BlueCross BlueShield of Arizona
An Independent Licensee of the Blue Cross and Blue Shield Association

PHARMACY COVERAGE GUIDELINES
SECTION: DRUGS

ORIGINAL EFFECTIVE DATE: 11/21/19
LAST REVIEW DATE: 11/21/19
LAST CRITERIA REVISION DATE:
ARCHIVE DATE:

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

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

PHARMACY COVERAGE GUIDELINES
SECTION: DRUGS

ORIGINAL EFFECTIVE DATE: 11/21/19
LAST REVIEW DATE: 11/21/19
LAST CRITERIA REVISION DATE:
ARCHIVE DATE:

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

Criteria:

- **Criteria for initial therapy:** Noxafil (posaconazole) delayed release tablet or Noxafil (posaconazole) 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 is 13 years of age or older

  3. A confirmed diagnosis of **ONE** of the following: (confirmed by culture, skin or blood tests, or biopsy)
     - Invasive aspergillosis
       - 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
       - Treatment of invasive aspergillus refractory or intolerant of conventional therapy
     - Candida infection:
       - 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
       - Treatment of oropharyngeal candidiasis (OPC), including oropharyngeal candidiasis refractory (rOPC) to itraconazole and/or fluconazole
       - Treatment of esophageal candidiasis refractory to conventional therapy
     - Treatment of non-meningeal & meningeal infections of coccidioidomycosis refractory to conventional therapy
     - Treatment of non-immunosuppressed pulmonary cryptococcal infections
     - As salvage and step-down therapy for mucormycosis

  4. For brand Noxafil: Individual has failure, intolerance, or contraindication to generic Noxafil

  5. **ALL** of the following baseline tests have been completed before initiation of treatment with continued monitoring as clinically appropriate:

- Liver function tests
- Comprehensive metabolic panel
- If present, correction of hypokalemia, hypomagnesemia, and hypocalcemia
- Complete blood count

6. There are **NO** contraindications
   - Contraindications include:
     - Hypersensitivity to posaconazole, other azole antifungal agents, or any component of the formulation
     - 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)

Initial approval duration: 6 months

- **Criteria for continuation of coverage (renewal request):** Noxafil (posaconazole) delayed release tablet or Noxafil (posaconazole) 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
   - Response is defined as:
     - No evidence of disease progression
     - 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 level 4 adverse drug effects that may exclude continued use
   - Contraindications as listed in the criteria for initial therapy section
   - Significant adverse effect such as:
     - Life-threatening cardiac arrhythmias
     - Torsades de pointe
     - QT interval prolongation
     - Hepatotoxicity

5. There are no significant interacting drugs

Renewal duration: 12 months

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

Description:

Noxafil (posaconazole) is an azole antifungal agent. It is available as delayed-release tablets and an oral suspension. Noxafil (posaconazole) delayed-release tablets and oral suspension are not interchangeable 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 tablets or 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) oral suspension is indicated for the treatment of oropharyngeal candidiasis (OPC), including OPC refractory (rOPC) to itraconazole and/or fluconazole.

The duration of prophylaxis with Noxafil (posaconazole) for invasive *Aspergillus* and *Candida* infections is based on recovery from neutropenia or immune suppression. The duration of treatment of OPC with Noxafil (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.

Off-label guideline recommended uses include: treatment of invasive Aspergillus for refractory or intolerant of conventional therapy; treatment of esophageal Candidiasis refractory to conventional therapy; treatment of non-meningeal and meningeal infections of Coccidioidomycosis refractory to conventional therapy; treatment of non-immunosuppressed pulmonary Cryptococcal infections; and as salvage and step-down therapy for Mucormycosis.

Resources:

Noxafil (posaconazole) product information accessed 10-18-19 at DailyMed

Posaconazole product information accessed 10-18-19 at DailyMed

UpToDate: Treatment and prevention of invasive aspergillosis. Current through Sep 2019, accessed 10-21-19

UpToDate: Treatment of chronic pulmonary aspergillosis. Current through Sep 2019, accessed 10-21-19

UpToDate: Treatment of oropharyngeal and esophageal candidiasis. Current through Sep 2019, accessed 10-21-19