

Clinical Policy: Infectious Disease Agents: Antifungals for Onychomycosis & Systemic Infections

Reference Number: OH.PHAR.PPA.70

Effective Date: 01/01/2020

Last Review Date: N/A

Line of Business: Medicaid

[Coding Implications](#)

[Revision Log](#)

See [Important Reminder](#) at the end of this policy for important regulatory and legal information.

Description:

INFECTIOUS DISEASE AGENTS: AGENTS FOR ONYCHOMYCOSIS

NO PA REQUIRED "PREFERRED"	PA REQUIRED "NON-PREFERRED"
GRIFULVIN®V tablets (griseofulvin, microsize)	ITRACONAZOLE (generic of Sporanox®)
GRISEOFULVIN suspension (generic of Grifulvin®V)	LAMISIL Granules (terbinafine)
GRIS-PEG® (griseofulvin, ultramicrosize)	ONMEL® (itraconazole)
TERBINAFINE (generic of Lamisil®)	SPORANOX® 100mg/10ml oral solution (itraconazole)

INFECTIOUS DISEASE AGENTS: AGENTS FOR SYSTEMIC INFECTIONS

NO PA REQUIRED "PREFERRED"	PA REQUIRED "NON-PREFERRED"
FLUCONAZOLE (generic of Diflucan®)	CRESEMBA® (isavuconazonium)
FLUCONAZOLE suspension (generic of Diflucan®)	ITRACONAZOLE capsules (generic of Sporanox®)
FLUCYTOSINE (generic of Ancobon®)	NOXAFIL® (posaconazole)
KETOCONAZOLE (generic of Nizoral®)	ORAVIG® (miconazole)
	SPORANOX® 100mg/10ml oral solution (itraconazole)
	VORICONAZOLE (generic of Vfend®)
	TOLSURA (itraconazole)

FDA Approved Indication(s):

Antifungals are indicated for the treatment of:

- aspergillosis
- blastomycosis
- bone and joint infections
- candidemia
- candidiasis
- candidiasis prophylaxis
- candiduria
- cryptococcal meningitis
- cryptococcosis
- cystitis

Infections

- endocarditis
- esophageal candidiasis
- histoplasmosis
- intraabdominal abscess
- intraabdominal infections
- meningitis
- mucormycosis
- onychomycosis
- oropharyngeal candidiasis (thrush)
- peritonitis
- pneumonia
- pyelonephritis
- sinusitis
- skin and skin structure infections
- tinea barbae
- tinea capitis
- tinea corporis
- tinea cruris
- tinea pedis
- urinary tract infection (UTI)
- vulvovaginal candidiasis

Policy/Criteria

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

It is the policy of Buckeye Health Plan, an affiliate of Centene Corporation[®], that Sporanox, Lamisil Granules, Onmel, Cresemba, Noxafil, Oravig, Vfend, and Tolsura are **medically necessary** when the following criteria are met:

I. Initial Approval Criteria**A. For Sporanox, Lamisil Granules, Onmel, Noxafil, Oravig, Vfend, and Tolsura (must meet all):**

1. FDA-approved or supported by standard pharmacopeias;
2. The member meets one of the following (a, b, or c):
 - a. Documentation that the member has a serious illness that causes them to be immunocompromised [i.e. AIDS, cancer, organ (solid or non-solid) transplant];
 - b. Documentation that there have been therapeutic failures to no less than a 7 day trial of at least one medication not requiring prior approval UNLESS there is a reason the member cannot be changed to a preferred medication. Acceptable reasons include:
 - Allergies to all medications not requiring prior approval.
 - Contraindication to or drug-to-drug interaction with medications not requiring prior approval.

- History of unacceptable/toxic side effects to medications not requiring prior approval.
- c. Documentation that the member is completing a course of therapy with a medication which was initiated in the hospital OR if the member has just become Medicaid eligible and is already on course of treatment.

NOTE: An off-label use may be approvable for a medication (such as Nizoral) for advanced prostate cancer or for Cushing's Syndrome when standard treatments have failed.

Approval duration: For the duration of the prescription (up to 180 days).

B. For Cresemba (isavuconazonium) (must meet all):

1. Diagnosis of invasive aspergillosis or invasive mucormycosis;
2. Age \geq 18 years;
3. Prescribed by or in consultation with an infectious disease specialist;
4. The member meets one of the following (a, b, or c):
 - a. Documentation that the member has a serious illness that causes them to be immunocompromised [i.e. AIDS, cancer, organ (solid or non-solid) transplant];
 - b. Documentation that there have been therapeutic failures to no less than a 7 day trial of at least one medication not requiring prior approval UNLESS there is a reason the member cannot be changed to a preferred medication. Acceptable reasons include:
 - Allergies to all medications not requiring prior approval.
 - Contraindication to or drug-to-drug interaction with medications not requiring prior approval.
 - History of unacceptable/toxic side effects to medications not requiring prior approval.
 - c. Documentation that the member is completing a course of therapy with a medication which was initiated in the hospital OR if the member has just become Medicaid eligible and is already on course of treatment.

Approval duration: For the duration of the prescription (up to 180 days).

C. Other diagnoses/indications:

1. There are no pharmacy and therapeutic committee approved off-label use criteria for the diagnosis;
2. Use is supported by one of the following (a, b, or c):
 - a. The National Comprehensive Cancer Network (NCCN) Drug Information and Biologics Compendium level of evidence 1 or 2A;
 - b. Evidence from at least two high-quality, published studies in reputable peer-reviewed journals or evidence-based clinical practice guidelines that provide all of the following (i – iv):
 - i. Adequate representation of the member's clinical characteristics, age, and diagnosis;
 - ii. Adequate representation of the prescribed drug regimen;
 - iii. Clinically meaningful outcomes as a result of the drug therapy in question;
 - iv. Appropriate experimental design and method to address research questions;
 - c. Micromedex DrugDex[®] with strength of recommendation Class I, IIa, or IIb;

3. Prescribed by or in consultation with an appropriate specialist for the diagnosis;
4. Failure of an adequate trial of at least two FDA-approved drugs for the indication and/or drugs that are considered the standard of care, when such agents exist for the same indication at maximum indicated doses, unless no such drugs exist, at maximum indicated doses, unless contraindicated or clinically significant adverse effect are experienced;
5. Dosing regimen and duration are within dosing guidelines recommended by clinical practice guidelines and/or medical literature.

Approval duration: For the duration of the prescription (up to 180 days).

II. Diagnoses/Indications for which coverage is NOT authorized:

Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policy – CP.PMN.53 for Medicaid or evidence of coverage documents.

III. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

- ER: Extended Release
- FDA: Food and Drug Administration
- PA: Prior Authorization
- UTI: Urinary Tract Infection

Appendix B: Therapeutic Alternatives

This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may not be a formulary agent for all relevant lines of business and may require prior authorization.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
griseofulvin microsize tablets (Grifulvin V)	<p>Tinea corporis, tinea cruris, tinea capitis, tinea barbae 500 mg given either once daily or in 2 to 4 divided doses per day</p> <p>Tinea pedis or tinea unguium (onychomycosis) 750 to 1000 mg given either once daily or in 2 to 4 divided doses</p>	1 g daily
griseofulvin suspension (Grifulvin V)	<p>Tinea corporis, tinea cruris, tinea capitis, tinea barbae 500 mg given either once daily or in 2 to 4 divided doses per day</p> <p>Tinea pedis or tinea unguium (onychomycosis) 750 to 1000 mg given either once daily or in 2 to 4 divided doses</p>	1 g daily

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
griseofulvin ultramicrosize tablets (Gris-PEG)	<p>Tinea corporis, tinea cruris, tinea capitis, tinea barbae 300 to 375 mg given either once daily or in 2 to 4 divided doses per day</p> <p>Tinea pedis or tinea unguium (onychomycosis) 660 to 750 mg given either once daily or in 2 to 4 divided doses</p>	750 mg daily
terbinafine (Lamisil)	<p>Onychomycosis 250 mg once daily. Treatment should continue for 6 weeks for treatment of fingernails, and 12 weeks for treatment of toenails.</p>	250 mg daily
fluconazole (Diflucan)	<p>Candidemia and invasive (non-CNS) candidiasis 800 mg (12 mg/kg) once, then 400 mg (6 mg/kg) once daily</p> <p>Oropharyngeal candidiasis (thrush) 200 mg once, then 100 mg once daily for 7 to 14 days</p> <p>Esophageal candidiasis 200 mg once, then 100 mg once daily. Alternately, 200 to 400 mg (3 to 6 mg/kg/dose) once daily. Treat for 14 to 21 days and for at least 2 weeks after the resolution of symptoms.</p> <p>Vulvovaginal candidiasis (VVC) 150 mg as a single dose</p>	400 mg/day. However, doses up to 12 mg/kg/day, not to exceed 800 mg/day have been recommended for severe infections.
flucytosine (Ancobon)	<p>Candidemia and disseminated (non-CNS) candidiasis 50 to 150 mg/kg/day in divided doses every 6 hours in combination with amphotericin B.</p> <p>Urinary tract infection (UTI), including symptomatic cystitis, caused by Candida 25 mg/kg/dose 4 times daily, with or without amphotericin B.</p>	150 mg/kg/day

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
flucytosine (Ancobon) - continued	<p>Pyelonephritis caused by Candida 5 mg/kg/dose 4 times daily for 2 weeks, with or without amphotericin B.</p> <p>Cryptococcosis 50 to 150 mg/kg/day in divided doses every 6 hours, or alternately, an initial dosage of 25 mg/kg/dose 4 times daily in combination with amphotericin B or fluconazole.</p>	150 mg/kg/day
ketoconazole (Nizoral)	<p>Chromomycosis 200 mg once daily. Serious infection may require 400 mg once daily.</p> <p>Coccidioidomycosis, histoplasmosis, and paracoccidioidomycosis 200 to 400 mg once daily. For coccidioidomycosis, 400 mg once daily is recommended.</p> <p>Blastomycosis 200 to 400 mg once daily.</p>	400 mg/day

Therapeutic alternatives are listed as Brand name[®] (generic) when the drug is available by brand name only and generic (Brand name[®]) when the drug is available by both brand and generic.

Appendix C: Contraindications/Boxed Warnings

- Contraindication(s):
 - Azole Antifungal Hypersensitivity
 - Hepatic Disease
 - Hepatitis
 - Milk Protein Hypersensitivity
 - Porphyria
 - Pregnancy
 - Short QT Syndrome
- Boxed warning(s):
 - Bone Marrow Suppression
 - Heart Failure
 - Hepatotoxicity
 - QT Prolongation
 - Renal Impairment
 - Ventricular Dysfunction

IV. Dosage and Administration

- Varies by drug product. See FDA approved dosing and administration AND Appendix B.

V. Product Availability

Drug Name	Availability
Cresemba	Capsules: 186 mg
Fluconazole	Oral suspension: 10 mg/mL, 40 mg/mL
Fluconazole	Tablets: 50 mg, 100 mg, 150 mg, 200 mg
Flucytosine	Capsules: 250 mg, 500 mg
Griseofulvin Microsize	Oral suspension: 125 mg/5 mL
Griseofulvin Microsize	Tablets: 500 mg
Gris-PEG	Tablets: 250 mg
Griseofulvin Ultramicrosize	Tablets: 125 mg, 250 mg
Itraconazole	Capsules: 100 mg
Itraconazole	Oral solution: 10 mg/mL
Ketoconazole	Tablets: 200 mg
Noxafil	Oral suspension: 200 mg/5 mL
Onmel	Tablets: 200 mg
Oravig	Buccal Tablets: 50 mg
Posaconazole	Tablets (Delayed-Release): 100 mg
Terbinafine	Tablets: 250 mg
Tolsura	Capsules: 65 mg
Voriconazole	Oral suspension: 40 mg/mL
Voriconazole	Tablets: 50 mg, 200 mg

VI. References

- Cresemba (isavuconazonium) [package insert]. Northbrook, IL; Astellas Pharma Inc.; Revised 04/2018.
- Fluconazole. Clinical Pharmacology. Elsevier. Tampa, FL. Available at <https://www.clinicalpharmacology-ip.com>. Accessed November 15, 2019.
- Itraconazole. Clinical Pharmacology. Elsevier. Tampa, FL. Available at <https://www.clinicalpharmacology-ip.com>. Accessed November 15, 2019.
- Posaconazole. Clinical Pharmacology. Elsevier. Tampa, FL. Available at <https://www.clinicalpharmacology-ip.com>. Accessed November 15, 2019.
- Voriconazole. Clinical Pharmacology. Elsevier. Tampa, FL. Available at <https://www.clinicalpharmacology-ip.com>. Accessed November 15, 2019.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
New policy created.	10.19	N/A

Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical

policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. “Health Plan” means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan’s affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

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Note:

For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.

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