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Next Review Date… **11/1/2024**
Coverage Policy Number **IP0536**

Posaconazole PowderMix for Delayed-Release Oral Suspension for Individual and Family Plans

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Related Coverage Resources

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. 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.

Overview

This policy supports medical necessity review for posaconazole powder-mix for delayed-release oral suspension (**Noxafil® PowderMix Kit**).

Coverage for posaconazole powder-mix for delayed-release oral suspension (**Noxafil® PowderMix Kit**) varies across plans and requires the use of preferred products in addition to the criteria listed below. Refer to the customer's benefit plan document for coverage details.

Receipt of sample product does not satisfy any criteria requirements for coverage.

Initial Approval Criteria

Posaconazole powder-mix for delayed-release oral suspension (Noxafil PowderMix Kit) is considered medically necessary when the individual meets ONE of the following criteria:

1. Documentation of **BOTH** of the following:
    a. **ONE** of the following:
        i. Inability to swallow oral tablets
        ii. Weight less than or equal to 40 kg
    b. **ONE** of the following:
        i. Treatment or Prophylaxis of *Aspergillus* Infection.
        ii. Prophylaxis for systemic *Candida* Infection.
        iii. Treatment of Oropharyngeal and/or Esophageal Candidiasis.
        iv. Prophylaxis for systemic Fungal Infection in an individual with Cancer and Neutropenia.
        v. Prophylaxis for systemic Fungal Infection in an individual with Graft-versus-Host Disease.
        vi. Treatment of systemic Fungal Infection in an individual with Human Immunodeficiency Virus (HIV) Infection (examples, Histoplasmosis, Coccidioidomycosis).
        vii. Treatment of chronic suppressive Esophageal Candidiasis in an individual with HIV Infection.
        viii. Treatment of systemic Fungal Infection that is Susceptible to Noxafil.
        ix. Treatment of invasive Fusariosis.
        x. Maintenance treatment of Mucormycosis.
        xi. Treatment of *Scedosporium* Infection.

2. Continuation of therapy for individual currently receiving posaconazole powder-mix delayed-release oral suspension (Noxafil PowderMix Kit) to complete a course of therapy.

When coverage is available and medically necessary, the dosage, frequency, duration of therapy, and site of care should be reasonable, clinically appropriate, and supported by evidence-based literature and adjusted based upon severity, alternative available treatments, and previous response to therapy.

Continuation of Therapy

Continuation of posaconazole powder-mix delayed-release oral suspension (Noxafil PowderMix Kit) is considered medically necessary for **ALL** covered diagnoses when initial criteria are met AND beneficial response is demonstrated.

Authorization Duration

Aspergillus Infection – prophylaxis approval up to 6 months
Aspergillus Infection – treatment approval up to 3 months
Candida Infection (Systemic) – prophylaxis approval up to 6 months
Oropharyngeal Candidiasis – treatment approval up to 3 months
Fungal Infection (Systemic) in an individual with Cancer and Neutropenia – prophylaxis approval up to 6 months
Fungal Infection (Systemic) in an individual with Graft-versus-Host Disease – prophylaxis approval up to 6 months
Fungal Infection (Systemic) in an individual with Human Immunodeficiency Virus (HIV) Infection (examples, Histoplasmosis, Coccidioidomycosis) – treatment approval up to 3 months
Esophageal Candidiasis in an individual with HIV Infection – chronic suppressive treatment approval up to 6 months
Fungal Infection (Systemic) that is Susceptible to Noxafil – treatment approval up to 3 months
Fusariosis, Invasive – treatment approval up to 3 months
Mouth and Esophageal Infection (Refractory to Other Azole Antifungals) – treatment approval up to 3 months
Mucormycosis – maintenance treatment approval up to 6 months
Scedosporium Infection – treatment approval up to 3 months
Individual currently receiving Posaconazole powder-mix delayed-release oral suspension (Noxafil® PowderMix Kit) approval up to 3 months to complete course of therapy.

Conditions Not Covered

Any other use is considered experimental, investigational or unproven.

Background

OVERVIEW

Noxafil, 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: posaconazole delayed-release tablets, in patients ≥ 2 years of age who weigh > 40 kg; Noxafil 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: posaconazole delayed-release tablets, in patients ≥ 13 years of age.
- Treatment of oropharyngeal candidiasis including oropharyngeal candidiasis refractory to itraconazole and/or fluconazole: Noxafil oral suspension, in patients ≥ 13 years of age.

The duration of Noxafil therapy is varied. In a pivotal study, where Noxafil 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 Noxafil therapy was 80 days.[1]

GUIDELINES

The Infectious Diseases Society of America (IDSA) guidelines for aspergillosis (2016) recommend Noxafil 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 1.2022 – June 2, 2022) note Noxafil as one of the drugs of choice for the treatment of fluconazole-refractory oropharyngeal candidiasis.[3] NCCN also recommends Noxafil for antifungal prophylaxis in neutropenic patients with acute myeloid leukemia or myelodysplastic syndrome receiving induction or re-induction chemotherapy, patients who are allogeneic HSCT recipients, or patients with significant GVHD receiving immunosuppressive therapy, and patients with chronic severe neutropenia. Treatment should continue until neutropenia is resolved or until resolution of GVHD.[4] NCCN notes that posaconazole has shown activity as a second-line agent against a broad spectrum of invasive fungal infections. The IDSA notes Noxafil as having high-quality evidence for prophylaxis of candidiasis.

The guidelines for prevention and treatment of opportunistic infections in adults and adolescents with human immunodeficiency virus (HIV) infections (last updated April 2022) note Noxafil as an option for treatment of patients with coccidiodomycosis, or histoplasmosis; and as chronic suppressive treatment of esophageal candidiasis.[4]

The NCCN Guidelines for Prevention and Treatment of Cancer-Related Infections (version 1.2022 - June 2, 2022) include Noxafil as one of the antifungal therapies for the following: treatment of mouth and esophageal infections (e.g., oral thrush) refractory to fluconazole; invasive fusariosis; Scedosporium infections; and maintenance treatment of mucormycosis.[5] Noxafil is active against Candida and Aspergillus species, some Mucorales spp, some of the rarer molds, and against dimorphic fungi.

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.