BlueCross BlueShield
Federal Employee Program
Federal Employee Program®
1310 G Street, N.W.
Washington, D.C. 20005
202.942.1000
Fax 202.942.1125

5.01.018

Section:	Prescription Drugs	**Effective Date:**	January 1, 2023
Subsection:	Anti-infective Agents	**Original Policy Date:**	July 1, 2001
Subject:	Itraconazole	**Page:**	1 of 5

Last Review Date: December 2, 2022

Itraconazole

Description

Sporanox (itraconazole); Tolsura* (itraconazole)

*Prior authorization for the brand formulation applies only to formulary exceptions due to being a non-covered medication.

Background
Itraconazole is an oral azole antifungal agent indicated for the treatment of blastomycosis, histoplasmosis, aspergillosis, onychomycosis and oropharyngeal or esophageal candidiasis. FDA-approved indications vary by dosage form, and dosage forms are not interchangeable. Itraconazole works by inhibiting the production of ergosterol (principal sterol in fungal cell membrane) and inhibiting cell membrane formation (1).

Regulatory Status
FDA-approved indications: Sporanox oral solution is indicated for the treatment of oropharyngeal and esophageal candidiasis. Only the oral solution has demonstrated effective for oral and/or esophageal candidiasis (2).

Sporanox capsules and Tolsura capsules are indicated for the treatment of blastomycosis (pulmonary and extrapulmonary), histoplasmosis (including chronic cavitary pulmonary disease and disseminated, non-meningeal histoplasmosis), and aspergillosis (pulmonary and extrapulmonary) in patients who are intolerant of or who are refractory to amphotericin B therapy (2-3).

Sporanox capsules are also indicated for the treatment of onychomycosis in non-immunocompromised patients (3).

Tolsura Limitations of Use: (4)
Tolsura is not indicated for the treatment of onychomycosis and it is not interchangeable or substitutable with other itraconazole products.

Itraconazole has a boxed warning for congestive heart failure, cardiac effects and drug interactions. Do not administer itraconazole in patients with evidence of ventricular dysfunction, such as congestive heart failure (CHF) or a history of CHF. Coadministration of a number of CYP3A4 substrates are contraindicated with itraconazole (2-4).

Itraconazole has warnings regarding hepatic effects, cardiac dysrhythmias, cardiac disease, interaction potential, interchangeability, hydroxypropyl-β-cyclodextrin, and treatment of severely neutropenic patients (2-4)

There are three major forms of aspergillosis: invasive, saprophytic and allergic. The Infectious Disease Society of America (IDSA) recommends the use of itraconazole and corticosteroids for the treatment of allergic bronchopulmonary aspergillosis (5).

The safety and efficacy of itraconazole in patients less than 18 years of age have not been established (2-4).

Related policies
Cresemba, 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.

Itraconazole may be considered **medically necessary** in patients 18 years of age or older for the treatment of susceptible fungal infections and if the conditions indicated below are met.

Itraconazole may be considered **investigational** for patients below 18 years of age and for all other indications.

Prior-Approval Requirements

Age 18 years of age or older

Diagnoses

Patient must have **ONE** of the following

Sporanox oral solution ONLY

1. Candidiasis
   a. Must be unresponsive or refractory to fluconazole
   b. Includes oropharyngeal and esophageal candidiasis

Sporanox capsules ONLY

1. Onychomycosis
   a. Not immunocompromised
   b. Not have evidence of ventricular dysfunction, such as congestive heart failure or a history of CHF

Sporanox capsules and Tolsura capsules

1. Aspergillosis – invasive or saprophytic
   a. Must be refractory or intolerant to amphotericin B
2. Aspergillosis – allergic bronchopulmonary
3. Blastomycosis
4. Coccidioidomycosis
5. Histoplasmosis
6. Sporotrichosis

AND ALL of the following for **ALL** diagnoses:

a. 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 a diagnosis of Onychomycosis or Candidiasis
1 year for all other diagnoses

Prior – Approval *Renewal* Limits

Same as above

Rationale

Summary

Itraconazole is an oral azole antifungal agent indicated for the treatment of blastomycosis, histoplasmosis, aspergillosis, onychomycosis and oropharyngeal or esophageal candidiasis. FDA-approved indications vary by dosage form, and dosage forms are not interchangeable. Itraconazole works by inhibiting the production of ergosterol (principal sterol in fungal cell membrane) and inhibiting cell membrane formation. Itraconazole has a boxed warning for congestive heart failure, cardiac effects and drug interactions. Itraconazole has warnings regarding hepatic effects, interchangeability, hydroxypropyl-β-cyclodextrin, and treatment of severely neutropenic patients. The safety and efficacy of itraconazole in patients less than 18 years of age have not been established (1-4).

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

References

1. Itraconazole. Clinical Pharmacology [database online]. Tampa, FL: Elsevier; Revision year 2018. Available from: http://www.clinicalkey.com.
2. Sporanox oral solution [package insert]. Titusville, NJ: Janssen Pharmaceuticals; September 2020.
3. Sporanox capsules [package insert]. Titusville, NJ: Janssen Pharmaceuticals; December 2019.
4. Tolsura [package insert]. Greenville, NC: Mayne Pharma International Pty Ltd; April 2022.
5. Patterson TF, Thompson GR, Denning DW, et al. Practice Guidelines for the Diagnosis and Management of Aspergillosis: 2016 Update by the Infectious Diseases Society of America. *Clinical Infectious Diseases.* 2016; 63:112-146.

Policy History

Date	Action
December 2012	Annual editorial review and reference update.
March 2013	Addition of age and contraindication for CHF Addition of Onmel as a line extension
September 2014	Annual editorial review and reference update

September 2015	Annual editorial review and reference update. Addition of identified types of aspergillosis- allergic bronchopulmonary and aspergillosis – invasive or saprophytic
March 2016	Annual editorial review Policy number changed from 5.03.18 to 5.01.18
December 2017	Annual editorial review and reference update
November 2018	Annual editorial review
January 2019	Addition of Tolsura. Policy renamed Itraconazole
March 2019	Annual review
June 2019	Annual review. Added requirement to monitor for QTc prolongation per SME
September 2019	Removed diagnosis of other fungal infection if patient is diabetic or immune compromised
December 2019	Annual review. Moved Tolsura to MFE with PA only.
December 2020	Annual review and reference update
June 2021	Annual editorial review and reference update. Removed Onmel from policy due to being discontinued. Criteria revised so that Sporanox Oral Solution is the only formulation approved for candidiasis to align with PI
December 2021	Annual review
June 2022	Annual review and reference update
December 2022	Annual review and reference update. Changed policy number to 5.01.018

Keywords

This policy was approved by the FEP® Pharmacy and Medical Policy Committee on December 2, 2022 and is effective on January 1, 2023.