Noxafil

**Description**

Noxafil (posaconazole) delayed-release tablets

Noxafil (posaconazole) oral suspension

**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: (1)

- Noxafil delayed-release tablets and oral suspension are 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 transplant (HSCT) patients with graft-versus-host disease (GVHD) or those with hematologic malignancies with prolonged neutropenia from chemotherapy.
- Noxafil delayed-release tablets and oral suspension are indicated in patients 13 years of age and older.
- Noxafil oral suspension is also indicated for the treatment of oropharyngeal candidiasis, including oropharyngeal candidiasis refractory to itraconazole and/or fluconazole.
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 efficacy of Noxafil delayed-release tablets and oral suspension in patients less than 13 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 in patients 13 years of age or older for the treatment of susceptible fungal infections and if the conditions indicated below are met.

Noxafil may be considered investigational in patients less than 13 years of age and for all other indications.

Prior-Approval Requirements

Age
13 years of age or older

Diagnoses
Patient must have the following:

Delayed-release tablets and oral suspension:
1. Prophylaxis of invasive Aspergillosis or Candida infections AND ONE of the following:
   a. Patient is severely immunocompromised
   b. Patient is post-HSCT with GVHD
   c. Patient has hematologic malignancies with prolonged neutropenia from chemotherapy
Oral suspension only:
2. Oropharyngeal candidiasis

AND ALL of the following:
   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 6 months for oropharyngeal candidiasis
1 year for fungal prophylaxis

Prior – Approval Renewal Limits

Duration 6 months for oropharyngeal candidiasis
1 year for fungal prophylaxis

Rationale

Summary
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. The safety and efficacy of Noxafil delayed-release tablets and oral suspension in patients less than 13 years of age have not been established (1).
Prior approval is required to ensure the safe, clinically appropriate and cost effective use of Noxafil while maintaining optimal therapeutic outcomes.

References

Policy History

<table>
<thead>
<tr>
<th>Date</th>
<th>Action</th>
</tr>
</thead>
<tbody>
<tr>
<td>July 2019</td>
<td>Addition to PA</td>
</tr>
<tr>
<td>September 2019</td>
<td>Annual review</td>
</tr>
</tbody>
</table>

This policy was approved by the FEP® Pharmacy and Medical Policy Committee on September 13, 2019 and is effective on October 1, 2019.