envolve Pharmacy Solutions

Clinical Policy: Itraconazole (Onmel, Sporanox)
Reference Number: ERX.NPA.25
Effective Date: 06.01.15
Last Review Date: 08.17
Line of Business: Commercial [Prescription Drug Plan] Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

Description
Itraconazole (Omnel®, Sporanox®) 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
- 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 (which may include office chart notes and lab results) supporting that member has met all approval criteria

It is the policy of health plans affiliated with Envolve Pharmacy Solutions™ 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. At the time of request, member is not currently receiving any of the medications in Appendix B;
  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:
  Fingernail disease: 2 months

Toenail disease: 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. At the time of request, member is not currently receiving any of the medications in Appendix B ;
6. 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. At the time of request, member is not currently receiving any of the medications in Appendix B;
5. Dose does not exceed 200 mg (20 mL) per day.

Approval duration: 4 weeks

D. **Aspergillosis, Blastomycosis, Histoplasmosis**
1. Diagnosis of aspergillosis, blastomycosis, or histoplasmosis;
2. Request is for Sporanox capsules;
3. If member has aspergillosis, failure of amphotericin B at up to maximally indicated doses unless contraindicated or clinically significant adverse effects are experienced;
4. At the time of request, member is not currently receiving any of the medications in Appendix B;
5. Dose does not exceed 400 mg per day (4 capsules per day).

Approval duration:
Blastomycosis: 6 months
Histoplasmosis: 6 weeks
Aspergillosis: 3 months

E. **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. At the time of request, member is not currently receiving any of the medications in Appendix B ;
4. Dose does not exceed 400 mg per day (4 capsules per day).

Approval duration: 3 months

F. **Other diagnoses/indications**
1. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized)

II. **Continued Therapy**

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

1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions or member has previously met initial approval criteria;
2. Member has not received more than 90 days of treatment;
3. If request is for a dose increase, new dose does not exceed 400 mg per day (4 capsules per day).

Approval duration:
Fingernail disease: Up to 2 months of total treatment
Toenail disease: Up to 3 months of total treatment

B. Oropharyngeal/Esophageal Candidiasis (must meet all)**:**
1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions or member has previously met initial approval criteria;
2. Member is responding positively to therapy;
3. 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, Aspergillosis (must meet all)**:**
1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions or member has previously met initial approval criteria;
2. Member is responding positively to therapy;
3. 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 a health plan affiliated with Envolve Pharmacy Solutions Centene benefit or member has previously met initial approval criteria;
2. Member is responding positively response to therapy;
3. If request is for a dose increase, new dose does not exceed 400 mg per day (4 capsules per day).

Approval duration: 6 months

E. Other diagnoses/indications (must meet 1 or 2)**:**
1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions and documentation supports positive response to therapy.
   Approval duration: Duration of request or 12 months (whichever is less); or
2. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized)

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 – ERX.PA.01 or evidence of coverage documents

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key
FDA: Food and Drug Administration

Appendix B: Drugs Interacting with Itraconazole
Itraconazole increases the plasma concentration of the following drug therapies. In some cases, serious cardiovascular events, including QT prolongation, torsades de pointes, ventricular tachycardia, cardiac arrest, and/or sudden death have occurred.

- Cisapride
- Disopyramide
- Dofetilide

- Dronedarone
- Eplerenone
- Ergot alkaloids (e.g., dihydroergotamine, ergometrine [ergonovine])
- Ergotamine
- Felodipine
- Irinotecan
- Ivabradine
- Lovastatin
- Lurasidone
- Methadone
- Methylergometrine (methylergonovine)
- Nisoldipine
- Oral midazolam
- Pimozide
- Quinidine
- Ranolazine
- Simvastatin
- Ticagrelor
- Triazolam

In patients with varying degrees of renal or hepatic impairment, colchicine, fesoterodine, telithromycin and solifenacin are also contraindicated.

Appendix C: Therapeutic Alternatives

Drug	Dosing Regimen	Dose Limit/ Maximum Dose
Lamisil® (terbinafine)	250 mg by mouth once daily	250 mg/day
Diflucan® (fluconazole)	200 mg on the first day, followed by 100 mg once daily	400 mg/day
Nystatin suspension	Swish 4 to 6 ml by mouth 4 times per day	20 mL/day
Mycelex Troche® (clotrimazole)	Dissolve a 10 mg troche slowly and completely in the mouth 5 times daily for 14 days	50 mg/day
Amphotericin B	0.25-0.3 mg/kg/dose IV once daily with doses increased by 5-10 mg/day up to a full dose of 0.5-0.7 mg/kg/dose IV once daily	1-1.5 mg/kg/day IV

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 200mg 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
Itraconzole (Onmel)	Onychomycosis	toenail: 200 mg (one tablet) once daily for 12 consecutive weeks	200mg/day

envolve Pharmacy Solutions

VI. Product Availability

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

VII. References

1. Sporanox Prescribing Information. Titusville, NJ: Janssen Pharmaceuticals, Inc.; April 2015. 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. Accessed June 2017.
2. Sporanox oral solution Prescribing Information. Titusville, NJ: Janssen Pharmaceuticals, Inc., October 2016. Available at https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=ae50721d-ee15-4ee7-9fe7-afd98c56461b. Accessed June 2017.
3. Sporanox® monograph. Clinical Pharmacology. Accessed January 2017.
4. 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.
5. 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.
6. 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.
7. 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.
8. 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.
   Onmel Prescribing Information. Greensboro, NC: Merz Pharmaceutical, LLC. November 2012. Available at http://www.onmel.com/. Accessed June 23, 2017.
9. 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.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy created.	06/15	06/15
Updated to new template (converted algorithm to bulleted criteria, added background and references). Separated criteria by diagnosis. Removed safety criteria ("Previously used Onmel safely") as this is outside the scope of a PBM. Modified requirement of fluconazole trial duration from ≥ 3 weeks to ≥ 2 weeks in treatment of candidiasis per literature review. Modified approval duration of candidiasis prophylaxis in setting of hematologic malignancy from 4 weeks to 3 months to match aspergillosis prophylaxis approval duration per literature review; removed trial duration of fluconazole for candidiasis prophylaxis as duration of fluconazole therapy is moot (failure would mean infection at any point while on prophylaxis therapy). Added requirement for trial/failure of amphotericin B in treatment of aspergillosis per FDA labeling.	07/16	09/16
Converted to new template. Removed requirement of generic trial of itraconazole for onychomycosis; Removed "If request is	06/17	08/17

Reviews, Revisions, and Approvals	Date	P&T Approval Date
for Onmel, failure of generic itraconazole capsules, unless contraindicated" for candidiasis because Onmel is only approved for onychomycosis; changed 14 day trial to 21 day duration of fluconazole trial for esophageal candidiasis per IDSA guideline; Removed lab results dated within the past 14 days are consistent with diagnosis for blastomycosis, histoplasmosis and aspergillosis; Added DDIs per black box warning that such interactions can be fatal; Separated continued approval criteria. Updated approval durations to be in line with current IDSA guidelines. Separated toenail and finger nail durations per IDSA. Changed Aspergillosis, Blastomycosis, and Histoplasmosis approval duration from 6 months per IDSA.		

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.

This Clinical Policy is not intended to dictate to providers how to practice medicine, nor does it constitute a contract or guarantee regarding payment or results. 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 policy is the property of Envolve Pharmacy Solutions. Unauthorized copying, use, and distribution of this Policy or any information contained herein is strictly prohibited. By accessing this policy, you agree to be bound by the foregoing terms and conditions, in addition to the Site Use Agreement for Health Plans associated with Envolve Pharmacy Solutions.

©2015 Envolve Pharmacy Solutions. All rights reserved. All materials are exclusively owned by Envolve Pharmacy Solutions and are protected by United States copyright law and international copyright law. No part of this publication may be reproduced, copied, modified, distributed, displayed, stored in a retrieval system, transmitted in any form or by any means, or otherwise published without the prior written permission of Envolve Pharmacy Solutions. You may not alter or remove any trademark, copyright or other notice contained herein.