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Section:	Prescription Drugs	**Effective Date:**	January 1, 2026
Subsection:	Anti-infective Agents	**Original Policy Date:**	July 26, 2019
Subject:	Noxafil	**Page:**	1 of 5

Last Review Date: December 12, 2025

Noxafil

Description

Noxafil* (posaconazole) delayed-release tablets

Noxafil (posaconazole) oral suspension

Noxafil PowderMix (posaconazole) for delayed-release oral suspension

*Prior authorization for the brand formulation applies only to formulary exceptions due to being a non-covered medication.

Background
Noxafil (posaconazole) blocks the synthesis of ergosterol, which is a vital component of fungal cell membranes, through the inhibition of cytochrome P-450 dependent enzyme lamosterol 14α-demethylase responsible for the conversion of lamosterol to ergosterol in the fungal cell membrane. This results in an accumulation of methylated sterol precursors and a depletion of ergosterol within the cell membrane thus weakening the structure and function of the fungal cell membrane. This may be responsible for the antifungal activity of posaconazole (1).

Regulatory Status
FDA-approved indications: Noxafil is an azole antifungal indicated as follows: (1)

- **Noxafil delayed-release tablets** are indicated for the treatment of invasive aspergillosis in adults and pediatric patients 13 years of age and older.
- Noxafil is indicated for the 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) patients with graft-versus-host disease (GVHD) or those with hematologic malignancies with prolonged neutropenia from chemotherapy as follows:
    - **Noxafil delayed-release tablets:** adults and pediatric patients 2 years of age

and older who weigh greater than 40 kg
    - **Noxafil oral suspension**: adults and pediatric patients 13 years of age and older
    - **Noxafil PowderMix for delayed-release oral suspension**: pediatric patients 2 years of age and older who weigh 40 kg or less
- **Noxafil oral suspension** is also indicated for the treatment of oropharyngeal candidiasis (OPC), including OPC refractory (rOPC) to itraconazole and/or fluconazole in adult and pediatric patients aged 13 years and older.

Off-Label Uses: (2-5)
- Refractory coccidioidomycosis
- Invasive mucormycosis

Noxafil is contraindicated if coadministered with sirolimus, CYP3A4 substrates, HMG-CoA reductase inhibitors primarily metabolized through CYP3A4, or ergot alkaloids (1).

Liver function tests should be evaluated at the start of and during the course of Noxafil therapy. Patient management should include evaluation of hepatic function (particularly liver function tests and bilirubin). Discontinuation of Noxafil must be considered if clinical signs and symptoms consistent with liver disease develop that may be attributable to Noxafil (1).

The safety and effectiveness of Noxafil in pediatric patients less than 2 years of age have not been established (1).

Related policies
Cresemba, Itraconazole, Ketoconazole, Vfend

Policy

This policy statement applies to clinical review performed for pre-service (Prior Approval, Precertification, Advanced Benefit Determination, etc.) and/or post-service claims.

Noxafil may be considered **medically necessary** if the conditions indicated below are met.

Noxafil may be considered **investigational** for all other indications.

Prior-Approval Requirements

Diagnoses

Patient must have **ONE** of the following:

1. Prophylaxis of invasive *Aspergillus* infection (aspergillosis) or invasive *Candida* infection (candidiasis) in a patient who is severely immunocompromised (e.g., post HSCT with GVHD, hematologic malignancies with prolonged neutropenia) **AND ONE** of the following:
   a. **Noxafil PowderMix:** 2 years of age or older **AND** weigh 40kg or less
   b. **Noxafil delayed-release tablets:** 2 years of age or older **AND** weigh > 40kg
   c. **Noxafil oral suspension:** 13 years of age or older

2. Treatment of refractory coccidioidomycosis **OR** invasive mucormycosis **AND ONE** of the following:
   a. **Noxafil PowderMix:** 2 years of age or older **AND** weigh 40kg or less
   b. **Noxafil delayed-release tablets:** 2 years of age or older **AND** weigh > 40kg
   c. **Noxafil oral suspension:** 13 years of age or older

Noxafil oral suspension ONLY:

1. Treatment of oropharyngeal candidiasis in patients 13 years of age or older

Noxafil delayed-release tablets ONLY:

1. Treatment of invasive *Aspergillus* infection (aspergillosis) in patients 13 years of age or older

AND ALL of the following for **ALL** formulations and indications:

a. Liver function tests will be monitored during therapy with Noxafil
b. Prescriber agrees to monitor for QTc prolongation

Prior – Approval *Renewal* Requirements

Same as above

Policy Guidelines

Pre - PA Allowance

None

Prior - Approval Limits

Duration:

- 3 months for **treatment** of invasive *Aspergillus* infection (aspergillosis)*
- 6 months for **treatment** of oropharyngeal candidiasis
- 12 months for **prophylaxis** of invasive *Aspergillus* infection (aspergillosis)*
- 12 months for **prophylaxis** of *Candida* infection (candidiasis)*
- 12 months for **treatment** of refractory coccidioidomycosis or invasive mucormycosis*

*__**with an approved FE only**__ for Noxafil **brand** 100 mg delayed-release tablet

Prior – Approval *Renewal* Limits

Same as above

Rationale

Summary

Noxafil (posaconazole) is a triazole antifungal that blocks the synthesis of ergosterol, which is a vital component of fungal cell membranes. Noxafil formulations are indicated for use in aspergillosis and candidiasis. Studies have also shown that Noxafil can be used off-label in refractory coccidioidomycosis and invasive mucormycosis. Patients on Noxafil should have liver function tests and QTc prolongation monitored. The safety and effectiveness of Noxafil in pediatric patients less than 2 years of age have not been established (1-5).

Prior approval is required to ensure the safe, clinically appropriate, and cost-effective use of Noxafil while maintaining optimal therapeutic outcomes.

References

1. Noxafil [package insert]. Whitehouse Station, NJ: Merch Sharp & Dohme Corp.; October 2024.
2. Galgiani JN, Ampel NM, et. al. *2016 Infectious Diseases Society of America (IDSA)*: Clinical Practice Guideline for the Treatment of Coccidioidomycosis. Clin Infect Dis. 2016 Sep 15;63(6):e112-46.
3. Anstead GM, Corcoran G, et al. Refractory coccidioidomycosis treated with posaconazole. Clin Infect Dis2005; 40:1770–6.
4. Vehreschild JJ, Birtel A, et al. Mucormycosis treated with posaconazole: review of 96 case reports. Crit Rev Microbiol. 2013;39(3): 310-24.
5. Cox GM. Up To Date: Mucormycosis (zygomycosis). Version 53.0. June 15, 2021.

Policy History

Date	Action
July 2019	Addition to PA
September 2019	Annual review
December 2020	Annual review and reference update
June 2021	Added Noxafil PowderMix. Added requirement that patients requesting Noxafil delayed-release tablets for prophylaxis of *Aspergillus* or *Candida* infections must weigh more than 40 kg per new PI. Added new indication for Noxafil delayed-release tablets: the treatment of invasive aspergillosis in adults and pediatric patients 13 years of age and older per new PI.
September 2021	Annual review
December 2021	Annual review and reference update. Addition of off-label indications refractory coccidioidomycosis and invasive mucormycosis per SME
September 2022	Annual review and reference update
December 2022	Annual review
June 2023	Annual review
June 2024	Annual review
June 2025	Annual review and reference update
December 2025	Annual review. Per FEP, Noxafil brand delayed-release tablet requires an FE

Keywords

This policy was approved by the FEP® Pharmacy and Medical Policy Committee on December 12, 2025 and is effective on January 1, 2026.