

MEDICATION COVERAGE POLICY

PHARMACY AND THERAPEUTICS ADVISORY COMMITTEE



POLICY	Fungal Infections	P&T DATE	12/8/2020
THERAPEUTIC CLASS	Infectious Diseases	REVIEW HISTORY	12/19, 12/18, 12/16,
LOB AFFECTED	Medi-Cal	(MONTH/YEAR)	11/15, 5/15, 9/13, 6/08

This policy has been developed through review of medical literature, consideration of medical necessity, generally accepted medical practice standards, and approved by the HPSJ Pharmacy and Therapeutic Advisory Committee.

OVERVIEW

Prescription and OTC antifungal medications are used to treat a wide range of fungal infections in an outpatient setting. Generally, mild, localized infections may be treated with prescription or OTC topical antifungal products. Prescription oral and/or IV antifungal agents are required for more severe, disseminated infections. Relative to the growing public health concern of antibiotic-resistant bacterial infections, less is known about antifungal-resistant fungal infections. Nevertheless, the CDC recommends appropriate use of antifungal agents to reduce drug resistance.¹ The purpose of this Fungal Infections Coverage Policy is to review the coverage criteria of HPSJ's formulary antifungal agents (Table 1).

Table 1: Available Antifungal Medications (Current as of 9/2020)

Generic Name (Brand Name)	Available Strengths/ Dosage Forms	Form. Limits	Avg Cost Per 30 Days	Notes
AZOLES				
FLUCONAZOLE (DIFLUCAN)	50 mg tablet	-	\$21.55	
	100 mg tablet	-	\$5.66	
	200 mg tablet	-	\$34.02	
	150 mg tablet	-	\$2.21	
	40 mg/ml oral suspension	-	\$41.47	
	10 mg/ml oral suspension	-	\$21.55	
ISAVUCONAZONIUM SULFATE (CRESEMBA)	186 mg Capsule	NF	\$5,018.50	
	372 mg IV solution	NF	--	
ITRACONAZOLE (SPORANOX, ONMEL)	100 mg capsule	PA; PL; SP	\$132.26	Restricted to use by infectious disease or transplant specialists or failure of terbinafine for onychomycosis or fluconazole for oral candidiasis.
	10 mg/ml oral solution	NF	--	
	200 mg tablet	NF	--	
POSACONAZOLE (NOXAFIL)	200 mg/5 ml (40 mg/ml) oral suspension	PA; PL; SP	--	Restricted to use by infectious disease or transplant specialists.
	100 mg DR tablet	PA; PL; SP	\$4,262.52	
VORICONAZOLE (VFEND)	50 mg tablet	PA	\$292.20	Restricted to treatment failure of Fluconazole for Candidiasis
	200 mg tablet	PA	\$334.14	
IMIDAZOLE				
CLOTTRIMAZOLE	10 mg troche	--	\$48.75	
KETOCONAZOLE (NIZORAL)	200 mg tablet	PA	--	Reserved for treatment failure or intolerance to other systemic antifungal medications.

MICONAZOLE (ORAVIG)	50 mg Buccal tablets	NF	--	
ECHINOCANDIN				
ANIDULAFUNGIN (ERAXIS)	50 mg IV Solution	NF	--	
	100 mg IV Solution	NF	\$187.45	
CASPOFUNGIN (CANCIDAS)	50 mg IV Solution	SP,PA	\$893.00	Approval is determined by medical necessity criteria.
	70 mg IV Solution	SP,PA	--	
MICA FUNGIN (MYCAMINE)	50 mg IV Solution	NF	\$1,714.17	
	100 mg IV Solution	NF	\$935.00	
	MYCAMINE 50 mg IV Solution	NF	\$858.33	
MISCELLANEOUS				
AMPHOTERICIN B LIPOSOAML (AMBISOME)	50 mg IV Suspension	NF	--	
AMPHOTERICIN B CHOLESTERYL SULFATE COMPLEX (AMPHOTEC)	50 mg IV Suspension	NF	--	
	100 mg IV Suspension			
AMPHOTERICIN B (FUNGIZONE)	50 mg IV Solution	NF	--	
AMPHOTERICIN B LIPID COMPLEX (ABELCET)	5 mg IV Suspension	NF	--	
FLUCYTOSINE (ANCOBON)	250 mg capsule	SP,PA	--	Approval is determined by medical necessity criteria.
	500 mg capsule	SP,PA	--	
GRISEOFULVIN (GRIFULVIN V, GRIS-PEG)	125 mg/5 ml microsize oral suspension	--	\$88.67	
	500 mg microsize tablet	--	\$311.24	
	125 mg ultramicrosize tablet	--	\$164.55	
	250 mg ultramicrosize tablet	--	\$121.18	
NYSTATIN (MYCOSTATIN)	500,000 unit tablet	--	\$34.32	
	50 million unit oral powder	--	--	
	150 million unit oral powder	--	--	
	500 million unit oral powder	--	--	
	100,000 Unit/ml Oral Suspension	--	\$8.51	
TERBINAFINE HCL (LAMISIL, TERBINEX)	250 mg tablet	QL	\$4.40	Limit 1 tablet per day and 3 fills per year.
	125 mg granules packet	NF		

PA = Prior Authorization Required; QL = Quantity Limit; PL = Prescriber Limit; SP = Specialty Pharmacy; NF = Non-formulary

Generic Name (Brand Name)	Available Strengths/ Dosage Forms	Form. Limits	Avg Cost Per 30 Days	Notes
TOPICAL AGENTS				
CICLOPIROX (LOPROX, CICLODAN, PENLAC)	1% shampoo	--	\$46.02	For Onychomycosis: Must have completed oral Terbinafine treatment for 6 weeks for fingernail infection or 12 weeks for toenail infections. For other types of fungal infections: Must have tried and failed first line agents within the last 2 months.
	0.77% cream	--	\$13.49	
	0.77% gel	--	\$19.57	
	8% solution	--	\$13.41	
IMIDAZOLE				
BUTOCONAZOLE (GYNEZOL-1)	2% Vaginal cream	NF	--	
CLOTRIMAZOLE (GYNE-LOTTRIMIN, LOTTRIMIN AF, DESENEK)	1% vaginal cream (7-day)	--	\$4.49	
	2% vaginal cream (3-day)	--	\$7.71	
	1% topical cream	--	\$2.22	
	1% topical solution	--	\$25.54	
CLOTRIMAZOLE/ BETAMETHASONE (LOTRISONE)	1%-0.05% topical cream	QL	\$9.39	Restricted to 45g per 30 days
	Topical lotion	--	\$78.48	
ECONAZOLE NITRATE (ECOZA)	1% topical cream	--	\$15.86	
KETOCONAZOLE (NIZORAL A-D, KETODAN, EXTINA, XOLEGEL)	1% shampoo	--	\$12.75	
	2% shampoo	--	\$13.32	
	2% topical cream	--	\$28.37	
	KETODAN , EXTINA 2% FORAM	NF	--	
	XOLEGEL 2%	NF	--	
MICONAZOLE NITRATE (MONISTAT, MICATIN, FUNGOID TINCTURE)	2% topical ointment	--	\$4.79	
	2% topical spray	--	\$5.51	
	2% topical spray powder	--	\$5.49	
	2% topical cream	--	\$3.25	
	2% topical tincture	--	\$466.53	
	2% vaginal cream (7-day)	--	\$3.68	
	100 mg vaginal suppository	--	\$2.91	
	4% vaginal cream (200 mg/5 gram) (3-day)	--	\$9.17	
	2% vaginal kit (200 mg/9 gram suppository) (3-day)	--	--	
	2% vaginal kit (1,200 mg ovule) (1-day)	--	--	
OXICONAZOLE (OXISTAT)	1% topical cream	--	--	
	1% topical lotion	--	--	
SERTACONAZOLE (ERTACZO)	2% topical cream	NF	--	
SULCONAZOLE (EXELDERM)	1% topical cream	NF	--	
	1% topical solution			

TIOCONAZOLE (VAGISTAT-1)	6.5% vaginal ointment (1-day)	--	\$11.36	
MISCELLENEOUS				
EFINACONAZOLE (JUBLIA)	10% topical solution	NF	--	
NAFTIFINE (NAFTIN)	1% topical cream	NF	--	
	1% topical gel			
NYSTATIN (NYSTOP)	100,000 unit/gram topical cream	--	\$9.49	
	100,000 unit/gram topical ointment	--	\$15.38	
	100,000 unit/gram topical powder	--	\$64.78	
NYSTATIN/ TRIAMCINOLONE (MYCOLOG-II)	100,000 unit/gram-0.1% topical cream	--	\$14.72	
	100,000 unit/gram-0.1% topical ointment	--	\$16.16	
TAVABOROLE (KERYDIN)	5% topical solution	NF	--	
TERBINAFINE HCL (LAMISIL AT)	1% topical cream	--	\$13.03	
TERCONAZOLE (TERAZOL)	80 mg vaginal suppository (3-day)	--	\$81.75	
	0.8% vaginal cream (3-day)	--	\$26.59	
	0.4% vaginal cream (7-day)	--	\$28.93	
TOLNAFTATE	1% topical spray powder	-	\$6.99	
	1% topical cream	-	\$4.48	
	1% topical powder	-	\$5.28	
	1% topical solution	-	--	

PA = Prior Authorization Required; QL = Quantity Limit; PL = Prescriber Limit; SP = Specialty Pharmacy; NF = Non-formulary

⊕ EVALUATION CRITERIA FOR APPROVAL/EXCEPTION CONSIDERATION

Below are the coverage criteria and required information for each agent. These coverage criteria have been reviewed & approved by the HPSJ Pharmacy & Therapeutics (P&T) Advisory Committee. For conditions not covered under this Coverage Policy, HPSJ will make the determination based on Medical Necessity as described in HPSJ Medical Review Guidelines (UM06).

Oral Antifungals

Clotrimazole (Mycelex), Fluconazole (Diflucan), Flucytosine (Ancobon), Griseofulvin (Grifulvin V, Gris-Peg), Itraconazole (Sporanox), Ketoconazole (Nizoral), Nystatin, Posaconazole (Noxafil), Terbinafine HCl (Lamisil, Terbinex), Voriconazole (Vfend)

Flucytosine (Ancobon)

- Coverage Criteria:** *Approval is determined by medical necessity criteria.*
- Limits:** None
- Required Information for Approval:** Relevant clinical documentation
- Other Notes:** Medication is to be dispensed by HPSJ's designated specialty pharmacy.

Itraconazole (Sporanox)

- Coverage Criteria:** *Itraconazole is restricted to failure of terbinafine for onychomycosis or fluconazole for oral candidiasis.*
- Limits:** None

- Required Information for Approval:** For onychomycosis, clinic notes or prescription fill history indicating patient has tried terbinafine. For oral candidiasis, clinic notes or prescription fill history indicating patient has tried fluconazole.
- Other Notes:** Medication is to be dispensed by HPSJ's designated specialty pharmacy. Must be prescribed by infectious disease or transplant specialists.

Ketoconazole (Nizoral)

- Coverage Criteria:** *Ketoconazole is reserved for treatment failure or intolerance to other systemic antifungal medications.*
- Limits:** None
- Required Information for Approval:** Prescription fill history indicating patient has tried other antifungal medications or clinic notes documenting treatment failure or intolerance to other antifungal medication.
- Other Notes:** None

Posaconazole (Noxafil)

- Coverage Criteria:** *Posaconazole is restricted to use by infectious disease or transplant specialists.*
- Limits:** None
- Required Information for Approval:** N/A
- Other Notes:** Medication is to be dispensed by HPSJ's designated specialty pharmacy. Must be prescribed by infectious disease or transplant specialists.

Terbinafine (Lamisil, Terbinex)

- Coverage Criteria:** *None*
- Limits:** 1 tablet per day and 3 fills per year
- Required Information for Approval:** N/A
- Other Notes:** None

Voriconazole (Vfend)

- Coverage Criteria:** *Voriconazole is reserved for treatment of aspergillosis. For candidiasis, reserved for failure of fluconazole.*
- Limits:** None
- Required Information for Approval:** For aspergillosis, histopathologic or cytopathologic examinations showing fungal hyphae in tissue biopsy specimens. For candidiasis, prescription fill history indicating patient has tried fluconazole.
- Other Notes:** Medication is to be dispensed by HPSJ's designated specialty pharmacy. Must be prescribed by infectious disease or transplant specialists.

Clotrimazole (Mycelex), Fluconazole (Diflucan), Griseofulvin (Grifulvin V, Gris-Peg), Nystatin

- Coverage Criteria:** *None*
- Limits:** None
- Required Information for Approval:** N/A
- Other Notes:** None

Topical Antifungals

Ciclopirox, Clotrimazole, Clotrimazole/betamethasone, Econazole nitrate, Efinaconazole (Jublia), Ketoconazole (Nizoral A-D), Miconazole nitrate, Naftifine (Naftin), Nystatin (Nystop, Nyamyc), Nystatin/triamcinolone, Oxiconazole (Oxistat), Sertaconazole (Ertaczo), Terbinafine HCl, Terconazole, Tioconazole, Tolnaftate

Ciclopirox, Clotrimazole, Econazole nitrate, Ketoconazole, Miconazole nitrate, Nystatin, Nystatin/triamcinolone, Oxiconazole, Terbinafine HCl, Terconazole, Tioconazole, Tolnaftate

- Coverage Criteria:** *for Ciclopirox*
- Limits:** None
- Required Information for Approval:**
 - **For Onychomycosis:**
 - Must have completed oral Terbinafine treatment for 6 weeks for fingernail infection or 12 weeks for toenail infections.
 - **For other types of fungal infections:**
 - Must have tried and failed first line agents within the last 2 months.
- Other Notes:** None

- Non-Formulary:** Efinaconazole (Jublia), Naftifine (Naftin), Sertaconazole (Ertaczo)

Clotrimazole/betamethasone

- Coverage Criteria:** None
- Limits:** 45 g per 30 days
- Required Information for Approval:** N/A
- Other Notes:** None

CLINICAL JUSTIFICATION

HPSJ’s fungal infection management policy is based on recommendations by the *Infectious Diseases Society of America (IDSA)*, *British Association of Dermatologists (BAD)*, and *American Academy of Dermatology (AAD)*. In general, mild, localized infections may be treated with topical antifungal products. Oral and/or IV antifungal agents are required for more severe, disseminated infections. One exception to this trend is for the treatment of onychomycosis—for which topical agents can be used but are often ineffective due to their poor penetration of the entire nail unit. In contrast, oral agents such as terbinafine, penetrate the nail unit rapidly and sustain therapeutic concentrations, resulting in higher efficacy and shorter treatment duration. For this reason, oral terbinafine for 6 weeks (for fingernail infection) to 12 weeks (for toenail infection) is considered first-line treatment of onychomycosis.^{2,3,4} Therefore, HPSJ has maintained non-formulary status for topical agents used for onychomycosis. The quantity limit of oral terbinafine to 12-weeks supply per year is to encourage appropriate use of terbinafine.

REFERENCES

1. Fungal Diseases: Antifungal Resistance. Centers for Disease Control and Prevention Web Site. <http://www.cdc.gov/fungal/antifungal-resistance.html>. Updated October 23, 2014. Accessed November 7, 2015.
2. Del Rosso JQ. The Role of Topical Antifungal Therapy for Onychomycosis and the Emergence of Newer Agents. *J Clin Aesthet Dermatol.* 2014;7(7):10–18.
3. Elewski, BE. Onychomycosis: Pathogenesis, Diagnosis, and Management. *Clin Microbiol Rev.* 1998;11(3):415–429.
4. Fungal Diseases: Fungal Nail Infections. Centers for Disease Control and Prevention Web Site. <http://www.cdc.gov/fungal/nail-infections.html>. Updated September 30, 2014. Accessed November 7, 2015.
5. Pappas P., Kauffman C., Andes D., et al. Clinical Practice Guideline for the Management of Candidiasis: 2016 Update by the Infectious Diseases Society of America.
6. Christenson J., Peterson G., et al. Challenges and Opportunities in the Management of Onychomycosis. *Journal of Fungi*

REVIEW & EDIT HISTORY

Document Changes	Reference	Date	P&T Chairman
Creation of Policy	Antifungal review 6-08.docx	6/2008	Allen Shek, PharmD
Update to Policy	Oral Ketoconazole Safety Review 2013-09-17.docx	9/2013	Jonathan Szkotak, PharmD
Update to Policy	Antifungal Class Review 5-2015.docx	5/2015	Jonathan Szkotak, PharmD
Update to Policy	HPSJ Coverage Policy – Infectious disease – Fungal infections 2015-11.docx	11/2015	Johnathan Yeh, PharmD
Update to Policy	HPSJ Coverage Policy – Infectious disease – Fungal infections 2018-12.docx	12/2018	Matthew Garrett, PharmD
Update to Policy	HPSJ Coverage Policy – Infectious disease – Fungal infections 2019-12.docx	12/2019	Matthew Garrett, PharmD
Review of Policy	Fungal Infections	12/2020	Matthew Garrett, PharmD

Note: All changes are approved by the HPSJ P&T Committee before incorporation into the utilization policy