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: 07/26/2023

INSTRUCTIONS FOR USE

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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 patients ≥ 2 years of age who weigh > 40 kg; oral suspension, in 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 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]

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 1.2023 – June 28, 2023) 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. 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 June 2023) note posaconazole as an option for treatment of patients with coccidioidomycosis, or histoplasmosis; and as chronic suppressive treatment of esophageal candidiasis.[4]

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 3 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 (HIV) Infection – Treatment.** Approve for 3 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 6 months.

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

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

14. **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 experimental, investigational or unproven for ANY other use(s).

REFERENCES

1. Noxafil® intravenous infusion, delayed-release tablets, oral suspension, and delayed-release oral suspension [prescribing information]. Whitehouse Station, NJ: Merck; January 2022.
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 June 14, 2023. Accessed on July 14, 2023.
5. The NCCN Prevention and Treatment of Cancer-Related Infections Clinical Practice Guidelines in Oncology (version 1.2023 – June 28, 2023). ©2023 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on July 14, 2023.

HISTORY

Type of Revision	Summary of Changes	Review Date
Annual Revision	***Aspergillus* Infection – Treatment:** This indication was moved from Other Uses with Supportive Evidence to FDA-Approved Indications; posaconazole delayed-release tablet is now indicated for this condition. **Esophageal Candidiasis in a Patient with Human Immunodeficiency Virus (HIV) Infection – Chronic Suppressive Treatment:** This indication was added to the Other Uses with Supportive Evidence section. **Patient is Currently Receiving Noxafil:** This was revised from "Patient Currently Receiving Intravenous Noxafil or Oral Noxafil (Tablets or Oral Suspension)".	06/29/2022
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 cancer predisposing neutropenic patients to risk of fungal infections were added as a Note.	07/26/2023