PRIOR AUTHORIZATION WITH STEP THERAPY POLICY

POLICY: Tolsura™ (itraconazole capsules – Mayne Pharma)

DATE REVIEWED: 06/10/2020

OVERVIEW

Tolsura, a branded itraconazole product, is indicated for the treatment of the following fungal infections in immunocompromised and non-immunocompromised adult patients: 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.[1] Limitations of use: Tolsura is not indicated for the treatment of onychomycosis. Tolsura is not interchangeable or substitutable with other itraconazole products due to the differences in the dosing between Tolsura and other itraconazole products. Compared with itraconazole capsules, the bioavailability of Tolsura is greater (relative bioavailability is 173% with 21% less variability).[2] The recommended dose for the treatment of blastomycosis or histoplasmosis is 130 mg (2 x 65 mg capsules) once daily (QD). The dose is 130 mg (2 x 65 mg capsules) QD or twice daily (BID) for the treatment of aspergillosis.[1] A loading dose of 130 mg (2 x 65 mg capsules) three times a day (TID) may be necessary for the treatment of life-threatening infections. Tolsura is available as 65 mg capsules.

Itraconazole capsule (Sporanox, generics) is indicated for the treatment of the following fungal infections in immunocompromised and non-immunocompromised patients: 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.[3] Itraconazole capsule is also indicated for the treatment of the following fungal infections in non-immunocompromised patients: onychomycosis of the toenail, with or without fingernail involvement, due to dermatophytes (tinea unguium); and onychomycosis of the fingernail due to dermatophytes (tinea unguium). The dose of itraconazole capsule (100 mg capsules) for the treatment of systemic fungal infections and onychomycosis range from 200 mg/day to 400 mg/day; a 600 mg/day loading dose (for 3 days) is recommended for life-threatening infections.

Itraconazole oral solution (Sporanox, generics) is indicated for the treatment of oropharyngeal and esophageal candidiasis.[4] The prescribing information notes that itraconazole oral solution was not investigated in severely neutropenic patients with oropharyngeal and/or esophageal candidiasis and it is not recommended for initiation of treatment in patients at immediate risk of systemic candidiasis. The recommended dose of itraconazole oral solution (10 mg/mL) range from 100 mg (10 mL) to 200 mg (20 mL) per day. Itraconazole oral solution should not be used interchangeably with itraconazole capsule. Drug exposure is greater with the oral solution than with the capsules when the same dose of drug is given. Although itraconazole oral solution is not FDA-approved for the treatment of systemic fungal infections, both the capsule and liquid formulation of itraconazole are listed as options for use in the treatment and prophylaxis of systemic fungal infections by the Infectious Diseases Society of America (IDSA), American Thoracic Society (ATS) and the National Comprehensive Cancer Network (NCCN).[5-7] Many guidelines note improved bioavailability of the oral solution compared with the capsule formulation.[5,8,9] Therapeutic drug monitoring of itraconazole is recommended.

Clinical Efficacy/Guidelines

Tolsura has not yet been incorporated into guidelines. Conventional itraconazole (capsule and/or oral solution) is a treatment option for systemic fungal infections, including invasive aspergillosis, blastomycosis, and histoplasmosis.[5,6,10]

POLICY STATEMENT

Prior authorization is recommended for prescription benefit coverage of Tolsura. This Prior Authorization Policy also contains a Step Therapy component. When clinically appropriate, patients are directed to try one Preferred Step 1 agent (itraconazole capsules or oral solution) prior to Tolsura (Step 2). All approvals are provided for the duration noted below.

Automation: None.

RECOMMENDED AUTHORIZATION CRITERIA

Coverage of Tolsura is recommended in those who meet the following criteria:

FDA-Approved Indications

1. **Blastomycosis – Pulmonary Or Extrapulmonary – Treatment.** Approve for 3 months if the patient meets one of the following criteria (A or B):
   - **A)** The patient has tried one of itraconazole capsules or oral solution; OR
   - **B)** The patient is currently receiving Tolsura for this condition.

2. **Histoplasmosis (Including Chronic Cavitary Pulmonary Disease and Disseminated, Non-Meningeal) – Treatment.** Approve for 3 months if the patient meets one of the following criteria (A or B):
   - **A)** The patient has tried one of itraconazole capsules or oral solution; OR
   - **B)** The patient is currently receiving Tolsura for this condition.

3. **Aspergillosis – Pulmonary Or Extrapulmonary – Treatment.** Approve for 3 months if the patient meets one of the following criteria (A or B):
   - **A)** The patient has tried one of itraconazole capsules or oral solution; OR
   - **B)** The patient is currently receiving Tolsura for this condition.

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Tolsura not been shown to be effective, or there are limited or preliminary data or potential safety concerns that are not supportive of general approval for the following conditions. Rationale for non-coverage for these specific conditions is provided below. (Note: This is not an exhaustive list of Conditions Not Recommended for Approval.)

1. **Onychomycosis.** Treatment of onychomycosis is noted as a Limitation of Use in the prescribing information.

2. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

REFERENCES

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2. Lindsay J, Mudge S, Thompson GR. Effects of food and omeprazole on a novel formulation of super bioavailability itraconazole in healthy subjects. *Antimicrob Agents Chemother*. 2018;62(12): e01723-18.
3. Sporanox® capsule [prescribing information]. Titusville, NJ: Janssen Pharmaceuticals, Inc.; March 2019.

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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. *Clin Infect Dis.* 2016;63(4):e1-e60.
6. Limper AH, Know KS, Sarosi GA, et al. An official American Thoracic Society statement: treatment of fungal infections in adult pulmonary and critical care patients. *Am J Respir Crit Care Med*. 2011;183:96-128.
7. The NCCN Prevention and Treatment of Cancer-Related Infections Clinical Practice Guidelines in Oncology (version2.2020 – June 5, 2020). ©2019 National Comprehensive Cancer Network, Inc. Available at: http://www.nccn.org. Accessed on June 5, 2020.
8. Pappas PG, Kauffman CA, Andes DR, et al. Clinical practice guidelines for the management of candidiasis: 2016 update by the Infectious Diseases Society of America. *Clin Infect Dis.* 2016;62(4):e1-50.
9. Panel on Opportunistic Infections in HIV-Infected Adults and Adolescents. Guidelines for the prevention and treatment of opportunistic infections in HIV-infected adults and adolescents: recommendations from the Centers for Disease Control and Prevention, the National Institutes of Health, and the HIV Medicine Association of the Infectious Diseases Society of America. Available at: http://aidsinfo.nih.gov/contentfiles/lvguidelines/adult_oi.pdf. Accessed on June 5, 2020.
10. Wheat J, Freifeld AG, Kleiman MB, et al. Clinical practice guidelines for the management of patients with histoplasmosis: 2007 update by the Infectious Diseases Society of America. *Clin Infect Dis.* 2007;45:807-825.