

Policy and Procedure

PHARMACY PRIOR AUTHORIZATION POLICY AND CRITERIA ORPTCINF002.1225	ANTI-INFECTIVE AGENTS ANTIFUNGAL AGENTS See Table 1 for Applicable Medications
Effective Date: 2/1/2026	Review/Revised Date: 06/98, 11/00, 05/02, 02/03, 06/03, 06/04, 09/04, 09/05, 02/06, 12/06, 10/08, 12/08, 04/09, 10/09, 02/10, 01/11, 02/12, 12/12, 12/14, 12/15, 05/16, 10/16, 08/17, 11/17, 05/18, 08/18, 11/18, 04/19, 11/19, 10/20, 10/21, 10/22, 01/23, 10/23, 04/24, 11/24, 11/25 (MTW)
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Approved by: Oregon Region Pharmacy and Therapeutics Committee	

SCOPE:

Providence Health Plan and Providence Health Assurance as applicable (referred to individually as “Company” and collectively as “Companies”).

APPLIES TO:

Commercial
Medicaid

POLICY CRITERIA:

COVERED USES:

All Food and Drug Administration (FDA). Some medically accepted indications not otherwise excluded from the benefit.

Coverage for Medicaid is limited to a condition that has been designated a covered line item number by the Oregon Health Services Commission listed on the Prioritized List of Health Care Services when all applicable indication-specific criteria below are met or if the Early and Periodic Screening, Diagnostic and Treatment (EPSDT) benefit applies.

REQUIRED MEDICAL INFORMATION:

1. For **oropharyngeal or esophageal candidiasis** (posaconazole and voriconazole only): Documented failure, intolerance, or contraindication to fluconazole and itraconazole solution
2. For the **treatment** of invasive *Aspergillus* or disseminated *Candida* infections:
 - a. Confirmed diagnosis (Fungal culture and other relevant laboratory studies [including histopathology] must be documented)
 - b. For posaconazole or isavuconazonium: Documented failure, intolerance, or contraindication to voriconazole
3. For the treatment of blastomycosis or histoplasmosis: Documented failure, intolerance, or contraindication to itraconazole

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4. For prophylaxis of invasive Aspergillus or Candida infections: posaconazole or voriconazole may be covered for severely immunocompromised patients. For example:
 - a. Hematopoietic stem cell transplant recipient with graft-versus-host disease
 - b. Current diagnosis of cancer currently undergoing chemotherapy or radiation
 - c. HIV/AIDS (as secondary prophylaxis for patients with frequent or severe recurrences)
 - d. Lung transplant or high-risk non-lung solid organ transplant recipients
5. For treatment of mucormycosis: isavuconazonium or posaconazole may be covered
6. For empiric antifungal therapy in patients with febrile neutropenia: voriconazole or posaconazole may be covered
7. For recurrent vulvovaginal candidiasis (RVVC) (oteseconazole only) must meet all the following criteria:
 - a. Documentation that patient is NOT of reproductive potential
 - b. Documentation of three or more episodes of symptomatic vulvovaginal candidiasis
 - c. Documentation of compatible clinical symptoms (such as vulvovaginal irritation, burning, pruritus, characteristic discharge, or edema/erythema)
 - d. Documented failure, intolerance, or contraindication to BOTH of the following:
 - i. A 7- to 14-day topical azole course
 - ii. An oral fluconazole dose (specifically, oral fluconazole given every third day for a total of three doses)

For reauthorization:

Documentation supporting continued use of the requested agent for the intended diagnosis (such as continued active disease, length of therapy is supported by literature or guidelines, for prophylaxis patient continues to be severely immunocompromised)

EXCLUSION CRITERIA: N/A

AGE RESTRICTIONS: N/A

PRESCRIBER RESTRICTIONS:

Must be prescribed by, or in consultation with, one of the following:

- Infectious disease specialist
- Hematologist
- Oncologist
- Pulmonologist

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COVERAGE DURATION:

For prophylaxis of invasive *Aspergillus* or *Candida* infections: initial authorization and reauthorization will be approved for one year

For recurrent vulvovaginal candidiasis (RVVC): initial authorization and reauthorization will be approved for six months.

For other covered uses: Initial authorization will be approved for three months. Reauthorization will be approved for up to one year.

Requests for indications that were approved by the FDA within the previous six (6) months may not have been reviewed by the health plan for safety and effectiveness and inclusion on this policy document. These requests will be reviewed using the New Drug and or Indication Awaiting P&T Review; Prior Authorization Request ORPTCOPS047.

Requests for a non-FDA approved (off-label) indication requires the proposed indication be listed in either the American Hospital Formulary System (AHFS), Drugdex, or the National Comprehensive Cancer Network (NCCN) and is considered subject to evaluation of the prescriber's medical rationale, formulary alternatives, the available published evidence-based research and whether the proposed use is determined to be experimental/investigational.

Coverage for Medicaid is limited to a condition that has been designated a covered line item number by the Oregon Health Services Commission listed on the Prioritized List of Health Care Services.

Coverage decisions are made on the basis of individualized determinations of medical necessity and the experimental or investigational character of the treatment in the individual case.

INTRODUCTION:

Posaconazole, voriconazole, itraconazole, oteseconazole, and isavuconazonium (prodrug of isavuconazole) are “azole” antifungal agents used in a variety of infectious disease states. All five agents are considered to be active against *Candida* infections, among other severe fungal infections.

FDA APPROVED INDICATIONS:

Posaconazole (Noxafil®):

- Injection, delayed-release tablets, and oral suspension: prophylaxis of invasive *Aspergillus* and *Candida* infections in patients, 13 years of age and older, who are at high risk of developing these infections due to being severely immunocompromised, such as HSCT recipients with GVHD or those with hematologic malignancies with prolonged neutropenia from chemotherapy
- Oral suspension: treatment of oropharyngeal candidiasis (OPC), including OPC refractory (rOPC) to itraconazole and/or fluconazole

- Injection and delayed-release tablets: treatment of invasive aspergillosis in adults and pediatric patients 13 years of age and older

Itraconazole (Sporanox®) – does not require prior authorization

- Capsules:
 - Treatment of the following fungal infections in immunocompromised and non-immunocompromised patients:
 - Blastomycosis, pulmonary and extrapulmonary
 - Histoplasmosis, including chronic cavitary pulmonary disease and disseminated, non-meningeal histoplasmosis, and
 - Aspergillosis, pulmonary and extrapulmonary, in patients who are intolerant of or who are refractory to amphotericin B therapy.
 - Treatment of the following fungal infections in non-immunocompromised patients:
 - Onychomycosis of the toenail, with or without fingernail involvement, due to dermatophytes (tinea unguium)
 - Onychomycosis of the fingernail due to dermatophytes (tinea unguium)
- Solution: treatment of oropharyngeal and esophageal candidiasis

Voriconazole (Vfend®): Pediatric patients two years of age and older for the treatment of

- Invasive Aspergillosis
- Candidemia in non-neutropenic patients and the following Candida Infections: disseminated infections in skin and infections in abdomen, kidney, bladder wall, and wounds
- Esophageal Candidiasis
- Serious fungal infections caused by *Scedosporium apiospermum* (Asexual Form of *Pseudallescheria boydii*) and *Fusarium spp.* Including *Fusarium solani*, in patient's intolerant of, or refractory to, other therapy

Isavuconazonium sulfate (Cresemba®): Treatment of invasive aspergillosis and mucormycosis:

- Injection: adults and pediatric patients one year of age and older
- Capsule: adults and pediatric patients six years of age and older who weigh 16 kilograms and greater

Oteseconazole (Vivjoa®):

- Reduce the incidence of recurrent vulvovaginal candidiasis (RVVC) in females with a history of RVVC who are NOT of reproductive potential
 - Female patients who are not of reproductive potential are defined as: patients who are biological females who are postmenopausal or who have another reason for permanent infertility (tubal ligation, hysterectomy, etc.)

POSITION STATEMENT:

To promote appropriate utilization and antimicrobial stewardship, posaconazole, voriconazole, oteseconazole, and isavuconazonium will be restricted to use for guideline and evidence-supported indications. In addition, these medications must be prescribed by, or in consultation with, an appropriate specialist.

These antifungal agents may be clinically appropriate or agents of choice for prophylaxis or treatment of conditions not outlined in this policy.

Fluconazole continues to be the standard, first-line treatment for several types of **Candida infections** and is recommended by guidelines from the Infectious Diseases Society of America (IDSA). Other agents are typically reserved for infections that are resistant to fluconazole.²

Because *Candida* species are commensal; their culture from sputum, the mouth, the vagina, urine, stool, or skin does not necessarily signify an invasive, progressive infection. A characteristic clinical lesion must also be present, histopathologic evidence of tissue invasion (e.g., yeasts, pseudohyphae, or hyphae in tissue specimens) must be documented, and other etiologies must be excluded. Positive cultures of specimens taken from normally sterile sites, such as blood, cerebrospinal fluid, pericardium, pericardial fluid, or biopsied tissue provide definitive evidence that systemic therapy is needed.

Urine mycotoxin tests are not approved by FDA for accuracy or for clinical use. Mycotoxins are metabolites of some fungi that can cause illness in humans and animals, primarily after ingestion of contaminated foods. Low levels of mycotoxins are found in many foods; therefore, mycotoxins are found in the urine of healthy persons. Mycotoxin levels that predict disease have not been established.

For prophylaxis of invasive aspergillosis, posaconazole is the preferred agent in HSCT recipients with GVHD who are at high risk for invasive aspergillosis and in patients with AML or myelodysplastic syndrome who are at high risk. Voriconazole is recommended as the first-line agent for the treatment of an active aspergillosis infection.³ Isavuconazonium is not recommended for the prophylaxis of aspergillosis or mucormycosis. In patients with HIV, routine primary prophylaxis is not recommended in patients due to low attributable morbidity and mortality and highly effective therapies available for treatment⁴. Secondary prophylaxis is recommended for patients with low CD4 counts and frequent or severe recurrences. It is reasonable to discontinue secondary prophylaxis with CD4 count has increased to over 200 cells/mm³ following initiation of antiretroviral therapy.

Itraconazole is recommended as first-line therapy for the treatment of **histoplasmosis and blastomycosis** by guidelines from the European

Confederation of Medical Mycology/International Society for Human and Animal Mycology, American Thoracic Society, and US Department of Health and Human Services.^{4,5,6}

For onychomycosis, secondary risk factors or comorbidities include but are not limited to:

- Use for an immunocompromised patient (e.g., current chemotherapy/radiation, HIV/AIDS)
- A fungal infection of the extremity in the presence of a severe circulatory disorder
- A diabetic and fungal state that poses significant risk unless treated with systemic antifungal therapy
- An infected nail that cannot be removed and leads to recurrent cellulitis (more than one episode)
- Pain limiting normal activity

Dermatomycosis is a fungal infection of the skin. Dermatophyte tinea infections (e.g., tinea corporis, tinea capitis) are caused by a group of fungi called dermatophytes. Another common fungal infection of the skin is pityriasis versicolor (tinea versicolor). This is not a dermatophyte infection but is caused by yeasts which can lead to patches of the skin becoming scaly and discolored. Topical or systemic antifungal drugs are effective therapies. Most superficial cutaneous fungal infections can be managed with topical therapy. Use of oral antifungals may be practical where the involvement is extensive or chronic, or where application of a topical is not feasible or has not been effective. Depending on the location and type of infection, oral systemic options may include terbinafine, griseofulvin, itraconazole and fluconazole.^{7,8,9} Per the Oregon Health Authority minor fungal infections of skin, such as dermatophytosis or candidiasis, are only covered for Medicaid members when complicated by an immunocompromised host.

Mucormycosis is a rare invasive fungal infection caused by molds belonging to the order Mucorales. The five most common clinical presentations are rhinocerebral, pulmonary, cutaneous, gastrointestinal, and disseminated mucormycosis. Some of the risk factors for mucormycosis are malignancy, hematopoietic stem cell or solid organ transplant, poorly controlled diabetes, skin trauma and iron overload. First line treatment is usually liposomal amphotericin B. Posaconazole and isavuconazole both have activity against most Mucorales and are often used for step-down or salvage therapy. Surgical debridement or resection is also often required. Treatment duration is individualized and often relies on clinical and radiographic resolution as well as reversal of immunosuppression, if present and possible. Some individuals may require life-long therapy.

Recurrent vulvovaginal candidiasis (RVCC) infection is estimated to affect less than 5% of women.¹⁶ IDSA guidelines define recurrent vulvovaginal candidiasis as at least 4 episodes of symptomatic infection within one year, usually caused by azole-susceptible *C. albicans*. IDSA guidelines and CDC 2021 vulvovaginal candidiasis guideline recommend 10-14 days of induction therapy with a topical azole agent or oral fluconazole, followed by fluconazole, 150 mg weekly for 6 months, for recurring vulvovaginal candidiasis.^{16,2} CDC 2021 vulvovaginal candidiasis guideline states that these women should be managed in consultation with a specialist. A diagnosis may be confirmed with a fungal culture or wet slide (10% KOH or saline mount). Women with a positive result should be treated. However, women with signs and symptoms of RVCC and a negative wet slide result should still be considered for treatment.¹⁶

Early and Periodic Screening Diagnostic and Treatment (EPSDT) Review

The Early and Periodic Screening, Diagnostic and Treatment (EPSDT) benefit includes comprehensive preventative health care services for Medicaid members until they turn age 21 and for members with qualifying special health care needs (Youth with Special Healthcare Needs (YSHCN)) as they turn 21. This benefit applies when a condition is determined to impact the ability to grow, develop or participate in school and the applicable criteria above are met.

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16. Vulvovaginal candidiasis (VVC). Sexually Transmitted Infections Treatment Guidelines, 2021. Centers for Disease Control and Prevention (CDC). Available at: [Vulvovaginal Candidiasis - STI Treatment Guidelines \(cdc.gov\)](#). (Accessed on November 20, 2025)

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Table 1. Medications covered by this policy

Generic Name	Brand Name	Covered Uses
Isavuconazonium sulfate	Cresemba®	<ul style="list-style-type: none"> • Treatment of invasive <i>Aspergillus</i> or disseminated <i>Candida</i> infections • For treatment of invasive mucormycosis
Posaconazole	Noxafil®	<ul style="list-style-type: none"> • Treatment of oropharyngeal or esophageal candidiasis • Treatment of invasive <i>Aspergillus</i> or disseminated <i>Candida</i> infections • Prophylaxis of invasive <i>Aspergillus</i> or <i>Candida</i> infections • Treatment of blastomycosis or histoplasmosis • For treatment of mucormycosis • For empiric antifungal therapy in patients with febrile neutropenia
Voriconazole	Vfend®	<ul style="list-style-type: none"> • Treatment of oropharyngeal or esophageal candidiasis • Treatment of invasive <i>Aspergillus</i> or disseminated <i>Candida</i> infections • Treatment of blastomycosis or histoplasmosis • Prophylaxis of invasive <i>Aspergillus</i> or <i>Candida</i> infections • For empiric antifungal therapy in patients with febrile neutropenia
Oteseconazole	Vivjoa®	<ul style="list-style-type: none"> • To reduce the incidence or recurrent vulvovaginal candidiasis (RVVC) in females with a history of RVVC who are NOT of reproductive potential <ul style="list-style-type: none"> ○ Female patients who are not of reproductive potential are defined as: patients who are biological females who are postmenopausal or who have another reason for permanent infertility (tubal ligation, hysterectomy, etc.)