BlueCross BlueShield Arizona

An Independent Licensee of the Blue Cross Blue Shield Association

PHARMACY COVERAGE GUIDELINE

NOXAFIL® (posaconazole) delayed release tablet
NOXAFIL® (posaconazole) oral suspension
NOXAFIL® (posaconazole) delayed release oral suspension packet
Posaconazole delayed release tablet
Posaconazole oral suspension
Generic Equivalent (if available)

This Pharmacy Coverage Guideline (PCG):
- Provides information about the reasons, basis, and information sources we use for coverage decisions
- Is not an opinion that a drug (collectively "Service") is clinically appropriate or inappropriate for a patient
- Is not a substitute for a provider's judgment (Provider and patient are responsible for all decisions about appropriateness of care)
- Is subject to all provisions e.g. (benefit coverage, limits, and exclusions) in the member's benefit plan; and
- Is subject to change as new information becomes available.

Scope
- This PCG applies to Commercial and Marketplace plans
- This PCG does not apply to the Federal Employee Program, Medicare Advantage, Medicaid or members of out-of-state Blue Cross and/or Blue Shield Plans

Instructions & Guidance
- To determine whether a member is eligible for the Service, read the entire PCG.
- This PCG is used for FDA approved indications including, but not limited to, a diagnosis and/or treatment with dosing, frequency, and duration.
- Use of a drug outside the FDA approved guidelines, refer to the appropriate Off-Label Use policy.
- The "Criteria" section outlines the factors and information we use to decide if the Service is medically necessary as defined in the Member's benefit plan.
- The "Description" section describes the Service.
- The "Definition" section defines certain words, terms or items within the policy and may include tables and charts.
- The "Resources" section lists the information and materials we considered in developing this PCG
- **We do not accept patient use of samples as evidence of an initial course of treatment, justification for continuation of therapy, or evidence of adequate trial and failure.**
- Information about medications that require prior authorization is available at www.azblue.com/pharmacy. You must fully complete the request form and provide chart notes, lab workup and any other supporting documentation. The prescribing provider must sign the form. Fax the form to BCBSAZ Pharmacy Management at (602) 864-3126 or email it to Pharmacyprecert@azblue.com.

Criteria:

- **Criteria for initial therapy:** Noxafil (posaconazole) delayed release tablet, Noxafil (posaconazole) oral suspension, Noxafil (posaconazole) delayed release oral suspension packet, posaconazole delayed release tablet, posaconazole oral suspension, and/or generic equivalent (if available) are considered ***medically necessary*** and will be approved when **ALL** of the following criteria are met:

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1. Prescriber is a physician specializing in the patient's diagnosis or is in consultation with an Infectious Disease, HIV/AIDS specialist, Hematologist, Oncologist, or Transplant Surgeon depending upon indication or use

2. Individual's age is consistent with FDA label for product, indication, and formulation and is **ONE** of the following:
    a. Treatment of invasive aspergillosis with delayed release tablet: *13 years of age or older*
    b. Treatment of oropharyngeal candidiasis (OPC), including refractory oropharyngeal candidiasis (rOPC) with oral suspension: *13 years of age or older*
    c. Prophylaxis of invasive aspergillosis or candida infection with:
        i. Delayed release tablet: *2 years of age or older who weigh **greater than 40 kg***
        ii. Oral suspension: *13 years of age or older*
        iii. Delayed release oral suspension: *2 years of age and older who **weigh 40 kg or less***

3. Individual has a confirmed diagnosis of **ONE** of the following (confirmed by culture, skin or blood tests, or biopsy):
    a. **Prophylaxis** of invasive aspergillus infection in a patient who is at high risk of developing this infection due to being severely immunocompromised, such as hematopoietic stem cell transplant (HSCT) recipient with graft-versus-host disease (GVHD) or patient with hematologic malignancies with prolonged neutropenia from chemotherapy

    b. **Prophylaxis** of candida infections in a patient who is at high risk of developing this infection due to being severely immunocompromised, such as hematopoietic stem cell transplant (HSCT) recipient with graft-versus-host disease (GVHD) or patient with hematologic malignancies with prolonged neutropenia from chemotherapy

    c. **Treatment** of invasive aspergillus refractory or intolerant to voriconazole or liposomal amphotericin

    d. **Treatment** of oropharyngeal candidiasis (OPC), including oropharyngeal candidiasis refractory (rOPC) to fluconazole (using daily dose of 400 mg) and itraconazole

    e. **Treatment** of esophageal candidiasis refractory to fluconazole (using a maximum dose of 800 mg daily) and itraconazole therapy

4. Individual has received and completed **ALL** the following **baseline tests** before initiation of treatment and with continued monitoring of the individual as clinically appropriate:
    a. Serum potassium, magnesium, and calcium levels are within the normal range
    b. For Noxafil (posaconazole) delayed release oral suspension use in a pediatric patient there is an assessment of Hereditary Fructose Intolerance
    c. Liver function tests and bilirubin

5. For **brand Noxafil delayed release tablet**: Individual has failure, contraindication per FDA label, intolerance, or is not a candidate for **generic posaconazole delayed release tablet**

6. For **brand Noxafil oral suspension**: Individual has failure, contraindication per FDA label, intolerance, or is not a candidate for **generic posaconazole oral suspension**

7. **If available**: Individual has failure after adequate trial, contraindication per FDA label, intolerance, or not a candidate for generic **equivalent of Noxafil PowderMix for delayed-release oral suspension** [Note: Failure, contraindication or intolerance to the generic should be reported to the FDA] (see Definitions section)

8. There are **NO** FDA-label contraindications such as:
    a. Hypersensitivity to any other azole antifungal agent
    b. Co-administration with sirolimus, ergot alkaloids (e.g., ergotamine, dihydroergotamine), HMG-CoA reductase inhibitors that are primarily metabolized through CYP3A4 (e.g., atorvastatin, lovastatin, simvastatin), or CYP3A4 substrates that prolong the QT interval (e.g., pimozide, quinidine)
    c. Venetoclax: in patients with chronic lymphocytic leukemia (CLL) or small lymphocytic lymphoma (SLL) at initiation and during the ramp up phase
    d. For delayed release oral suspension: known or suspected hereditary fructose intolerance (HFI)

Initial approval duration: 6 months

- **Criteria for continuation of coverage (renewal request):** Noxafil (posaconazole) delayed release tablet, Noxafil (posaconazole) oral suspension, Noxafil (posaconazole) delayed release oral suspension packet, posaconazole delayed release tablet, posaconazole oral suspension, and/or generic equivalent (if available) are considered ***medically necessary*** and will be approved when **ALL** of the following criteria are met **(samples are not considered for continuation of therapy)**:

1. Individual continues to be seen by a physician specializing in the patient's diagnosis or is in consultation with an Infectious Disease, HIV/AIDS specialist, Hematologist, Oncologist, or Transplant Surgeon depending upon indication or use

2. Individual's condition has responded while on therapy with response defined as **TWO** of the following:
    a. Documented evidence of efficacy, disease stability and/or improvement
    b. When used **for treatment of invasive aspergillosis**
        i. Survival with a complete or survival with a partial clinical, radiologic or mycologic improvement
    c. When used **for prophylaxis of aspergillosis or candida**
        i. A reduction in occurrence of a proven or probable breakthrough invasive fungal infection
        ii. Reduced need for use of systemic antifungal therapy
    d. When used for **treatment of oropharyngeal or esophageal candida infections**

i. Complete or partial resolution of all ulcers and/or plaques and symptoms
ii. A reduction in recurrence of signs or symptoms after initial cure or improvement
iii. Absence of colony forming units in quantitative culture

3. Individual has been adherent with the medication

4. For **brand Noxafil delayed release tablet**: Individual has failure, contraindication per FDA label, intolerance, or is not a candidate for **generic posaconazole delayed release tablet**

5. For **brand Noxafil oral suspension**: Individual has failure, contraindication per FDA label, intolerance, or is not a candidate for **generic posaconazole oral suspension**

6. **If available**: Individual has failure after adequate trial, contraindication per FDA label, intolerance, or not a candidate for **generic equivalent of Noxafil PowderMix for delayed-release oral suspension** [Note: Failure, contraindication or intolerance to the generic should be reported to the FDA] (see Definitions section)

7. Individual has not developed any contraindications or other significant adverse drug effects that may exclude continued use as follows:
   a. Contraindications as listed in the criteria for initial therapy section
   b. Significant adverse effect such as:
      i. Life-threatening cardiac arrhythmias
      ii. Torsades de pointe
      iii. QT interval prolongation
      iv. Hepatotoxicity

Renewal duration: 12 months

- Criteria for a request for non-FDA use or indication, treatment with dosing, frequency, or duration outside the FDA-approved dosing, frequency, and duration, refer to one of the following Pharmacy Coverage Guideline:

1. **Off-Label Use of Non-Cancer Medications**

2. **Off-Label Use of Cancer Medications**

Description:

Noxafil (posaconazole) is an azole antifungal agent. It is available as delayed-release tablets, an oral suspension, a delayed release oral suspension, and an injection for intravenous use. Noxafil (posaconazole) oral suspension is not substitutable with delayed-release tablets or delayed oral suspension due to the differences in the dosing of

each formulation. Posaconazole has been shown to be active against most isolates both *in vivo* and in clinical infections *Aspergillus species* and *Candida species.*

Noxafil (posaconazole) delayed-release tablet or oral suspension or delayed release oral suspension is indicated for 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 transplantation (HSCT) recipients with graft versus host disease (GVHD) or those with hematologic malignancies with prolonged neutropenia from chemotherapy. Noxafil (posaconazole) delayed-release tablet is indicated for the treatment of invasive aspergillosis. Noxafil (posaconazole) oral suspension is indicated for the treatment of oropharyngeal candidiasis (OPC), including OPC refractory (rOPC) to itraconazole and/or fluconazole.

Generic Posaconazole delayed release tablet is indicated for the treatment of invasive aspergillosis and 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 transplantation (HSCT) recipients with graft versus host disease (GVHD) or those with hematologic malignancies with prolonged neutropenia from chemotherapy.

Posaconazole oral suspension is indicated for the treatment of oropharyngeal candidiasis, including oropharyngeal candidiasis refractory to itraconazole and/or fluconazole in adults and pediatric patients 13 years of age and older. It is also 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) recipients with graft-versus-host disease (GVHD) or those with hematologic malignancies with prolonged neutropenia from chemotherapy.

The duration of prophylaxis with posaconazole for invasive *Aspergillus* and *Candida* infections is based on recovery from neutropenia or immune suppression. The duration of treatment of OPC with posaconazole is for a total of 14 days while the duration of treatment of rOPC is based on the severity of the patient's underlying disease and clinical response.

Posaconazole blocks the synthesis of ergosterol, a key component of the fungal cell membrane, through the inhibition of cytochrome P-450 dependent enzyme lanosterol 14α-demethylase responsible for the conversion of lanosterol 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.

Definitions:

U.S. Food and Drug Administration (FDA) MedWatch Forms for FDA Safety Reporting
MedWatch Forms for FDA Safety Reporting | FDA

Noxafil is an azole antifungal indicated as follows:

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- ***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) recipients 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 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*

Noxafil oral suspension is not substitutable with **Noxafil delayed-release tablets** or **Noxafil PowderMix for delayed-release oral suspension** due to the differences in the dosing of each formulation.

Posaconazole is an azole antifungal indicated as follows:

- ***Posaconazole delayed-release tablets*** are indicated for the treatment of invasive aspergillosis in adults and pediatric patients *13 years of age and older*
- ***Posaconazole*** 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) recipients with graft-versus-host disease (GVHD) or those with hematologic malignancies with prolonged neutropenia from chemotherapy as follows:
  - ***Posaconazole delayed-release tablets***: adults and pediatric patients *2 years of age and older* who weigh greater than 40 kg
  - ***Posaconazole oral suspension***: adults and pediatric patients *13 years of age and older*
- ***Posaconazole oral suspension*** is 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*

Posaconazole oral suspension is not substitutable with **Posaconazole delayed-release tablets** or **Noxafil PowderMix for delayed-release oral suspension** due to the differences in the dosing of each formulation.

Resources:

Noxafil (posaconazole) suspension, tablet, solution, powder for suspension product information, revised by Merck Sharp & Dohme LLC. 10-2024, at DailyMed http://dailymed.nlm.nih.gov. Accessed June 27, 2025.

Posaconazole delayed release tablet, revised by Camber Pharmaceutical, Inc. 01-2022. Available at DailyMed http://dailymed.nlm.nih.gov. Accessed June 27, 2025.

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Posaconazole suspension product information, revised by Hikma Pharmaceuticals USA, Inc. 12-2024. Available at DailyMed http://dailymed.nlm.nih.gov. Accessed June 27, 2025.

Patterson TF. Treatment and prevention of invasive aspergillosis. In: UpToDate, Kauffman CA, White N (Eds), UpToDate, Waltham MA.: UpToDate Inc. Available at http://uptodate.com. Literature current through July 2025. Topic last updated March 03, 2025. Accessed August 20, 2025.

Kosmidis C. Chronic pulmonary aspergillosis: Treatment. In: UpToDate, Kauffman CA, White N (Eds), UpToDate, Waltham MA.: UpToDate Inc. Available at http://uptodate.com. Literature current through July 2024. Topic last updated March 12, 2025. Accessed August 20, 2025.

Kauffman CA, Vazquez JA. Esophageal candidiasis in adults. In: UpToDate, Baddley JW, Bogorodskaya M (Eds), UpToDate, Waltham MA.: UpToDate Inc. Available at http://uptodate.com. Literature current through July 2025. Topic last updated May 30, 2025. Accessed August 20, 2025.

Roifman CM. Chronic mucotaneous candidiasis. In: UpToDate, Orange JS, TePas E (Eds), UpToDate, Waltham MA.: UpToDate Inc. Available at http://uptodate.com. Literature current through July 2025. Topic last updated September 04, 2024. Accessed August 20, 2025.

Kauffman CA, Vazquez JA. Oropharyngeal candidiasis in adults. In: UpToDate, Baddley JW, Bogorodskaya M (Eds), UpToDate, Waltham MA.: UpToDate Inc. Available at http://uptodate.com. Literature current through July 2025. Topic last updated May 30, 2025. Accessed August 20, 2025.

Vazques JA. Management of candidemia and invasive candidiasis in adults. In: UpToDate, Kauffman CA, Hall KK (Eds), UpToDate, Waltham MA.: UpToDate Inc. Available at http://uptodate.com. Literature current through July 2025. Topic last updated December 16, 2024. Accessed August 20, 2025.