PRIOR AUTHORIZATION CRITERIA

BRAND NAME*
(generic)

NOXAFIL (all dosage forms)
(posaconazole)

Status: CVS Caremark Criteria ***REG***
Type: Initial Prior Authorization ***Ref # 3405-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

Treatment of Invasive Aspergillosis

Noxafil injection and **Noxafil delayed-release tablets** are indicated for the treatment of invasive aspergillosis in adults and pediatric patients 13 years of age and older.

Prophylaxis of Invasive Aspergillus and Candida Infections

Noxafil is indicated for the 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 as follows:

- **Noxafil Injection:** adults and pediatric patients 2 years of age and older
- **Noxafil delayed-release tablets:** adults and pediatric patients 2 years of age and older who weigh greater than 40 kg
- **Noxafil oral suspension:** adults and pediatric patients 13 years of age and older
- **Noxafil PowderMix for delayed-release oral suspension:** pediatric patients 2 years of age and older who weigh 40 kg or less

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 in adults and pediatric patients 13 years of age and older.

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 injection or Noxafil delayed-release tablets are being prescribed for the treatment of invasive aspergillosis

OR

- Noxafil oral suspension (immediate-release) is being prescribed for the treatment of moderate to severe oropharyngeal candidiasis

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 is indicated for the 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 as follows: Noxafil

injection in adults and pediatric patients 2 years of age and older, Noxafil delayed-release tablets in adults and pediatric patients 2 years of age and older who weigh greater than 40 kg, Noxafil oral suspension in adults and pediatric patients 13 years of age and older, and Noxafil PowderMix for delayed-release oral suspension in pediatric patients 2 years of age and older who weigh 40 kg or less. Noxafil injection and Noxafil delayed-released tablets are also indicated for the treatment of invasive aspergillosis in adults and pediatric patients 13 years of age and older. Additionally, Noxafil oral suspension is indicated for the treatment of oropharyngeal candidiasis, including oropharyngeal candidiasis refractory to itraconazole and/or fluconazole in adults and pediatric patients 13 years of age and older.[1]

Noxafil oral suspension is not substitutable with Noxafil delayed-release tablets or Noxafil PowderMix for delayed-release oral suspension due to the differences in the dosing of each formulation.[1]

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.[1] 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.

For the treatment of invasive aspergillosis, a loading dose of Noxafil injection or Noxafil delayed-release tablets should be administered on the first day. Starting on the second day, a maintenance dose of Noxafil injection or Noxafil delayed-release tablets should be administered once daily for a total recommended treatment duration of 6 to 12 weeks. Switching between the intravenous and delayed-release tablets is acceptable; a loading dose is not required when switching between formulations.[1] Therefore, approvals for this indication will be for 3 months to allow for treatment of invasive aspergillosis at the maximum recommended duration of therapy.

The Infectious Diseases Society of America (IDSA) recommends use of posaconazole for moderate to severe oropharyngeal candidiasis in patients who are refractory to fluconazole; therefore, moderate to severe disease will be required for use of posaconazole suspension for the treatment of oropharyngeal candidiasis.[4]

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.[1] The Infectious Diseases Society of America (IDSA) recommends for fluconazole-refractory disease, itraconazole solution, 200mg once daily or posaconazole suspension 400mg twice daily for 3 days then 400mg daily, for up to 28 days.[4] Therefore, approvals for Noxafil oral suspension (immediate-release) for the treatment of moderate to severe oropharyngeal candidiasis will be for 1 month.

REFERENCES

1. Noxafil [package insert]. Whitehouse Station, NJ: Merck & Co., Inc.; June 2021.
2. Lexicomp Online, AHFS DI (Adult and Pediatric) Online. Hudson, Ohio: UpToDate, Inc.; 2021; Accessed January 12, 2021.
3. Micromedex (electronic version). IBM Watson Health, Greenwood Village, Colorado, USA. Available at: https://www.micromedexsolutions.com. Accessed January 12, 2021.
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**.**

Written by:	UM Development (JK)
Date Written:	11/2019 (created REG version of 3094-A 05-2019 removing the trial/failure requirement)
Revised:	(ME) 02/2020 (no clinical changes); (NZ) 02/2021 (DOA update), 06/2021 (updated to include newly FDA-approved dosage form Noxafil PowderMix for delayed-release oral suspension); (CJH) 06/2021 (updated q-set to include new indication for treatment of aspergillosis for Noxafil injection and Noxafil delayed-release tabs)
Reviewed:	Medical Affairs (CHART) 11/21/2019, (CHART) 02/27/2020, 02/25/2021, 06/17/2021, 07/15/2021 External Review: 12/2019 (FYI), 06/2020, 06/2021, 08/2021 (FYI)

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	Which drug is being requested? [Note: Please check the drug being requested.] [] Noxafil Injection (if checked, go to 3) [] Noxafil delayed-release tablets (if checked, go to 3) [] Noxafil oral suspension (immediate-release) (if checked, go to 4) [] Noxafil PowderMix for delayed-release oral suspension (if checked, deny)		
3	Is the requested drug being prescribed for the treatment of invasive aspergillosis? [No further questions.]	Yes	No
4	Is the requested drug being prescribed for the treatment of moderate to severe oropharyngeal candidiasis?	Yes	No

Mapping Instructions			
	Yes	**No**	**DENIAL REASONS – DO NOT USE FOR MEDICARE PART D**
1.	Approve, 6 months	Go to 2	
2.	1=3, 2=3, 3=4, 4=Deny		You do not meet the requirements of your plan. Your plan covers this drug when you are at high risk of specific types of fungal infections. Your request has been denied based on the information we have. [Short Description: No approvable diagnosis- prophylaxis of Aspergillus and Candida infections]
3.	Approve, 3 months	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 specific types of fungal infections - You are using it to treat a specific type of fungal infection Your request has been denied based on the information we have. [Short Description: No approvable diagnosis- prophylaxis of Aspergillus and Candida infections OR treatment of aspergillosis]
4.	Approve, 1 month	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 specific types of fungal infections - You are using it to treat a moderate to severe fungal infection of the mouth and throat Your request has been denied based on the information we have. [Short Description: No approvable diagnosis- prophylaxis of Aspergillus and Candida infections OR treatment of oropharyngeal candidiasis]