading dose: 372 mg (2 capsules) every 8 hours for 48 hours (12 capsules or 6 doses);
- b. Maintenance dose: 372 mg (2 capsules) per day.

Approval duration: 3 months for capsules (refer to HIM.PA.103 for intravenous)

C. Other diagnoses/indications

1. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): HIM.PHAR.21 for health insurance marketplace.

II. Continued Therapy

A. All Indications in Section I (must meet all):

1. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
2. Member is responding positively to therapy;
3. If request is for a dose increase, new dose does not exceed 372 mg (2 capsules) per day.

Approval duration: 6 months for capsules (refer to HIM.PA.103 for intravenous)

B. Other diagnoses/indications (must meet 1 or 2):

1. Currently receiving medication via Centene benefit and documentation supports positive response to therapy.
Approval duration: Duration of request or 6 months (whichever is less); or
2. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): HIM.PHAR.21 for health insurance marketplace.

III. Diagnoses/Indications for which coverage is NOT authorized:

- A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policies – HIM.PHAR.21 for health insurance marketplace or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

FDA: Food and Drug Administration

Appendix B: Therapeutic Alternatives

This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may not be a formulary agent for all relevant lines of business and may require prior authorization.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
voriconazole (Vfend [®])	Aspergillosis IV: 6 mg/kg/dose IV every 12 hours on day 1, followed by 4 mg/kg/dose IV every 12 hours. If	Weight ≥ 40 kg: 12 mg/kg/day IV; 800 mg/day PO

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
	<p>patient is unable to tolerate maintenance therapy, reduce dose to 3 mg/kg/dose IV every 12 hours.</p> <p><u>PO:</u> <i>Adults weighing 40 kg or more:</i> 200 mg PO every 12 hours beginning after at least 7 days of IV voriconazole therapy. Increase to 300 mg PO every 12 hours for inadequate response; if not tolerated, taper by 50 mg increments to minimum 200 mg PO every 12 hours. <i>Adults weighing less than 40 kg:</i> 100 mg PO every 12 hours beginning after at least 7 days of IV voriconazole therapy. Increase to 150 mg PO every 12 hours for inadequate response; if not tolerated, reduce dose to minimum 100 mg PO every 12 hours.</p> <p>Clinical practice guidelines suggest voriconazole as primary therapy. Treat for at least 6 to 12 weeks with duration dependent on extent and length of immunosuppression, infection site, and disease improvement.</p>	<p>Weight < 40 kg: 12 mg/kg/day IV; 400 mg/day PO</p>
amphotericin B	<p>Mucormycosis <i>Adults:</i> 0.25 to 0.3 mg/kg/dose IV every 24 hours; may increase dose by 5 to 10 mg/day to a final dose of 0.5 to 0.7 mg/kg/day.</p>	<p>1 mg/kg/day or 1.5 mg/kg given every other day</p>

Therapeutic alternatives are listed as Brand name[®] (generic) when the drug is available by brand name only and generic (Brand name[®]) when the drug is available by both brand and generic.

Appendix C: Contraindications/Boxed Warnings

- Contraindication(s):
 - Hypersensitivity to Cresemba.
 - Coadministration of strong CYP3A4 inhibitors, such as ketoconazole or high-dose ritonavir (400 mg every 12 hours), with Cresemba is contraindicated because strong CYP3A4 inhibitors can significantly increase the plasma concentration of isavuconazole.
 - Coadministration of strong CYP3A4 inducers, such as rifampin, carbamazepine, St. John’s wort, or long acting barbiturates with Cresemba is contraindicated because strong CYP3A4 inducers can significantly decrease the plasma concentration of isavuconazole.
 - Cresemba is contraindicated in patients with familial short QT syndrome. Cresemba shortened the QTc interval in a concentration-related manner.
- Boxed warning(s): none reported

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
Invasive aspergillosis or invasive mucormycosis	Loading dose: 372 mg (IV or 2 capsules PO) every 8 hours for a total of 6 doses in 48 hours	Loading dose: 1,116 mg/day
	Maintenance dose (starting 12 to 24 hours after the last loading dose): 372 mg (IV or 2 capsules PO) QD	Maintenance dose: 372 mg/day

VI. Product Availability

- Capsule: 186 mg of isavuconazonium sulfate (equivalent to 100 mg of isavuconazole)
- Single-dose vial for injection: 372 mg of isavuconazonium sulfate (equivalent to 200 mg of isavuconazole)

VII. References

1. Cresemba Prescribing Information. Northbrook, IL: Astellas Pharma US, Inc.; April 2018. Available at: <https://www.cresemba.com/>. Accessed May 21, 2019.
2. Patterson TF, Thompson GR, 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 Aug 15;63(4):e1-e60. doi: 10.1093/cid/ciw326.
3. 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. Mar 2017, 102(3) 433-444.
4. Centers for Disease Control and Prevention. Fungal Diseases: Treatment of Mucormycosis. Last updated December 30, 2015. Available at: <https://www.cdc.gov/fungal/diseases/mucormycosis/treatment.html>. Accessed April 27, 2018.
5. Clinical Pharmacology [database online]. Tampa, FL: Gold Standard, Inc.; 2019. Available at: <http://www.clinicalpharmacology-ip.com/>.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy created.	04.17	08.17
3Q 2018 annual review: no significant changes; added age; removed requirements related to confirmation of diagnosis and duration of trial since specialist is involved in care and duration of antifungal treatment should be determined on an individual basis; combined continued therapy since criteria for aspergillosis and mucormycosis are the same; references reviewed and updated.	04.30.18	08.18
3Q 2019 annual review: no significant changes; reference reviewed and updated.	05.21.19	08.19

Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted

standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. “Health Plan” means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan’s affiliates, as applicable.

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Note:

For Health Insurance Marketplace members, when applicable, this policy applies only when the prescribed agent is on your health plan approved formulary. Request for non-formulary drugs must be reviewed using the formulary exception policy.

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