Brexafemme® (ibrexafungerp)

Policy # 00766
Original Effective Date: 12/13/2021
Current Effective Date: 03/10/2025

Applies to all products administered or underwritten by Blue Cross and Blue Shield of Louisiana and its subsidiary, HMO Louisiana, Inc.(collectively referred to as the "Company"), unless otherwise provided in the applicable contract. Medical technology is constantly evolving, and we reserve the right to review and update Medical Policy periodically.

When Services May Be Eligible for Coverage

Coverage for eligible medical treatments or procedures, drugs, devices or biological products may be provided only if:

- *Benefits are available in the member's contract/certificate, and*
- *Medical necessity criteria and guidelines are met.*

Vulvovaginal Candidiasis

Based on review of available data, the Company may consider Brexafemme®‡ (ibrexafungerp) for the treatment of vulvovaginal candidiasis to be **eligible for coverage**** when the patient selection criteria are met.

Patient Selection Criteria

Coverage eligibility for Brexafemme (ibrexafungerp) will be considered when the following criteria are met:

- Patient has a diagnosis of vulvovaginal candidiasis; AND
- Patient is a post-menarchal pediatric female OR an adult female; AND
- Patient is NOT pregnant; AND
- Patient has tried and failed (e.g., intolerance or inadequate response) generical oral fluconazole for the current infection unless there is clinical evidence or patient history that suggests the use of the generic oral fluconazole will be ineffective or cause an adverse reaction to the patient; AND
  *(Note: This specific patient selection criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met)*
- Patient has tried and failed a topical antifungal preparation (either prescription or over the counter) for the current infection unless there is clinical evidence or patient history that suggests the use of these products will be ineffective or cause an adverse reaction to the patient. Examples include clotrimazole, miconazole, terconazole, tioconazole, butoconazole (Gynazole-1®)‡.
  *(Note: This specific patient selection criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met)*

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Recurrent Vulvovaginal Candidiasis

Based on review of available data, the Company may consider Brexafemme (ibrexafungerp) to reduce in the incidence of recurrent vulvovaginal candidiasis to be **eligible for coverage**** when the patient selection criteria are met.

Patient Selection Criteria

Coverage eligibility for Brexafemme (ibrexafungerp) will be considered when the following criteria are met:

- Patient has a diagnosis of recurrent vulvovaginal candidiasis (RVVC); AND
- Patient has a documented history of greater than or equal to 3 episodes of vulvovaginal candidiasis in a 12-month period; AND
- Patient is a post-menarchal pediatric female OR an adult female; AND
- Patient is NOT pregnant; AND
- Patient has received an initial short course of oral therapy with generic fluconazole (100 mg, 150 mg, or 200 mg) dosed every third day for three doses to attempt mycologic remission unless there is clinical evidence or patient history that suggests the use of generic oral fluconazole will be ineffective or cause an adverse reaction to the patient; AND
  *(Note: This specific patient selection criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met)*
- Patient has tried and failed (e.g., intolerance or inadequate response) a maintenance antifungal regimen of generic oral fluconazole (100 mg, 150 mg, or 200 mg) once weekly for at least 6 months of therapy unless there is clinical evidence or patient history that suggests the use of generic oral fluconazole will be ineffective or cause an adverse reaction to the patient.
  *(Note: This specific patient selection criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met)*

When Services Are Considered Not Medically Necessary

Based on review of available data, the Company considers the use of Brexafemme (ibrexafungerp) when the patient has not tried and failed the pre-requisite medications listed in the patient selection criteria for the current vulvovaginal candidiasis infection to be **not medically necessary.****

Based on review of available data, the Company considers the use of Brexafemme (ibrexafungerp) when the patient has not received a short course of oral therapy with generic fluconazole to attempt mycologic remission of recurrent vulvovaginal candidiasis infection to be **not medically necessary.****

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Based on review of available data, the Company considers the use of Brexafemme (ibrexafungerp) when the patient has not tried and failed a maintenance antifungal regimen of generic oral fluconazole for at least 6 months to be **not medically necessary.****

When Services Are Considered Investigational

Coverage is not available for investigational medical treatments or procedures, drugs, devices or biological products.

Based on review of available data, the Company considers use of Brexafemme (ibrexafungerp) when the patient selection criteria are not met (with the exception of those denoted as **not medically necessary****) to be **investigational.***

Background/Overview

Brexafemme is a triterpenoid antifungal indicated for the treatment of adult and post-menarchal pediatric females with vulvovaginal candidiasis (VVC). It is also indicated to reduce the incidence of recurrent vulvovaginal candidiasis infections (RVVC). Brexafemme is contraindicated in pregnancy. The recommended dose is 300 mg twice a day for one day for VVC and the same dose every month for a duration of 6 months for RVVC. Brexafemme is available in 150 mg tablets. VVC is one of the most common causes of vaginal itching and discharge. VVC can be further classified into complicated and uncomplicated cases. Uncomplicated cases are typically caused by *C. albicans* and are most commonly sporadic or infrequent with mild to moderate symptoms. Complicated cases typically have severe symptoms, occur frequently, and are not usually caused by *C. albicans*. RVVC is categorized as a complicated case of VVC infection. Options for therapy for uncomplicated VVC include oral fluconazole as well as topical products available via prescription [butoconazole (Gynazole-1), terconazole] or over the counter (clotrimazole, miconazole, tioconazole). Oral fluconazole and the intravaginal antifungals appear to be equally effective in the treatment of VVC. The recommended treatment for RVVC consists of an induction regimen using the previously mentioned agents and a maintenance treatment regimen with oral fluconazole for a duration of 6 months. Brexafemme was not studied head to head with any of these products, so there can be no claims of superiority made. Brexafemme, similarly to fluconazole, cannot be used in pregnancy. Existing treatment options offer an equally efficacious and economically advantageous option for therapy as compared to Brexafemme.

FDA or Other Governmental Regulatory Approval

U.S. Food and Drug Administration (FDA)

Brexafemme is a triterpenoid antifungal indicated for the treatment of adult and post-menarchal pediatric females with vulvovaginal candidiasis (VVC). In November of 2022, Brexafemme received an additional indication to reduce the incidence of recurrent vulvovaginal candidiasis infection (RVVC).

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Rationale/Source

This medical policy was developed through consideration of peer-reviewed medical literature generally recognized by the relevant medical community, U.S. Food and Drug Administration approval status, nationally accepted standards of medical practice and accepted standards of medical practice in this community, technology evaluation centers, reference to federal regulations, other plan medical policies, and accredited national guidelines.

Vulvovaginal Candidiasis

Two randomized placebo-controlled clinical trials (Trial 1and Trial 2) with a similar design were conducted to evaluate the safety and efficacy of a single day of Brexafemme 600 mg (two 150 mg tablets per dose, administered 12 hours apart) for the treatment of vulvovaginal candidiasis (VVC). Non-pregnant post-menarchal females with a diagnosis of VVC were eligible. A diagnosis of VVC was defined as (a) minimum composite vulvovaginal signs and symptoms (VSS) score of ≥4 with at least two signs or symptoms having a score of 2 (moderate) or greater; (b) positive microscopic examination with 10% KOH (potassium hydroxide) in a vaginal sample revealing yeast forms (hyphae/pseudohyphae) or budding yeasts, and (c) normal vaginal pH (≤4.5). The total composite VSS score was based on the vulvovaginal signs (erythema, edema, excoriation) and vulvovaginal symptoms (itching, burning, or irritation) where each was scored as 0= absent, 1= mild, 2= moderate, or 3= severe. Study visits included the test of cure (TOC, Day 8 to 14) visit and a follow-up (Day 21 to 29) visit. The modified intent to treat (MITT) population included randomized subjects with a baseline culture positive for *Candida* species who took at least 1 dose of study medication. Trial 1 was conducted in the United States. The MITT population consisted of 190 patients treated with Brexafemme and 100 patients treated with placebo. The median VSS score at baseline was 9 (range 4-18). The majority (92%) of the subjects were culture-positive with *C. albicans*. Trial 2 was conducted in the United States (39%) and Bulgaria (61%). The MITT population consisted of 189 patients treated with Brexafemme and 89 patients treated with placebo. The median VSS score at baseline was 10 (range 4-18). The majority (89%) of the subjects were culture-positive with *C. albicans*.

Efficacy was assessed by clinical outcome at the TOC visit. A complete clinical response was defined as the complete resolution of signs and symptoms (VSS score of 0). Additional endpoints included a negative culture for *Candida* spp. at the TOC visit, and clinical outcome at the follow-up visit. Statistically significantly greater percentages of patients experienced a complete clinical response at TOC (Trial 1: 50% vs. 28%, p=0.001; Trial 2: 63.5% vs. 44.9%, p=0.009), negative culture at TOC (Trial 1: 49.5% vs. 19%, p<0.001; Trial 2: 58.7% vs. 29.2%, p<0.001), and complete clinical response at follow-up (Trial 1: 59.5% vs. 44.0%, p=0.007; Trial 2: 72.5% vs. 49.4%, p=0.006) with treatment with Brexafemme compared to placebo.

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Recurrent Vulvovaginal Candidiasis

A randomized placebo-controlled clinical trial (Trial 3) was conducted to evaluate the safety and efficacy of Brexafemme 300 mg (two 150 mg tablets) administered approximately 12 hours apart (e.g., in the morning and in the evening) for one day, for a total daily dosage of 600 mg (four 150 mg tablets) administered once monthly for six months. Trial 3 was conducted in the United States (33%), Bulgaria (28%), Poland (12%), and Russia (28%). Non-pregnant post-menarchal females presenting with a symptomatic VVC episode and a history of recurrent VVC (at least 3 episodes of VVC in the previous 12 months) were eligible. The symptomatic episode at screening was treated with 3 doses of fluconazole 150 mg 3 days apart. To be randomized, patients had to have a culture confirmed VVC episode at screening and had to achieve significant resolution of their vulvovaginal signs and symptoms (defined as a total composite score ≤ 2 on the VSS Scale) after fluconazole treatment. Patients were randomized at a 1:1 ratio to receive double-blind Brexafemme or placebo administered as a single-day treatment repeated every 4 weeks for a total of 6 single-day treatments. Study visits included the test of cure (TOC) at week 24 (4 weeks after the last dose) and a follow-up visit at week 36. The intent to treat (ITT) population was all randomized patients, which consisted of 130 patients treated with Brexafemme and 130 patients treated with placebo.

Efficacy was assessed as the percentage of patients with clinical success, defined as subjects with No Culture Proven, Presumed or Suspected Recurrence of VVC requiring antifungal therapy up to TOC at week 24. Clinical success was also assessed at the week 36 follow-up visit.

Statistically significantly greater percentages of patients experienced clinical success at TOC compared to placebo. The clinical success rate at TOC was lower for patients in the United States when compared to patients outside the United States (ex-US) for both Brexafemme and placebo groups. In both regions, the Brexafemme group had a higher clinical success rate compared to placebo (US: 33% vs 23% and ex-US: 81% vs 68% in Brexafemme vs placebo arms, respectively) and the difference between the treatment groups was consistent [US:10.1% (-9.0, 29.1) and ex-US: 12.9% (0.04, 25.7)]. Clinical success at week 36 was also greater for Brexafemme compared to placebo.

The purpose of this policy is to ensure that Brexafemme is used per its FDA approved indication as well as to ensure that the most efficacious and economically advantageous products are used prior to Brexafemme.

References

1. Brexafemme [package insert]. Scynexis, Inc. Jersey City, New Jersey. Updated November 2022.
2. Brexafemme Drug Evaluation. Updated June 2021.
3. Candida vulvovaginitis: Treatment. UpToDate. Accessed October 2021.

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11/04/2021	Medical Policy Committee review
11/10/2021	Medical Policy Implementation Committee approval. New policy.
11/03/2022	Medical Policy Committee review
11/09/2022	Medical Policy Implementation Committee approval. No change to coverage
02/02/2023	Medical Policy Committee review
02/08/2023	Medical Policy Implementation Committee approval. Added new indication, recurrent vulvovaginal candidiasis, to policy with criteria. Updated criteria for the vulvovaginal candidiasis indication that requires a patient to not be pregnant and removed the recurrent vulvovaginal candidiasis definition criterion. Updated background and rationale sections accordingly.
02/01/2024	Medical Policy Committee review
02/14/2024	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
02/06/2025	Medical Policy Committee review
02/12/2025	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.

Next Scheduled Review Date: 02/2026

*Investigational – A medical treatment, procedure, drug, device, or biological product is Investigational if the effectiveness has not been clearly tested and it has not been incorporated into standard medical practice. Any determination we make that a medical treatment, procedure, drug, device, or biological product is Investigational will be based on a consideration of the following:

A. Whether the medical treatment, procedure, drug, device, or biological product can be lawfully marketed without approval of the U.S. Food and Drug Administration (FDA) and whether such approval has been granted at the time the medical treatment, procedure, drug, device, or biological product is sought to be furnished; or
B. Whether the medical treatment, procedure, drug, device, or biological product requires further studies or clinical trials to determine its maximum tolerated dose, toxicity, safety, effectiveness, or effectiveness as compared with the standard means of treatment or diagnosis, must improve health outcomes, according to the consensus of opinion among experts as shown by reliable evidence, including:
    1. Consultation with technology evaluation center(s);
    2. Credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community; or
    3. Reference to federal regulations.

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**Medically Necessary (or "Medical Necessity") - Health care services, treatment, procedures, equipment, drugs, devices, items or supplies that a Provider, exercising prudent clinical judgment, would provide to a patient for the purpose of preventing, evaluating, diagnosing or treating an illness, injury, disease or its symptoms, and that are:

A. In accordance with nationally accepted standards of medical practice;
B. Clinically appropriate, in terms of type, frequency, extent, level of care, site and duration, and considered effective for the patient's illness, injury or disease; and
C. Not primarily for the personal comfort or convenience of the patient, physician or other health care provider, and not more costly than an alternative service or sequence of services at least as likely to produce equivalent therapeutic or diagnostic results as to the diagnosis or treatment of that patient's illness, injury or disease.

For these purposes, "nationally accepted standards of medical practice" means standards that are based on credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community, Physician Specialty Society recommendations and the views of Physicians practicing in relevant clinical areas and any other relevant factors.

‡ Indicated trademarks are the registered trademarks of their respective owners.

NOTICE: If the Patient's health insurance contract contains language that differs from the BCBSLA Medical Policy definition noted above, the definition in the health insurance contract will be relied upon for specific coverage determinations.

NOTICE: Medical Policies are scientific based opinions, provided solely for coverage and informational purposes. Medical Policies should not be construed to suggest that the Company recommends, advocates, requires, encourages, or discourages any particular treatment, procedure, or service, or any particular course of treatment, procedure, or service.

NOTICE: Federal and State law, as well as contract language, including definitions and specific contract provisions/exclusions, take precedence over Medical Policy and must be considered first in determining eligibility for coverage.