PHARMACY COVERAGE GUIDELINES
SECTION: DRUGS

ORIGINAL EFFECTIVE DATE: 11/21/2019
LAST REVIEW DATE: 11/18/2021
LAST CRITERIA REVISION DATE: 11/18/2021
ARCHIVE DATE:

NOXAFIL® (posaconazole) delayed release tablet
NOXAFIL® (posaconazole) oral suspension
NOXAFIL® PowderMix (posaconazole) delayed release oral suspension
Posaconazole delayed release tablet

Coverage for services, procedures, medical devices and drugs are dependent upon benefit eligibility as outlined in the member's specific benefit plan. This Pharmacy Coverage Guideline must be read in its entirety to determine coverage eligibility, if any.

This Pharmacy Coverage Guideline provides information related to coverage determinations only and does not imply that a service or treatment is clinically appropriate or inappropriate. The provider and the member are responsible for all decisions regarding the appropriateness of care. Providers should provide BCBSAZ complete medical rationale when requesting any exceptions to these guidelines.

The section identified as "Description" defines or describes a service, procedure, medical device or drug and is in no way intended as a statement of medical necessity and/or coverage.

The section identified as "Criteria" defines criteria to determine whether a service, procedure, medical device or drug is considered medically necessary or experimental or investigational.

State or federal mandates, e.g., FEP program, may dictate that any drug, device or biological product approved by the U.S. Food and Drug Administration (FDA) may not be considered experimental or investigational and thus the drug, device or biological product may be assessed only on the basis of medical necessity.

Pharmacy Coverage Guidelines are subject to change as new information becomes available.

For purposes of this Pharmacy Coverage Guideline, the terms "experimental" and "investigational" are considered to be interchangeable.

This Pharmacy Coverage Guideline does not apply to FEP or other states' Blues Plans.

Information about medications that require precertification is available at www.azblue.com/pharmacy.

Some large (100+) benefit plan groups may customize certain benefits, including adding or deleting precertification requirements.

All applicable benefit plan provisions apply, e.g., waiting periods, limitations, exclusions, waivers and benefit maximums.

Precertification for medication(s) or product(s) indicated in this guideline requires completion of the request form in its entirety with the chart notes as documentation. **All requested data must be provided.** Once completed the form must be signed by the prescribing provider and faxed back to BCBSAZ Pharmacy Management at (602)

PHARMACY COVERAGE GUIDELINES
SECTION: DRUGS

ORIGINAL EFFECTIVE DATE: 11/21/2019
LAST REVIEW DATE: 11/18/2021
LAST CRITERIA REVISION DATE: 11/18/2021
ARCHIVE DATE:

NOXAFIL® (posaconazole) delayed release tablet
NOXAFIL® (posaconazole) oral suspension
NOXAFIL® PowderMix (posaconazole) delayed release oral suspension
Posaconazole delayed release tablet

864-3126 or emailed to Pharmacyprecert@azblue.com. **Incomplete forms or forms without the chart notes will be returned.**

Criteria:

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

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 age is consistent with FDA label for product and indication and is one of the following:
    a. Treatment of invasive aspergillosis with delayed release tablet: 13 years of age or older

    b. 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. Delayed release oral suspension: 2 years of age or older who weigh 40 kg or less
        iii. Oral suspension: 13 years of age or older

    c. Treatment of oropharyngeal candidiasis (OPC), including refractory oropharyngeal candidiasis (rOPC) with oral suspension: 13 years of age or older

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

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

    b. Candida infection:
        i. Prophylaxis of candida infections in patients who are at high risk of developing this infection due to being severely immunocompromised, such as hematopoietic stem cell transplant (HSCT) recipients with graft-versus-host disease (GVHD) or patients with hematologic malignancies with prolonged neutropenia from chemotherapy

ii. Treatment of oropharyngeal candidiasis (OPC), including oropharyngeal candidiasis refractory (rOPC) to fluconazole and itraconazole

iii. Treatment of esophageal candidiasis refractory to fluconazole (using 800 mg daily) and itraconazole therapy

4. For brand Noxafil delayed release tablet: Individual has failure, contraindication per FDA label, or intolerance to generic posaconazole delayed release tablet

5. 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. For delayed release oral suspension: known or suspected hereditary fructose intolerance (HFI)

6. There are no significant interacting drugs

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 is considered ***medically necessary*** and will be approved when **ALL** of the following criteria are met:

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 responded while on therapy
   a. Response is defined as:
      i. No evidence of disease progression
      ii. Documented evidence of efficacy, disease stability and/or improvement

3. Individual has been adherent with the medication

4. Individual has not developed any contraindications or other significant adverse drug effects that may exclude continued use
   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

5. There are no significant interacting drugs

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 a Non-cancer Medications**

2. **Off-Label Use of a Cancer Medication for the Treatment of Cancer without a Specific Coverage Guideline**

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.

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.

Resources:

Noxafil (posaconazole) product information, revised by Merck Sharp & Dohme Corp. 07-2021, at DailyMed http://dailymed.nlm.nih.gov. Accessed September 08, 2021.

Posaconazole product information, revised by Par Pharmaceutical Inc. 07-2021. Available at DailyMed http://dailymed.nlm.nih.gov. Accessed September 08, 2021.

Patterson TF. Treatment and prevention of invasive aspergillosis. In: UpToDate, Kauffman CA, Bond S (Eds), UpToDate, Waltham MA.: UpToDate Inc. Available at http://uptodate.com. Accessed September 08, 2021.

Denning DW. Treatment of chronic pulmonary aspergillosis. In: UpToDate, Kauffman CA, Bond S (Eds), UpToDate, Waltham MA.: UpToDate Inc. Available at http://uptodate.com. Accessed September 98, 2021.

Kauffman CA. Esophageal candidiasis in adults. In: UpToDate, Marr KA, Bogorodskaya M (Eds), UpToDate, Waltham MA.: UpToDate Inc. Available at http://uptodate.com. Accessed September 08, 2021.

Kauffman CA. Oropharyngeal candidiasis in adults. In: UpToDate, Marr KA, Bogorodskaya M (Eds), UpToDate, Waltham MA.: UpToDate Inc. Available at http://uptodate.com. Accessed September 08, 2021.

Kauffman CA. Management of candidemia and invasive candidiasis in adults. In: UpToDate, Marr KA, Baron EL (Eds), UpToDate, Waltham MA.: UpToDate Inc. Available at http://uptodate.com. Accessed September 08, 2021.