BlueCross BlueShield
Federal Employee Program

NOXAFIL (posaconazole) delayed-release tablets
NOXAFIL (posaconazole) oral suspension
NOXAFIL POWDERMIX (posaconazole) for delayed-release oral suspension

RATIONALE FOR INCLUSION IN PA PROGRAM

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: Noxafil is an azole antifungal indicated as follows: (1)

- **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) patients 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 also 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.

<u>Off-Label Uses:</u> (2-5)

- Refractory coccidioidomycosis
- Invasive mucormycosis

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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 effectiveness of Noxafil in pediatric patients less than 2 years of age have not been established (1).

Summary

Noxafil (posaconazole) is a triazole antifungal that blocks the synthesis of ergosterol, which is a vital component of fungal cell membranes. Noxafil formulations are indicated for use in aspergillosis and candidiasis. Studies have also shown that Noxafil can be used off-label in refractory coccidioidomycosis and invasive mucormycosis. Patients on Noxafil should have liver function tests and QTc prolongation monitored. The safety and effectiveness of Noxafil in pediatric patients less than 2 years of age have not been established (1-5).

Prior approval is required to ensure the safe, clinically appropriate, and cost-effective use of Noxafil while maintaining optimal therapeutic outcomes.

References

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