



## Drug Quantity Management – Per Rx Antifungals – Itraconazole

### Table of Contents

National Formulary Medical Necessity .....	1
Conditions Not Covered.....	3
Background.....	3
References .....	5
Revision History.....	6

### Product Identifier(s)

**Effective 1/1/23 to 2/6/23:** 108311

**Effective 2/7/23:** 21995

#### **INSTRUCTIONS FOR USE**

*The following Coverage Policy applies to health benefit plans administered by Cigna Companies. Certain Cigna Companies and/or lines of business only provide utilization review services to clients and do not make coverage determinations. References to standard benefit plan language and coverage determinations do not apply to those clients. Coverage Policies are intended to provide guidance in interpreting certain standard benefit plans administered by Cigna Companies. Please note, the terms of a customer's particular benefit plan document [Group Service Agreement, Evidence of Coverage, Certificate of Coverage, Summary Plan Description (SPD) or similar plan document] may differ significantly from the standard benefit plans upon which these Coverage Policies are based. For example, a customer's benefit plan document may contain a specific exclusion related to a topic addressed in a Coverage Policy. In the event of a conflict, a customer's benefit plan document always supersedes the information in the Coverage Policies. In the absence of a controlling federal or state coverage mandate, benefits are ultimately determined by the terms of the applicable benefit plan document. Coverage determinations in each specific instance require consideration of 1) the terms of the applicable benefit plan document in effect on the date of service; 2) any applicable laws/regulations; 3) any relevant collateral source materials including Coverage Policies and; 4) the specific facts of the particular situation. Coverage Policies relate exclusively to the administration of health benefit plans. Coverage Policies are not recommendations for treatment and should never be used as treatment guidelines. In certain markets, delegated vendor guidelines may be used to support medical necessity and other coverage determinations.*

### National Formulary Medical Necessity

#### Drugs Affected

- Sporanox® (itraconazole capsules and oral solution – generic)
- Onmel™ (itraconazole tablets)
- Tolsura® (itraconazole capsules)

This Drug Quantity Management program has been developed to prevent stockpiling, waste, and address potential order entry error of itraconazole. If the Drug Quantity Management rule is not met for the requested medication at the point of service, coverage will be determined by the Criteria below. Approvals are provided for the duration noted below.

## Drug Quantity Limits

Product	Strength and Form	Retail Maximum Quantity per Rx	Home Delivery Maximum Quantity per Rx
Sporanox (itraconazole capsules, generic)	100 mg capsules	30 capsules	90 capsules
Sporanox (itraconazole oral solution, generic)	10 mg/mL oral solution in 150 mL bottles	300 mL (2 bottles)*	300 mL (2 bottles)
Onmel (itraconazole tablets)	200 mg tablets	14 tablets	42 tablets
Tolsura (itraconazole capsules)	65 mg capsules	60 capsules	180 capsules

\* This provides a quantity sufficient for a dose of 20 mL per day for 14 days.

## Criteria

### Cigna covers quantities as medically necessary when the following criteria are met:

#### Itraconazole 100 mg capsules (Sporanox, generic)

1. If the individual has blastomycosis, histoplasmosis, or aspergillosis, approve the requested quantity sufficient for a 30-day supply per dispensing at retail and a 90-day supply per dispensing at home delivery for up to 1 year.
2. If the individual has onychomycosis of the fingernail or toenail and the request is for continuous dosing (i.e., 200 mg daily for 6 to 12 weeks), approve 60 capsules per dispensing at retail and home delivery for up to 90 days if the individual meets ONE of the following criteria (A or B):  
**A)** Individual has completed at least one complete course of pulse therapy with itraconazole; OR  
**Note:** One complete course of pulse therapy with itraconazole is defined as two consecutive pulses for fingernails and three consecutive pulses for toenails and each pulse consists of 200 mg twice daily (BID) for 1 week followed by a 3-week period without itraconazole.  
**B)** Individual cannot tolerate the adverse effects of pulse therapy dosing.
3. If the medication is being requested for the prevention or treatment of other superficial and systemic mycoses (suspected or confirmed), approve up to 180 capsules per dispensing at retail and 540 capsules per dispensing at home delivery for 1 year.

#### Itraconazole 10 mg/mL oral solution (Sporanox, generic)

1. If the individual has oropharyngeal candidiasis that is unresponsive/refractory to treatment with fluconazole, approve the requested quantity, not to exceed 600 mL per dispensing at retail and at home delivery.  
**Note:** This provides a quantity sufficient for up to 20 mL per day for up to 4 weeks.
2. If the individual has esophageal candidiasis, approve the requested quantity, not to exceed 600 mL per dispensing at retail and at home delivery.  
**Note:** This provides a quantity sufficient for up to 20 mL per day for up to 4 weeks.

#### Onmel 200 mg tablets

1. If the individual has blastomycosis, histoplasmosis, or aspergillosis, approve the requested quantity sufficient for a 30-day supply per dispensing at retail and a 90-day supply per dispensing at home delivery for 1 year.
2. If the individual has onychomycosis of the fingernail or toenail and the request is for continuous dosing (i.e., 200 mg daily for 6 to 12 weeks), approve 30 tablets per dispensing at retail and home delivery for up to 90 days if the individual meets ONE of the following criteria (A or B):  
**A)** Individual has completed at least one complete course of pulse therapy with itraconazole; OR  
**Note:** One complete course of pulse therapy with itraconazole is defined as two consecutive pulses for fingernails and three consecutive pulses for toenails and each pulse consists of 200 mg twice daily (BID) for 1 week followed by a 3-week period without itraconazole.  
**B)** Individual cannot tolerate the adverse effects of pulse therapy dosing.

3. If the medication is being requested for the prevention or treatment of other superficial and systemic mycoses (suspected or confirmed), approve up to 90 tablets per dispensing at retail and 270 tablets per dispensing at home delivery for 1 year.

#### Tolsura 65 mg capsules

1. If the individual has life-threatening histoplasmosis, blastomycosis, or aspergillosis, approve a one-time override for up to 126 capsules at retail and home delivery.  
Note: This quantity provides a 30-day supply to accommodate the loading dose (130 mg three times daily for 3 days [18 capsules]) followed by up to 260 mg twice daily (BID) for 27 days (108 capsules).<sup>1</sup>
2. If the individual has aspergillosis, approve up to 120 capsules per dispensing at retail and 360 capsules per dispensing at home delivery for up to 1 year.
3. If the individual has been receiving 130 mg per day and has not experienced improvement, approve a quantity of 120 capsules per dispensing at retail and 360 capsules per dispensing at home delivery for up to 1 year.
4. If the individual has progressive histoplasmosis or blastomycosis, approve a quantity of 120 capsules per dispensing at retail and 360 capsules per dispensing for up to 1 year.

#### Itraconazole 100 mg capsules (Sporanox, generic) and Onmel 200 mg tablets

1. No overrides are recommended for the following indications:
  - A. Tinea versicolor.
  - B. Tinea capitis.
  - C. Tinea corporis.
  - D. Tinea cruris.
  - E. Tinea pedis (any type including moccasin or plantar).
  - F. Tinea manuum.
  - G. Tinea imbricate.
  - H. Tinea faciei.
  - I. Vaginal candidiasis, acute or recurrent.

## Conditions Not Covered

Any other exception is considered not medically necessary.

## Background

### Overview

Sporanox capsules (generic) and oral solution (generic), Onmel tablets, and Tolsura capsules all contain itraconazole, an azole antifungal.<sup>1,5,8,10</sup>

Itraconazole capsules (Sporanox, generic) and Tolsura, are indicated for the treatment of the following fungal infections in immunocompromised and non-immunocompromised patients<sup>1,5</sup>:

- Pulmonary and extapulmonary **blastomycosis**;
- **Histoplasmosis**, including chronic cavitory pulmonary disease and disseminated, nonmeningeal histoplasmosis;
- Pulmonary and extrapulmonary **aspergillosis**, in patients who are intolerant of or who are refractory to amphotericin B therapy.

In addition, itraconazole capsules (Sporanox, generic) are indicated for the treatment of the following fungal infections in non-immunocompromised patients<sup>1</sup>:

- **Onychomycosis of the toenail**, with or without fingernail involvement, due to dermatophytes (tinea unguium);
- **Onychomycosis of the fingernail** due to dermatophytes (tinea unguium).

Itraconazole oral solution (Sporanox, generic) is indicated for the treatment of **oropharyngeal and esophageal candidiasis**.<sup>10</sup>

Onmel is indicated for the treatment of **onychomycosis of the toenail** caused by *Trichophyton rubrum* or *T. mentagrophytes*.<sup>8</sup>

## Dosing

### Itraconazole capsules (Sporanox, generic)

For the treatment of blastomycosis or histoplasmosis, the recommended dose is 200 mg once daily (QD).<sup>1</sup> If there is no obvious improvement, or if there is evidence of progressive fungal disease, the dose should be increased in 100 mg increments to a maximum of 400 mg/day. Doses above 200 mg/day should be given in two divided doses. For the treatment of aspergillosis, the dose is 200 to 400 mg/day.<sup>1</sup> In life-threatening situations, a loading dose of 200 mg three times daily (TID) [600 mg/day] for the first 3 days of treatment is recommended. Treatment should be continued for a minimum of 3 months and until clinical parameters and laboratory test indicate that the active fungal infection has subsided; inadequate treatment may lead to recurrence of the active infection. Doses up to 200 mg TID are recommended in guidelines.<sup>2-4</sup>

According to the prescribing information, for the treatment of toenail onychomycosis with or without fingernail involvement, the recommended dose is 200 mg QD for 12 weeks.<sup>1</sup> For the treatment of fingernail-only onychomycosis, the recommended dose is two treatment-pulses, each consisting of 200 mg twice daily (BID) [400 mg/day] for 1 week. Pulses are separated by a 3-week period without itraconazole; therefore, two treatment-pulses occur over a 2-month period.

Off-label dosing in onychomycosis has also been described.<sup>6</sup> A treatment-pulse dosing regimen in toenail onychomycosis consists of three treatment-pulses (200 mg BID for 1 week, followed by 3 weeks of no itraconazole, over a 3 month period).<sup>6</sup> Daily continuous dosing has been used in fingernail onychomycosis (200 mg BID for 6 weeks). A meta-analysis of treatments for toenail onychomycosis determined that mycotic cure rates were 63% for itraconazole with treatment-pulse dosing and 59% for itraconazole with continuous daily dosing. Clinical cure rates were the same for itraconazole with pulse dosing and continuous dosing (70% for both).

Itraconazole capsules (Sporanox, generic) have been used off-label for the treatment of tinea versicolor, pityriasis versicolor, tinea capitis, tinea barbae, tinea faciei, tinea manuum, tinea imbricata, tinea pedis (either nonmoccasin or chronic type or the plantar-type or moccasin-type dry chronic), tinea corporis, and acute or recurrent vaginal candidiasis. Thirty capsules are adequate for one course of treatment of these conditions. It has also been used to treat or prevent various other suspected or confirmed systemic and superficial fungal conditions that are not listed above.<sup>9</sup>

### Itraconazole Oral Solution (Sporanox, generic)

For the treatment of oropharyngeal and esophageal candidiasis, the solution should be vigorously swished in the mouth (10 mL at a time) and swallowed.<sup>10</sup>

The recommended dose for the treatment of oropharyngeal candidiasis is 200 mg (20 mL) daily for 1 to 2 weeks.<sup>10</sup> Generally, signs and symptoms of oropharyngeal candidiasis resolve within several days. For patients with oropharyngeal candidiasis unresponsive/refractory to treatment with fluconazole tablets, the recommended dose is 100 mg (10 mL) BID. For patients responding to therapy, clinical response will be seen in 2 to 4 weeks. Patients may be expected to relapse shortly after discontinuing therapy. Limited data on the safety of long-term use (> 6 months) of itraconazole oral solution are available.

For the treatment of esophageal candidiasis, the recommended dose is 100 mg (10 mL) daily for a minimum of 3 weeks.<sup>10</sup> Treatment should continue for 2 weeks following resolution of symptoms. Doses up to 200 mg (20 mL) per day may be used based on the patient's response and medical judgment.

Itraconazole oral solution (Sporanox, generic) and itraconazole capsules (Sporanox, generic) should not be used interchangeably.<sup>10</sup>

### Onmel tablets

The dose of Onmel is one tablet QD for 12 weeks for toenail onychomycosis.<sup>5</sup> Pulse regimens of itraconazole for fingernail and toenail onychomycosis are also effective (as described above).<sup>6</sup>

### Tolsura capsules

The dose of Tolsura is 130 mg to 260 mg/day for the treatment of blastomycosis, histoplasmosis, and aspergillosis.<sup>8</sup> Tolsura is not approved for the treatment of onychomycosis. For the treatment of blastomycosis and histoplasmosis, the recommended dose is 130 mg QD; if there is no obvious improvement, or there is evidence of progressive fungal disease, the dose should be increased in 65 mg increments to a maximum of 260 mg/day (130 mg BID). For the treatment of aspergillosis, the recommended dose is 130 mg QD or 260 mg BID. For all three approved indications, in life-threatening situations, a loading dose of 130 mg TID (390 mg/day) is recommended to be given for the first 3 days, followed by the appropriate recommended dosing based on indication. Treatment should be continued for a minimum of 3 months and until clinical parameters and laboratory tests indicate that the active fungal infection has subsided. An inadequate period of treatment may lead to recurrence of active infection.

### **Availability**

Itraconazole capsules (Sporanox, generic) are available as 100 mg capsules and itraconazole oral solution (Sporanox, generic) is available as a 10 mg/mL oral solution in 150 mL bottles.<sup>1,10</sup> Onmel is available as a 200 mg tablet (supplied as a 14 tablet blister pack) and Tolsura is available as a 65 mg capsule.<sup>5,8</sup>

## References

1. Sporanox<sup>®</sup> capsules [prescribing information]. Titusville, NJ: Janssen Pharmaceuticals; December 2019.
2. Chapman SW, Dismukes WE, Proia LA, et al. Clinical practice guidelines for the management of blastomycosis: 2008 update by the Infectious Diseases Society of America. *Clin Infect Dis*. 2008;46:1801-1812.
3. Patterson TF, Thompson III 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: 112-146.
4. Wheat LJ, Friefeld AG, Kleiman MB, et al. Clinical practice guidelines for the management of patients with histoplasmosis: 2007 Update by the Infectious Disease Society of America. *Clin Infect Dis*. 2007;45:807-825.
5. Onmel<sup>™</sup> tablets [prescribing information]. Greensboro, NC: Merz Pharmaceuticals; November 2012.
6. Westerberg DP and Voyack MJ. Onychomycosis: Current trends in diagnosis and treatment. *Am Fam Physician*. 2013;88(11):762-770. Available at: <https://www.aafp.org/afp/2013/1201/afp20131201p762.pdf>. Accessed on March 24, 2022.
7. Pajaziti L, Vasili E; Treatment of Onychomycosis – a Clinical Study. *Med Arch*. 2015;69(3): 173-176.
8. Tolsura<sup>®</sup> capsules [prescribing information]. Greenville, NC: Mayne Pharma; June 2020.
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. Updated February 22, 2022. Available at: [https://clinicalinfo.hiv.gov/sites/default/files/guidelines/documents/Adult\\_OI.pdf](https://clinicalinfo.hiv.gov/sites/default/files/guidelines/documents/Adult_OI.pdf). Accessed on March 28, 2022.
10. Sporanox<sup>®</sup> oral solution [prescribing information]. Titusville, NJ: Janssen Pharmaceuticals; September 2020.

## Revision History

Type of Revision	Summary of Changes	Approval Date
Annual Revision	<p><b>Itraconazole 100 mg capsules (Sporanox, generic).</b> Override criteria in onychomycosis of the fingernail or toenail were updated to approve 60 capsules per dispensing (previously, “a quantity sufficient for continuous therapy”, was approved). Continuous dosing was specified as 200 mg every day for 6 to 12 weeks (previously 90 days). Criteria for patients who could not tolerate the side effects of 200 mg twice daily dosing were modified to patient cannot tolerate “pulse therapy” dosing.</p> <p>Override criteria for the prevention or treatment of other superficial and systemic mycoses (suspected or confirmed) were updated to approve up to 190 capsules per dispensing (previously, 120 capsules per dispensing were approved).</p> <p><b>Onmel 200 mg tablets.</b> Onmel quantity limit was changed to 14 tablets per Rx (previously 15 tablets per Rx).</p> <p>Override criteria in onychomycosis of the fingernail or toenail were updated to approve 30 tablets per dispensing (previously, “a quantity sufficient for continuous therapy”, was approved). Continuous dosing was specified as 200 mg every day for 6 to 12 weeks (previously 90 days). Criteria for patients who could not tolerate the side effects of 200 mg twice daily dosing were modified to patient cannot tolerate “pulse therapy” dosing.</p> <p>Override criteria for the prevention or treatment of other superficial and systemic mycoses (suspected or confirmed) were updated to approve up to 90 tablets per dispensing (previously, 60 tablets per dispensing were approved).</p> <p><b>Tolsura 65 mg capsules.</b> Override criteria were added for patients with life-threatening histoplasmosis, blastomycosis, or aspergillosis, to approve a one-time override of up to 126 capsules (previously this was not addressed).</p> <p>Override criteria for patients with “progressive disease” was clarified to apply to patients with progressive histoplasmosis or blastomycosis.</p>	04/06/2022
Selected Revision	<p>Policy was updated to reflect the existing quantity limits when a product is obtained via home delivery.</p> <p>Itraconazole oral solution was added to the policy with override criteria approving additional quantities for patients with oropharyngeal candidiasis that is unresponsive/refractory to treatment with fluconazole and for patients with esophageal candidiasis.</p>	09/21/2022

“Cigna Companies” refers to operating subsidiaries of Cigna Corporation. All products and services are provided exclusively by or through such operating subsidiaries, including Cigna Health and Life Insurance Company, Connecticut General Life Insurance Company, Evernorth Behavioral Health, Inc., Cigna Health Management, Inc. and HMO or service company subsidiaries of Cigna Health Corporation. The Cigna name, logo, and other Cigna marks are owned by Cigna Intellectual Property, Inc. © 2023 Cigna.