

## **Clinical Policy: Itraconazole (Sporanox, Onmel)**

Reference Number: CP.PMN.124

Effective Date: 11.01.06

Last Review Date: 05.19

Line of Business: Commercial, HIM\*, Medicaid

[Revision Log](#)

See [Important Reminder](#) at the end of this policy for important regulatory and legal information.

### **Description**

Itraconazole (Sporanox<sup>®</sup>, Onmel<sup>®</sup>) is an azole antifungal agent.

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*\*For Health Insurance Marketplace (HIM), if request is through pharmacy benefit, Onmel and brand Sporanox capsule are non-formulary and cannot be approved using these criteria; refer to the formulary exception policy, HIM.PA.103.*

### **FDA Approved Indication(s)**

Onmel is indicated for the treatment of onychomycosis of the toenail caused by *Trichophyton rubrum* or *T. mentagrophytes*.

Sporanox capsules are indicated in:

- Immunocompromised and non-immunocompromised patients for the treatment of:
  - Blastomycosis, pulmonary and extrapulmonary
  - Histoplasmosis, including chronic cavitary pulmonary disease and disseminated, nonmeningeal histoplasmosis
  - Aspergillosis, pulmonary and extrapulmonary, in patients who are intolerant of or who are refractory to amphotericin B therapy
- Non-immunocompromised patients for the treatment of:
  - Onychomycosis of the toenail, with or without fingernail involvement, due to dermatophytes (tinea unguium)
  - Onychomycosis of the fingernail due to dermatophytes (tinea unguium)

Sporanox oral solution is indicated for the treatment of oropharyngeal and esophageal candidiasis.

### **Policy/Criteria**

*Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.*

It is the policy of health plans affiliated with Centene Corporation<sup>®</sup> that Onmel and Sporanox are **medically necessary** when the following criteria are met:

#### **I. Initial Approval Criteria**

##### **A. Onychomycosis (must meet all):**

1. Diagnosis of onychomycosis;
2. Request is for Sporanox capsules or Onmel tablets (toenails only);
3. Member meets one of the following (a or b):

- a. For fingernail disease: Failure of a 6-week trial of oral terbinafine at 250 mg/day, unless contraindicated or clinically significant adverse effects are experienced;
- b. For toenail disease: Failure of a 12-week trial of oral terbinafine at 250 mg/day, unless contraindicated or clinically significant adverse effects are experienced;
4. Dose does not exceed (a or b):
  - a. Sporanox capsules: 400 mg (4 capsules) per day;
  - b. Onmel tablets: 200 mg (1 tablet) per day.

**Approval duration:**

**Medicaid/Commercial** – Fingernail disease: 2 months; toenail disease: 3 months

**HIM** – Fingernail disease: 2 months; toenail disease: 3 months for generic Sporanox  
(Refer to HIM.PA.103 for Onmel and brand Sporanox)

**B. Oropharyngeal Candidiasis (must meet all):**

1. Diagnosis of oropharyngeal candidiasis;
2. Request is for Sporanox oral solution;
3. Failure of a 14-day trial of nystatin suspension or clotrimazole troches/lozenges, unless contraindicated or clinically significant adverse effects are experienced;
4. Failure of a 14-day trial of fluconazole, unless contraindicated or clinically significant adverse effects are experienced;
5. Dose does not exceed 200 mg (20 mL) per day.

**Approval duration: 4 weeks**

**C. Esophageal Candidiasis (must meet all):**

1. Diagnosis of esophageal candidiasis;
2. Request is for Sporanox oral solution;
3. Failure of a 21-day trial of fluconazole at up to maximally indicated doses, unless contraindicated or clinically significant adverse effects are experienced;
4. Dose does not exceed 200 mg (20 mL) per day.

**Approval duration: 4 weeks**

**D. Aspergillosis (must meet all):**

1. Diagnosis of aspergillosis;
2. Request is for Sporanox capsules;
3. Failure of a 3-month trial of voriconazole at up to maximally indicated doses, unless contraindicated or clinically significant adverse effects are experienced;  
*\*Prior authorization may be required for voriconazole*
4. Dose does not exceed 400 mg (4 capsules) per day.

**Approval duration:**

**Medicaid/Commercial** – 3 months

**HIM** – 3 months for generic Sporanox (Refer to HIM.PA.103 for brand Sporanox)

**E. Blastomycosis or Histoplasmosis (must meet all):**

1. Diagnosis of blastomycosis or histoplasmosis;
2. Request is for Sporanox capsules;
3. Dose does not exceed 400 mg (4 capsules) per day.

**Approval duration:**

**Medicaid/Commercial** – Blastomycosis: 6 months; Histoplasmosis: 6 weeks  
**HIM** – Blastomycosis: 6 months; Histoplasmosis: 6 weeks for generic Sporanox (*Refer to HIM.PA.103 for brand Sporanox*)

**F. Hematologic Malignancy (off-label) (must meet all):**

1. Diagnosis of hematologic malignancy;
2. Request is for Sporanox;
3. Member meets one of the following (a or b):
  - a. Request is for prophylaxis of aspergillosis;
  - b. Request is for prophylaxis of candidiasis, and member has failed fluconazole at up to maximally indicated doses unless contraindicated or clinically significant adverse effects are experienced;
4. Dose does not exceed (a or b):
  - a. Capsules: 400 mg (4 capsules) per day;
  - b. Oral solution: 200 mg (20 mL) per day.

**Approval duration:**

**Medicaid/Commercial** – 3 months

**HIM** – 3 months for oral solution and generic capsules (*Refer to HIM.PA.103 for brand capsules*)

**G. Other diagnoses/indications**

1. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.CPA.09 for commercial, HIM.PHAR.21 for health insurance marketplace, and CP.PMN.53 for Medicaid.

**II. Continued Therapy**

**A. Onychomycosis (must meet all):**

1. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
2. Member is responding positively to therapy;
3. Member has not received more than 90 days of treatment;
4. If request is for a dose increase, new dose does not exceed (a or b):
  - a. Sporanox capsules: 400 mg (4 capsules) per day;
  - b. Onmel tablets: 200 mg (1 tablet) per day.

**Approval duration:**

**Medicaid/Commercial** - Fingernail disease: up to 2 months total; toenail disease: up to 3 months total

**HIM** - Fingernail disease: up to 2 months total; toenail disease: up to 3 months total for generic Sporanox (*Refer to HIM.PA.103 for Onmel and brand Sporanox*)

**B. Oropharyngeal/Esophageal Candidiasis (must meet all):**

1. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
2. Member is responding positively to therapy;
3. Request is for Sporanox oral solution;

4. If request is for a dose increase, new dose does not exceed 200 mg (20 mL) per day.

**Approval duration: 2 weeks**

**C. Blastomycosis, Histoplasmosis, or Aspergillosis (must meet all):**

1. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
2. Member is responding positively to therapy;
3. Request is for Sporanox capsules;
4. If request is for a dose increase, new dose does not exceed 400 mg per day (4 capsules) per day.

**Approval duration:**

**Medicaid/Commercial** – Blastomycosis: 6 months; Histoplasmosis: 6 weeks; Aspergillosis: 3 months

**HIM** – Blastomycosis: 6 months; Histoplasmosis: 6 weeks; Aspergillosis: 3 months for generic Sporanox (*Refer to HIM.PA.103 for brand Sporanox*)

**D. Hematologic Malignancy (off-label) (must meet all):**

1. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
2. Request for Sporanox;
3. Member is responding positively to therapy;
4. If request is for a dose increase, new dose does not exceed (a or b):
  - a. Sporanox capsules: 400 mg (4 capsules) per day;
  - b. Sporanox oral solution: 200 mg (20 mL) per day.

**Approval duration:**

**Medicaid/Commercial** – 6 months

**HIM** – 6 months for oral solution and generic capsules (*Refer to HIM.PA.103 for brand capsules*)

**E. Other diagnoses/indications (must meet 1 or 2):**

1. Currently receiving medication via Centene benefit and documentation supports positive response to therapy.

**Approval duration: Duration of request or 6 months (whichever is less); or**

2. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.CPA.09 for commercial, HIM.PHAR.21 for health insurance marketplace, and CP.PMN.53 for Medicaid.

**III. Diagnoses/Indications for which coverage is NOT authorized:**

- A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policies – CP.CPA.09 for commercial, HIM.PHAR.21 for health insurance marketplace, and CP.PMN.53 for Medicaid or evidence of coverage documents.

**IV. Appendices/General Information**

*Appendix A: Abbreviation/Acronym Key*

FDA: Food and Drug Administration

*Appendix B: Therapeutic Alternatives*

*This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may not be a formulary agent for all relevant lines of business and may require prior authorization.*

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
terbinafine (Lamisil <sup>®</sup> )	250 mg PO QD	500 mg per day
nystatin suspension	400,000 to 600,000 units (4 to 6 mL) per dose swished in the mouth QID	2.4 million units per day
clotrimazole troches/lozenges (Mycelex <sup>®</sup> )	10 mg troche PO 5 times daily for 14 days	Varies
fluconazole (Diflucan <sup>®</sup> )	400 mg PO per day	800 mg per day
voriconazole (Vfend <sup>®</sup> )	Weight ≥ 40 kg: 200 mg PO every 12 hours Weight < 40 kg: 100 mg PO every 12 hours	Weight ≥ 40 kg: 800 mg per day Weight < 40 kg: 400 mg per day

*Therapeutic alternatives are listed as Brand name<sup>®</sup> (generic) when the drug is available by brand name only and generic (Brand name<sup>®</sup>) when the drug is available by both brand and generic.*

*Appendix C: Contraindications/Boxed Warnings*

- Contraindication(s):
  - Itraconazole should not be administered for the treatment of onychomycosis in patients with evidence of ventricular dysfunction such as congestive heart failure (CHF) or a history of CHF.
  - Concomitant coadministration of itraconazole with the following drugs: methadone, dofetilide, quinidine, ergot alkaloids (such as dihydroergotamine, ergometrine (ergonovine), ergotamine, methylergometrine (methylergonovine)), felodipine, pimozide, oral midazolam, triazolam, nisoldipine, cisapride, lovastatin, simvastatin.
  - Additional product-specific drug-drug interactions include:
    - Onmel: levacetylmethadol (levomethadyl)
    - Sporanox (capsules and oral solution): disopyramide, dronedarone, irinotecan, lurasidone, ivabradine, ranolazine, eplerenone, ticagrelor and, in subjects with varying degrees of renal or hepatic impairment, colchicine, fesoterodine, and solifenacin.
    - Sporanox capsules: telithromycin
    - Sporanox oral solution: isavuconazole, naloxegol, lomitapide, avanafil
  - Pregnancy, or women contemplating pregnancy
  - Hypersensitivity to itraconazole

- Boxed warning(s):
  - CHF or history of CHF (see contraindications)
  - Drug-drug interactions (see contraindications)

**V. Dosage and Administration**

Drug Name	Indication	Dosing Regimen	Maximum Dose
Itraconazole (Sporanox) capsule	Blastomycosis	200 mg PO QD	400 mg/day
	Histoplasmosis	200 mg PO QD	400 mg/day
	Aspergillosis	200 to 400 mg PO QD	400 mg/day
	Onychomycosis	200 mg PO QD (toenails with or without fingernail involvement)  200 mg PO BID for 1 week, followed by no drug for 3 weeks, then another week of 200 mg PO BID or 200 mg PO QD for 6 weeks (fingernails only)	400 mg/day
	In life-threatening situations	Loading dose of 200 mg PO TID given for the first 3 days of treatment	600 mg/day
Itraconazole (Sporanox) oral solution	Oropharyngeal candidiasis	200 mg (20 mL) PO daily for 1 to 2 weeks; swish in the mouth (10 mL at a time) for several seconds and swallow	200 mg (20 mL)/day
	Esophageal candidiasis	100 mg (10 mL) PO daily for a minimum treatment of three weeks	200 mg (20 mL)/day
Itraconazole (Onmel)	Onychomycosis	Toenail: 200 mg (one tablet) PO QD for 12 consecutive weeks	200 mg/day

**VI. Product Availability**

Drug Name	Availability
Itraconazole (Sporanox)	Capsules: 100 mg Oral solution: 10 mg/mL
Itraconazole (Onmel)	Tablets: 200 mg

**VII. References**

1. Sporanox Oral Solution Prescribing Information. Titusville, NJ: Janssen Pharmaceuticals, Inc.; April 2018. Available at: <http://www.janssenlabels.com/package-insert/product-monograph/prescribing-information/SPORANOX-Oral+Solution-pi.pdf>. Accessed February 26, 2019.
2. Sporanox Capsules Prescribing Information. Titusville, NJ: Janssen Pharmaceuticals, Inc., May 2018. Available at: [https://www.accessdata.fda.gov/drugsatfda\\_docs/label/2018/020083s062lbl.pdf](https://www.accessdata.fda.gov/drugsatfda_docs/label/2018/020083s062lbl.pdf). Accessed February 26, 2019.
3. Onmel Prescribing Information. Greensboro, NC: Merz Pharmaceuticals, LLC. November 2012. Available at: <http://www.onmel.com/>. Accessed February 26, 2019.

4. Clinical Pharmacology [database online]. Tampa, FL: Gold Standard, Inc.; 2019. Available at: <http://www.clinicalpharmacology-ip.com/>.
5. 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(12):1801.
6. Pappas PG, Kauffman CA, Andes DR et al. Clinical practice guidelines for the management of candidiasis: 2016 update by the Infectious Disease Society of America. Clin Infect Dis. 2016 Feb 15;62(4):e1-50. doi: 10.1093/cid/civ933.
7. Wheat LJ, 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(7):807.
8. 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 Aug 15;63(4):e1-e60. doi: 10.1093/cid/ciw326.
9. Ameen M, Lear JT, Madan V, et al. British Association of Dermatologists' guidelines for the management of onychomycosis 2014. Br J Dermatology. 2014;171:937-58.
10. Freifeld AG, Bow EJ, Sepkowitz KA et al. Clinical practice guideline for the use of antimicrobial agents in neutropenic patients with cancer: 2010 update by the infectious diseases society of america. Clin Infect Dis. 2011 Feb 15;52(4):e56-93. doi: 10.1093/cid/cir073.
11. 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](http://aidsinfo.nih.gov/contentfiles/lvguidelines/adult_oi.pdf). Accessed February 26, 2019.
12. 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: [http://aidsinfo.nih.gov/contentfiles/lvguidelines/oi\\_guidelines\\_pediatics.pdf](http://aidsinfo.nih.gov/contentfiles/lvguidelines/oi_guidelines_pediatics.pdf). Accessed February 26, 2019.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Updated references. Clarified “other” to be other FDA labeled indications in criteria for approval.	04.15	04.15
Removed onychomycosis requirement of pathologic (KOH prep, fungal culture, or nail biopsy) and approval requirement of only 84 capsules, added age requirement and maximum dose; For Oropharyngeal/Esophageal Candidiasis added age requirement, request for oral solution and maximum dose; For Blastomycosis, Histoplasmosis or Aspergillosis added age requirement, maximum dose and increased continued approval from 14 days to 6 months; Removed Other FDA Labeled Indications;	02.16	05.16



Reviews, Revisions, and Approvals	Date	P&T Approval Date
<p>Revised background information to clearly include indications and MOA; References updated and added.</p>		
<p>Added 6 week trial of terbinafine for fingernails and 12 week trial of terbinafine for toenail onychomycosis and limited trial to one course instead of 2 courses. Removed requirement of multiple toes and/or fingers involved or member having a diagnosis of diabetes mellitus, peripheral vascular disease, or is immunocompromised for onychomycosis per specialist feedback. Separated approval durations for onychomycosis for ingernails only: 2 months and toenails: 3 months per PI, guideline and clinical pharmacology. Separated initial criteria for oropharyngeal and esophageal candidiasis. Esophageal candidiasis requires a trial of fluconazole only per IDSA guidelines. Added 14 day duration of nystatin or clotrimazole trial and fluconazole trial for oropharyngeal candidiasis per IDSA guideline. Added 21 day duration of fluconazole trial for esophageal candidiasis per IDSA guideline. Changed approval duration from 8 weeks to 4 weeks for oropharyngeal and esophageal candidiasis per IDSA guideline and PI. Changed continued approval duration for oropharyngeal and esophageal candidiasis from 8 weeks to 2 weeks per IDSA guideline and PI. Added Request is for Sporanox capsules for onychomycosis, blastomycosis, histoplasmosis, and aspergillosis. Clarified continued approval duration for blastomycosis, histoplasmosis, and aspergillosis per IDSA guidelines. Added continued approval criteria for onchomycosis. Converted to new template Removed age criteria as age is not an absolute contraindication per FDA labeling Updated references</p>	03.17	05.17
<p>2Q 2018 annual review: policies combined for Medicaid, Commercial, and HIM; added Onmel to policy; added age; added 3 months trial of voriconazole for aspergillosis per IDSA; added criteria for hematologic malignancy; references reviewed and updated.</p>	02.06.18	05.18
<p>2Q 2019 annual review: no significant changes; removed age requirement due to lack of age restriction in guidelines; corrected</p>	02.26.19	05.19



Reviews, Revisions, and Approvals	Date	P&T Approval Date
dosing typo in continued therapy section for blastomycosis, histoplasmosis, and aspergillosis; references reviewed and updated.		

**Important Reminder**

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. “Health Plan” means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan’s affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

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**Note:**

**For Medicaid members**, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.

**For Health Insurance Marketplace members**, when applicable, this policy applies only when the prescribed agent is on your health plan approved formulary. Request for non-formulary drugs must be reviewed using the formulary exception policy: HIM.PA.103.

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