Oral Antifungal Agents

Override(s)	Approval Duration
Prior Authorization^ Quantity Limit	• Onychomycosis: 12 weeks or three 1 month fills per rolling calendar year per incidence of onychomycosis • All other indications: 1 year

Medications	Quantity Limit
itraconazole 100mg capsule	May be subject to quantity limit

^ For the following drug: itraconazole
If the reject is **Product Service Not Covered** due to *benefit exclusion (nail bed [finger/toe] fungus or onychomycosis),* may approve all non onychomycosis diagnoses without regard to the below criteria.

APPROVAL CRITERIA

Requests for itraconazole capsules for the treatment of **onychomycosis** may be approved based on the following criteria:

I. Individual has **no relevant comorbidity** (normal immune system, and no disorder which predisposes to infection in the extremities); **AND**

A. Evidence of functional impairment (such as loss of one or more toenails, pain, or swelling) is present; **AND**
B. Individual has a confirmed fungal infection (such as, potassium hydroxide [KOH] preparation, fungal culture, nail biopsy or physical exam);

OR

II. Individual has **a relevant comorbidity** (abnormal immune system [including infection with HIV, on immunosuppressant agents] or disorder which predisposes to infection in the extremities [such as, diabetes]); **AND**

A. Individual has confirmed fungal infection (e.g. potassium hydroxide [KOH] preparation, fungal culture, nail biopsy or physical exam);

Itraconazole capsules may not be approved for the following:

I. Individual with ventricular dysfunction (including congestive heart failure) requesting itraconazole for the treatment of onychomycosis.

Requests for **itraconazole** capsules may be approved for the following **non-onychomycosis** indications:

I. Blastomycosis, pulmonary and extrapulmonary; **OR**
II. Histoplasmosis, including chronic cavitary pulmonary disease and disseminated, non-meningeal histoplasmosis; **OR**
III. Invasive Aspergillosis, pulmonary and extrapulmonary, in individuals refractory to or intolerant or contraindicated to treatment with amphotericin B; **OR**
IV. Paracoccidioidomycosis (AHFS); **OR**
V. Sporotrichosis (capsules) (AHFS); **OR**
VI. Cryptococcus (capsules) if alternative regimens have failed or are not available or are contraindicated (AHFS); **OR**
VII. Treatment or suppressive therapy of coccidioidomycosis ((AHFS); **OR**
VIII. Primary prophylaxis to prevent first episode of histoplasmosis in individual diagnosed with human immunodeficiency (HIV) infection with CD4 T-cell counts less than 150/mm^3 and at risk because of occupational exposure or residing in areas where histoplasmosis is highly endemic (AHFS); **OR**
IX. Secondary prophylaxis (prevention of recurrence) of histoplasmosis in immunosuppressed individual or individual diagnosed with HIV-infection who has been adequately treated for histoplasmosis (AHFS); **OR**
X. Basidiobolomycosis (AHFS); **OR**
XI. Allergic Bronchopulmonary aspergillosis (DrugPoints, B IIa); **OR**
XII. Prophylaxis of invasive fungal infection (DrugPoints, B IIa); **OR**
XIII. Chronic pulmonary aspergillosis (cavitary or necrotizing) (DrugPoints, B IIa) ; **OR**
XIV. Chromomycosis caused by various dematiaceous fungi (such as, *Cladosporium, Exophiala, Fonsecaea, Phialophora*) (AHFS): **OR**
XV. Treatment or suppressive therapy of penicilliosis caused by *Penicillium marneffei* (AHFS, CDC/NIH/IDSA); **OR**
XVI. Microsporidosis (AHFS); **OR**
XVII. Transitioning from inpatient treatment to an outpatient setting and requires continued therapy for an organism susceptible to itraconazole.

Requests for itraconazole capsules may be approved for the following:

I. Tinea infections (**EXCEPT** for Tinea unguium) (DrugPoints B IIa) where the individual has had a trial and inadequate response or intolerance to at least one prior topical antifungal therapy including, but not limited to:
    - Miconazole; **OR**
    - Ciclopirox; **OR**
    - Tolnaftate; **OR**
    - Clotrimazole; **OR**
    - Ketoconazole; **OR**
    - Econazole; **OR**
    - Nystatin; **OR**
    - Butenafine; **OR**
    - Terbinafine; **OR**

- Tolnaftate.

*Note: Onychomycosis is also known as tinea unguium, nail fungus, and dermatophytosis of the nails. Itraconazole has black box warnings for congestive heart failure, cardiac effects and drug interactions. Itraconazole can cause or exacerbate congestive heart failure (CHF). If signs or symptoms of CHF occur during treatment, reassess the benefit-risk of continuing treatment. Itraconazole should not be administered for the treatment of onychomycosis in individuals with evidence of ventricular dysfunction including CHF or a history of CHF. Itraconazole has significant drug interactions that can result in serious adverse events and are contraindications to use. Coadministration of methadone, disopyramide, dofetilide, dronedarone, quinidine, ergot alkaloids (such as dihydroergotamine, ergometrine (ergonovine), ergotamine, methylergometrine (methylergonovine)), irinotecan, lurasidone, oral midazolam, pimozide, triazolam, felodipine, nisoldipine, ranolazine, eplerenone, cisapride, lovastatin, simvastatin, ticagrelor and, in subjects with varying degrees of renal or hepatic impairment, colchicine, fesoterodine, telithromycin and solifenacin with itraconazole is contraindicated. Coadministration of these agents with itraconazole can cause elevated plasma concentrations of these drugs which may increase or prolong both the pharmacologic effects and/or adverse reactions to these drugs. One example is increased plasma concentrations of some of these drugs leading to QT prolongation and ventricular tachyarrhythmias including torsades de pointes, a potentially fatal arrhythmia.

Key References:

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2. Centers for Disease Control and Prevention (CDC). Sexually Transmitted Infection Treatment Guidelines, 2021. Available at https://www.cdc.gov/std/treatment-guidelines/toc.htm. Accessed: October 9, 2022.
3. DailyMed. Package inserts. U.S. National Library of Medicine, National Institutes of Health website. http://dailymed.nlm.nih.gov/dailymed/about.cfm. Accessed: October 8, 2022.
4. DrugPoints® System [electronic version]. Truven Health Analytics, Greenwood Village, CO. Updated periodically.
5. Galgiani JN, Ampel NM, Blair JE, et.al. 2016 Infectious Diseases Society of America (IDSA) Clinical Practice Guideline for the Treatment of Coccidioidomycosis. *Clin Infect Dis.* 2016; 63(6):e112-146.
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7. Nieman LK, Biller BMK, Findling JW, et al. Treatment of Cushing's Syndrome: An Endocrine Society Clinical Practice Guideline. *J Clin Endocrinol Metab*. 2015. 100: 2807–2831.

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9. Panel on Opportunistic Infections in HIV-Exposed and HIV-Infected Children. Guidelines for the prevention and treatment of opportunistic infections in HIV-Exposed and HIV-Infected Children. Department of Health and Human Services. Available at https://clinicalinfo.hiv.gov/en/guidelines/hiv-clinical-guidelines-pediatric-opportunistic-infections/whats-new-guidelines. Accessed: October 9, 2022.
10. Pappas PG, Kauffman CA, Andes D, et al. Clinical Practice Guideline for the Management of Candidiasis: 2016 Update by the Infectious Diseases Society of America. *Clin Infect Dis.* 2016; 62(4):E1-50.
11. 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 (IDSA). *Clin Infect Dis.* 2016. 63(4): e1-e60.

Federal and state laws or requirements, contract language, and Plan utilization management programs or polices may take precedence over the application of this clinical criteria.