PRIOR AUTHORIZATION POLICY

POLICY: Antifungals – Cresemba (Oral) Prior Authorization Policy
- Cresemba® (isavuconazonium sulfate capsules – Astellas)

REVIEW DATE: 07/16/2025; selected revision 08/06/2025

INSTRUCTIONS FOR USE

THE FOLLOWING COVERAGE POLICY APPLIES TO HEALTH BENEFIT PLANS ADMINISTERED BY CIGNA COMPANIES. CERTAIN CIGNA COMPANIES AND/OR LINES OF BUSINESS ONLY PROVIDE UTILIZATION REVIEW SERVICES TO CLIENTS AND DO NOT MAKE COVERAGE DETERMINATIONS. REFERENCES TO STANDARD BENEFIT PLAN LANGUAGE AND COVERAGE DETERMINATIONS DO NOT APPLY TO THOSE CLIENTS. COVERAGE POLICIES ARE INTENDED TO PROVIDE GUIDANCE IN INTERPRETING CERTAIN STANDARD BENEFIT PLANS ADMINISTERED BY CIGNA COMPANIES. PLEASE NOTE, THE TERMS OF A CUSTOMER'S PARTICULAR BENEFIT PLAN DOCUMENT [GROUP SERVICE AGREEMENT, EVIDENCE OF COVERAGE, CERTIFICATE OF COVERAGE, SUMMARY PLAN DESCRIPTION (SPD) OR SIMILAR PLAN DOCUMENT] MAY DIFFER SIGNIFICANTLY FROM THE STANDARD BENEFIT PLANS UPON WHICH THESE COVERAGE POLICIES ARE BASED. FOR EXAMPLE, A CUSTOMER'S BENEFIT PLAN DOCUMENT MAY CONTAIN A SPECIFIC EXCLUSION RELATED TO A TOPIC ADDRESSED IN A COVERAGE POLICY. IN THE EVENT OF A CONFLICT, A CUSTOMER'S BENEFIT PLAN DOCUMENT ALWAYS SUPERSEDES THE INFORMATION IN THE COVERAGE POLICIES. IN THE ABSENCE OF A CONTROLLING FEDERAL OR STATE COVERAGE MANDATE, BENEFITS ARE ULTIMATELY DETERMINED BY THE TERMS OF THE APPLICABLE BENEFIT PLAN DOCUMENT. COVERAGE DETERMINATIONS IN EACH SPECIFIC INSTANCE REQUIRE CONSIDERATION OF 1) THE TERMS OF THE APPLICABLE BENEFIT PLAN DOCUMENT IN EFFECT ON THE DATE OF SERVICE; 2) ANY APPLICABLE LAWS/REGULATIONS; 3) ANY RELEVANT COLLATERAL SOURCE MATERIALS INCLUDING COVERAGE POLICIES AND; 4) THE SPECIFIC FACTS OF THE PARTICULAR SITUATION. EACH COVERAGE REQUEST SHOULD BE REVIEWED ON ITS OWN MERITS. MEDICAL DIRECTORS ARE EXPECTED TO EXERCISE CLINICAL JUDGMENT WHERE APPROPRIATE AND HAVE DISCRETION IN MAKING INDIVIDUAL COVERAGE DETERMINATIONS. WHERE COVERAGE FOR CARE OR SERVICES DOES NOT DEPEND ON SPECIFIC CIRCUMSTANCES, REIMBURSEMENT WILL ONLY BE PROVIDED IF A REQUESTED SERVICE(S) IS SUBMITTED IN ACCORDANCE WITH THE RELEVANT CRITERIA OUTLINED IN THE APPLICABLE COVERAGE POLICY, INCLUDING COVERED DIAGNOSIS AND/OR PROCEDURE CODE(S). REIMBURSEMENT IS NOT ALLOWED FOR SERVICES WHEN BILLED FOR CONDITIONS OR DIAGNOSES THAT ARE NOT COVERED UNDER THIS COVERAGE POLICY (SEE "CODING INFORMATION" BELOW). WHEN BILLING, PROVIDERS MUST USE THE MOST APPROPRIATE CODES AS OF THE EFFECTIVE DATE OF THE SUBMISSION. CLAIMS SUBMITTED FOR SERVICES THAT ARE NOT ACCOMPANIED BY COVERED CODE(S) UNDER THE APPLICABLE COVERAGE POLICY WILL BE DENIED AS NOT COVERED. COVERAGE POLICIES RELATE EXCLUSIVELY TO THE ADMINISTRATION OF HEALTH BENEFIT PLANS. COVERAGE POLICIES ARE NOT RECOMMENDATIONS FOR TREATMENT AND SHOULD NEVER BE USED AS TREATMENT GUIDELINES. IN CERTAIN MARKETS, DELEGATED VENDOR GUIDELINES MAY BE USED TO SUPPORT MEDICAL NECESSITY AND OTHER COVERAGE DETERMINATIONS.

CIGNA NATIONAL FORMULARY COVERAGE:

OVERVIEW

Cresemba, an azole antifungal, is indicated in adults and pediatric patients ≥ 6 years of age who weigh ≥ 16 kg for the following uses:[1]
- **Invasive aspergillosis.**
- **Invasive mucormycosis.**

Cresemba is also available for use as an intravenous (IV) infusion.[1] Switching between the IV and oral formulation is acceptable as the two formulations are bioequivalent. A loading dose is not required when switching between formulations. Patients are typically transitioned from the IV formulation to the oral formulation while in the hospital or upon discharge. In the pivotal study involving patients with invasive aspergillosis, patients were initiated on IV Cresemba before transitioning to oral Cresemba therapy. The mean treatment duration was 47 days, of which patients received IV Cresemba for 8 to 9 days.

Guidelines/Recommendations

The Infectious Diseases Society of America (IDSA) [2016] recommends Cresemba as a treatment option for invasive aspergillosis and different invasive syndromes of *Aspergillus* (e.g., invasive pulmonary aspergillosis, invasive sinus aspergillosis, aspergillosis of the central nervous system).[2] Treatment of invasive aspergillosis should be continued for a minimum of 6 to 12 weeks, depending on the degree and duration of immunosuppression, site of disease, and evidence of disease improvement.

The global guideline for the diagnosis and management of mucormycosis (2019) recommends Cresemba as a treatment option with moderate strength. The duration of therapy to treat mucormycosis is unknown, but in general weeks to month of therapy are required.[5] In an open-label, non-comparative study that included a subset of patients with invasive mucormycosis, patients were treated with either IV or oral Cresemba. The median duration of Cresemba therapy was 102 days for patients classified as primary, 33 days for refractory, and 85 days for intolerant.[1]

Other Uses with Supportive Evidence

The National Comprehensive Cancer Network (NCCN) Guidelines for Prevention and Treatment of Cancer-Related Infections (version 1.2025 – June 20, 2025) note that use of Cresemba may be considered for patients who have invasive or refractory aspergillosis or mucormycosis or who have intolerance to amphotericin B formulations.[3] NCCN also notes Cresemba as a treatment option for the prevention of fungal infections in patients with significant graft-versus-host disease (GVHD) [especially grade 3/4] who are receiving immunosuppressive therapy; treatment should continue until resolution of significant GVHD. Cresemba is also a treatment option for these groups of patients with neutropenia: patients with myelodysplastic syndrome, patients with acute myeloid leukemia, and patients who are allogeneic hematopoietic cell transplant recipients; treatment should continue until resolution of neutropenia.

The guidelines for prevention and treatment of opportunistic infections in adults and adolescents with human immunodeficiency virus (HIV) infections (last updated April 2025) note Cresemba as a treatment option for patients with HIV and esophageal candidiasis.[4] Cresemba is also an option for patients with HIV and coccidioidomycosis.

The global guideline for the diagnosis and management of cryptococcosis (2024) note Cresemba as an alternative treatment option for patients with cryptococcal meningitis.[6] This is a moderate strength recommendation as Cresemba and other triazole drugs have not been formally studied in cryptococcosis.

POLICY STATEMENT

Prior Authorization is recommended for prescription benefit coverage of Cresemba capsules. All approvals are provided for the duration noted below. In cases where the approval is authorized in months, 1 month is equal to 30 days.

- **Cresemba® (isavuconazonium sulfate capsules - Astellas)**

is(are) covered as medically necessary when the following criteria is(are) met for FDA-approved indication(s) or other uses with supportive evidence (if applicable):

FDA-Approved Indications

1. ***Aspergillus* Infection – Treatment.** Approve for 6 months.

2. **Mucormycosis – Treatment.** Approve for 6 months.

Other Uses with Supportive Evidence

3. **Esophageal Candidiasis in a Patient with Human Immunodeficiency Virus Infection – Treatment.** Approve for 3 months.

4. **Fungal Infection (Systemic) in a Patient with Human Immunodeficiency Virus Infection – Treatment.** Approve for 3 months.

5. **Fungal Infection (Systemic) in a Patient With Cancer and Neutropenia – Prophylaxis.** Approve for 6 months.
   Note: Examples of cancers predisposing neutropenic patients to risk of fungal infections include: myelodysplastic syndrome, acute myeloid leukemia, patients post-allogeneic hematopoietic cell transplant.

6. **Fungal Infection (Systemic) in a Patient with Graft-versus-Host Disease – Prophylaxis**. Approve for 6 months.

7. **Coccidioidomycosis in a Patient with Human Immunodeficiency Virus Infection – Treatment.** Approve for 6 months.

8. **Cryptococcal Meningitis – Treatment.** Approve for 12 months.

9. **Fungal Infection (Systemic) That Is Susceptible to Cresemba – Treatment.** Approve for 3 months.

10. **Patient is Currently Receiving Cresemba.** Approve for 3 months to complete the course of therapy.

CONDITIONS NOT COVERED

- **Cresemba® (isavuconazonium sulfate capsules - Astellas)**

is(are) considered not medically necessary for ANY other use(s); criteria will be updated as new published data are available.

REFERENCES

1. Cresemba® capsules [prescribing information]. Northbrook, IL: Astellas Pharma; April 2025
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;63(4):e1-e60.
3. The NCCN Prevention and Treatment of Cancer-Related Infections Clinical Practice Guidelines in Oncology (version 1.2025 – June 20, 2025). ©2025 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on July 1, 2025.
4. Panel on Opportunistic Infections in HIV-Infected Adults and Adolescents. Guidelines for the prevention and treatment of opportunistic infections in HIV-infected adults and adolescents: recommendations from the Centers for Disease Control and Prevention, the National Institutes of Health, and the HIV Medicine Association of the Infectious Diseases Society of America. Available at: https://clinicalinfo.hiv.gov/sites/default/files/guidelines/documents/adult-adolescent-oi/guidelines-adult-adolescent-oi.pdf. Last updated April 23, 2025. Accessed on July 1, 2025. Cornely OA, Izquierdo AA, Arenz D, et al. Global guideline for the diagnosis and management of mucormycosis: an initiative of the European confederation of medical mycology in cooperation with the mycoses study group education and research consortium. *Lancet Infect Dis*. 2019;19(12): e405-421.
5. Chang CC, Harrison TS, Bicanic TA, et al. Global guideline for the diagnosis and management of cryptococcosis: an initiative of the ECMM and ISAHM in cooperation with the ASM. *Lancet Infect Dis*. 2024;24(8): e485.

HISTORY

Type of Revision	Summary of Changes	Review Date
Annual Revision	**Fungal Infection (Systemic) in a Patient with Graft-versus-Host Disease – Prophylaxis:** This condition of approval was added to the policy. **Fungal Infection (Systemic) in a Patient with Cancer and Neutropenia – Prophylaxis:** This indication was previously worded as "Fungal Infection (Systemic) in a Patient At Risk of Neutropenia – Prophylaxis" and was revised to align with NCCN. Examples of cancers predisposing neutropenic patients to risk of fungal infections were added as a Note.	07/26/2023
Update	Added the new indication of adults and pediatric patients ≥ 6 years of age who weigh ≥ 16 kg. No criteria changes.	01/10/2024
Annual Revision	No criteria changes.	07/31/2024
Annual Revision	**Aspergillus Infection – Treatment**: The duration of approval was changed to 6 months. Previously it was 3 months. **Mucormycosis – Treatment**: The duration of approval was changed to 6 months. Previously it was 3 months. **Esophageal Candidiasis (Systemic) in a Patient with Human Immunodeficiency Virus:** Updated to as written. Previously this condition of approval was titled "Candidiasis (Systemic) in a Patient with Human Immunodeficiency Virus." **Coccidioidomycosis in a Patient with Human Immunodeficiency Virus – Treatment**: New condition of approval was added to Other Uses with Supportive Evidence. **Cryptococcal Meningitis – Treatment:** New condition of approval was added to Other Uses with Supportive Evidence.	07/16/2025

Selected Revision	**Esophageal Candidiasis in a Patient with Human Immunodeficiency Virus**: Updated to as written. Previously this condition of approval was titled "Esophageal Candidiasis (Systemic) in a Patient with Human Immunodeficiency Virus." **Fungal Infection (Systemic) in a Patient with Human Immunodeficiency Virus**: New condition of approval was added to the Other Uses with Supportive Evidence.	08/06/2025