Pharmacy Medical Necessity Guidelines:
Oral Antifungal Agents

Effective: September 15, 2026

Prior Authorization Required	√	Type of Review – Care Management	
Not Covered		Type of Review – Clinical Review	√
Pharmacy (RX) or Medical (MED) Benefit	RX	Department to Review	RXUM
These pharmacy medical necessity guidelines apply to the following: ☒ Tufts Health RITogether – A Rhode Island Medicaid Plan		**Fax Numbers:** RXUM: 617.673.0939	

Note: This guideline does not apply to Medicare Members (includes dual eligible Members).

OVERVIEW

FOOD AND DRUG ADMINISTRATION-APPROVED INDICATIONS

Flucytosine:

- Flucytosine is indicated only in the treatment of serious infections caused by susceptible strains of *Candida* and/or *Cryptococcus.*
    - *Candida*: Septicemia, endocarditis and urinary system infections have been effectively treated with flucytosine. Limited trials in pulmonary infections justify the use of flucytosine.
    - *Cryptococcus*: Meningitis and pulmonary infections have been treated effectively. Studies in septicemias and urinary tract infections are limited, but good responses have been reported.
- Flucytosine should be used in combination with amphotericin B for the treatment of systemic candidiasis and cryptococcosis because of the emergence of resistance.

Posaconazole:

- Posaconazole oral suspension is indicated for the treatment of oropharyngeal candidiasis, including oropharyngeal candidiasis refractory to itraconazole and/or fluconazole in patients at least 13 years of age.
- Posaconazole oral suspension and delayed-release tablets are indicated as 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 recipients with graft-vs-host disease or those with hematologic malignancies with prolonged neutropenia from chemotherapy. The delayed-release tablets are approved in adults and pediatric patients 2 years of age and older weighing more than 40 kilograms. The oral suspension is approved in patients 13 years of age and older. Noxafil PowderMix for delayed-release oral suspension is approved in pediatric patients 2 years of age and older who weigh 40 kilograms or less.
- Posaconazole oral suspension and delayed-release tablets are indicated for the treatment of invasive aspergillosis. The delayed-release tablets are approved in adults and pediatric patients 2 years of age and older who weigh greater than 40 kilograms. Noxafil PowderMix for delayed-release oral suspension is approved in pediatric patients 2 years of age and older who weigh 10 kilograms to 40 kilograms.

Voriconazole:

- Voriconazole is indicated for use in patients at least 2 years for the treatment of invasive aspergillosis; candidemia (nonneutropenic) and disseminated candidiasis in skin, abdomen, kidney, bladder wall, and wounds; esophageal candidiasis; and serious infections cause by *Scedosporium apiospermum* and *Fusarium* species including *Fusarium solani*, in patients intolerant of, or refractory to, other therapy.

COVERAGE GUIDELINES

The plan may authorize coverage of an oral antifungal agent for Members when **ALL** of the following criteria for a particular regimen are met:

Flucytosine

1. Documented diagnosis of cryptococcal meningitis

OR

2. Documented diagnosis of candida endocarditis

OR

3. Documented diagnosis of a cryptococcal pulmonary infection AND documentation of clinical inappropriateness of treatment with at least one first-line agent (e.g., fluconazole, itraconazole, or voriconazole)

OR

4. Documented diagnosis of candida septicemia AND documentation of clinical inappropriateness of treatment with one other agent (e.g., fluconazole, voriconazole, amphotericin B, or an echinocandin)

OR

5. Documented diagnosis of candiduria AND documentation of clinical inappropriateness of treatment with ONE of the following: fluconazole or amphotericin B

Posaconazole

1. Documented diagnosis of Zygomycosis (mucormycosis)

OR

2. Documented diagnosis of hematologic malignancy with neutropenia, hematopoietic stem cell transplant, or graft-versus-host disease requiring prevention of invasive aspergillus and candida fungal infections

OR

3. Documented diagnosis of esophageal candidiasis AND documented failure of or clinical inappropriateness of therapy with at least TWO of the following: oral fluconazole, itraconazole, and voriconazole

OR

4. Documented diagnosis of oropharyngeal candidiasis AND documented failure of or clinical inappropriateness of therapy with ALL of the following: oral fluconazole and itraconazole

OR

5. Documented diagnosis of invasive aspergillosis

Voriconazole

1. Documented diagnosis of an invasive aspergillus infection

OR

2. Documented diagnosis of a serious infection case by scedosporium or fusarium species

OR

3. Documented diagnosis of esophageal candidiasis AND documented failure of or clinical inappropriateness to fluconazole and itraconazole

OR

4. Documented diagnosis of oropharyngeal candidiasis AND documented failure of or clinical inappropriateness of treatment with ALL of the following: fluconazole, itraconazole, posaconazole

OR

5. Documented diagnosis of candidemia and disseminated candidiasis infections AND documented failure of or clinical inappropriateness to oral fluconazole

OR

6. Documented diagnosis of prevention of invasive aspergillus and candida fungal infections AND documentation of hematologic malignancy with neutropenia, hematopoietic stem cell transplant, or graft-versus-host disease

LIMITATIONS

1. Approval will be limited to one complete course of therapy.
2. Requests for brand-name products, which have AB-rate generics, will be reviewed according to Brand Name criteria.

CODES

None

REFERENCES

1. Ancobon (flucytosine) [package insert]. Bridgewater, NJ: Bausch Health US, LLC; February 2022.
2. Cox GM. Candida infections of the bladder and kidneys. UpToDate. Available at: www.uptodate.com. Accessed: 4 August 2023.
3. Kauffman CA. Chronic disseminated candidiasis (hepatosplenic candidiasis). UpToDate. Available at: www.uptodate.com. Accessed 3 August 2023.
4. Kauffman CA. Esophageal candidiasis in adults. UpToDate. Available at: www.uptodate.com. Accessed 3 August 2023.

5. Noxafil (posaconazole) [prescribing information]. Whitehouse Station, NJ: Merck & Co Inc; January 2026.
6. Vazquez JA. Management of candidemia and invasive candidiasis in adults. UpToDate. Available at: www.uptodate.com. Accessed 4 August 2023.
7. Vfend (voriconazole) [prescribing information]. New York, NY: Pfizer; October 2022.
8. Perfect JR, Dismukes WE, Dromer F, et al. Clinical practice guidelines for the management of cryptococcal disease: 2010 update by the Infectious Diseases Society of America. *Clin Infect Dis*. 2010;50(3):291-322.

APPROVAL HISTORY

October 11, 2022: Reviewed by Pharmacy & Therapeutics Committee.

Subsequent endorsement date(s) and changes made:

1. September 12, 2023: Effective October 1, 2023, updated posaconazole criteria for esophageal and oropharyngeal candidiasis to remove requirement that the request is for the oral suspension. Updated flucytosine criteria for candiduria to allow approval if member has tried fluconazole or amphotericin B rather than both.
2. September 10, 2024: Administrative change to fax number.
3. September 9, 2025: No changes
4. September 15, 2026: Administrative update to the overview section for expanded indication for posaconazole in pediatric patients 2 years of age and older for treatment of invasive aspergillosis for tablet and delayed-release oral suspension.

BACKGROUND, PRODUCT AND DISCLAIMER INFORMATION

Pharmacy Medical Necessity Guidelines have been developed for determining coverage for plan benefits and are published to provide a better understanding of the basis upon which coverage decisions are made. The plan makes coverage decisions on a case-by-case basis considering the individual member's health care needs. Pharmacy Medical Necessity Guidelines are developed for selected therapeutic classes or drugs found to be safe, but proven to be effective in a limited, defined population of patients or clinical circumstances. They include concise clinical coverage criteria based on current literature review, consultation with practicing physicians in the service area who are medical experts in the particular field, FDA and other government agency policies, and standards adopted by national accreditation organizations. The plan revises and updates Pharmacy Medical Necessity Guidelines annually, or more frequently if new evidence becomes available that suggests needed revisions.

For self-insured plans, coverage may vary depending on the terms of the benefit document. If a discrepancy exists between a Pharmacy Medical Necessity Guideline and a self-insured Member's benefit document, the provisions of the benefit document will govern.

Treating providers are solely responsible for the medical advice and treatment of members. The use of this policy is not a guarantee of payment or a final prediction of how specific claim(s) will be adjudicated. Claims payment is subject to member eligibility and benefits on the date of service, coordination of benefits, referral/authorization and utilization management guidelines when applicable, and adherence to plan policies and procedures and claims editing logic.

Provider Services