ibrexafungerp (Brexafemme®)

EOCCO POLICY

Policy Type:PA/SP Pharmacy Coverage Policy: EOCCO269

Description

ibrexafungerp (Brexafemme) is an orally administered triterpenoid antifungal.

Length of Authorization

- Initial:
  - i. Acute vulvovaginal candidiasis (VVC): one month
  - ii. Recurrent vulvovaginal candidiasis (RVVC): 6 months
- Renewal: Cannot be renewed

Quantity Limits

Product Name	Indication	Dosage Form	Quantity Limit
ibrexafungerp (Brexafemme)	Treatment of vulvovaginal candidiasis (VVC)	150mg tablet	4 tablets/1 day
	Reduction in the incidence of recurrent vulvovaginal candidiasis (RVVC)		

Initial Evaluation

I. **Ibrexafungerp (Brexafemme)** may be considered medically necessary when the following criteria are met:
   A. Member is 12 years of age or older; **AND**
   B. Member has experienced menarche; **AND**
   C. A diagnosis of one of the following:
      1. **Acute vulvovaginal candidiasis (VVC)**; **AND**
         i. Treatment with fluconazole 150mg (Diflucan) has been ineffective, contraindicated, or not tolerated; **OR**
      2. Recurrent vulvovaginal candidiasis (RVVC); AND
         i. Member has a history of three or more acute vulvovaginal candidiasis (VVC) episodes within the last 12 months; **AND**
         ii. Member is currently experiencing signs and symptoms consistent with an acute episode of VVC (e.g., vulvovaginal pain, pruritis or irritation, abnormal vaginal discharge, etc.); **AND**
         iii. Diagnosis of acute VVC has been confirmed by positive KOH or culture; **AND**
         iv. Member has been treated with weekly oral fluconazole for a period of 6 months; **OR**

a. Treatment with fluconazole is not tolerated or contraindicated; **OR**
b. Antifungal susceptibility testing has been conducted and confirms fluconazole resistance; **OR**
c. Member has experienced a recurrence during or following maintenance therapy with fluconazole

II. Ibrexafungerp (Brexafemme) is considered investigational when used for all other conditions, including but not limited to:
   A. Allergic bronchopulmonary aspergillosis
   B. Blastomycosis
   C. Coccidioidomycosis
   D. Histoplasmosis
   E. Invasive candidiasis
   F. Invasive and/or chronic pulmonary aspergillosis
   G. Mucocutaneous candidiasis

Renewal Evaluation

I. Please see initial evaluation

Supporting Evidence

I. Ibrexafungerp (Brexafemme) was initially approved by the FDA in 2021 for the treatment of acute vulvovaginal candidiasis (VVC) in adult and post-menarche pediatric females. In 2022, the FDA granted approval for a second indication, reduction in the incidence of recurrent vulvovaginal candidiasis (RVVC).

II. **Acute Vulvovaginal Candidiasis**
   - In the setting of acute VVC, ibrexafungerp (Brexafemme) was studied in two identically designed randomized, double-blind, placebo-controlled, Phase 3 trials in 558 total post-menarche females aged 12 years and older (VANISH-303 and VANISH-306). The primary efficacy outcome was clinical cure (defined as complete resolution of signs and symptoms) at day 10 test-of-cure (TOC) visit. The key secondary outcomes included mycological eradication (negative culture for growth of yeast [candida species]) at TOC and clinical cure at follow-up visit (day 25). Ibrexafungerp (Brexafemme) was statistically significant compared to placebo for all primary and key secondary endpoints in both the VANISH-303 and VANISH-306 trials.

- Ibrexafungerp (Brexafemme) was also studied against fluconazole in a Phase 2b, multicenter, randomized, double-blind, double-dummy, active-controlled, dose-finding study (DOVE) in 186 patients with moderate-to-severe acute VVC. The primary endpoint was percentage of patients with clinical cure at the TOC (day 10), which was 53% for ibrexafungerp (Brexafemem) and 58% for fluconazole. This study was not statistically powered; thus, the clinical significance of these results cannot be determined.

III. **Recurrent Vulvovaginal Candidiasis**

- In the setting of RVVC, ibrexafungerp (Brexafemme) was studied in one randomized, double-blind, placebo-controlled trial (CANDLE) of 260 post-menarche females aged 12 years and older who had a diagnosis of RVVC, defined as at least three prior episodes of acute VVC in the past 12 months. The trial consisted of an acute phase and a maintenance phase. All patients received fluconazole 150mg on days 1, 4, and 7 during the acute phase to treat their current infection. Patients who responded to fluconazole therapy with significant resolution of their vulvovaginal signs and symptoms, defined as total composite score of ≤ 2 on the VSS Scale) then entered the maintenance phase. Patients in the maintenance phase were randomized to receive ibrexafungerp (Brexafemme) or placebo once monthly for 6 months.
- The primary endpoint was percentage of patients with clinical success (defined as no mycologically proven, presumed, or suspected recurrence of VVC) up to the test-of-cure (TOC) visit at week 24 post-dose. The secondary endpoint was percentage of patients with no mycologically proven recurrence (defined as an episode of VVC with total composite VSS Score of ≥3 and a culture positive for Candida spp. That required antifungal treatment), also at TOC (24 weeks). For the primary endpoint, 65.4% of patients in the ibrexafungerp (Brexafemme) group met the primary endpoint compared to 53.1% of patients in the placebo group (p=0.02); this was sustained over the three-month follow-up period (p=0.034). For the secondary endpoint, 70.8% of patients in the ibrexafungerp (Brexafemme) group met the secondary endpoint compared to 58.5% of patients in the placebo group (p=0.019), which was also sustained over the follow-up period (p=0.029).

IV. Patients enrolled in the trial were aged 12 years and older who had already experienced menarche (i.e., first menstrual cycle). The safety and/or efficacy of ibrexafungerp (Brexafemme) in pediatric patients who are either under the age of 12 years or have not experienced menarche has not been evaluated.

V. The safety profile for ibrexafungerp (Brexafemme) was consistent between the acute VVC and RVVC trials. The most commonly reported side effects include diarrhea (~15%), nausea (~11%), abdominal pain (~11%), headache (~17%), and dizziness (~2%). Although ibrexafungerp (Brexafemme) carries a contraindication for use during pregnancy due to risk of embryo-fetal toxicity, women of childbearing age were included in the clinical trial and were advised to not

become pregnant during the trial duration. FDA label recommends verifying pregnancy status prior to initiating therapy with ibrexafungerp (Brexafemme), and prior to each dose when using for RVVC.

VI. Clinical guidelines, including those published by the Centers for Disease Control and Prevention (CDC) and Infectious Disease Society of America (IDSA), indicate that diagnosis of VVC can typically be made via the presentation of infection signs/symptoms: pruritis, irritation, vaginal soreness, external dysuria, and dyspareunia accompanied by signs of vulvar edema, erythema, excoriation, fissures and white, thick, curd-like vaginal discharge. For complicated VVC and RVVC, diagnosis should be confirmed with a wet-mount preparation with use of saline and 10% potassium hydroxide (KOH). If KOH is negative, a culture for *Candida* should be obtained.

VII. For the treatment of acute VVC, IDSA and CDC guidelines carry a strong recommendation for topical (intravaginal) antifungals or oral fluconazole 150mg for acute, uncomplicated VVC. The same medications can be used for complicated and/or recurrent VVC, but at extended treatment durations of 10 – 14 days. Topical antifungals, such as miconazole and clotrimazole, are available in multiple over the counter (OTC) formulations, while oral fluconazole remains prescription only.

VIII. RVVC is usually defined as having at least three episodes of acute VVC within one year and are typically caused by azole-susceptible *C. albicans*. Clinical guidelines recommend beginning treatment with induction therapy with a 10-to-14-day course of a topical azole or oral fluconazole, followed by maintenance therapy with fluconazole 150mg once weekly for six months. If oral fluconazole is not feasible, topical clotrimazole (200mg cream twice weekly or 500mg vaginal suppository once weekly) or other intermittent oral or topical antifungal treatment is recommended. After cessation of maintenance therapy, IDSA approximates a 40-50% recurrence rate. Ibrexafungerp (Brexafemme) may be considered medically necessary if oral fluconazole has been not tolerated, is contraindicated, fluconazole resistance is confirmed, or if members experience recurrence of acute VVC symptoms anytime during or after maintenance therapy with fluconazole.

IX. According to results of the CANDLE trial, nearly 70% of participants who completed the maintenance regimen with ibrexafungerp (Brexafemme) did not experience a recurrent episode for up to 36 weeks (approximately nine months). However, rates of recurrence beyond nine months or safety and efficacy of retreatment with ibrexafungerp (Brexafemme) has not been established. Due to lack of adequate safety and efficacy data to establish an appropriate timeline for retreatment, renewal requests will be evaluated against initial policy criteria.

Investigational or Not Medically Necessary Uses

I. Ibrexafungerp (Brexafemme) has not been FDA-approved, or sufficiently studied for safety and efficacy for the conditions or settings listed below:

A. Allergic bronchopulmonary aspergillosis
B. Blastomycosis
C. Coccidioidomycosis
D. Histoplasmosis
E. Invasive candidiasis
F. Invasive and/or chronic pulmonary aspergillosis
G. Mucocutaneous candidiasis

References

1. Centers for Disease Control and Prevention (CDC). 2015 Sexually Transmitted Diseases Treatment Guideline: Vulvovaginal candidiasis. Accessed July 19, 2021.
2. Pappas PG, et al. Clinical Practice Guideline for the Management of Candidiasis: 2016 Update by the Infectious Diseases Society of America. Clinical Infectious Diseases. 2016;62(4):e1-50.
3. Azie N, et al. Efficacy and Safety of oral ibrexafungerp (SCY-078) vs. Placebo in Subjects with Acute Vulvovaginal Candidiasis (VANISH 303). Scynexis, Inc. 2020. [presented at ACOG Annual Clinical and Scientific Meeting, May 2021].
4. Sobel R, et al. Efficacy and Safety of oral ibrexafungerp (SCY-078) vs. Placebo in Subjects with Acute Vulvovaginal Candidiasis (VANISH 306). Scynexis, Inc. 2020. [presented at ACOG Annual Clinical and Scientific Meeting, May 2021].
5. New Drug Review: ibrexafungerp (Brexafemme). IPD Analytics. June 2021.
6. Cadet R, et al. A Phase 2b, dose-finding study evaluating oral ibrexafungerp vs fluconazole in vulvovaginal candidiasis (DOVE). Obstet Gynecol. 2019;133 (suppl):113S–114S.
7. Centers for Disease Control and Prevention (CDC). 2015 Sexually Transmitted Diseases Treatment Guideline: Vulvovaginal candidiasis. Accessed July 19, 2021.
8. Pappas PG, et al. Clinical Practice Guideline for the Management of Candidiasis: 2016 Update by the Infectious Diseases Society of America. Clinical Infectious Diseases. 2016;62(4):e1-50.
9. Brexafemme [Prescribing Information]. Scynexis, Inc.: Jersey City, NJ. November 2022.
10. Scynexis, Inc. Ibrexafungerp: a novel oral triterpenoid antifungal for the treatment of patients with vulvovaginal candidiasis (VVC). AMCP Dossier. June 30, 2021.

Related Policies

Policies listed below may be related to the current policy. Related policies are identified based on similar indications, similar mechanisms of action, and/or if a drug in this policy is also referenced in the related policy.

Policy Name	Disease state
oteseconazole (Vivjoa™)	Recurrent vulvovaginal candidiasis (RVVC)

Policy Implementation/Update:

Action and Summary of Changes	Date
Policy created	03/2023