**Executive Summary**

**Purpose:** Ensure appropriate utilization and control of systemic antifungal therapies

**Why Issue Selected:** Systemic antifungals include amphotericin B, variousazole 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:**

<table>
<thead>
<tr>
<th>Drug</th>
<th>Date Range FFS 1-1-2021 to 12-31-2021</th>
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<tbody>
<tr>
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<tr>
<td>BREXAFEMME 150 MG TABLET</td>
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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 Tolssura (itraconazole):
  o Documented trial of generic itraconazole in the past 90 days AND
  o Documented diagnosis of aspergillosis, blastomycosis, or histoplasmosis
- For Noxafil (posaconazole):
  o Documented diagnosis of aspergillosis OR
  o 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):
  o Documented diagnosis of aspergillosis, opportunistic mycoses, or mycosis NOS OR
  o Documented diagnosis of appropriate specified candidiasis AND documented trial of itraconazole or fluconazole in the past 90 days
- For Brexafemme (ibrexafungerp):
  o Participant is aged 12 years or older AND
  o Participant is not currently pregnant AND
  o Documented diagnosis of acute VVC AND
  o 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
  o 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: X

Disposition of Edit

SmartPA Clinical Proposal Form
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Denial: Exception code “0682” (Clinical Edit)
Rule type: CE

**Default Approval Period**

90 Days

**References**