

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

Reference Number: CP.PMN.124

Effective Date: 11.01.06

Last Review Date: 05.18

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.

*\*For Health Insurance Marketplace (HIM), Onmel is 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
- For the treatment of histoplasmosis, including chronic cavitary pulmonary disease and disseminated, nonmeningeal histoplasmosis
- For the treatment of aspergillosis, pulmonary and extrapulmonary, in patients who are intolerant of or who are refractory to amphotericin B therapy

Sporanox capsules are indicated in non-immunocompromised patients:

- For the treatment of onychomycosis of the toenail, with or without fingernail involvement, due to dermatophytes (*tinea unguium*)
- For the treatment of 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. Age  $\geq$  3 years;

3. Request is for Sporanox capsules or Onmel tablets (toenails only);
4. 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;
5. Dose does not exceed (a or b):
  - a. Sporanox capsules: 400 mg per day (4 capsules per day);
  - b. Onmel tablets: 200 mg per day (1 tablet per day).

**Approval duration:**

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

**HIM** - Approve Sporanox only for fingernail disease: 2 months; toenail disease: 3 months (*Refer to HIM.PA.103 for Onmel*)

**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 maximally indicated dose 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. Age  $\geq$  3 years;
3. Request is for Sporanox capsules;
4. If member has aspergillosis, failure of a 3 month trial of voriconazole at maximally indicated dose unless contraindicated or clinically significant adverse effects are experienced;

*\*Voriconazole may require a prior authorization*

5. Dose does not exceed 400 mg per day (4 capsules per day).

**Approval duration: 3 months**

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

1. Diagnosis of blastomycosis, histoplasmosis, or aspergillosis;
2. Request is for Sporanox capsules;

3. Dose does not exceed 400 mg per day (4 capsules per day).

**Approval duration: Blastomycosis: 6 months; Histoplasmosis: 6 weeks**

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

1. Diagnosis of hematologic malignancy;
2. 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 maximally indicated dose unless contraindicated or clinically significant adverse effects are experienced;
3. Dose does not exceed (a or b):
  - a. Sporanox capsules: 400 mg per day (4 capsules per day);
  - b. Sporanox oral solution: 200 mg (20 mL) per day.

**Approval duration: 3 months**

**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. Sporanox capsules: 400 mg per day (4 capsules per day);
  - b. Onmel tablets: 200 mg per day (1 tablet per day).

**Approval duration:**

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

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

**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 600 mg per day (4 capsules per day).

**Approval duration: Blastomycosis: 6 months; histoplasmosis: 6 weeks; aspergillosis: 3 months**

**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 Sporanax;
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 per day (4 capsules per day);
  - b. Sporanox oral solution: 200 mg (20 mL) per day.

**Approval duration: 6 months**

**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*

Not applicable

*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®)	250 mg once daily	500 mg per day

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
Nystatin suspension	400,000 to 600,000 units (4 to 6 mL) per dose swished in the mouth 4 times per day	2.4 million units per day
Clotrimazole troches/lozenges (Mycelex <sup>®</sup> )	10 mg troche 5 times daily for 14 days	Varies
Fluconazole (Diflucan <sup>®</sup> )	400 mg per day	800 mg per day
Voriconazole (Vfend <sup>®</sup> )	≥ 40 kg: 200 mg every 12 hours < 40 kg: 100 mg every 12 hours	≥ 40 kg: 800 mg per day < 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.*

**V. Dosage and Administration**

Drug Name	Indication	Dosing Regimen	Maximum Dose
Itraconazole (Sporanox) capsule	Blastomycosis	200 mg once daily	400 mg/day
	Histoplasmosis	200 mg once daily	400 mg/day
	Aspergillosis	200 to 400 mg daily	400 mg/day
	Onychomycosis	200 mg once daily (toenails with or without fingernail involvement)  200 mg PO twice daily for 1 week, followed by no drug for 3 weeks, then another week of 200 mg PO twice daily or 200 mg daily for 6 weeks (fingernails only)	400 mg/day
	In life-threatening situations	Loading dose of 200 mg three times daily given for the first 3 days of treatment	600 mg/day
Itraconazole (Sporanox) oral solution	Oropharyngeal candidiasis	200 mg (20 mL) 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) daily for a minimum treatment of three weeks	200 mg (20 mL)/day
Itraconazole (Onmel)	Onychomycosis	toenail: 200 mg (one tablet) once daily 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 Prescribing Information. Titusville, NJ: Janssen Pharmaceuticals, Inc.; October 2017. Available at: [http://www.janssen.com/us/sites/www\\_janssen\\_com\\_usa/files/products-documents/040501150916\\_sporanox\\_oral\\_solution\\_eos\\_code\\_update\\_only\\_sept\\_20151.pdf](http://www.janssen.com/us/sites/www_janssen_com_usa/files/products-documents/040501150916_sporanox_oral_solution_eos_code_update_only_sept_20151.pdf). Accessed January 2018.
2. Sporanox oral solution Prescribing Information. Titusville, NJ: Janssen Pharmaceuticals, Inc., October 2017. Available at <https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=ae50721d-ee15-4ee7-9fe7-afd98c56461b>. Accessed January 2018.
3. Onmel Prescribing Information. Greensboro, NC: Merz Pharmaceutical, LLC. November 2012. Available at <http://www.onmel.com/>. Accessed January 2018.
4. Sporanox® monograph. Clinical Pharmacology. Accessed April 2018.
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.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
References updated.	08.14	08.14
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; Revised background information to clearly include indications and MOA; References updated and added.	02.16	05.16

Reviews, Revisions, and Approvals	Date	P&T Approval Date
<ul style="list-style-type: none"> <li>- 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.</li> <li>- 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.</li> <li>- Separated approval durations for onychomycosis for ingernails only: 2 months and toenails: 3 months per PI, guideline and clinical pharmacology.</li> <li>- Separated initial criteria for oropharyngeal and esophageal candidiasis. Esophageal candidiasis requires a trial of fluconazole only per IDSA guidelines.</li> <li>- Added 14 day duration of nystatin or clotrimazole trial and fluconazole trial for oropharyngeal candidiasis per IDSA guideline.</li> <li>- Added 21 day duration of fluconazole trial for esophageal candidiasis per IDSA guideline.</li> <li>- Changed approval duration from 8 weeks to 4 weeks for oropharyngeal and esophageal candidiasis per IDSA guideline and PI.</li> <li>- Changed continued approval duration for oropharyngeal and esophageal candidiasis from 8 weeks to 2 weeks per IDSA guideline and PI.</li> <li>- Added Request is for Sporanox capsules for onychomycosis, blastomycosis, histoplasmosis, and aspergillosis.</li> <li>- Clarified continued approval duration for blastomycosis, histoplasmosis, and aspergillosis per IDSA guidelines.</li> <li>- Added continued approval criteria for onchomycosis.</li> <li>- Converted to new template</li> <li>- Removed age criteria as age is not an absolute contraindication per FDA labeling</li> <li>- Updated references</li> </ul>	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

**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.

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