

## Clinical Policy: Posaconazole (Noxafil)

Reference Number: AZ.CP.PHAR.30

Effective Date: 11.16.16

Last Review Date: 09.12.18

Line of Business: Arizona Medicaid

[Revision Log](#)

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

### Description

Posaconazole (Noxafil<sup>®</sup>) is a broad-spectrum oral triazole antifungal agent.

### FDA approved indication

Noxafil is indicated:

- Prophylaxis of invasive *Aspergillus* and *Candida* infections in patients who are at high risk of developing these infections due to being severely immunocompromised, such as hematopoietic stem cell transplant (HSCT) recipients with graft versus host disease (GVHD) or those with hematologic malignancies with prolonged neutropenia from chemotherapy
- Oral Suspension: Treatment of oropharyngeal candidiasis, including oropharyngeal candidiasis refractory to itraconazole and/or fluconazole

### 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 Centene Corporation<sup>®</sup> that Noxafil is **medically necessary** when the following criteria are met:

#### I. Initial Approval Criteria

##### A. Prophylaxis of Invasive *Aspergillus* and *Candida* Infections:

1. One of the following (a or b):
  - a. Authorization is requested by an infectious disease, oncologist, or HIV/AIDS specialist physician;
  - b. Discharge from hospital for continuation of therapy.

**Approval duration: Up to One Year**

##### B. Oropharyngeal Candidiasis:

1. One of the following (a, b, or c):
  - a. Authorization is requested by an infectious disease, oncologist, or HIV/AIDS specialist physician;
  - b. Discharge from hospital for continuation of therapy;
  - c. Failure or clinically significant adverse effects to one of the following: clotrimazole troches, nystatin suspension, fluconazole.

**Approval duration: 14 days; Refractory to itraconazole and/or fluconazole: Up to One Year**

**C. Allergic Bronchopulmonary Aspergillosis:**

1. Failure or clinically significant adverse events to itraconazole or voriconazole unless contraindicated or clinically significant adverse effects are experienced.

**Approval duration: Up to One Year**

**D. 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. All Indications in Section I (must meet all):**

1. Currently receiving medication via a health plan affiliated with Centene Corporation or member has previously met initial approval criteria;
2. Member is responding positively to therapy.

**Approval duration: Oropharyngeal candidiasis: Refer to the initial authorization limit; All other indications: Up to One Year**

**B. 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 12 months (whichever is less); or**

2. Refer to CP.PMN.53 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 – CP.PMN.53 or evidence of coverage documents

**IV. Appendices/General Information**

*Appendix A: Abbreviation/Acronym Key*

N/A

*Appendix B: General Information*

- A variety of dosing regimens of 800 mg/day were given in two to four divided doses during clinical studies for treatment of certain refractory invasive fungal infections in immunocompromised patients refractory to or intolerant of conventional antifungal therapy.
- Cases of elevated cyclosporine levels resulting in rare serious adverse events, including nephrotoxicity and leukoencephalopathy, and death were reported in clinical efficacy studies. Dose reduction and more frequent clinical monitoring of cyclosporine and tacrolimus should be performed when Noxafil therapy is initiated. Use of sirolimus is contraindicated due to the sirolimus blood levels increasing nine fold. Concomitant administration of posaconazole with CYP3A4 substrates such as simvastatin, pimozone and quinidine are also contraindicated due to increased plasma concentrations. Concomitant use of efavirenz, rifabutin, or phenytoin with posaconazole should be

limited to patients for whom the potential benefit outweighs the risk. Increased monitoring of digoxin, glipizide, vinka alkaloids, calcium channel blockers, metaclopramide gastric acid suppressors with posaconazole and appropriate dose adjustments are recommended.

- Concomitant administration of azole antifungals including Noxafil with vincristine has been associated with neurotoxicity and other serious adverse reactions; reserve azole antifungals, including Noxafil, for patients receiving a vinca alkaloid, including vincristine, who have no alternative antifungal treatment options.
- Liver function tests should be evaluated at the start of and during the course of therapy. Discontinuation of Noxafil should be considered if clinical signs and symptoms are consistent with development of liver disease.
- Noxafil is indicated with a IIb rating by Micromedex as salvage therapy for the treatment of allergic bronchopulmonary aspergillosis. This use is also supported by The Sanford Guide to Antimicrobial Therapy.

*Appendix C: Therapeutic Alternatives*

| <b>Drug</b>                          | <b>Dosing Regimen</b>  | <b>Dose Limit/<br/>Maximum Dose</b> |
|--------------------------------------|--|-------------------------------------|
| Clotrimazole troches                 | Oropharyngeal candidiasis: 1 lozenge (10 mg) PO 5 times per day  | 5 lozenges (50mg)/day               |
| Fluconazole (Diflucan <sup>®</sup> ) | Prevention of candidiasis-Bone Marrow Transplant: 400 mg PO or IV once daily<br><br>Vaginal candidiasis: 150 mg PO as a single dose if uncomplicated, 150 mg PO every 72 hr for 3 doses if complicated<br><br>Esophageal candidiasis: 200 mg PO or IV on the first day, then 100 mg once daily<br><br>Candida UTI and peritonitis: 50-200 mg PO or IV per day<br><br>Cryptococcal meningitis: 400 mg PO or IV on the first day, then 200 mg once daily for 10 to 12 weeks after the cerebrospinal fluid becomes culture negative. For suppression of relapse of cryptococcal meningitis in patients with HIV infection use 200 mg PO once daily<br><br>Systemic candidiasis (candidemia, disseminated candidiasis, pneumonia): Up to 400 mg PO or IV once daily<br><br>Oropharyngeal candidiasis: 200 mg PO on day 1 then 100 mg PO QD for 14 days | 400 mg/day<br>Tough                 |

| Drug                      | Dosing Regimen  | Dose Limit/<br>Maximum Dose   |
|---------------------------|---|---|
| Itraconazole (Sporanox®)* | <p>Blastomycosis or Histoplasmosis, disseminated:<br/>200 mg PO daily, up to 200 mg twice daily</p> <p>Aspergillosis invasive, refractory: 200 mg PO 3 times daily for 3 days, then 200 mg PO daily</p> <p>Esophageal candidiasis: 100-200 mg (10-20 ml) swish/swallow daily</p> <p>Oropharyngeal candidiasis: 200 mg (20 ml) swish/swallow daily</p>   | <p>600mg/day</p> <p>Oral Solution: Safety &amp; efficacy beyond 6 months is unknown</p> <p>Note: Capsules and oral solution are not interchangeable</p> |
| Nystatin suspension       | Oropharyngeal candidiasis: 4 – 6 ml (400,000 to 600,000 units) PO 4 times a day   | 2.4 MU per day  |
| Voriconazole (Vfend®)*    | <p>Invasive Aspergillosis, Candidemia in other nonneutropenic patients and other deep tissue Candida infections, Scedopporiosis and Fusariosis:<br/>6 mg/kg IV every 12 hours for 2 doses then either 3- 4 mg/kg IV every 12 hours or 200 mg PO every 12 hours (≥ 40 kg) or 100 mg PO every 12 hours (&lt; 40 kg)</p> <p>Esophageal candidiasis: 200 mg PO every 12 hr (≥ 40 kg) or 100 mg every 12 hr (&lt; 40 kg); treat for a minimum of 14 days and until 7 days after resolution of symptoms</p> | 800 mg/day  |

\* Requires Prior Authorization

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.

**V. Dosage and Administration**

| Indication                                 | Dosing Regimen   | Maximum Dose  |
|--|--|---|
| Prophylaxis of invasive fungal infections: | <p>Oral Suspension: 200 mg (5 mL) PO three times a day</p> <p>Delayed Release Tablets: 300mg PO twice a day on day 1 then 300mg once daily</p> | 800 mg/day PO for oral suspension; 600 mg/day PO for delayed release tablet |
| Oropharyngeal candidiasis:                 | Oral Suspension: Loading dose of 100 mg (2.5 mL) PO twice a day on the first day, then 100 mg (2.5 mL) daily                                   | 800 mg/day PO for oral suspension; 600 mg/day PO for delayed release tablet |
| Oropharyngeal candidiasis refractory to    | Oral Suspension: 400 mg (10 mL) PO twice a day   | 800 mg/day PO for oral suspension; 600 mg/day PO for                        |

|   |   |   |
|---|---|---|
| itraconazole and/or fluconazole:                      |   | delayed release tablet  |
| Treatment of allergic bronchopulmonary aspergillosis: | Oral Suspension:200 mg (5 mL) PO four times daily until stabilization of disease then 400 mg (10 mL) twice daily thereafter | 800 mg/day PO for oral suspension; 600 mg/day PO for delayed release tablet |

**VI. Product Availability**

- Oral suspension 40 mg/ml, 105 ml of oral suspension in a 123 ml bottle (glass amber type IV) with a measuring spoon (polystyrene) with 2 graduations: 2.5 ml and 5 ml
- IV solution: 300mg/16.7 ml (18 mg/ml)
- Delayed Release Capsules: 100 mg

**VII. References**

1. Noxafil [Prescribing Information] Whitehouse Station, NJ: Merck and Company, Inc; January 2018 .
2. Micromedex® Healthcare Series [Internet database]. Greenwood village, Colo: Thomson Healthcare. Updated periodically. Accessed September 12, 2018.
3. Keating G. Posaconazole. *Drugs*. 2005;65:1553-1567.
4. Sporanox capsules [Prescribing Information]Titusville, NJ : Janssen Pharmaceutical; October 2016
5. Vfend [Prescribing Information] New York, NY: Pfizer; February 2015.
6. Diflucan [Prescribing Information]. New York, NY: Pfizer; October 2014.
7. Sanford JP. *The Sanford Guide to Antimicrobial Therapy*. 40th edition. Sperryville, VA: Antimicrobial Therapy, Inc; 2011.
8. Restrepo A, Tobon A, Clark B et al. Salvage treatment of histoplasmosis with posaconazole. *J Infect* 2007; 54:319-327.
9. Ulmann AJ, Cornely A, Burchardt A, et al. Pharmacokinetics, safety, and efficacy of posaconazole in patients with persistent febrile neutropenia or refractory invasive fungal infection. *Antimicrob Agents Chemother* 2006; 50:658-666.

| Reviews, Revisions, and Approvals   | Date     | P&T Approval Date |
|---|----------|-------------------|
| Converted to new template; minor changes to verbiage and grammar. References updated. | 06.10.17 | 11.17             |
| Annual Review – Used CP.HNMC.07 as template. Updated references                       | 09.12.18 |                   |

**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.

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.

©2016 Centene Corporation. All rights reserved. All materials are exclusively owned by Centene Corporation 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 Centene Corporation. You may not alter or remove any trademark, copyright or other notice contained herein. Centene® and Centene Corporation® are registered trademarks exclusively owned by Centene Corporation.