



© Copyright 2024 Oregon State University. All Rights Reserved

**Drug Use Research & Management Program**  
Oregon State University, 500 Summer Street NE, E35  
Salem, Oregon 97301-1079  
**Phone** 503-947-5220 | **Fax** 503-947-2596



## Drug Class Update: Antifungals

**Date of Review:** December 2025

**Date of Last Review:** December 2023

**Dates of Literature Search:** 10/01/2023 - 07/09/2025

### Current Status of PDL Class:

See **Appendix 1**.

### Purpose for Class Update:

Evidence for the use of topical, oral and vaginal antifungals was reviewed by the Oregon Pharmacy & Therapeutics (P&T) Committee December 2023. Literature examining the comparative evidence published since the last review will be evaluated and presented.

### Plain Language Summary:

- Providers prescribe antifungal medicines to treat infections that are caused by fungus. Antifungals can be applied on the skin, injected or infused into the bloodstream, or taken by mouth.
- People with weakened immune systems are more likely to get a fungal infection. The National Institutes of Health recently published antifungal treatment recommendations for people with human immunodeficiency virus (HIV), which weakens the immune system. Antifungal treatment recommendations were also updated for people with fungal infections.
- Cresemba (isavuconazonium) received approval from the U.S. Food and Drug Administration (FDA) for invasive aspergillosis or invasive mucormycosis.
- FDA issued new warnings and precautions for 4 antifungal treatments to assist providers in monitoring patients for specific side effects.
- Oregon Health Authority (OHA) will pay for antifungals to treat serious fungal infections. Antifungals can be covered for minor fungal infections if people have conditions that could lead to complications. The Drug Use Research and Management group does not recommend any changes to this policy to OHA.

### Research Questions:

1. Is there new comparative evidence related to efficacy for the oral and topical antifungals for important outcomes (e.g., clinical cure or mycological cure)?
2. Is there new comparative evidence for harms for oral and topical antifungals?
3. Are there any populations based on certain demographic characteristics (i.e., age, sex, race, ethnicity, socioeconomic status, comorbidities) who may benefit more or suffer more harm from specific antifungal agents?

### Conclusions:

- A search of the literature identified one new guideline, one new indication and 6 antifungal safety updates.

Author: Kathy Sentena, PharmD

- The National Institutes of Health (NIH) updated guidance related to the prevention and treatment of opportunistic infections in adults and adolescents with human immunodeficiency virus (HIV). Recommendations align with current policy for the coverage of antifungals for patients who are immunocompromised.<sup>1</sup>
- A new indication for the use of isavuconazonium injection was approved in December of 2023 for invasive aspergillosis (IA) and invasive mucormycosis (IM) treatment in pediatric patients 1 year and older and for the capsules to be used in those patients 6 years and older for the same indications who weigh 16 kg or greater.<sup>2</sup> Evidence used to obtain the approval in pediatric patients (n=31) was from a phase 2, open-label, noncomparative study in patients 1 to less than 18 years with probable or definitive IA or IM which demonstrated a reduction in mortality.
- There were 6 new safety updates since the last review that pertain to the following drugs: itraconazole, posaconazole, miconazole, and voriconazole (**Table 4**).<sup>3-6</sup>

#### Recommendations:

- No changes to the Oregon Health Plan (OHP) fee-for-service preferred drug list (PDL) for the antifungals drug class.
- After evaluation of drug costs in executive session, make the following products preferred: terbinafine tablets, miconazole (solution and powder), ciclopirox (gel, solution and cream), ketoconazole (shampoo and cream), clotrimazole cream, clotrimazole-betamethasone cream, and nystatin-triamcinolone cream.

#### Summary of Prior Reviews and Current Policy:

- The antifungals were reviewed in December of 2023. After the executive session, terconazole, butoconazole, miconazole kits, miconazole 3 vaginal suppositories were designated non-preferred. Clotrimazole (cream and tablet), clotrimazole 3-day cream, miconazole 3- and 7-day creams, miconazole suppositories, terconazole cream and tioconazole ointment are preferred vaginal antifungals.
- Oral antifungals that are preferred are clotrimazole, fluconazole, and nystatin. Preferred topical antifungals are miconazole, and nystatin.
- The OHP does not fund the treatment of candidiasis of the mouth, skin, nails or dermatophytosis of nail, groin, scalp, and other dermatophytosis in immune competent patients. Coverage for these conditions in those under 21 years may be available through the Early and Periodic Screening, Diagnostic, and Treatment (EPSDT) program on a case-by-case basis.
- Ninety-eight percent of the oral antifungal utilization was for preferred therapies in the first quarter of 2025. For the topical antifungals, 71% of utilization was for preferred therapies and 96% for vaginal antifungals.

#### Background:

Oral and topical antifungal drugs are used to treat a wide spectrum of infections (**Table 1**). Fungal infections can occur on the skin and nails, mucosal surfaces, genitourinary tract, gastrointestinal tract and systemically.<sup>7</sup> Fungal infections of the skin, hair and nails are caused by dermatophyte infections and lead to conditions such as tinea pedis, tinea corporis, tinea cruris, tinea capitis and dermatophyte onychomycosis.<sup>7</sup> Mucosal fungal infections include oropharyngeal candidiasis, esophageal candidiasis and vulvovaginal candidiasis. Serious fungal infections are usually seen in individuals with compromised immune systems, such as prolonged neutropenia, allogenic hematopoietic stem cell transplant and acquired immunodeficiencies.

**Table 1. Antifungals Categories**<sup>7,8</sup>

Class	Drug Examples	Mechanism	Used For
Azoles	Fluconazole Isavuconazole	Inhibit ergosterol synthesis (cell membrane disruption)	Candidiasis, dermatophytosis, systemic mycoses (i.e., aspergillosis)

	Itraconazole Ketoconazole Oteseconazole Posaconazole Voriconazole		
Polyenes	Amphotericin B Nystatin	Bind ergosterol, form membrane pores	Systemic infections (Amphotericin B), superficial candidiasis (Nystatin)
Echinocandins	Caspofungin Micafungin Anidulafungin	Inhibit 1,3-β-D-glucan synthase (cell wall)	Invasive candidiasis, aspergillosis, empiric therapy in neutropenia
Allylamines	Terbinafine Naftifine	Inhibit squalene epoxidase (ergosterol synthesis)	Dermatophyte infections: onychomycosis, tinea pedis, tinea corporis, tinea cruris
Pyrimidine Analogues	Flucytosine	Converted to 5-FU, inhibits DNA/RNA synthesis	Cryptococcal meningitis (with Amphotericin B), Candida (with Amphotericin B)
Other	Griseofulvin	Disrupts mitotic spindle (inhibits mitosis)	Tinea capitis, tinea corporis (especially in children)
	Tolnaftate	Inhibits squalene epoxidase (topical)	Topical treatment for tinea infections
	Ciclopirox	Disrupts membrane transport, metal chelation	Topical use in dermatomycoses, onychomycosis, seborrheic dermatitis
	Selenium sulfide Zinc pyrithione	Cytostatic effect on epidermal cells, antifungal	Shampoos for seborrheic dermatitis, tinea versicolor

Choice of antifungal depends on indication, causative organism and resistance patterns. Fungal infections are commonly caused by yeasts, which are unicellular, or less commonly by molds, which are filamentous. Causative organism helps direct antifungal selection. Serious fungal infections typically require oral or intravenous antifungal therapy.<sup>9,10</sup> Antifungals can be categorized as azoles, echinocandins, polyenes, allylamines or nucleoside analogs (**Table 1**). Fluconazole is most commonly recommended first-line for a majority of fungal infections due to efficacy and tolerability.<sup>7</sup> Of the azole antifungals, posaconazole and isavuconazole have the broadest spectrum of action and are not associated with nephrotoxicity. There is wide variability between the different antifungals in their bioavailability and types of drug interactions (due to metabolism via the cytochrome P450 enzyme system). Gastrointestinal issues are the most common adverse reactions associated with antifungal therapy. Hepatic manifestations from mild elevations in liver enzymes to hepatic failure have occurred. For these reasons, transaminase monitoring is recommended for patients receiving extended treatment with antifungal therapy. Drug monitoring is recommended for itraconazole, voriconazole, and posaconazole to ensure efficacy and avoid toxicity.<sup>9</sup>

Important outcomes to determine antifungal efficacy include symptom improvement, clinical cure (clinical symptoms), mycological cure (negative mycological test) and mortality.

#### Methods:

A Medline literature search for new systematic reviews and randomized controlled trials (RCTs) assessing clinically relevant outcomes to active controls, or placebo, if needed, was conducted. The Medline search strategy used for this review is available in **Appendix 3**, which includes dates, search terms and limits

used. The OHSU Drug Effectiveness Review Project, Agency for Healthcare Research and Quality (AHRQ), National Institute for Health and Clinical Excellence (NICE), Department of Veterans Affairs, the Oregon Mental Health Clinical Advisory Group (MHCAG), the Scottish Intercollegiate Guidelines Network (SIGN), and Canada’s Drug Agency (CDA-AMA) resources were manually searched for high quality and relevant systematic reviews. When necessary, systematic reviews are critically appraised for quality using the AMSTAR tool and clinical practice guidelines using the AGREE tool. The FDA website was searched for new drug approvals, indications, and pertinent safety alerts.

The primary focus of the evidence is on high quality systematic reviews and evidence-based guidelines. Randomized controlled trials will be emphasized if evidence is lacking or insufficient from those preferred sources.

**New Systematic Reviews:**  
None identified.

After review, 12 systematic reviews were excluded due to poor quality (e.g, indirect network-meta analyses or failure to meet AMSTAR criteria), wrong study design of included trials (e.g., observational), comparator (e.g., no control or placebo-controlled), or outcome studied (e.g., non-clinical).<sup>11–23</sup>

**New Guidelines:**  
High Quality Guidelines:

NIH – Guidelines for the Prevention and Treatment of Opportunistic Infections in Adults and Adolescents with HIV  
In December 2024, recommendations for the treatment of opportunistic infection in those individuals with HIV were updated.<sup>1</sup> Opportunistic infections can be more frequent or more severe from immunosuppression from HIV. The main updates pertaining to the use of antifungals were for the treatment of coccidioidomycosis and histoplasmosis.<sup>1</sup>

For the treatment of coccidioidomycosis, isavuconazole sulfate was added as a treatment alternative for mild to moderate pulmonary infections (**Table 2**).<sup>1</sup> Coccidioidomycosis often presents with focal pneumonia, diffuse pneumonia, extrathoracic involvement, including meningitis. The recommended fluconazole dose for the treatment of coccidioidal meningitis was updated.<sup>1</sup> The use of azole antifungals during pregnancy was modified. Primary antifungal prophylaxis for coccidioidomycosis is not recommended (Grade A, Level III evidence).<sup>1</sup>

**Table 2. Antifungals for the Treatment of Coccidioidomycosis in Adults and Adolescents<sup>1</sup>**

Indication	Medication	Dose	Strength of Recommendation	Quality of Evidence
<i>Mild to Moderate Pulmonary Infections</i>				
Preferred Therapy	Fluconazole	400 mg PO once daily	A	II
	Itraconazole	200 mg PO three times daily for three days and the twice daily	A	II
Alternative Therapy	Voriconazole	Loading dose 400 mg PO twice daily on day 1, followed by 200 mg PO twice daily	B	II

	Posaconazole delayed-release tablet	300 mg PO twice daily on Day 1, followed by 300 mg once daily	B	III
	Isavuconazole sulfate	372 mg (isavuconazole 200 mg) PO every 8 hours for 6 doses followed by 372 mg PO once daily	B	III
<i>Severe Pulmonary or Extrapulmonary Infections (Except Meningitis)</i>				
Preferred Therapy	Amphotericin B deoxycholate*	0.7 to 1.0 mg/kg IV daily	A	III
	Lipid formulation amphotericin B*	3-5 mg/kg IV daily	A	III
Alternative Therapy	Amphotericin B deoxycholate or lipid formulation amphotericin B. with a triazole as initial therapy	Doses as above	C	III
<i>Meningeal Infection</i>				
Preferred Therapy	Fluconazole	800-1,200 mg PO once daily	A	III
Alternative Therapy	Itraconazole	200 mg PO 2-3 times daily	B	II
	Voriconazole	200-400 mg PO twice daily	B	III
	Posaconazole delayed release tablet	300 mg PO twice daily on day 1, followed by 300 mg PO once daily	C	III
	Isavuconazole sulfate	372 mg (isavuconazole 200 mg) every 8 hours for 6 doses, followed by isavuconazole sulfate 372 mg PO once daily	C	III
	Intrathecal amphotericin B deoxycholate when triazole antifungals are not effective	No dosing provided.	A	III
<i>Treatment in Pregnancy</i>				
Preferred Therapy During First Trimester	Lipid formulation amphotericin B	3-5 mg/kg IV daily	A	III
	Amphotericin B deoxycholate	0.7-1 mg/kg IV daily	A	III
After the first trimester	Fluconazole or itraconazole		A	III
Key: * Use until clinical improvement and then switch to triazole (fluconazole 400 mg PO daily or itraconazole 200 mg PO twice daily) Abbreviations: IV = intravenous; kg = kilogram; mg = milligram; PO = by mouth				

Histoplasmosis develops due to inhalation of microconidia.<sup>1</sup> Infections in the lungs and disseminated infection is common. People with CD4 counts less than 150 cells/mm<sup>3</sup> and have a risk due to occupational exposure or in areas with a high incidence of histoplasmosis are candidates for preventative therapy (**Table 3**).<sup>1</sup> For the treatment of histoplasmosis, the importance of monitoring serum concentrations of itraconazole and voriconazole were updated. Random itraconazole serum concentrations should be monitored 2 weeks after initiation to verify absorption and assess changes in hepatic metabolism due to drug interactions.<sup>1</sup>

Random levels of itraconazole should be measured in all patients after 2 weeks of treatment for histoplasmosis and should be 1.0-2.0 mcg/mL. Voriconazole trough levels for histoplasmosis should be measured 5 days after initiation, with goal levels of 1-5 mcg/mL.<sup>1</sup> Serum concentration of voriconazole can vary due to varying metabolism and drug interactions. Serum concentrations of voriconazole greater than 5 mcg/mL are associated with neurotoxicity and hepatotoxicity. Posaconazole serum concentrations for histoplasmosis should be higher than 1 mcg/mL and should be measured after 5 days of therapy.<sup>1</sup>

**Table 3. Antifungal Treatments for Histoplasmosis<sup>1</sup>**

Indication	Medication	Dose	Strength of Recommendation	Quality of Evidence
<i>Preventative Therapy</i>				
Preferred	Itraconazole	200 mg PO once daily	B	I
<i>Severe Disseminated Disease</i>				
Preferred Induction	Liposomal Amphotericin B	3 mg/kg IV daily	A	I
Alternate Induction	Amphotericin B lipid complex	5 mg/kg IV daily	A	III
Maintenance Therapy	Itraconazole	200 mg PO 3 times daily for 3 days, then 200 mg 2 times a day	A	II
Alternate Therapy	Posaconazole	300 mg extended-release tablet PO twice daily for 1 day, then 300 mg PO once daily	B	III
	Voriconazole	400 mg PO 2 times a day for 1 day, then 200 mg twice daily	B	III
	Fluconazole	800 mg once daily	C	II
<i>Histoplasmosis Meningitis</i>				
Preferred Induction	Liposomal amphotericin B	5 mg/kg IV daily	A	III
Alternative Induction	Amphotericin B deoxycholate	0.7 – 1.0 mg/kg IV daily	B	III
Preferred Maintenance	Itraconazole	200 mg PO 2-3 times a day	A	III
Alternate Maintenance	Voriconazole	400 mg PO twice daily for day 1, then 200 mg PO twice daily	B	III
	Fluconazole	800 mg PO once daily	C	II
Preferred Long-Term Suppressive Therapy	Itraconazole	200 mg PO once daily	A	III
Alternative Long-Term Suppressive Therapy	Fluconazole	400 mg PO once daily	C	II
	Voriconazole	200 mg PO twice daily	B	III
	Posaconazole	300 mg PO daily	B	III
<i>Treatment in Pregnancy</i>				
Preferred 1 <sup>st</sup> trimester Therapy	Amphotericin B	Dose not given	A	III

Preferred 2 <sup>nd</sup> /3 <sup>rd</sup> trimester Therapy	Itraconazole	Dose not given	C	III
Abbreviations: IV = intravenous; kg = kilogram; mg = milligram; PO = by mouth				

After review, one guideline was excluded due to poor quality.<sup>24</sup>

#### New Formulations or Indications:

Cresemba® (isavuconazonium): A new indication for isavuconazonium 372 mg injection was approved in December 2023 for use in pediatric patients 1 year of age and older for the treatment of IA and IM.<sup>2</sup> The isavuconazonium 74.5 mg and 186 mg capsules also received approval for the treatment of IA and IM in pediatric patients 6 years of age and older who weigh at least 16 kg.<sup>2</sup> Evidence used to obtain the approval in pediatric patients (n=31) was from a phase 2, open-label, noncomparative study in patients 1 to less than 18 years with probable or definitive IA or IM.<sup>25</sup> The primary endpoint was all-cause mortality at day 42. All-cause mortality was 6.5% on day 42. Successful response rates were 54.8% at the end of treatment.<sup>25</sup>

#### New FDA Safety Alerts:

**Table 4. Description of New FDA Safety Alerts**

Generic Name	Brand Name	Month / Year of Change	Location of Change (Boxed Warning, Warnings, CI)	Addition or Change and Mitigation Principles (if applicable)
Itraconazole <sup>3</sup>	Sporanox®	October 2024	Warnings	Risk of pseudoaldosteronism characterized by new onset of hypertension or worsening hypertension and abnormal lab values (i.e., hypokalemia, low serum renin and aldosterone and elevated 11-deoxycortisol). Blood pressure and potassium levels should be monitored and discontinuing itraconazole may be appropriate.
Itraconazole <sup>3</sup>	Sporanox®	October 2023	Precautions	Finerenone, voclosporin, mobocertinib, entrectinib and pemigatinib were added to the drug interaction precautions section.
Itraconazole <sup>3</sup>	Sporanox®	December 2024	Adverse Reactions	Bradycardia has been reported in post-marketing reports.
Metronidazole <sup>5</sup>	Flagyl®	March 2024	Warnings	Risk of severe cutaneous adverse reactions (SCARs) and hearing impairment have been reported. Metronidazole should be discontinued immediately if signs of SCARs develop, including skin rash, blisters, fever or other signs of hypersensitivity.
Posaconazole <sup>4</sup>	Noxafil®	October 2024	Warnings	Risk of pseudoaldosteronism characterized by new onset of hypertension or worsening hypertension and abnormal lab values (i.e., hypokalemia, low serum renin and aldosterone and elevate 11-deoxycortisol). Blood pressure and potassium levels should be monitored and discontinuing itraconazole may be appropriate.

Voriconazole <sup>6</sup>	Vfend®	March 2025	Contraindications and drug interactions	Concomitant use of voriconazole and finerenone is contraindicated. Coadministration may result in significant increases in finerenone exposure and risk for serious adverse reactions.
---------------------------	--------	------------	---	--

### Randomized Controlled Trials:

A total of 128 citations were manually reviewed from the initial literature search. After further review, all citations were excluded because of wrong study design (eg, observational), comparator (eg, no control or placebo-controlled), or outcome studied (eg, non-clinical).

### References:

1. Panel on Guidelines for the Prevention and Treatment of Opportunistic Infections in Adults and Adolescents With HIV. Guidelines for the Prevention and Treatment of Opportunistic Infections in Adults and Adolescents With HIV. National Institutes of Health, HIV Medicine Association, and Infectious Diseases Society of America. December 2024. Available at <https://clinicalinfo.hiv.gov/en/guidelines/adult-and-adolescent-opportunistic-infection>. Accessed July 2, 2025.
2. Food and Drug Administration. Cresemba (Isavuconazonium sulfate). Drug Safety-related Labeling Changes (SrLC). May 2021.
3. Sporanox (itraconazole)[prescribing information]. Titusville, NJ; Janssen Pharmaceuticals, Inc. December 2024.
4. Noxafil (Posaconazole) [prescribing information]. Whitehouse Station, NJ; Merck and Co., Inc. June 2021.
5. Flagyl (metronidazole) [prescribing information]. New York, NY; Pfizer Labs. July 2024.
6. Food and Drug Administration. Vfend (voriconazole). Drug Safety-related Labeling Changes (SrLC). September 2020.
7. Goldstein A, Goldstein B. Dermatophyte (tinea) infections. UpToDate. May 2025. Accessed June 23, 2025.
8. Lewis R. Pharmacology of echinocandins. UpToDate. 2019. Accessed August 24, 2019.
9. Patterson TF, Thompson GR, Denning DW, et al. Practice Guidelines for the Diagnosis and Management of Aspergillosis: 2016 Update by the Infectious Diseases Society of America. *Clin Infect Dis*. 2016;63(4):e1-e60. doi:10.1093/cid/ciw326
10. Pappas PG, Kauffman CA, Andes DR, et al. Clinical Practice Guideline for the Management of Candidiasis: 2016 Update by the Infectious Diseases Society of America. *Clin Infect Dis*. Published online December 16, 2015:civ933. doi:10.1093/cid/civ933.
11. de Oliveira VF, Taborda M, Katayose JT, et al. Isavuconazole in chronic pulmonary aspergillosis: What is the evidence? *Journal of Infection and Chemotherapy*. 2025;31(6):102704. doi:10.1016/j.jiac.2025.102704.
12. Abo Zeid M, Elrosasy A, Alkousheh H, et al. A comprehensive evaluation of Naftifine's efficacy and safety in treating dermatophyte infections; systematic review and meta-analysis. *Archives of Dermatological Research*. 2025;317(1):522. doi:10.1007/s00403-025-04044-x.



13. Keyvanfar A, Najafiarab H, Talebian N, et al. Drug-resistant oral candidiasis in patients with HIV infection: a systematic review and meta-analysis. *BMC Infectious Diseases*. 2024;24(1):546. doi:10.1186/s12879-024-09442-6.
14. Motta Guimaraes MG, Pinheiro Martin Tapioca F, Costa Neves F, Nunes Freitas Teixeira S, Santana Passos LC. The efficacy of fluconazole for anti-fungal prophylaxis in peritoneal dialysis patients: A systematic review and meta-analysis. *Nefrologia*. 2024;44(2):173-179. doi:10.1016/j.nefro.2024.04.002.
15. Niu X, Al-Hatmi AMS, Vitale RG, et al. Evolutionary trends in antifungal resistance: a meta-analysis. *Microbiology Spectrum*. 2024;12(4):e0212723. doi:10.1128/spectrum.02127-23.
16. Rehman OU, Nadeem ZA, Fatima E, et al. The Efficacy of Ketoconazole Containing Regimens in Castration-Resistant Prostate Cancer: A Systematic Review and Meta-Analysis. [Review]. *Clinical Genitourinary Cancer*. 2024;22(2):483-490. doi:10.1016/j.clgc.2024.01.003.
17. Adelhoefer SJ, Gonzalez MR, Bedi A, et al. Candida spondylodiscitis: a systematic review and meta-analysis of seventy two studies. [Review]. *International Orthopaedics*. 2024;48(1):5-20. doi:10.1007/s00264-023-05989-2.
18. Kato H, Hagihara M, Shibata Y, et al. Comparison of mortality between echinocandins and polyenes for an initial treatment of candidemia: A systematic review and meta-analysis. *Journal of Infection & Chemotherapy*. 2021;27(11):1562-1570. doi:10.1016/j.jiac.2021.06.017.
19. Muthu V, Dhooria S, Sehgal IS, et al. Nebulized amphotericin B for preventing exacerbations in allergic bronchopulmonary aspergillosis: A systematic review and meta-analysis. *Pulmonary Pharmacology & Therapeutics*. 2023;1:102226. doi:10.1016/j.pupt.2023.102226.
20. Viecceli C, Mattos ACV, Hirakata VN, et al. Ketoconazole as second-line treatment for Cushing's disease after transsphenoidal surgery: systematic review and meta-analysis. *Frontiers in Endocrinology*. 2023;1:1145775. doi:10.3389/fendo.2023.1145775.
21. Xie J, Zeng J, Zheng S. The efficacy and safety of fluconazole in preventing invasive fungal infection in very low birth weight infants: a systematic review and meta-analysis. [Review]. *Italian Journal of Pediatrics*. 2023;49(1):51. doi:10.1186/s13052-023-01460-5.
22. Huang Y, Shen C, Shen Y, Cui H. Assessing the Efficacy of Clotrimazole and Metronidazole Combined Treatment in Vaginitis: A Meta-Analysis. *Alternative Therapies in Health & Medicine*. 2024;30(1):186-191.
23. Weng J, Du X, Fang B, et al. Efficacy and safety of isavuconazole versus voriconazole for the treatment of invasive fungal infections: a meta-analysis with trial sequential analysis. *BMC Infectious Diseases*. 2025;25(1):230. doi:10.1186/s12879-025-10627-w.
24. Agarwal R, Sehgal IS, Muthu V, et al. Revised ISHAM-ABPA working group clinical practice guidelines for diagnosing, classifying and treating allergic bronchopulmonary aspergillosis/mycoses. *European Respiratory Journal*. 2024;63(4). doi:10.1183/13993003.00061-2024.
25. FDA Approves Expanded Use of CRESEMBA® (isavuconazonium sulfate) in Children with Invasive Aspergillosis and Invasive Mucormycosis. Astellas Pharma US, Inc. News Room. Accessed June 26, 2025. Available at: <https://newsroom.astellas.us/2023-12-08-FDA-Approves-Expanded-Use-of-CRESEMBA-R-isavuconazonium-sulfate-in-Children-with-Invasive-Aspergillosis-and-Invasive-Mucormycosis>. Accessed July 2, 2025.

## Appendix 1: Current Preferred Drug List

### Antifungals, Oral

<u>Generic</u>	<u>Brand</u>	<u>Form</u>	<u>PDL</u>
clotrimazole	CLOTRIMAZOLE	TROCHE	Y
fluconazole	DIFLUCAN	SUSP RECON	Y
fluconazole	FLUCONAZOLE	SUSP RECON	Y
fluconazole	DIFLUCAN	TABLET	Y
fluconazole	FLUCONAZOLE	TABLET	Y
nystatin	MYCOSTATIN	ORAL SUSP	Y
nystatin	NYSTATIN	ORAL SUSP	Y
nystatin	NYSTATIN	TABLET	Y
flucytosine	ANCOBON	CAPSULE	N
flucytosine	FLUCYTOSINE	CAPSULE	N
griseofulvin ultramicrosize	GRISEOFULVIN ULTRAMICROSIZED	TABLET	N
griseofulvin, microsize	GRISEOFULVIN	ORAL SUSP	N
griseofulvin, microsize	GRISEOFULVIN	TABLET	N
ibrexafungerp citrate	BREXAFEMME	TABLET	N
isavuconazonium sulfate	CRESEMBA	CAPSULE	N
itraconazole	TOLSURA	CAP SD DSP	N
itraconazole	ITRACONAZOLE	CAPSULE	N
itraconazole	SPORANOX	CAPSULE	N
itraconazole	ITRACONAZOLE	SOLUTION	N
itraconazole	SPORANOX	SOLUTION	N
ketoconazole	KETOCONAZOLE	TABLET	N
miconazole	ORAVIG	MA BUC TAB	N
oteseconazole	VIVJOA	CAPSULE	N
posaconazole	NOXAFIL	ORAL SUSP	N
posaconazole	POSACONAZOLE	ORAL SUSP	N
posaconazole	NOXAFIL	SUSPDR PKT	N
posaconazole	NOXAFIL	TABLET DR	N
posaconazole	POSACONAZOLE	TABLET DR	N
terbinafine HCl	TERBINAFINE HCL	TABLET	N
voriconazole	VFEND	SUSP RECON	N
voriconazole	VORICONAZOLE	SUSP RECON	N
voriconazole	VFEND	TABLET	N
voriconazole	VORICONAZOLE	TABLET	N

**Antifungals, Topical**

<u>Generic</u>	<u>Brand</u>	<u>Form</u>	<u>PDL</u>
miconazole nitrate	ANTIFUNGAL CREAM	CREAM (G)	Y
miconazole nitrate	MICONAZOLE NITRATE	CREAM (G)	Y
nystatin	NYSTATIN	CREAM (G)	Y
nystatin	NYSTATIN	OINT. (G)	Y
acetic ac/resorcino/salicyl ac	ANTIFUNGAL NAIL	TINCTURE	N
butenafine HCl	ATHLETE'S FOOT	CREAM (G)	N
butenafine HCl	BUTENAFINE HCL	CREAM (G)	N
ciclopirox	CICLOPIROX	GEL (GRAM)	N
ciclopirox	CICLOPIROX	SHAMPOO	N
ciclopirox	CICLODAN	SOLUTION	N
ciclopirox	CICLOPIROX	SOLUTION	N
ciclopirox olamine	CICLODAN	CREAM (G)	N
ciclopirox olamine	CICLOPIROX	CREAM (G)	N
ciclopirox olamine	LOPROX	CREAM (G)	N
ciclopirox olamine	CICLOPIROX	SUSPENSION	N
ciclopirox olamine	LOPROX	SUSPENSION	N
ciclopirox/skin cleanser no.28	CICLODAN	COMBO. PKG	N
ciclopirox/skin cleanser no.40	LOPROX	COMBO. PKG	N
ciclopirox/skin cleanser no.40	LOPROX	KIT SS-CLN	N
ciclopirox/urea/camph/men/euc	CICLODAN	SOLUTION	N
ciclopirox/urea/camph/men/euc	CICLOPIROX	SOLUTION	N
clotrimazole	ANTIFUNGAL	CREAM (G)	N
clotrimazole	ATHLETE'S FOOT	CREAM (G)	N
clotrimazole	CLOTRIMAZOLE	CREAM (G)	N
clotrimazole	FUNGOID	CREAM (G)	N
clotrimazole	LOTRIMIN AF	CREAM (G)	N
clotrimazole	MICOTRIN AC	CREAM (G)	N
clotrimazole	MYCOZYL AC	CREAM (G)	N
clotrimazole	TRIMAZOLE	CREAM (G)	N
clotrimazole	ALEVAZOL	OINT. (G)	N
clotrimazole	ATHLETE'S FOOT	SOLUTION	N
clotrimazole	CLOTRIMAZOLE	SOLUTION	N
clotrimazole	FUNGOID	SOLUTION	N
clotrimazole/betamethasone dip	CLOTRIMAZOLE-BETAMETHASONE	CREAM (G)	N
clotrimazole/betamethasone dip	CLOTRIMAZOLE-BETAMETHASONE	LOTION	N
econazole nitrate	ECONAZOLE NITRATE	CREAM (G)	N

efinaconazole	JUBLIA	SOL W/APPL	N
ketoconazole	KETOCONAZOLE	CREAM (G)	N
ketoconazole	KETOCONAZOLE	FOAM	N
ketoconazole	KETODAN	FOAM	N
ketoconazole	KETOCONAZOLE	SHAMPOO	N
ketoconazole/skin cleanser 28	KETODAN	COMBO. PKG	N
luliconazole	LULICONAZOLE	CREAM (G)	N
luliconazole	LUZU	CREAM (G)	N
miconazole nitrate	ATHLETE'S FOOT SPRAY	AERO POWD	N
miconazole nitrate	THERA ANTIFUNGAL	CREAM(ML)	N
miconazole nitrate	ALOE VESTA	OINT.(ML)	N
miconazole nitrate	ANTIFUNGAL POWDER	POWDER	N
miconazole nitrate	MICONAZOLE NITRATE	POWDER	N
miconazole nitrate	MICONAZORB AF	POWDER	N
miconazole nitrate	MICOTRIN AP	POWDER	N
miconazole nitrate	MYCOZYL AP	POWDER	N
miconazole nitrate	THERA ANTIFUNGAL	POWDER	N
miconazole nitrate	MICONAZOLE NITRATE	SOL W/APPL	N
miconazole nitrate	FUNGOID TINCTURE	TINCTURE	N
miconazole nitrate/zinc ox/pet	MICONAZOLE-ZINC OXIDE-PETROLTM	OINT. (G)	N
miconazole nitrate/zinc ox/pet	VUSION	OINT. (G)	N
naftifine HCl	NAFTIFINE HCL	CREAM (G)	N
naftifine HCl	NAFTIFINE HCL	GEL (GRAM)	N
naftifine HCl	NAFTIN	GEL (GRAM)	N
nystatin	KLAYESTA	POWDER	N
nystatin	NYAMYC	POWDER	N
nystatin	NYSTATIN	POWDER	N
nystatin	NYSTOP	POWDER	N
nystatin/triamcinolone acet	MYCONEL	CREAM (G)	N
nystatin/triamcinolone acet	MYTREX	CREAM (G)	N
nystatin/triamcinolone acet	N.T.A.	CREAM (G)	N
nystatin/triamcinolone acet	NYSTATIN-TRIAMCINOLONE	CREAM (G)	N
nystatin/triamcinolone acet	MYTREX	OINT. (G)	N
nystatin/triamcinolone acet	N.T.A.	OINT. (G)	N
nystatin/triamcinolone acet	NYSTATIN-TRIAMCINOLONE	OINT. (G)	N
oxiconazole nitrate	OXICONAZOLE NITRATE	CREAM (G)	N
oxiconazole nitrate	OXISTAT	LOTION	N
sertaconazole nitrate	ERTACZO	CREAM (G)	N
tavaborole	TAVABOROLE	SOL W/APPL	N
terbinafine HCl	ATHLETE'S FOOT	CREAM (G)	N

terbinafine HCl	ATHLETE'S FOOT AF	CREAM (G)	N
terbinafine HCl	TERBINAFINE	CREAM (G)	N
tolnaftate	ATHLETE'S FOOT	AERO POWD	N
tolnaftate	TOLNAFTATE	AERO POWD	N
tolnaftate	ANTIFUNGAL CREAM	CREAM (G)	N
tolnaftate	TOLNAFTATE	CREAM (G)	N
tolnaftate	TRITOLNACIDE C	CREAM(ML)	N
tolnaftate	TOLNAFTATE	POWDER	N
tolnaftate	ANTIFUNGAL	SOLUTION	N
tolnaftate	MICOMITIN	SOLUTION	N
tolnaftate	MICOTRIN AL	SOLUTION	N
tolnaftate	MYCOZYL AL	SOLUTION	N
tolnaftate	TOLNAFI-AL	SOLUTION	N
tolnaftate	TRITOLNACIDE S	SOLUTION	N
undecylenic ac/zinc undecylena	ANTIFUNGAL CREAM	CREAM (G)	N
undecylenic ac/zinc undecylena	UNDEX-25	OINT. (G)	N
undecylenic acid	TRIPENICOL C	CREAM(ML)	N
undecylenic acid	TRIPENICOL S	SOLUTION	N

#### Antifungals, Vaginal

<u>Generic</u>	<u>Brand</u>	<u>Form</u>	<u>PDL</u>
clotrimazole	3-DAY VAGINAL CREAM	CREAM/APPL	Y
clotrimazole	CLOTRIMAZOLE	CREAM/APPL	Y
clotrimazole	CLOTRIMAZOLE-3	CREAM/APPL	Y
clotrimazole	CLOTRIMAZOLE	TABLET	Y
miconazole nitrate	MICONAZOLE 3	CMB PF CRM	Y
miconazole nitrate	MICONAZOLE 7	CREAM/APPL	Y
miconazole nitrate	MICONAZOLE NITRATE	CREAM/APPL	Y
miconazole nitrate	MICONAZOLE-7	CREAM/APPL	Y
miconazole nitrate	YEAST-X	CREAM/APPL	Y
miconazole nitrate	MICONAZOLE 7	SUPP.VAG	Y
miconazole nitrate	MICONAZOLE NITRATE	SUPP.VAG	Y
terconazole	TERCONAZOLE	CREAM/APPL	Y
tioconazole	TIOCONAZOLE-1	OIN/PF APP	Y
butoconazole nitrate	GYNAZOLE 1	CRM/PF APP	N
clotrimazole	VAGINAL 3-DAY	COMBO. PKG	N
miconazole nitrate	MICONAZOLE 1	KIT	N
miconazole nitrate	MICONAZOLE 3	KIT	N
miconazole nitrate	MICONAZOLE NITRATE	KIT	N
miconazole nitrate	MICONAZOLE 3	SUPP.VAG	N

terconazole

TERCONAZOLE

SUPP.VAG

N

**Appendix 3: Medline Search Strategy**Database(s): **Ovid MEDLINE(R) ALL** 1946 to June 19, 2025

Search Strategy:

#	Searches	Results
1	clotrimazole.mp. or Clotrimazole/	3432
2	Fluconazole/ or fluconazole.mp.	17714
3	nystatin.mp. or Nystatin/	5723
4	flucytosine.mp. or Flucytosine/	4168
5	griseofulvin.mp. or Griseofulvin/	4167
6	ibrexafungerp.mp.	161
7	isavuconazonium.mp.	110
8	itraconazole.mp. or Itraconazole/	12662
9	ketoconazole.mp. or Ketoconazole/	10169
10	miconazole.mp. or Miconazole/	3624
11	oteseconazole.mp.	58
12	posaconazole.mp.	3938
13	terbinafine.mp. or Terbinafine/	3846
14	voriconazole.mp. or Voriconazole/	9592
15	acetic acid.mp. or Acetic Acid/	58997
16	butenafine.mp.	117
17	ciclopirox.mp. or Ciclopirox/	752
18	clotrimazole.mp. or Clotrimazole/	3432
19	econazole.mp. or Econazole/	1075
20	efinaconazole.mp.	270

21	ketokonazole.mp.	24
22	luliconazole.mp.	238
23	naftifine.mp.	233
24	oxiconazole.mp.	124
25	sertaconazole.mp.	171
26	tavaborole.mp.	160
27	tolnaftate.mp. or Tolnaftate/	310
28	undecylenic.mp.	404
29	terconazole.mp.	268
30	tioconazole.mp.	260
31	butoconazole.mp.	72
32	terconazole.mp.	268
33	1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25 or 26 or 27 or 28 or 29 or 30 or 31 or 32	119823
34	limit 33 to (english language and humans and yr="2023 -Current")	3546
35	limit 34 to (clinical trial, phase iii or guideline or meta analysis or practice guideline or "systematic review")	128

Appendix 4: Key Inclusion Criteria

Population	Patients with active fungal infections
Intervention	Oral, topical, or vaginal antifungal therapies
Comparator	Placebo or active treatment
Outcomes	Mycological cure
Setting	Outpatient

Appendix 5: Prior Authorization Criteria

Antifungals

Goal(s):

- Approve use of antifungals only for OHP-funded diagnoses. Minor fungal infections of skin, such as dermatophytosis and candidiasis are only funded when complicated by an immunocompromised host.
- Allow case-by-case review for members covered under the EPSDT program.

Length of Authorization:

- See criteria

Requires PA:

- Non-preferred drugs

Covered Alternatives:

- Current PMPDP preferred drug list per OAR 410-121-0030 at
- Searchable site for Oregon FFS Drug Class listed at [www.orpdl.org/drugs/](http://www.orpdl.org/drugs/)

Table 1: Examples of FUNDED indications (07/08/2025)

ICD-10	Description
B37.1	Candidiasis of the lung
B37.3	Candidiasis of vulva and vagina (vaginitis and cervicitis)
B37.42, B37.49	Candidiasis of other urogenital sites
B37.5-37.6, B37.81-37.84, B37.89	Candidiasis of other specified sites



B37.7	Disseminated Candidiasis
B38.0-B38.4, B38.7, B38.9	Coccidiomycosis various sites
B39.0-39.5, B39.9, G02, I32, I39, J17	Histoplasmosis, subacute meningitis, acute bacterial meningitis
B40.9, B41.0, B41.9, B48.0	Blastomycosis
B42.0-42.9, B43.9, B44.9-45.0, B45.7, B45.9, B46.9, B48.1-48.2, B48.8, B49	Rhinosporidiosis, Sporotrichosis, Chromoblastomycosis, Aspergillosis, Mycosis Mycetomas, Cryptococcosis, Allescheriosis, Zygomycosis, Dematiaceous Fungal Infection, Opportunistic Mycosis, Mycoses Nec and Nos
B44.81	Bronchopulmonary Aspergillus, Allergic
L03.019, L03.029, L03.039, L03.049	Cellulitis and abscess of finger and toe
L30.4	Severe intertrigo (see HERC guideline note 21 for definition of severe inflammatory skin disease)
N73.9-75.1, N76.0-N77.1	Acute inflammatory pelvic disease
P37.5	Neonatal Candida infection

**Table 2: Examples of NON-FUNDED indications (07/08/2025)**

ICD-10	Description
B36.0	Pityriasis versicolor
B36.2	Tinea blanca
B36.3	Black piedra
B36.8, B36.9	Mycoses, superficial
B37.2	Cutaneous candidiasis
B37.9	Candidiasis, unspecified
L20.0-20.84, L20.89-20.9	Other atopic dermatitis and related conditions
L21.0-21.1, L21.8-21.9,	Erythematous squamous dermatosis
L22	Diaper or napkin rash
L23.0, 23.81, L24.0-24.2, L24.81, L25.0, L25.1-25.5, L25.8-L25.9, L55.1-L55.2, L56.8, L57.8, L57.9, L58.9	Contact dermatitis and other eczema
L26, L30.4, L49.0-L49.9, L51.0, L51.8-L51.9, L52, L53.0-L53.2,	Erythematous conditions

L53.8, L53.9, L71.0-L71.1, L71.8, L92.0, L93.0, L93.2, L95.1, L98.2	
L43.8, L44.1-44.3, L44.9, L66.1	Lichen Planus
L70.0-70.2, L70.8	Rosacea or acne
R21	Rash and other nonspecific skin eruption

**Table 3: Diagnosis funded by OHP if criteria are met (7/08/25)**

ICD-10	Description
B35.0	Dermatophytosis of scalp and beard (tinea capitis/ tinea barbae)
B35.1	Tinea unguium (onychomycosis)
B35.2	Dermatophytosis of hand (tinea manuum)
B35.3	Dermatophytosis of foot (tinea pedis)
B35.5	Dermatophytosis of body (tinea corporis / tinea imbricate)
B35.6	Dermatophytosis of groin and perianal area (tinea cruris)
B35.8-B35.9	Deep seated dermatophytosis; dermatophytosis of other specified sites - unspecified site
B36.1	Tinea nigra
B37.83	Candidiasis of mouth

### Approval Criteria

1. What diagnosis is being treated?	Record ICD10 code	
2. Is the diagnosis funded by OHP? (See examples in Table 1)	<b>Yes:</b> Go to #3	<b>No:</b> Go to #8
3. Is the request for oteseconazole?	<b>Yes:</b> Go to #4	<b>No:</b> Go to #7
4. Does the patient have a diagnosis of recurrent vulvovaginal candidiasis (RVVC) defined as a history of 3 or more episodes of acute vulvovaginal candidiasis (VVC) in the previous 12 months?	<b>Yes:</b> Go to #5	<b>No:</b> Pass to RPh. Deny; medical appropriateness.

## Approval Criteria

5. Has the patient failed to have benefit with, or have contraindications or intolerance to, a course of oral fluconazole for recurrent vulvovaginal candidiasis?	<b>Yes:</b> Go to #6	<b>No:</b> Pass to RPh. Deny; medical appropriateness.
6. Is the patient of reproductive potential?	<b>Yes:</b> Pass to RPh. Deny; medical appropriateness.	<b>No:</b> Approve up to 18 capsules for 12 months
7. Will the prescriber consider a change to a preferred product? Message: <ul style="list-style-type: none"> <li>• Preferred products do not require PA.</li> <li>• Preferred products are evidence-based reviewed for comparative effectiveness and safety.</li> </ul>	<b>Yes:</b> Inform prescriber of preferred alternatives.	<b>No:</b> Approve for 3 months or course of treatment.
8. Is the prescriber a hematology, oncology or infectious disease specialty prescriber requesting voriconazole or posaconazole?	<b>Yes:</b> Approve for 3 months or course of treatment.	<b>No:</b> Go to #9
9. Is the diagnosis not funded by OHP? (see examples in Table 2).	<b>Yes:</b> If not eligible for EPSDT review: Pass to RPh. Deny; not funded by the OHP  If eligible for EPSDT review: Go to #10	<b>No:</b> Go to #10
10. Is the diagnosis funded by OHP if criteria are met? (see examples in Table 3).	<b>Yes:</b> Go to #11	<b>No:</b> Go to #16

## Approval Criteria

11. Is the patient immunocompromised (examples below)?

- Does the patient have a current (not history of) diagnosis of cancer **AND** is currently undergoing Chemotherapy or Radiation? Document therapy and length of treatment. **OR**
- Does the patient have a diagnosis of HIV/AIDS? **OR**
- Does the patient have sickle cell anemia?
- Poor nutrition, elderly or chronically ill?
- Other conditions as determined and documented by a RPh.

**Yes:** Record ICD-10 code. Approve as follows: (immunocompromised patient)

### ORAL & TOPICAL

- Course of treatment.
- If length of therapy is unknown, approve for 3 months.

**No:** Go to #12

## Approval Criteria

12. Is the patient currently taking an immunosuppressive drug? Document drug.

**Pass to RPh for evaluation if drug not in list.**

Immunosuppressive drugs include but are not limited to:

azathioprine	leflunomide
basiliximab	mercaptopurine
cyclophosphamide	methotrexate
cyclosporine	mycophenolate
etanercept	rituximab
everolimus	sirolimus
hydroxychloroquine	tacrolimus
infliximab	

**Yes:** Approve as follows:  
(immunocompromised patient)

### ORAL & TOPICAL

- Course of treatment.
- If length of therapy is unknown, approve for 3 months.

**No:** Go to #13

## Approval Criteria

13. Is the request for treatment of a foot condition and does the member meet criteria for high-risk foot care?

Antifungals are funded when all of the following criteria are met:

- 1) The patient is at high risk for nail/foot complications due to severe circulatory insufficiency and/or areas of desensitization OR resides in an institutional setting (e.g., skilled nursing/rehabilitation facility, group home, etc.)  
AND
- 2) There is clinical evidence of mycosis of the toenail;  
AND
- 3) The patient has documented marked limitation of ambulation, pain, and/or secondary bacterial infection resulting from the thickening and dystrophy of the infected toenail plate.

**Yes:** Approve as follows:

### ORAL & TOPICAL

- Course of treatment.
- If length of therapy is unknown, approve for 3 months.

**No:** If not eligible for EPSDT review: Pass to RPh. Deny; not funded by the OHP

If eligible for EPSDT review: Go to #14

14. Is there documentation that the condition is of sufficient severity that it impacts the patient's health (e.g., quality of life, function, growth, development, ability to participate in school, perform activities of daily living, etc.)?

**Yes:** Go to #15

**No:** Pass to RPh. Deny; medical necessity.

## Approval Criteria

15. Is the request for a preferred product OR has the patient failed to have benefit with, or have contraindications or intolerance to, at least 2 preferred products?

**Message:**

Preferred products are evidence-based reviewed for comparative effectiveness and safety by the Oregon Pharmacy & Therapeutics Committee.

**Yes:** Approve for 12 months.

**No:** Pass to RPh. Deny; medical appropriateness.

Inform prescriber of covered alternatives in class and process appropriate PA.

16. RPh only: All other indications need to be evaluated to see if it is an OHP-funded diagnosis:

- If funded: may approve for treatment course with PRN renewals. If length of therapy is unknown, approve for 3-month intervals only.
- If not funded:
  - If the member is eligible for EPSDT review, is there documentation that the condition is of sufficient severity that it impacts the patient's health (e.g., quality of life, function, growth, development, ability to participate in school, perform activities of daily living, etc.)?
    - If yes, may approve for treatment course with PRN renewals. If length of therapy is unknown, approve for 3-month intervals only.
    - If No, deny (medical necessity)
  - If the member is not eligible for EPSDT, Deny; not funded by the OHP.
    - Deny non-fungal diagnosis (medical appropriateness)
    - Deny fungal ICD-10 codes that do not appear on the OHP list pending a more specific diagnosis code (not funded by the OHP).
    - Forward any fungal ICD-10 codes not found in the Tables 1, 2, or 3 to the Lead Pharmacist. These codes will be forwarded to DMAP to be added to the Tables for future requests.

P&T Review: 12/25 (KS); 12/23;12/22; 2/22; 11/19; 7/15; 09/10; 2/06; 11/05; 9/05; 5/05  
 Implemented: 1/1/24; 1/1/23; 4/1/22; 5/1/16; 8/15; 1/1/11; 7/1/06; 11/1/0; 9/1/0