Clinical Policy: Itraconazole (Sporanox)

Reference Number: PA.CP.PPA.07
Effective Date: 01/18
Last Review Date: 04/19

Coding Implications
Revision Log

Description
Itraconazole (Sporanox®, Onmel®)) is an azole antifungal agent.

FDA approved indication
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:
  - 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 (including office chart notes and lab results) supporting that member has met all approval criteria

It is the policy of Pennsylvania Health and Wellness ® that Sporanox is **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: Fingernails only: 2 months; Toenails: 3 months

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. 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; or 600mg/day for the first three treatment days.

Approval duration: 3 months

E. Blastomycosis or Histoplasmosis (must meet all)**:**
1. Diagnosis of blastomycosis or histoplasmosis;
2. Request is for Sporanox capsules;
3. Dose does not exceed 600 mg per day.

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

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 dose 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: 3 months

G. Other diagnoses/indications

1. Refer to PA.CP.PMN.53 if diagnosis is NOT specifically listed.

II. Continued Therapy

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

1. Currently receiving medication via Pennsylvania Health and Wellness benefit or member has previously met initial approval criteria or the Continuity of Care policy (PA.LTSS.PHAR.01) applies;
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: Allow 2 months of total treat for fingernails; Allow 3 months of total treatment for toenails

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

1. Currently receiving medication via Pennsylvania Health and Wellness benefit or member has previously met initial approval criteria or the Continuity of Care policy (PA.LTSS.PHAR.01) applies;
2. Documentation of positive response 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 Pennsylvania Health and Wellness benefit or member has previously met initial approval criteria or the Continuity of Care policy (PA.LTSS.PHAR.01) applies;
2. Documentation of positive response to therapy;
3. Request is for capsules;
4. If request is for a dose increase, new dose does not exceed 400 mg (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 Pennsylvania Health and Wellness benefit or member has previously met initial approval criteria or the Continuity of Care policy (PA.LTSS.PHAR.01) applies;
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. Capsules: 400 mg (4 capsules) per day;
   b. 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 Pennsylvania Health and Wellness benefit and documentation supports positive response to therapy or the Continuity of Care policy (PA.LTSS.PHAR.01) applies; or
2. Refer to PA.CP.PMN.53 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

Approval duration: 6 months

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 policy – PA.CP.PMN.53 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®)	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®)	10 mg troche PO 5 times daily for 14 days	Varies
fluconazole (Diflucan®)	400 mg PO per day	800 mg per day
voriconazole (Vfend®)	Weight ≥ 40 kg: 200 mg PO every 12 hours	Weight ≥ 40 kg: 800 mg per day

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
	Weight < 40 kg: 100 mg PO every 12 hours	Weight < 40 kg: 400 mg per day

Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) 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 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	400 mg/day

Drug Name	Indication	Dosing Regimen	Maximum Dose
		or 200 mg daily for 6 weeks (fingernails only)	
	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
Itraconzole (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
Itraconzole (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.
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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_pediatrics.pdf. Accessed February 26, 2019.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
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; References reviewed and updated.	02.16	
2Q 2019 annual review: removed age requirement due to lack of age restriction in guidelines; references reviewed and updated.	04.19	