

Clinical Policy: Isavuconazonium (Cresemba)

Reference Number: CP.PMN.154

Effective Date: 11.16.16

Last Review Date: 08.19

Line of Business: Commercial, Medicaid

[Revision Log](#)

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

Description

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

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 or Mucormycosis (must meet all):

1. Diagnosis of invasive aspergillosis or invasive mucormycosis;
2. Age \geq 18 years;
3. Prescribed by or in consultation with an infectious disease specialist;
4. Dose does not exceed the following:
 - a. Loading dose: 372 mg (2 capsules or 2 vials) every 8 hours for 48 hours (total 6 doses: 12 capsules or 6 vials);
 - b. Maintenance dose: 372 mg (2 capsules or 2 vials) per day.

Approval duration: 3 months

B. 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): CP.CPA.09 for commercial and CP.PMN.53 for Medicaid.

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 or 2 vials) per day.

Approval duration: 6 months

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 12 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): CP.CPA.09 for commercial and CP.PMN.53 for Medicaid.

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 – CP.CPA.09 for commercial and CP.PMN.53 for Medicaid, or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

FDA: Food and Drug Administration

Appendix B: Therapeutic Alternatives

Not applicable

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

Indication	Dosing Regimen	Maximum Dose
	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, Inc.; April 2018. Available at: 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
Converted to new template; minor changes to verbiage and grammar. References updated.	1.5.17	8.17
3Q 2018 annual review: new policy for Medicaid line of business; added age and prescriber requirements; re-auth: added positive response to therapy, modified max dose requirement to reflect dosage regimen for maintenance dose; references reviewed and updated.	04.30.18	08.18
3Q 2019 annual review: no significant changes; revised approval duration for commercial to 3/6 months for initial/continuation to align with Medicaid; clarified max dose requirements to add vial formulation; references 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.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

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Note:

For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.

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