Clinical Policy: Itraconazole (Sporanox)
Reference Number: CP.PPA.07
Effective Date: 11/06
Last Review Date: 05/17
Line of Business: Medicaid

Coding Implications
Revision Log

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

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

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

It is the policy of health plans affiliated with Centene Corporation® that Sporanox is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

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

1. Diagnosis of onychomycosis;
~~1.~~2. Request is for Sporanox capsules;
~~2. Age ≥ 18 years;~~
~~3. Failed two courses of oral terbinafine (Lamisil®), unless contraindication;~~
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. Multiple toes and/or fingers involved;~~, ~~with severe pain or erythema in surrounding tissue; OR~~
~~5. Criteria A and B are met and patient has diagnosis of diabetes mellitus, peripheral vascular disease, or is immunocompromised.~~
~~6.~~4. Dose does not exceed 400 mg per day (4 capsules per day).
Approval duration: Fingernails only: 2 months; Toenails: 3 months

B. Oropharyngeal~~/Esophageal Candidiasis~~ Candidiasis (must meet all)**:**
1. Diagnosis of oropharyngeal ~~or esophageal~~ candidiasis;
2. Request is for Sporanox oral solution;
~~2.~~3. Failure of a 14 day trial of nystatin suspension or clotrimazole troches/lozenges unless contraindicated or clinically significant adverse effects are experienced;
~~3. Age ≥ 18 years;~~
4. Failure of a 14 day trial of fluconazole ~~and nystatin suspension or clotrimazole troches/lozenges~~ unless ~~member experiences clinically significant adverse effects or has contraindication(s)~~contraindicated or clinically significant adverse effects are experienced;
5. Dose does not exceed 200 mg (20 mL~~l~~) per day.
Approval duration: ~~8 weeks~~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

~~C.~~**D. Blastomycosis, Histoplasmosis, or Aspergillosis** (must meet all)**:**
1. Diagnosis of blastomycosis, histoplasmosis, or aspergillosis;
~~1.~~2. Request is for Sporanox capsules;
~~2. Age ≥ 18 years;~~
3. Dose does not exceed ~~600~~ 400 mg per~~/~~ day (4 capsules per day).
Approval duration: ~~14 days~~Blastomycosis: 6 months; Histoplasmosis: 6 weeks; Aspergillosis: 3 months

~~D.~~**E. Other diagnoses/indications**
1. Refer to CP.PMN.53 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 Centene benefit or member has previously met initial approval criteria;
2. Dose does not exceed 400 mg per day (4 capsules/day);
3. Member has not received more than 90 days of treatment.

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~~1. Not a~~Applicable
Approval duration: ~~Not available for~~ **Allow 2 months of total treat for fingernails; Allow 3 months of total treatment for toenails~~continued therapy may not be approved~~**

B. Oro~~r~~pharyngeal/Esophageal Candidiasis (must meet all)**:**
1. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
2. Documentation of positive response to therapy;
3. If request is for a dose increase, new dose does not exceed 200 mg (20 mL~~l~~) per day.

Approval duration: ~~8~~ 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. Documentation of positive response to therapy;
3. If request is for a dose increase, new dose does not exceed 600 mg per~~/~~ day (4 capsules per day).

~~4.~~ **Approval duration: Blastomycosis: 6 months; Histoplasmosis: 6 weeks; Aspergillosis: 3 months~~6 months~~**

D. Other diagnoses/indications (must meet 1 or 2)**:**
1. Currently receiving medication via Centene benefit and documentation supports positive response to therapy; or
2. Refer to 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 – CP.PMN.53 or evidence of coverage documents~~;~~

~~**B.** [Indications/diagnoses/situations in which drug is unsafe/ineffective]~~

IV. Appendices/General Information

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

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
Blastomycosis	200 mg once daily	400 mg daily
Histoplasmosis	200 mg once daily	400 mg daily
Aspergillosis	200 to 400 mg daily	400 mg daily

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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 daily
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) ~~per day~~daily
Esophageal candidiasis	100 mg (10 mL) daily for a minimum treatment of three weeks	200 mg (20 mL) ~~per day~~daily
In life-threatening situations	*L~~l~~oading dose of 200 three times daily ~~be~~ given for the first 3 days of treatment*	*600 mg daily~~/day~~*

VI. Product Availability
Capsules: 100 mg
Oral solution: 10 mg/mL

VII. Workflow Document

Sporanox WF.docx Sporanox WF.docx

VIII. 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/040501-150916_sporanox_oral_solution_eos_code_update_only_sept_20151.pdf. Accessed ~~February 2016~~January 2017.
2. Sporanox® oral solution P~~p~~rescribing I~~i~~nformation. Titusville, NJ: Janssen Pharmaceuticals, Inc., October 2016. ~~Accessed February 2016 .~~Available at https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=ae50721d-ee15-4ee7-9fe7-afd98c56461b. Accessed January 2017.

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~~http://www.accessdata.fda.gov/drugsatfda_docs/label/2009/020657s011s018s019s021lbl.pdf~~

3. Sporanox® monograph. Clinical Pharmacology. Accessed ~~February 2016~~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.~~Clin Infect Dis. 2015.~~
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.

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Reviews, Revisions, and Approvals	Date	P&T Approval Date
Revise item "a" under Onychomycosis criteria for approval to state: "Diagnosis of onychomycosis by appropriate nail specimens for pathologic confirmation (KOH prep, fungal culture, or nail biopsy)" Add the following to item "d" under Onychomycosis criteria for approval: "Criteria a and b are met and" Remove the following item under Onychomycosis criteria for approval: "Edema, erythema or purulent drainage in surrounding tissue and positive fungal culture"	08/09	08/09
References updated. Added fluconazole prerequisite for treatment of oral candidiasis. Updated "Continued Approval" criteria.	08/10	08/10
References updated.	07/11	07/11
References updated.	08/12	08/12
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;	02/16	05/16

Reviews, Revisions, and Approvals	Date	P&T Approval Date
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.		
~~No c~~Clinical changes to criteria - 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. - Seperated 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	03~~1~~/17	05/17

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.

This clinical policy is the property of the Health Plan. Unauthorized copying, use, and distribution of this clinical policy or any information contained herein are strictly prohibited. Providers, members and their representatives are bound to the terms and conditions expressed herein through the terms of their contracts. Where no such contract exists, providers, members and their representatives agree to be bound by such terms and conditions by providing services to members and/or submitting claims for payment for such services.

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.