PRIOR AUTHORIZATION CRITERIA

BRAND NAME*
(generic)

NOXAFIL (all dosage forms)
(posaconazole)

Status: CVS Caremark Criteria
Type: Initial Prior Authorization ***Ref # 3094-A***

** Drugs that are listed in the target drug box include both brand and generic and all dosage forms and strengths unless otherwise stated. OTC products are not included unless otherwise stated.*

FDA-APPROVED INDICATIONS

Prophylaxis of Invasive Aspergillus and Candida Infections

Noxafil injection, delayed-release tablets, and oral suspension are indicated for 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.
Noxafil injection is indicated in patients 18 years of age and older.
Noxafil delayed-release tablets and oral suspension are indicated in patients 13 years of age and older.

Treatment of Oropharyngeal Candidiasis Including Oropharyngeal Candidiasis Refractory to Itraconazole and/or Fluconazole

Noxafil oral suspension is indicated for the treatment of oropharyngeal candidiasis, including oropharyngeal candidiasis refractory to itraconazole and/or fluconazole.

COVERAGE CRITERIA

The requested drug will be covered with prior authorization when the following criteria are met:

- The requested drug is being prescribed for the prevention of invasive Aspergillus and Candida infections in a patient who is at a high risk of developing these infections due to being severely immunocompromised

OR

- Noxafil oral suspension is being prescribed for the treatment of moderate to severe oropharyngeal candidiasis
  AND
  - The patient has experienced an inadequate treatment response to fluconazole AND itraconazole

  OR
  - The patient has experienced an intolerance to fluconazole AND itraconazole

  OR
  - The patient has a contraindication that would prohibit a trial of fluconazole AND itraconazole

RATIONALE

The intent of the criteria is to provide coverage consistent with product labeling, FDA guidance, standards of medical practice, evidence-based drug information, and/or published guidelines. Noxafil injection, delayed-release tablets, and oral suspension are indicated for 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. Noxafil injection is indicated in patients 18 years of age and older. Noxafil delayed-release tablets and oral suspension are indicated in patients 13 years of age and older. Noxafil oral suspension is indicated for the treatment of oropharyngeal candidiasis, including oropharyngeal candidiasis refractory to itraconazole and/or fluconazole.

Noxafil delayed-release tablets and oral suspension are not to be used interchangeably due to the differences in the dosing of each formulation.

The Infectious Diseases Society of America (IDSA) recommends clotrimazole, miconazole or nystatin for mild oropharyngeal candidiasis. For mild disease, clotrimazole troches or miconazole buccal tablets are recommended. Alternatives for mild disease include nystatin suspension. For moderate to severe oropharyngeal candidiasis, oral fluconazole is recommended. For fluconazole-refractory disease, itraconazole solution or posaconazole suspension are recommended. Fluconazole-refractory infections should be treated initially with itraconazole solution; between 64% and 80% of patients will respond to this therapy. Posaconazole suspension is efficacious in approximately 75% of patients with refractory oropharyngeal candidiasis.[4] Noxafil oral suspension will be approved for the treatment of moderate to severe oropharyngeal candidiasis when the patient has tried fluconazole and itraconazole as recommended in the guidelines.

For the treatment of oropharyngeal candidiasis (OPC) refractory to fluconazole the duration of therapy is based on the severity of the patient's underlying disease and clinical response. Forty-five subjects with refractory OPC were treated with posaconazole oral suspension 400 mg BID for 3 days, followed by 400 mg QD for 25 days with an option for further treatment during a 3-month maintenance period. Following a dosing amendment, a further 44 subjects were treated with posaconazole 400 mg BID for 28 days. The efficacy of posaconazole was assessed by the clinical success (cure or improvement) rate after 4 weeks of treatment. Therefore, approvals for Noxafil oral suspension will be for 6 months.

For the prophylaxis of invasive Aspergillus and Candida infections the duration of therapy is based on recovery from neutropenia or immunosuppression. Liver function tests should be evaluated at the start of and during the course of posaconazole therapy. Patients who develop abnormal liver function tests during posaconazole therapy should be monitored for the development of more severe hepatic injury. Patient management should include laboratory evaluation of hepatic function (particularly liver function tests and bilirubin). Discontinuation of posaconazole must be considered if clinical signs and symptoms consistent with liver disease develop that may be attributable to posaconazole. Therefore, approvals for prophylaxis of invasive Aspergillus and Candida infections will be for 6 months to allow for monitoring and for reevaluation of the underlying condition.

REFERENCES

1. Noxafil [package insert]. Whitehouse Station, NJ: Merck & Co., Inc.; March 2019.
2. Lexicomp Online, AHFS DI (Adult and Pediatric) Online. Hudson, OH: Wolters Kluwer Clinical Drug Information, Inc. http://online.lexi.com/. Accessed February 2020.
3. Micromedex (electronic version). Truven Health Analytics, Greenwood Village, Colorado, USA. http://www.micromedexsolutions.com/. Accessed February 2020.
4. Pappas P, Kauffman C, Andes D, et al. Clinical Practice Guidelines for the Management of Candidiasis: 2016 Update by the Infectious Diseases Society of America. *Clinical Infectious Diseases*. 2016;62:1-50.

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CRITERIA FOR APPROVAL

1	Is the requested drug being prescribed for the prevention of invasive Aspergillus and Candida infections in a patient who is at a high risk of developing these infections due to being severely immunocompromised? [If yes, then no further questions.]	Yes	No
2	Is this request for Noxafil oral suspension?	Yes	No
3	Is the requested drug being prescribed for the treatment of moderate to severe oropharyngeal candidiasis?	Yes	No

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4	Has the patient experienced an inadequate treatment response to fluconazole AND itraconazole? [If yes, then no further questions.]	Yes	No
5	Has the patient experienced an intolerance to fluconazole AND itraconazole? [If yes, then no further questions.]	Yes	No
6	Does the patient have a contraindication that would prohibit a trial of fluconazole AND itraconazole?	Yes	No

Mapping Instructions			
	Yes	**No**	**DENIAL REASONS – DO NOT USE FOR MEDICARE PART D**
1.	Approve, 6 months	Go to 2	
2.	Go to 3	Deny	You do not meet the requirements of your plan. Your plan covers this drug when you are at high risk of a fungal infection (Aspergillus or Candida). Your request has been denied based on the information we have. [Short Description: No approvable diagnosis]
3.	Go to 4	Deny	You do not meet the requirements of your plan. Your plan covers this drug when you meet any of these conditions: - You are at high risk of a fungal infection (Aspergillus or Candida) - You have a moderate to severe fungal infection of the mouth and throat (Oropharyngeal candidiasis) Your request has been denied based on the information we have. [Short Description: No approvable diagnosis]
4.	Approve, 6 months	Go to 5	
5.	Approve, 6 months	Go to 6	
6.	Approve, 6 months	Deny	You do not meet the requirements of your plan. Your plan covers this drug when you meet any of these conditions: - You have a moderate to severe fungal infection of the mouth and throat (Oropharyngeal candidiasis) - You tried fluconazole and itraconazole and they did not work for you, or you cannot use them. Your request has been denied based on the information we have. [Short Description: No inadequate response, intolerance or contraindication to fluconazole and itraconazole]