PRIOR AUTHORIZATION POLICY

POLICY: Antifungals – Posaconazole (Oral) Prior Authorization Policy
- Noxafil® (posaconazole delayed-release tablets [generic], oral suspension [generic], PowderMix for delayed-release oral suspension – Merck)

REVIEW DATE: 07/16/2025

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

Posaconazole, an azole antifungal, is indicated for the following uses:[1]

- **Prophylaxis of invasive *Aspergillus* and *Candida* infections** in patients who are at high risk of developing these infections due to being severely immunocompromised, such as hematopoietic stem cell transplant (HSCT) recipients with graft-versus-host disease (GVHD) or those with hematologic malignancies with prolonged neutropenia from chemotherapy: delayed-release tablets, in adults and pediatric patients ≥ 2 years of age who weigh > 40 kg; oral suspension, in adults and pediatric patients ≥ 13 years of age; Noxafil PowderMix for delayed-release oral suspension, in pediatric patients ≥ 2 years of age who weigh ≤ 40 kg.
- **Treatment of invasive aspergillosis** in adults and pediatric patients ≥ 13 years of age (delayed-release tablets).

- **Treatment of oropharyngeal candidiasis** including oropharyngeal candidiasis refractory to itraconazole and/or fluconazole, in patients ≥ 13 years of age (oral suspension).

The duration of posaconazole therapy is varied. In a pivotal study, where posaconazole oral suspension was compared with fluconazole capsules as prophylaxis for the prevention of invasive fungal infections in allogeneic HSCT recipients with GVHD, the mean duration of posaconazole therapy was 80 days.[1] The recommended total duration of therapy for the treatment of invasive aspergillosis is 6 to 12 weeks. The duration of therapy for other indications varies and is based on recovery from neutropenia, degree of immunosuppression, and severity of underlying disease and clinical response.

Guidelines

The Infectious Diseases Society of America (IDSA) guidelines for aspergillosis (2016) recommend posaconazole for treatment and prophylaxis of invasive aspergillosis.[2] The IDSA guidelines for candidiasis (2016) and the National Comprehensive Cancer Network (NCCN) Guidelines for the Prevention and Treatment of Cancer-Related Infections (version 1.2025 – June 20, 2025) note posaconazole as one of the drugs of choice for the treatment of fluconazole-refractory oropharyngeal candidiasis.[3,5] The IDSA notes posaconazole as having high-quality evidence for prophylaxis of candidiasis.

NCCN notes posaconazole is active against *Candida* and *Aspergillus* species, some *Mucorales spp*, some of the rarer molds, and against dimorphic fungi and *C. neoformans*. Posaconazole is noted 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. Posaconazole 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. NCCN also notes posaconazole as a treatment option for the treatment of the following infections: mouth and esophageal infections (e.g., oral thrush) refractory to fluconazole; invasive fusariosis; *Scedosporium* infections; and maintenance treatment of mucormycosis.[5] In addition, posaconazole is a treatment option for patients with invasive, refractory infections who have intolerance to amphotericin B formulations.

The guidelines for prevention and treatment of opportunistic infections in adults and adolescents with human immunodeficiency virus (HIV) infections (last updated April 2025) note posaconazole as an option for treatment of patients with coccidioidomycosis, or histoplasmosis; and as chronic suppressive treatment of esophageal candidiasis.[4]

Other Uses with Supportive Evidence

The global guideline for the diagnosis and management of cryptococcosis (2024) note posaconazole as an alternative treatment option for patients with cryptococcal

meningitis.[6] This is a moderate strength recommendation as posaconazole and other triazole drugs have not been formally studied in cryptococcosis.

The global guideline for the diagnosis and management of mucormycosis (2019) also recommends posaconazole as an alternative treatment option for mucormycosis.[7] Duration of therapy ranges from 1 week to almost 3 years, with a mean duration of approximately 6 months.

POLICY STATEMENT

Prior Authorization is recommended for prescription benefit coverage of Noxafil/posaconazole (oral). 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.

- **Noxafil® (posaconazole delayed-release tablets [generic], oral suspension [generic], PowderMix for delayed-release oral suspension - Merck)**

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 – Prophylaxis.** Approve for 6 months.

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

3. ***Candida* Infection (Systemic) – Prophylaxis.** Approve for 6 months.

4. **Oropharyngeal Candidiasis – Treatment.** Approve for 3 months.

Other Uses with Supportive Evidence

5. **Esophageal Candidiasis in a Patient with Human Immunodeficiency Virus (HIV) Infection – Chronic Suppressive Treatment**. Approve for 6 months.

6. **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.

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

8. **Fungal Infection (Systemic) in a Patient with Human Immunodeficiency Virus Infection – Treatment.** Approve for 6 months.

9. **Fusariosis, Invasive – Treatment.** Approve for 3 months.

10. **Mouth and Esophageal Infection (Refractory to Other Azole Antifungals) – Treatment.** Approve for 3 months.

11. **Mucormycosis – Maintenance Treatment.** Approve for 12 months.

12. ***Scedosporium* Infection – Treatment.** Approve for 3 months.

13. **Fungal Infection (Systemic) that is Susceptible to Posaconazole – Treatment.** Approve for 3 months.

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

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

CONDITIONS NOT COVERED

- **Noxafil® (posaconazole delayed-release tablets [generic], oral suspension [generic], PowderMix for delayed-release oral suspension - Merck)**

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

REFERENCES

1. Noxafil® intravenous infusion, delayed-release tablets, oral suspension, and delayed-release oral suspension [prescribing information]. Whitehouse Station, NJ: Merck; September 2024
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. Pappas PG, Kauffman CA, Andes DR, et al. Clinical practice guidelines for the management of candidiasis: 2016 update by the Infectious Diseases Society of America. *Clin Infect Dis*. 2016;62(4):e1-50.
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 July 9, 2024. Accessed on July 25, 2024.
5. 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.
6. 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.

HISTORY

Type of Revision	Summary of Changes	Review Date
Annual Revision	**Policy name change:** from Antifungals – Noxafil (Oral) PA to Antifungals – Posaconazole (Oral) PA. **Fungal Infection in a Patient with Human Immunodeficiency Virus (HIV) Infection (e.g., Histoplasmosis, Coccidioidomycosis) – Treatment:** The examples, histoplasmosis and coccidioidomycosis were removed. **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 National Comprehensive Cancer Network (NCCN) guidelines. Examples of cancers predisposing neutropenic patients to risk of fungal infections were added as a Note.	07/26/2023
Annual Revision	No criteria changes.	07/31/2024
Annual Revision	**Aspergillus Infection – Treatment.** The duration of approval for this condition was changed to 6 months. Previously, it was 3 months. **Mucormycosis – Maintenance Treatment**: The duration of approval for this condition was changed to 12 months. Previously, it was 6 months. **Cryptococcal Meningitis – Treatment**: New condition of approval was added to Other Uses with Supportive Evidence. **Fungal Infection (Systemic) in a Patient with Human Immunodeficiency Virus Infection – Treatment**: The duration of approval for this condition was changed to 6 months. Previously it was 3 months.	07/16/2025