



SmartPA Criteria Proposal

Drug/Drug Class:	Systemic Antifungals Clinical Edit
First Implementation Date:	2003
Proposed Date:	March 17, 2022
Prepared for:	MO HealthNet
Prepared by:	MO HealthNet/Conduent
Criteria Status:	<input type="checkbox"/> Existing Criteria <input checked="" type="checkbox"/> Revision of Existing Criteria <input type="checkbox"/> New Criteria

Executive Summary

Purpose: Ensure appropriate utilization and control of systemic antifungal therapies

Why Issue Selected: Systemic antifungals include amphotericin B, various azole derivatives, echinocandins, and flucytosine. The azoles that are available for systemic use can be classified into two groups: the triazoles (fluconazole, itraconazole, voriconazole, posaconazole, and isavuconazole) and the imidazoles (ketoconazole). Azole antifungals inhibit the synthesis of ergosterol, an important component of the fungal cell membrane, to treat chronic mycoses; lowered ergosterol levels result in the breakdown of the fungal membrane. The first azole, ketoconazole, has been supplanted by more effective, less toxic triazoles which are now often recommended as first-line drugs for many invasive fungal infections. These drugs have markedly changed the approach to antifungal therapy.

Brexafemme® (ibrexafungerp) was FDA approved in June 2021 for the treatment of adult and post-menarchal pediatric females with vulvovaginal candidiasis (VVC). It represents the first approved drug in a novel antifungal class, the triterpenoids, in more than 20 years and is also the first treatment for VVC that is both oral and non-azole. Brexafemme is also being assessed currently in clinical studies for the prevention of recurrent VVC, the treatment of fungal disease that has been intolerant or refractory to Standard of Care antifungal treatment, and the treatment of *Candida auris* infection, an organism that is often multi-drug resistant, associated with high mortality, and classified by the Centers for Disease Control and Prevention (CDC) as an Urgent Threat to public health.

Due to the high cost and specific approved indications, MO HealthNet will impose clinical criteria to ensure appropriate utilization of systemic antifungal therapies.

Program-Specific Information:

Date Range FFS 1-1-2021 to 12-31-2021			
Drug	Claims	Spend	Avg Spend per Claim
BREXAFEMME 150 MG TABLET	1	\$487.68	\$487.68
CRESEMBA 186 MG CAPSULE	23	\$112,454.69	\$4,889.33
CRESEMBA 372 MG VIAL	0	-	-
NOXAFIL 40 MG/ML SUSPENSION	19	\$96,021.08	\$5,053.74
NOXAFIL DR 100 MG TABLET	155	\$383,408.66	\$2,473.60
NOXAFIL 300 MG/16.7 ML VIAL	0	-	-
TOLSURA 65 MG CAPSULE	8	\$37,910.98	\$4,738.87

SmartPA Clinical Proposal Form

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VFEND 40 MG/ML SUSPENSION	25	\$24,249.69	\$969.98
VFEND 50 MG TABLET	18	\$8,498.75	\$472.15
VFEND 200 MG TABLET	117	\$20,960.82	\$179.15
VFEND IV 200 MG VIAL	3	\$30.81	\$10.27

Type of Criteria: Increased risk of ADE Preferred Drug List
 Appropriate Indications Clinical Edit

Data Sources: Only Administrative Databases Databases + Prescriber-Supplied

Setting & Population

- Drug class for review: Systemic Antifungals
- Age range: All appropriate MO HealthNet participants

Approval Criteria

- Documentation of a severely suppressed immune system **OR**
- Approval based on Clinical Consultant Review **OR**
- For Tolsura (itraconazole):
 - Documented trial of generic itraconazole in the past 90 days **AND**
 - Documented diagnosis of aspergillosis, blastomycosis, or histoplasmosis
- For Noxafil (posaconazole):
 - Documented diagnosis of aspergillosis **OR**
 - Documented diagnosis of appropriate specified candidiasis **AND** documented trial of generic itraconazole or fluconazole in the past 90 days
- For Cresemba (isavuconazonium sulfate): Documented diagnosis of aspergillosis or mucormycosis
- For Vfend (voriconazole):
 - Documented diagnosis of aspergillosis, opportunistic mycoses, or mycosis NOS **OR**
 - Documented diagnosis of appropriate specified candidiasis **AND** documented trial of itraconazole or fluconazole in the past 90 days
- **For Brexafemme (ibrexafungerp):**
 - **Participant is aged 12 years or older AND**
 - **Participant is not currently pregnant AND**
 - **Documented diagnosis of acute VVC AND**
 - **Documented therapeutic trial of oral fluconazole and at least 1 topical vaginal antifungal therapy for the current episode of VVC (defined as in the past 30 days) AND**
 - **Quantity limit of 4 tablets per claim and 8 tablets per year**

Denial Criteria

- Therapy will be denied if all approval criteria are not met

Required Documentation

Laboratory Results: Progress Notes:
 MedWatch Form: Other:

Disposition of Edit

Denial: Exception code "0682" (Clinical Edit)
Rule type: CE

Default Approval Period

90 Days

References

- TOLSURA® (itraconazole capsules) [package insert]. Greenville, NC: Mayne Pharma Inc.; June 2020.
- NOXAFIL® (posaconazole) [package insert]. Whitehouse Station, NJ: Merck & Co., Inc.; January 2022.
- CRESEMBA® (isavuconazonium sulfate) [package insert]. Northbrook, IL: Astellas Pharma Inc.; December 2021.
- VFEND® (voriconazole) [package insert]. New York, NY: Pfizer, Inc; October 2021.
- BREXAFEMME (ibrexafungerp tablets) [package insert]. Jersey City, NJ: Scynexis, Inc.; June 2021.
- Sanjay G. Revankar. Antifungal Drugs. Merck Manual. [Antifungal Drugs - Infectious Diseases - Merck Manuals Professional Edition](#). Updated April 2021. Accessed February 2, 2022.
- Holtry, B. Antifungal Agents. [Antifungal Agents - Anti-Infective Therapy - AntiinfectiveMeds.com](#). Updated December 1, 2020. Accessed February 2, 2022.
- Clinical Pharmacology. Azole Antifungals (systemic). Accessed February 2, 2022.
- IPD Analytics. New Drug Review: Brexafemme (ibrexafungerp tablets). June 2021.
- IPD Analytics. Infectious Disease: Antifungals. Accessed February 2, 2022.
- 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, Clinical Infectious Diseases, Volume 62, Issue 4, 15 February 2016, Pages e1–e50, <https://doi.org/10.1093/cid/civ933>
- Centers for Disease Control and Prevention. 2015 Sexually Transmitted Diseases Treatment Guidelines: Vulvovaginal Candidiasis. [Vulvovaginal Candidiasis - 2015 STD Treatment Guidelines \(cdc.gov\)](#). Accessed June 11, 2021.