

STEPS

New Drug Reviews

Ibrexafungerp (Brexafemme) for the Treatment of Vulvovaginal Candidiasis

Kelsea Woolfolk, PharmD, BCPS, and Jonathan Hughes, PharmD, BCPS, BCACP

Department of Pharmacy Services, Ascension Medical Group, Murfreesboro, Tennessee

Ibrexafungerp (Brexafemme) is an antifungal labeled for the treatment of vulvovaginal candidiasis in adult and postmenarchal adolescent female patients.¹ Ibrexafungerp inhibits glucan synthase, an enzyme necessary for creation of the fungal cell wall, which is active against most fluconazole (Diflucan)–resistant *Candida* species.

Safety

No serious adverse effects were reported in the phase 3 clinical studies of ibrexafungerp. Based on findings from animal studies that resulted in fetal malformations, the medication is contraindicated in pregnant patients. Patients of reproductive age should be tested for pregnancy before initiation of ibrexafungerp. Contraception should be used during treatment and for four days after the last dose. Use of ibrexafungerp should be avoided in premenarchal female patients because safety and effectiveness have not been established in this population.

Tolerability

Ibrexafungerp is generally well tolerated. The most common adverse effects are nausea, abdominal pain, and diarrhea (11% to 17%), with numbers needed to harm ranging from 7 to 15. Some patients may report dizziness and vomiting (3.3% and 2.0%, respectively, vs. 2.5% and 0.7% with

| Drug | Dosage | Dose form | Cost of full course* |
|----------------------------|---|---------------|----------------------|
| Ibrexafungerp (Brexafemme) | 300 mg taken twice per day 12 hours apart for total of 600 mg | 150-mg tablet | \$520 |

*—Estimated retail price of one course of treatment based on information obtained at <https://www.goodrx.com> (accessed July 5, 2022; zip code: 66211).

placebo). In clinical trials of 545 patients, less than 1% discontinued use of ibrexafungerp due to adverse effects.^{2,3}

Effectiveness

Ibrexafungerp has been evaluated in two randomized controlled trials of 545 patients with vulvovaginal candidiasis. Approximately 57% of patients treated with ibrexafungerp achieved complete clinical response (i.e., resolution of vulvovaginal erythema, edema, itching, burning, and irritation with no need for further antifungal therapy) eight to 14 days after completing treatment vs. 36% of patients who received placebo.^{2,3}

Most patients enrolled in each of the two trials had a positive culture for *C. albicans* (92% vs. 89%). Based on in vitro studies, ibrexafungerp is active against multiple isolates of *Candida* spp., including *C. krusei* and *C. glabrata*, and on mutations associated with fluconazole and echinocandin resistance.⁴ However, this potential advantage in the general population or an azole/echinocandin–resistant population has not yet been demonstrated in a phase 3 study. In a phase 2 randomized controlled trial of 186 patients with vulvovaginal candidiasis, ibrexafungerp produced cure rates similar to fluconazole (51.9% vs. 58.3%, respectively). However, patients in the ibrexafungerp group were less likely to require additional treatment compared with those receiving fluconazole (3.7% vs. 29.2%, respectively) following initial treatment.⁵

STEPS new drug reviews cover Safety, Tolerability, Effectiveness, Price, and Simplicity. Each independent review is provided by authors who have no financial association with the drug manufacturer.

This series is coordinated by Allen F. Shaughnessy, PharmD, assistant medical editor.

A collection of STEPS published in *AFP* is available at <https://www.aafp.org/afp/steps>.

Author disclosure: No relevant financial relationships.

STEPS

Price

Ibrexafungerp costs approximately \$520 for a two-dose regimen. It is significantly more expensive than a single-dose treatment of generic fluconazole, which costs about \$10, as well as over-the-counter options such as miconazole and clotrimazole cream, which generally cost about \$10 per tube.

Simplicity

Ibrexafungerp should be taken in two 300-mg doses 12 hours apart, for a total of 600 mg. For patients taking strong cytochrome P450 3A4 inhibitors (e.g., ketoconazole, itraconazole [Sporanox], clarithromycin [Biaxin], and ritonavir [Norvir]), the dosage of ibrexafungerp should be reduced to two 150-mg doses taken 12 hours apart.^{2,3} Ibrexafungerp is packaged in blister packs with four 150-mg tablets per pack. Ibrexafungerp can be taken with or without food.

Bottom Line

Compared with oral fluconazole, ibrexafungerp is a significantly more expensive treatment option for adolescent, adult, and postmenarchal patients with vulvovaginal candidiasis and has not been shown to be more effective to date.

Although the novel mechanism of ibrexafungerp may hold potential for patients who have not benefited from treatment with fluconazole or topical azole antifungals, clinical trials among these populations are still pending.

Address correspondence to Kelsea Woolfolk, PharmD, BCPS, at kelsea.woolfolk@ascension.org. Reprints are not available from the authors.

References

1. DailyMed. Drug label information. Brexafemme (ibrexafungerp tablet, film coated). Accessed June 17, 2022. <https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=c33be3a1-c4fd-512c-e053-2995a90a63eb>
2. Schwebke JR, Sobel R, Gersten JK, et al. Ibrexafungerp versus placebo for vulvovaginal candidiasis treatment: a phase 3, randomized, controlled superiority trial (VANISH 303). *Clin Infect Dis*. 2022;74(11):1979-1985.
3. Sobel R, Nyirjesy P, Ghannoum MA, et al. Efficacy and safety of oral ibrexafungerp for the treatment of acute vulvovaginal candidiasis: a global phase 3, randomised, placebo-controlled superiority study (VANISH 306). *BJOG*. 2022;129(3):412-420.
4. U.S. Food and Drug Administration. NDA multi-disciplinary review and evaluation - NDA 214900. Brexafemme (ibrexafungerp). Accessed June 21, 2022. <https://www.fda.gov/media/151040/download>
5. Nyirjesy P, Schwebke JR, Angulo DA, et al. Phase 2 randomized study of oral ibrexafungerp vs fluconazole in vulvovaginal candidiasis [published online ahead of print]. *Clin Infect Dis*. 2021;ciab841. ■