MEDICATION COVERAGE POLICY

PHARMACY AND THERAPEUTICS ADVISORY COMMITTEE

Health Plan of San Joaquin

POLICY	Fungal Infections	**P&T DATE**	12/14/2016
THERAPEUTIC CLASS	Infectious Diseases	**REVIEW HISTORY** (MONTH/YEAR)	5/15, 9/13, 6/08
LOB AFFECTED	Medi-Cal, SJHA		

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

Drug (Generic)	Strength & Dosage form	Drug (Brand)	Formulary Limits	Notes
ORAL AGENTS				
Clotrimazole	10 mg troche	Clotrimazole	-	
Fluconazole	50 mg tablet	Diflucan	-	
	100 mg tablet	Diflucan	-	
	200 mg tablet	Diflucan	-	
	150 mg tablet	Diflucan	-	
	40 mg/ml oral suspension	Diflucan	-	
	10 mg/ml oral suspension	Diflucan	-	
Flucytosine	250 mg capsule	Ancobon	PA	Approval is determined by medical necessity criteria.
	500 mg capsule	**Ancobon**	PA	
		Flucytosine	PA	
Griseofulvin	125 mg/5 ml microsize oral suspension	Grifulvin V	-	
	500 mg microsize tablet	Grifulvin V	-	
	125 mg ultramicrosize tablet	Gris-Peg	-	
	250 mg ultramicrosize tablet	Gris-Peg	-	
Itraconazole	100 mg capsule	Sporanox	PA; PL; SP	Restricted to use by infectious disease or transplant specialists or failure of terbinafine for onychomycosis or fluconazole for oral candidiasis.
Ketoconazole	200 mg tablet	Ketoconazole	PA	Reserved for treatment failure or intolerance to other systemic antifungal medications.
Nystatin	500,000 unit tablet	Mycostatin	-	
	50 million unit oral powder	Nystatin	-	
	150 million unit oral powder	Nystatin	-	
	500 million unit oral powder	Nystatin	-	
Posaconazole	200 mg/5 ml (40 mg/ml) oral suspension	**Noxafil**	PA; PL; SP	Restricted to use by infectious disease or transplant specialists.
	100 mg DR tablet	**Noxafil**	PA; PL; SP	
Terbinafine HCl	250 mg tablet	Lamisil, Terbinex	QL	Limit 1 tablet per day and 3 fills per year.
	125 mg granules packet	**Lamisil**	NF	
Voriconazole	50 mg tablet	Vfend	PA	Reserved for treatment of aspergillosis confirmed by biopsy of affected tissue. For candidiasis, reserved for failure of fluconazole.
	200 mg tablet	Vfend	PA	

***Bolded items** = Brand name drug cost/utilization*
PA = Prior Authorization Required; QL = Quantity Limit; PL = Prescriber Limit; SP = Specialty Pharmacy; NF = Non-formulary

Drug (Generic)	Strength & Dosage form	Drug (Brand)	Formulary Status	Notes
TOPICAL AGENTS				
Ciclopirox	0.77% gel	Loprox	NF	
	8% solution	Ciclodan, Penlac	NF	
Clotrimazole	1% vaginal cream (7-day)	Gyne-Lotrimin	-	
	2% vaginal cream (3-day)		-	
	1% topical cream	Lotrimin AF, Desenex	-	
	1% topical solution	Clotrimazole	-	
Clotrimazole/ betamethasone	1%-0.05% topical cream	Lotrisone	QL	Restricted to 45g per 30 days
Econazole nitrate	1% topical cream	Ecoza	-	
Efinaconazole	10% topical solution	**Jublia**	NF	
Ketoconazole	1% shampoo	**Nizoral A-D**	-	
	2% shampoo	Ketoconazole	-	
	2% topical cream	Ketoconazole	-	
Miconazole nitrate	2% topical ointment	**Aloe Vesta**	-	
		Critic-Aid Clear AF	-	
		DermaFungal	-	
	2% topical spray	Desenex Spray, Lotrimin AF	-	
	2% topical spray powder	Desenex Spray, Cruex, Lotrimin AF Powder	-	
	2% topical cream	Micatin, Inzo	-	
		Baza	-	
		Miconazole nitrate	-	
	2% topical tincture	**Fungoid Tincture**	-	
	2% vaginal cream (7-day)	**Monistat 7**	-	
		Miconazole nitrate	-	
	100 mg vaginal suppository	Miconazole nitrate	-	
	4% vaginal cream (200 mg/5 gram) (3-day)	Miconazole nitrate	-	
		Monistat 3	-	
	2% vaginal kit (200 mg/9 gram suppository) (3-day)	**Monistat 3 Combo Pack**	-	
		Miconazole 3 Combo Pack	-	
	2% vaginal kit (1,200 mg ovule) (1-day)	Monistat 1 Combo Pack	-	
Naftifine	2% topical cream	**Naftin**	NF	
Nystatin	100,000 unit/gram topical cream	Nystatin	-	
	100,000 unit/gram topical ointment	Nystatin	-	
	100,000 unit/gram topical powder	Nystatin	-	
		Nystop	-	
		Nyamyc	-	
Nystatin/ Triamcinolone	100,000 unit/gram-0.1% topical cream	Mycolog-II	-	
	100,000 unit/gram-0.1% topical ointment	Mycolog-II	-	
Oxiconazole	1% topical cream	**Oxistat**	NF	
Sertaconazole	2% topical cream	**Ertaczo**	NF	
Terbinafine HCl	1% topical cream	Lamisil AT	-	
Terconazole	80 mg vaginal suppository (3-day)	Terazol 3, Zazole	-	
	0.8% vaginal cream (3-day)		-	
	0.4% vaginal cream (7-day)	Terazole 7, Zazole	-	
Tioconazole	6.5% vaginal ointment (1-day)	Vagistat-1	-	
Tolnaftate	1% topical spray powder	Jock Itch Spray, Lamisil AF Defense, Tinactin	-	
	1% topical cream	Fungi-Guard, Medi-First Anti-Fungal, Tinactin	-	
	1% topical powder	Lamisil AF Defense, Anti-Fungal, Tinactin, Podactin	-	
		Anti-Fungal	-	
	1% topical solution	Tinaspore	-	

***Bolded items =** Brand name drug cost/utilization*
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 HSPJ 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:** None

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

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

- **Coverage Criteria:** ***None***
- **Limits:** None
- **Required Information for Approval:** N/A
- **Other Notes:** None
- **Non-Formulary:** Ciclopirox, Efinaconazole (Jublia), Naftifine (Naftin), Oxiconazole (Oxistat), 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.

NEWLY APPROVED MEDICATIONS NOT ON FORMULARY

None since last review

GUIDELINE & LITERATURE REVIEW

No updates since last review

CRITERIA REVIEW FOR UNNECESSARY BARRIERS

Current requirements are appropriate based on existing evidence

RECOMMENDATIONS

Review on an annual cycle

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.

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	Johanthan Yeh, PharmD

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