



## DRUG QUANTITY MANAGEMENT POLICY – PER RX

- POLICY:** Antifungals – Itraconazole Drug Quantity Management Policy – Per Rx
- Sporanox® (itraconazole capsules and oral solution – Janssen, generic)
  - Tolsura® (itraconazole capsules – Mayne)

**REVIEW DATE:** 04/03/2025

### **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. EACH COVERAGE REQUEST SHOULD BE REVIEWED ON ITS OWN MERITS. MEDICAL DIRECTORS ARE EXPECTED TO EXERCISE CLINICAL JUDGMENT WHERE APPROPRIATE AND HAVE DISCRETION IN MAKING INDIVIDUAL COVERAGE DETERMINATIONS. WHERE COVERAGE FOR CARE OR SERVICES DOES NOT DEPEND ON SPECIFIC CIRCUMSTANCES, REIMBURSEMENT WILL ONLY BE PROVIDED IF A REQUESTED SERVICE(S) IS SUBMITTED IN ACCORDANCE WITH THE RELEVANT CRITERIA OUTLINED IN THE APPLICABLE COVERAGE POLICY, INCLUDING COVERED DIAGNOSIS AND/OR PROCEDURE CODE(S). REIMBURSEMENT IS NOT ALLOWED FOR SERVICES WHEN BILLED FOR CONDITIONS OR DIAGNOSES THAT ARE NOT COVERED UNDER THIS COVERAGE POLICY (SEE "CODING INFORMATION" BELOW). WHEN BILLING, PROVIDERS MUST USE THE MOST APPROPRIATE CODES AS OF THE EFFECTIVE DATE OF THE SUBMISSION. CLAIMS SUBMITTED FOR SERVICES THAT ARE NOT ACCOMPANIED BY COVERED CODE(S) UNDER THE APPLICABLE COVERAGE POLICY WILL BE DENIED AS NOT COVERED. 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.

### **CIGNA NATIONAL FORMULARY COVERAGE:**

#### **OVERVIEW**

Sporanox capsules (generic) and oral solution (generic) and Tolsura capsules all contain itraconazole, an azole antifungal.<sup>1-3</sup>

Itraconazole capsules (Sporanox, generic) and Tolsura, are indicated for the treatment of the following fungal infections in immunocompromised and non-immunocompromised patients<sup>1,2</sup>:

- Pulmonary and extrapulmonary **blastomycosis**;
- **Histoplasmosis**, including chronic cavitary 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>3</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. 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>4-6</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. Continuous dosing of itraconazole 200 mg QD for 6 (fingernail) to 12 weeks (toenail) have also been described.<sup>7</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>2</sup>

The recommended dose for the treatment of oropharyngeal candidiasis is 200 mg (20 mL) daily for 1 to 2 weeks.<sup>2</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>2</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>2</sup>

### *Tolsura capsules*

The dose of Tolsura is 130 mg to 260 mg/day for the treatment of blastomycosis, histoplasmosis, and aspergillosis.<sup>3</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>1,2</sup> Tolsura is available as a 65 mg capsule.<sup>3</sup>

### **POLICY STATEMENT**

This Drug Quantity Management program has been developed to prevent stockpiling, waste, and address potential order entry error of the itraconazole products. 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 1 year, unless otherwise noted below. “One-time” approvals are provided for 30 days in duration.

### **Drug Quantity Limits**

<b>Product</b>	<b>Strength and Form</b>	<b>Retail Maximum Quantity per Rx</b>	<b>Home Delivery Maximum Quantity per Rx</b>
Sporanox® (itraconazole capsules, generic)	100 mg capsules	30 capsules	90 capsules
Sporanox® (itraconazole oral solution, generic)	10 mg/mL oral solution (150 mL bottles)	300 mL (2 bottles)*	300 mL (2 bottles)*
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.

**Antifungals – Itraconazole Drug Quantity Management Policy – Per Rx product(s) is(are) covered as medically necessary when the following criteria is(are) met. Any other exception is considered not medically necessary.**

**CRITERIA**

Itraconazole 100 mg capsules (Sporanox, generic)

1. If the patient has blastomycosis, histoplasmosis, or aspergillosis, approve the requested quantity not to exceed 180 capsules per dispensing at retail or 540 capsules per dispensing at home delivery.
2. If the patient has onychomycosis of the fingernail or toenail, approve 60 capsules per dispensing at retail for 90 days or 180 capsules per dispensing at home delivery for 90 days.
3. If the medication is being requested for the prevention or treatment of other superficial and systemic mycoses (suspected or confirmed), approve the requested quantity, not to exceed 180 capsules per dispensing at retail or 540 capsules per dispensing at home delivery.

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

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

Tolsura 65 mg capsules

1. If the patient has life-threatening histoplasmosis, blastomycosis, or aspergillosis, approve a one-time override for the requested quantity, not to exceed 234 capsules at retail or home delivery.  
Note: This provides a quantity sufficient for 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 (216 capsules).
2. If the patient has aspergillosis, approve the quantity requested, not to exceed 240 capsules per dispensing at retail or 720 capsules per dispensing at home delivery.  
Note: This provides a quantity sufficient for a 30-day supply at retail or 90-day supply at home delivery at a dose of up to 260 mg twice daily (BID).

- If the patient has been receiving 130 mg per day and has not experienced improvement, approve 120 capsules per dispensing at retail or 360 capsules per dispensing at home delivery.

Note: This provides a quantity sufficient for a 30-day supply at retail or 90-day supply at home delivery at a dose of up to 130 mg twice daily (BID).

- If the patient has progressive histoplasmosis or blastomycosis, approve 120 capsules per dispensing at retail or 360 capsules per dispensing.

Note: This provides a quantity sufficient for a 30-day supply at retail or 90-day supply at home delivery at a dose of up to 130 mg twice daily (BID).

## REFERENCES

- Sporanox® capsules [prescribing information]. Titusville, NJ: Janssen; December 2024.
- Sporanox® oral solution [prescribing information]. Titusville, NJ: Janssen; December 2024.
- Tolsura® capsules [prescribing information]. Greenville, NC: Mayne; October 2024.
- 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.
- 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.
- 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.
- Westerberg DP and Voyack MJ. Onychomycosis: Current trends in diagnosis and treatment. *Am Fam Physician*. 2013;88(11):762-770.

## HISTORY

Type of Revision	Summary of Changes	Review Date
Annual Revision	No criteria changes.	04/06/2023
Annual Revision	<p><b>Itraconazole 100 mg capsules (Sporanox, generic):</b></p> <ul style="list-style-type: none"> <li>Override criteria to approve for a quantity sufficient for a 30-day supply per dispensing at retail or a 90-day supply per dispensing at home delivery if the patient has blastomycosis, histoplasmosis, or aspergillosis were updated to approve the requested quantity, not to exceed 180 capsules per dispensing at retail or 540 capsules per dispensing at home delivery.</li> <li>Override criteria to approve 60 capsules per dispensing at retail or home delivery for up to 90 days for a patient with onychomycosis of the fingernail or toenail if they had completed one course of pulse therapy or cannot tolerate the adverse effects of pulse therapy were updated to approve 60 capsules per dispensing at retail or 180 capsules per dispensing at home delivery for 90 days if the patient has onychomycosis of the fingernail or toenail.</li> </ul> <p><b>Onmel 200 mg tablets:</b> Onmel 200 mg tablets were removed from the policy (obsolete).</p> <p><b>Tolsura 65 mg capsules:</b></p> <ul style="list-style-type: none"> <li>Criteria to approve a one-time override for the requested quantity, not to exceed 126 capsules at retail or home delivery if the patient</li> </ul>	04/19/2024

	<p>has life-threatening histoplasmosis, blastomycosis, or aspergillosis were updated to approve the requested quantity, not to exceed 234 capsules at retail or home delivery.</p> <ul style="list-style-type: none"> <li>• Criteria to approve the requested quantity, not to exceed 120 capsules per dispensing at retail or 720 capsules per dispensing at home delivery if the patient has aspergillosis were updated to approve the requested quantity, not to exceed 240 capsules per dispensing at retail or 720 capsules per dispensing at home delivery.</li> </ul> <p><b>Exclusions:</b> Exclusions to not provide additional quantities of itraconazole (Sporanox, generic) or Onmel 200 mg tablets for the treatment of tinea versicolor, tinea capitis, tinea corporis, tinea cruris, tinea pedis (any type including moccasin or plantar), tinea manuum, tinea imbricate, tinea faciei, or vaginal candidiasis, acute or recurrent, were removed.</p>	
Annual Revision	Policy statement was clarified to note that "one-time" approvals are provided for 30 days in duration.	04/03/2025

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