Pharmacy Policy Bulletin: J-0217 Noxafil (posaconazole) – Commercial and Healthcare Reform	
Number: J-0217	**Category:** Prior Authorization
Line(s) of Business: ☒ Commercial ☒ Healthcare Reform ☐ Medicare	**Benefit(s):** **Commercial:** **Prior Authorization (1.):** **1.** Other Managed Prior Authorization= Yes w/ Prior Authorization **Healthcare Reform:** Not Applicable
Region(s): ☒ All ☐ Delaware ☐ New York ☐ Pennsylvania ☐ West Virginia	**Additional Restriction(s):** None
Version: J-0217-011	**Original Date:** 05/01/2019
Effective Date: 07/18/2025	**Review Date:** 06/25/2025

Drugs Product(s):	• Noxafil (posaconazole) delayed-release tablets • Noxafil (posaconazole) oral suspension • Noxafil (posaconazole) PowderMix for delayed-release oral suspension

FDA-Approved Indication(s):	• Noxafil delayed-release tablets
	  ○ Prophylaxis of invasive *Aspergillus* and *Candida* infections in adult and pediatric patients 2 years of age and older who weigh > 40 kg and 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.
	  ○ Treatment of invasive aspergillosis in adults and pediatric patients 13 years of age and older
	• Noxafil oral suspension
	  ○ Prophylaxis of invasive *Aspergillus* and *Candida* infections in adult and pediatric patients 13 years of age and older who are at high risk of developing these infections due to being severely immunocompromised, such as HSCT recipients with GVHD or those with hematologic malignancies with prolonged neutropenia from chemotherapy.
	  ○ Treatment of oropharyngeal candidiasis (OPC), including OPC refractory (rOPC) to itraconazole and/or fluconazole in adult and pediatric patients aged 13 years and older.
	• Noxafil PowderMix for delayed-release oral suspension
	  ○ Prophylaxis of invasive Aspergillus and Candida infections in pediatric patients 2 years of age and older (who weigh 40 kg or less) who are at high risk of developing these infections due to being severely immunocompromised, such as HSCT recipients with GVHD or those with hematologic malignancies with prolonged neutropenia from chemotherapy.

Background:	• Noxafil is an antifungal that works by blocking the synthesis of ergosterol, a key component of the fungal cell membrane. It inhibits the cytochrome P450 dependent enzyme lanosterol 14α-demethylase, which is responsible for the conversion of lanosterol to ergosterol in the fungal cell membrane. This results in an accumulation of methylated sterol precursors and a decrease in ergosterol within the cell membrane which weakens the structure and function of the fungal cell membrane.
	• According to the National Cancer Comprehensive Cancer Network (NCCN) Guidelines for Prevention and Treatment of Cancer-Related Infections, posaconazole is considered a category 1 treatment for prophylaxis of fungal infections in patients with myelodysplastic syndrome or acute myeloid leukemia who are neutropenic after chemotherapy, and for patients with significant GVHD receiving immunosuppressive therapy. Posaconazole is a category 2B treatment for allogeneic hematopoietic cell transplant.
	• The 2016 Infectious Diseases Society of America Practice Guidelines for the Diagnosis and Management of Aspergillosis recommend primary treatment with voriconazole for treatment of invasive aspergillosis. The NCCN Guidelines for Prevention and Treatment of Cancer-Related infections recommend voriconazole as primary therapy for treatment of invasive aspergillosis (category 1).
	• The 2016 Infectious Diseases Society of America Clinical Practice Guideline for the Management of Candidiasis recommends oral fluconazole for moderate to severe disease. Posaconazole solution is recommended as a second-line agent for fluconazole-refractory disease. According to the NCCN Guidelines for Prevention and Treatment of Cancer-Related Infections, voriconazole, posaconazole, or an echinocandin can be considered for fluconazole-refractory disease.
	• Prescribing considerations:
	  ○ Noxafil (posaconazole) oral suspension is not substitutable with Noxafil delayed-release tablets due to the differences in the dosing of each formulation.
	  ○ Noxafil is metabolized through the cytochrome P450 enzyme system causing drug-drug interactions with other medications metabolized via CYP3A4. Coadministration of the following medications is contraindicated: sirolimus, pimozide, quinidine, HMG-CoA reductase inhibitors primarily metabolized through CYP3A4, and ergot alkaloids
	  ○ Warnings and precautions for Noxafil include: calcineurin-inhibitor toxicity, arrhythmias and QTc prolongation, electrolyte disturbances, hepatic toxicity, concomitant use with midazolam, and vincristine toxicity.

Approval Criteria

I. Initial Authorization

A. *Aspergillus* or *Candida* Infection Prophylaxis (No ICD-10 codes)

When a benefit, coverage of Noxafil (posaconazole) delayed-release tablets, oral suspension, or PowderMix for delayed-release oral suspension may be approved when all of the following criteria are met **(1. and 2.)**:

1. The member meets one (1) of the following **(a., b., or c.)**:

a. If the request is for Noxafil (posaconazole) delayed-release tablets, the member meets all of the following **(i., ii., and iii.)**:
   i. The member is 2 years of age or older.
   ii. The member weighs > 40 kg.
   iii. If the request is for brand Noxafil delayed-release tablets, the member has experienced therapeutic failure or intolerance to generic posaconazole delayed-release tablets.

b. If the request is for Noxafil (posaconazole) oral suspension, the member meets all of the following **(i., ii., and iii.)**:
   i. The member is 13 years of age or older.
   ii. The member is unable to swallow tablets
   iii. If the request is for brand Noxafil oral suspension, the member has experienced therapeutic failure or intolerance to generic posaconazole oral suspension.

c. If the request is for Noxafil PowderMix, the member meets all of the following **(i., ii., and iii.)**:
   i. The member is 2 years or age or older
   ii. The member weighs ≤ 40 kg.
   iii. If the member is 13 years of age or older, the member has experienced therapeutic failure or intolerance to plan-preferred generic posaconazole oral suspension.

2. The member is at high risk of developing invasive Aspergillosis or Candidiasis infection due to being severely immunocompromised (for example, HSCT recipients with GVHD, those with hematologic malignancies with prolonged neutropenia from chemotherapy).

B. Invasive Aspergillosis Infection Treatment (No ICD-10 codes)

When a benefit, coverage of Noxafil (posaconazole) delayed-release tablets may be approved when all of the following criteria are met **(1. through 4.)**:

1. The member is 13 years of age or older.
2. The member has a diagnosis of invasive aspergillosis infection.
3. The member has experienced therapeutic failure, contraindication, or intolerance to voriconazole.
4. If the request is for brand Noxafil delayed-release tablets, the member has experienced therapeutic failure or intolerance to generic posaconazole delayed-release tablets.

C. Oropharyngeal Candidiasis Treatment

When a benefit, coverage of Noxafil oral suspension may be approved when all of the following criteria are met **(1. through 4.)**:

1. The member is 13 years of age or older.
2. The member has a diagnosis of oropharyngeal candidiasis (thrush) (ICD-10: B37.0).
3. The member has experienced therapeutic failure or intolerance to generic fluconazole.
4. If the request is for brand Noxafil oral suspension, the member has experienced therapeutic failure or intolerance to generic posaconazole oral suspension.

II. Reauthorization

When a benefit, reauthorization of Noxafil (posaconazole) may be approved when the following criterion is met **(A.)**:

A. The prescriber attests that the member has experienced positive clinical response to therapy.

III. An exception to some or all of the criteria above may be granted for select members and/or circumstances based on state and/or federal regulations.

Limitations of Coverage

I. Coverage of drug(s) addressed in this policy for disease states outside of the FDA-approved indications should be denied based on the lack of clinical data to support effectiveness and safety in other conditions unless otherwise noted in the approval criteria.
II. For Commercial or HCR members with a closed formulary, a non-formulary product will only be approved if the member meets the criteria for a formulary exception in addition to the criteria outlined within this policy.

Authorization Duration

- Commercial and HCR Plans: If approved, up to a 12 month authorization may be granted.

Automatic Approval Criteria

None

References:

1. Noxafil [package insert]. Whitehouse Station, NJ: Merck & Co., Inc.; October 2024.
2. Pappas PG, Kauffman CA, Andes DR, et al. Clinical Practice Guideline for the Management of Candidiasis: 2016 Update by the Infectious Diseases Society of America. *Clin Infect Dis.* 2016;62(4):e1-e50.
3. 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.
4. National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology: Prevention and Treatment of Cancer-Related Infections Version 3.2024. Available at: https://www.nccn.org/professionals/physician_gls/pdf/infections.pdf. Accessed April 14, 2025.