# Ibrexafungerp (BREXAFEMME®)
# National Drug Monograph
# March 2022

**VA Pharmacy Benefits Management Services, Medical Advisory Panel, and VISN Pharmacist Executives**

*The purpose of VA PBM Services drug monographs is to provide a focused drug review for making formulary decisions. Updates will be made if new clinical data warrant additional formulary discussion. The Product Information or other resources should be consulted for detailed and most current drug information.*

## FDA Approval Information

### Description/Mechanism of Action

- Ibrexafungerp is a novel triterpenoid antifungal that was approved by the United States Food and Drug Administration (FDA) on 06/01/21 for the treatment of vulvovaginal candidiasis (VVC) in adult and post-menarchal pediatric females[1,2,3]
- The mechanism of action of ibrexafungerp is inhibition of β-1,3-D glucan synthetase which disrupts the formation of fungal cell walls[2]
- Mechanisms of resistance to ibrexafungerp include:
    - Mutations in the FKS genes of fungal glucan synthetase may confer some resistance, however the activity of ibrexafungerp was found to be minimally affected[4]
    - Mutations in the FKS2 gene of *Candida glabrata*[5]

### Indication(s) Under Review in This Document

- Treatment of VVC in adult and post-menarchal pediatric females (FDA-approved indication)

### Dosage Form(s) Under Review

- Ibrexafungerp 300mg (administered as two 150mg tablets) by mouth twice daily for one day for treatment of VVC in adult and post-menarchal pediatric females

## Clinical Evidence Summary

### Efficacy Considerations

- *In vitro*[6,7]
    - Concentration-dependent fungicidal activity *in vitro* against most *Candida* species
        - 50% minimum inhibitory concentrations ($\mathrm{MIC}_{50}$) of 0.5 to 1 µg/mL for *C. auris*, which has shown emerging multi-drug resistance
        - $\mathrm{MIC}_{50}$ for species often found to be less susceptible to fluconazole include 0.125 to 1 µg/mL for *C. glabrata*, 0.5 to 1 µg/mL for *Pichia kudriavzevii* (formerly known as *C. krusei*), and <0.03 to 1 µg/mL for *C. tropicalis*
    - The target site on glucan synthase to which ibrexafungerp binds is independent and only partially overlaps with that of echinocandins thus reducing the degree of resistance of fungal pathogens to ibrexafungerp
        - In terms of $\mathrm{MIC}_{50}$, FKS mutations resulted in a 2 to 4-fold increase for ibrexafungerp as compared to an 8.3 to >20-fold increase for caspofungin and an 8.3-fold increase for micafungin
    - Ibrexafungerp has been tested against *Candida* isolates resistant to fluconazole
        - $\mathrm{MIC}_{50}$ ranges were 0.06 to 2 µg/mL for *C. albicans*, 0.5 to 2 µg/mL for *C. glabrata*, 0.25 to 1 µg/mL for *C. tropicalis*, and 0.25 to 0.5 µg/mL for *C. parapsilosis*.
    - Ibrexafungerp possesses *in vitro* activity against *Aspergillus* species
        - *A. fumigatus:* $\mathrm{MEC}_{50}$ = <0.06-0.12 µg/mL and $\mathrm{MEC}_{90}$ = 0.12-0.25 µg/mL

- *A. flavus:* $MEC_{50}$ = <0.06-0.06 µg/mL and $MEC_{90}$ = <0.06-0.12 µg/mL
- *A. niger:* $MEC_{50}$ = <0.06-0.06 µg/mL
- *A. terreus*: $MEC_{50}$ = <0.06-0.06 µg/mL and $MEC_{90}$ = 0.125 µg/mL

○ Lacks activity vs. *Fusarium* spp and *Purpureocillium lilacinum* (formerly *Paecilomyces lilacinus*)

- *In vivo*
  - ○ Clinical efficacy data as summarized in Tables 1 and 2

**Table 1: Efficacy results from clinical trials for treatment of VVC**

| Study | Design, Purpose, Interventions | Demographics | Results |
|---|---|---|---|
| **DOVE**[8,9]<br>• Phase 2 Study | Design<br>• Multicenter, randomized, double-blind, double-dummy, active-controlled, dose finding study<br>Purpose<br>• To compare the efficacy, safety, and tolerability of IBX vs. FLU in mod/severe VVC<br>Interventions<br>• IBX:<br>○ 750mg PO for 1 day (n=28)<br>○ 300mg PO BID for 1 day (n=27)<br>○ 450mg PO BID for 1 day (n=22)<br>○ 150mg PO BID for 3 days (n=28)<br>○ 300mg PO BID for 3 days (n=27)<br>• FLU 150mg PO daily for 1 day (n=28)<br>Key Inclusion Criteria<br>• At least 18 years old<br>• Acute VVC at baseline with positive microscopic examination and vaginal pH ≤4.5<br>Key Exclusion Criteria<br>• Pregnancy<br>• Vaginal condition other than VVC<br>• Systemic and/or vaginal antifungal treatment 28 days prior to randomization<br>• Active menstruation at baseline<br>• Uncontrolled diabetes mellitus<br>• History of cervical/vaginal cancer<br>• HIV infection | Demographics<br>• Mean Age, years<br>- IBX: 34.4<br>- FLU: 33.8<br>• White, %<br>- IBX: 66.7<br>- FLU: 59.4<br>• BMI, $kg/m^2$<br>- IBX: 28.1<br>- FLU: 27.4 | **Ibrexafungerp dose of 300mg PO BID for 1 day showed the best combination of clinical efficacy and tolerability.**<br><br>The following results reported below compare outcomes of ibrexafungerp 300mg PO BID for 1 day and fluconazole 150mg PO daily for 1 day.<br><br>***Primary Outcome***<br>**Clinical Cure at Day 10:**<br>• **IBX 51.9% vs. FLU 58.3%**<br><br>*Secondary Outcomes*<br>Clinical Cure & Mycological Eradication at Day 10:<br>• IBX 37% vs. FLU 41.7%<br><br>Continued Clinical Response at Day 25<br>• IBX 40.7% vs. FLU 41.7%<br><br>*Post Hoc Analysis*<br>Antifungal Rescue Medication<br>• IBX 3.7% vs. FLU 29.2% |
| **VANISH 303**[10]<br>• Phase 3 Study | Design<br>• Multicenter, randomized, double-blind, placebo-controlled superiority study<br>Purpose<br>• Efficacy and safety of oral IBX vs. placebo for moderate/severe VVC<br>Intervention<br>• IBX 300mg PO BID for 1 day (n=249)<br>• PBO (n=127)<br>Key Inclusion Criteria<br>• At least 12 years old<br>• Diagnosis of acute VVC including positive microscopic examination and vaginal pH ≤4.5<br>• Use of effective contraception<br>Key Exclusion Criteria<br>• Conditions which may interfere with diagnosis or evaluation of response to therapy | Demographics<br>• Mean Age, years<br>- IBX: 33.5<br>- PBO: 36.0<br>• White, %<br>- IBX: 54.8<br>- PBO: 54.1<br>• BMI ≤35, %<br>- IBX: 76.6<br>- PBO: 77.6<br>• No Diabetes Mellitus, %<br>- IBX: 90.4<br>- PBO: 91.8<br>• *C. albicans*, %<br>- IBX: 92.0<br>- PBO: 91.8 | ***Primary Outcome***<br>**Clinical Cure at Day 11 ± 3:**<br>• **IBX 50.5% vs. PBO 28.6% (RR=1.71, 95% CI 1.205-2.431, P=0.001)**<br><br>***Secondary Outcomes***<br>Clinical Cure & Mycological Eradication at Day 11 ± 3:<br>• IBX 36.0% vs. PBO 12.6% (RR=3.19, 95% CI 1.772-5.756, **P<0.001**)<br>Clinical Cure & Mycological Eradication in Patients with *C. albicans* at Day 11 ± 3: |

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| | • Systemic and/or vaginal antifungal treatments within 28 days of baseline<br>• Pregnant or lactating patients<br>• Known HIV or other immune compromise<br>• Active cervical/vaginal cancer | | • IBX 37.4% vs. PBO 12.5% (RR=3.52, 95% CI 1.852-6.678, **P<0.001**)<br>Complete Resolution of Symptoms at Day 25:<br>• IBX 59.6% vs. PBO 44.9% (**P=0.009**) |
| **VANISH 306**[11]<br>• Phase 3 Study | Design<br>• Global, randomized, placebo-controlled, superiority study<br>Purpose<br>• Efficacy and safety of IBX vs. PBO in mod/severe VVC<br>Intervention<br>• IBX 300mg PO BID for 1 day (n=188)<br>• PBO (n=84)<br>Key Inclusion Criteria<br>• Same as VANISH 303<br>Key Exclusion Criteria<br>• Similar to VANISH 303 | Demographics<br>• Mean Age, years<br>- IBX: 33.7<br>- PBO: 33.5<br>• White, %<br>- IBX: 81.4<br>- PBO: 82.1<br>• BMI ≤35, %<br>- IBX: 88.8<br>- PBO: 82.1<br>• No Diabetes Mellitus, %<br>- IBX: 95.7<br>- PBO: 94.0<br>• *C. albicans*, %<br>- IBX: 87.8<br>- PBO: 90.5 | *Primary Outcome*<br>Clinical Cure, TOC:<br>• IBX 63.3% vs. PBO 44.0% (**P=0.007**)<br>*Secondary Outcomes*<br>Clinical Cure & Mycological Eradication:<br>• IBX 46.1% vs. PBO 28.4% (**P=0.022**)<br>Clinical Improvement, TOC:<br>• IBX 72.3% vs. PBO 54.8% (**P=0.01**)<br>Complete Resolution of Symptoms at Follow-Up:<br>• IB 73.9% vs. PBO 52.4% (**P=0.001**) |
| **SCY-078**[12]<br>• Phase 2 Study | Design<br>• Proof-of-concept, evaluator blinded study<br>Purpose<br>• Safety and efficacy of two dosing regimens of IBX in moderate-severe VVC vs. PO Fluconazole<br>Intervention<br>• Oral SCY-078 loading dose of 1250mg, followed by 750mg daily for 2 days (n=24)<br>• Oral SCY-078 loading dose of 1250mg, followed by 750mg daily for 4 days (n=26)<br>• Oral fluconazole 150mg for 1 day (n=20)<br>Key Inclusion Criteria<br>• Moderate to severe VVC confirmed by potassium hydroxide (KOH) test from vaginal secretion sample<br>• 3 episodes in past year confirmed to be caused by *Candida* spp. or responded to antifungal therapy | Demographics<br>• 70 subjects with culture-confirmed *Candida* spp. | *Efficacy Evaluation at Day 24*<br>Clinical Cure<br>• SCY-078 3-days 79.2% vs. SCY-078 5-days 73.1% vs. FLU 65%<br>*Efficacy Evaluation at Month 4*<br>Recurrences Requiring Antifungal Therapy:<br>• SCY-078 3-days 4.2% vs. SCY-078 5-days 3.8% vs. FLU 15%<br>Clinical Cure:<br>• SCY-078 3-days 87.%% vs. SCY-078 5-days 88.4% vs. FLU 65% |

Abbreviations: IBX = ibrexafungerp, FLU = fluconazole, PBO = placebo

**Table 2: Efficacy results from clinical trials for refractory invasive fungal infections (off-label)**

| Study | Design, Purpose, Interventions | Demographics | Results |
|---|---|---|---|
| **FURI**[13,14,15]<br>• Phase 3 Study<br>• Interim Analysis | Design<br>• Multicenter, open label, non-comparator, single arm study<br>Purpose<br>• Efficacy and safety of IBX in patients ≥18 years of invasive fungal infection refractory to (or intolerance to) SOC<br>Interventions | Demographics<br>• No complete demographics available as study is in progress | **Independent data review committee assessed treatment response of 41 patients enrolled in the FURI study**<br><br>The patients assessed by the independent data review committee had the following types of infections: intra-abdominal abscesses, |

| | | | |
|---|---|---|---|
| | • IBX 750mg PO BID X 2 days then 750mg daily for up to 180 days<br>Key Inclusion Criteria<br>• Eligible invasive and/or severe fungal disease refractory or intolerant to SOC<br>• Can receive enteral medication<br>Key Exclusion Criteria<br>• CNS involvement<br>• Lack of source control<br>• Hemodynamic instability<br>• Abnormal LFTs<br>• Pregnant or lactating | | oropharyngeal candidiasis, esophageal candidiasis, candidemia, and others<br><br>*Efficacy Results*<br>• 56% of all patients achieved complete or partial response<br>○ Outcomes by Pathogen:<br>- ***C. glabrata*: 9 (52.9%)**<br>- *C. albicans*: 5 (71.4%)<br>- *C.* krus*ei*: 2 (40.0%)<br>- *C. parapsilosis*: 3 (100%) |

Abbreviations: SOC = standard of care, NG = nasogastric, PEG = percutaneous endoscopic gastrostomy, IBX = ibrexafungerp, PK = pharmacokinetics, FLU = fluconazole

## Efficacy Summary

- The DOVE phase 2 trial was a dose-finding study that provided evidence that the IBX dose of 300mg PO BID for 1 day had comparable efficacy to fluconazole for the treatment of patients with acute VVC as the primary outcome of clinical cure at day 10 was similar between the two treatment groups.
- The VANISH 303 and 306 phase 3 studies provided evidence that IBX had superior efficacy compared to placebo for the treatment of acute VVC. Nearly all cases were caused by *C.albicans* with similar efficacy benefits seen in those subgroups.
- Overall, there is limited evidence currently available regarding use of ibrexafungerp for other indications such as prevention of recurrent VVC, invasive aspergillosis, and refractory invasive fungal infections. Additional ongoing and completed studies for these other indications as listed below:
    - Completed Studies:
        - Refractory invasive fungal infection – MSG-10 phase 2 study showed ibrexafungerp 1250mg PO followed by 750mg daily achieved a favorable global response rate similar to SOC treatment[16]
    - Ongoing Studies:
        - Prevention of recurrent VVC – CANDLE phase 3 study is currently ongoing[17]
        - Invasive aspergillosis – SCYNERGIA phase 2 study is currently ongoing[17]
        - Refractory invasive fungal infection – CARES phase 3 study is currently ongoing, however published case reports of 2 patients described efficacy of ibrexafungerp when initiated for candidemia due to *C. auris*[18]

## Safety Considerations

- Safety results from clinical trials as summarized in Tables 3 and 4

**Table 3: Safety results from clinical trials for treatment of VVC**

| Study | Results | Comments |
|---|---|---|
| **DOVE**[8,9]<br>• Phase 2 Study | The results reported below compare outcomes of ibrexafungerp 300mg PO BID X 1 day and fluconazole 150mg PO daily X 1 day.<br>Most Common Treatment-Related TEAEs<br>• Any Treatment-Related TEAE: IBX 46.7% vs. FLU 25.0%<br>• Diarrhea: IBX 16.7% vs. FLU 3.1%<br>• Nausea: IBX 10.0% vs. FLU 6.3%<br>• Abdominal Pain: IBX 3.3% vs. FLU 6.3%<br>• Somnolence: IBX 0% vs. FLU 6.3% | • Ibrexafungerp was reported to have been tolerated well overall with self-limited (generally 1-day duration) mild to moderate gastrointestinal TEAEs |
| **VANISH 303**[10]<br>• Phase 3 Study | Most Common Treatment-Related TEAEs<br>• ≥1 TEAE: IBX 39.7% vs. PBO 16.9% | • Ibrexafungerp was reported to be well-tolerated overall |

| | | |
|---|---|---|
| | ○ Mild: IBX 31.6% vs. PBO 13.7%<br>• Diarrhea: IBX 22.3% vs. PBO 4.0%<br>○ Mild: IBX 15.4% vs. PBO 3.2%<br>• Nausea: IBX 10.9% vs. PBO 4.0%<br>○ Mild: IBX 9.7% vs. PBO 4.0%<br>• Abdominal Pain: IBX 5.3% vs. PBO 0%<br>○ Mild: IBX 4.9% vs. PBO 0%<br>• Abdominal Discomfort: IBX 4.5% vs. PBO 1.6%<br>○ Mild: IBX 2.4% vs. PBO 1.6%<br>• Dizziness: IBX 3.6% vs. PBO 1.6%<br>○ Mild: IBX 2.8% vs. PBO 1.6% | • Majority of treatment-related TEAEs were gastrointestinal and mild in severity<br>• Of note, increased rates of treatment-related diarrhea and nausea were associated with ibrexafungerp |
| **VANISH 306**[11]<br>• Phase 3 Study | Most Common Treatment-Related TEAEs<br>• Any Treatment-Related TEAE: IBX 14.8% vs. PBO 4.0%<br>• Nausea: IBX 6.4% mild, 0.3% moderate, 0.3% severe<br>• Diarrhea: IBX 5.7% mild, 1.0% moderate<br>• No treatment-related treatment-emergent adverse effects occurred in ≥2% of patients in the placebo group | • Ibrexafungerp was reported to be well-tolerated overall<br>• Most frequently reported treatment-related TEAEs were gastrointestinal-related and mild to moderate in terms of severity |
| **SCY-078**[12]<br>• Phase 2 Study | • No severe or serious adverse events in any treatment group<br>• Higher rate of transient, mild to moderate severity gastrointestinal adverse effects such as nausea and diarrhea were reported in the SCY-078 treatment groups | • No further reporting of rates of adverse effects occurring in this study available |

Abbreviations: TEAE = treatment emergent adverse event, IBX = ibrexafungerp, FLU = fluconazole, PBO = placebo

**Table 4: Safety results from clinical trials for refractory invasive fungal infections (off-label)**

| Study | Results | Comments |
|---|---|---|
| **MSG-10**[16]<br>• Phase 2 Study | Most Common Treatment-Related TEAEs<br>• All TEAEs: IBX 500mg 100%, IBX 750mg 71%, SOC 88%<br>○ Mild: IBX 500mg 67%, IBX 750mg 14%, SOC 38%<br>• Diarrhea: IBX 500mg 33%, IBX 750mg 14%, SOC 13%<br>• Abdominal Pain: IBX 500mg 17%, IBX 750mg 14%, SOC 25%<br>• Vomiting: IBX 500mg 17%, IBX 750mg 14%, SOC 13%<br>• Headache: IBX 500mg 17%, IBX 750mg 29%, SOC 25% | • IBX safety profile was reported to be comparable to SOC overall<br>• Provides some evidence of tolerability vs. active therapy instead of PBO |

Abbreviations: TEAE = treatment emergent adverse event, IBX = ibrexafungerp, SOC = standard of care

- **Boxed warnings**[1]**:**
  - None
- **Contraindications**[1]**:**
  - **Pregnancy** – **Ibrexafungerp is contraindicated in pregnant patients as it may cause fetal harm based on the results of animal studies described below**. There is insufficient data on the use of ibrexafungerp in pregnant patients to draw sufficient conclusions regarding drug-associated risks of major birth defects, miscarriage, or any other adverse maternal/fetal outcomes. **The pregnancy status of female patients who have reproductive potential must be obtained prior to starting treatment with ibrexafungerp**. Effective contraception should be used during treatment and for 4 days after completion of treatment.
  - Patients who have hypersensitivity to ibrexafungerp
- **Other warnings / precautions**[1]:
  - **Risk of fetal toxicity** – In animal reproduction studies, ibrexafungerp was associated with fetal malformations when administered orally to pregnant rabbits during organogenesis
  - **Lactation** – Currently, no data available on the presence of ibrexafungerp in either human or animal milk, the effects on breast-fed infants, or the effects of ibrexafungerp on milk production
- **Adverse reactions**[1]**:**
  - **Common** – Diarrhea, nausea, abdominal pain, dizziness, vomiting

- **Serious Adverse Reactions** – No serious adverse reactions reported during clinical trials
- **Other Adverse Reactions (<2% of patients in clinical trials)** – Dysmenorrhea, flatulence, back pain, elevated transaminases, vaginal bleeding, rash/hypersensitivity reactions

- **Drug-drug interactions:**
  - Ibrexafungerp is a substrate of CYP3A4. Drugs that are inducers or inhibitors of CYP3A4 may affect the plasma concentrations, efficacy, and safety of ibrexafungerp
    - Strong CYP3A4 inhibitors (ex: ketoconazole or itraconazole) may significantly increase serum concentration of ibrexafungerp
      - Recommend reducing the ibrexafungerp dose to 150mg approximately 12 hours apart for one day
    - Strong/moderate CYP3A4 inducers (ex: rifampin, carbamazepine, phenytoin, St. John's wort, long-acting barbiturates, bosentan, efavirenz, or etravirine) have not been studied *in vivo* or *in vitro* but are likely to result in significant reduction of serum concentration of ibrexafungerp
      - Recommendation is to avoid concomitant administration
  - Ibrexafungerp is also an inhibitor of CYP3A4, P-gp, and OATP1B3 transporter. The effect of ibrexafungerp on the pharmacokinetics of these substrates is not considered to be clinically significant due to the short treatment duration of ibrexafungerp for acute VVC.

## Other Considerations

- **Pharmacokinetics (PK)[2,16]:**
  - Absorption –
    - For patients taking ibrexafungerp 300mg twice daily for 1 day for VVC, predicted $AUC_{24h}$ is 6832 ng·hr/mL and $C_{max}$ is 435 ng/mL when fasting vs. $AUC_{24h}$ of 9867 ng·hr/mL and $C_{max}$ of 629 ng/mL when taken with a meal.
    - Ibrexafungerp 1250mg PO followed by 750mg daily taken for invasive candidiasis is predicted to achieve target exposure in approximately 85% of the population
  - Distribution – $V_{ss}$ at steady state is approximately 600 L
  - Protein Binding – >99%, highly protein bound primarily to plasma albumin
  - Metabolism – CYP3A4 hydroxylates ibrexafungerp which subsequently undergoes glucuronidation and sulfation
  - Half-Life Elimination – Approximately 20 hours
  - Time to Peak – 4 to 6 hours
  - Excretion – Feces 90% with 51% as unchanged drug; Urine 1%
- **Special Populations[1]:**
  - Pregnancy – Use of ibrexafungerp is contraindicated in pregnant patients as it may cause fetal harm based on the results of animal studies. Current available data on use of ibrexafungerp in pregnant patients is insufficient to draw conclusions regarding risks of major birth defects, miscarriage, or other adverse maternal/fetal outcomes.
  - Lactation – There is currently no data regarding the presence of ibrexafungerp in human or animal milk, any effects ibrexafungerp may have on a breast-fed infant, or the effects of ibrexafungerp on milk production
  - Females of Reproductive Potential – Verify the pregnancy status in female patients with reproductive potential prior to starting ibrexafungerp treatment
  - Geriatric Use – In the clinical trials, there were insufficient numbers of patients age 65 years or older included to determine if there is a difference in response compared to younger patients. There were no observed clinically meaningful differences in the pharmacokinetics of ibrexafungerp administered to geriatric patients compared to younger patients.
- **Storage[1]:**
  - Store ibrexafungerp tablets at 68°F to 77°F (20°C to 25°C)

## Other Therapeutic Options

- Alternative treatments as listed in Table 5[19]

**Table 5 Treatment Alternatives for VVC**

| Drug | Formulary Status | Clinical Guidance | Other Considerations |
|---|---|---|---|
| **Ibrexafungerp** | TBD | • For treatment of VVC | • Two-dose regimen<br>• Only NON-Azole treatment regimen<br>• **Contraindicated in pregnancy** |
| Topical Azole Antifungal Agents | F | • For treatment of uncomplicated *Candida* vulvovaginitis | • No one agent is superior to another<br>• Duration varies from 3 to 7 days<br>• Therapy of choice in pregnant patients |
| Fluconazole | F | • For treatment of uncomplicated *Candida* vulvovaginitis | • Single-dose regimen<br>• Not recommended for use in pregnant patients<br>• Fluconazole is present in breast milk<br>• CYP3A4, CYP2C9, and CYP2C19 inhibitor |
| Boric acid vaginal suppositories | NF | • Must be compounded as they are not available commercially | • Can be fatal if swallowed |

# Projected Place in Therapy

- VVC is a common condition, affecting 25-50% of all women. Prior to IBX approval, treatment consisted exclusively of azole antifungal agents, either oral fluconazole or one of a variety of topical azole intravaginal creams or suppositories.
- Azole-resistant *Candida spp.* are uncommon but may be a cause of treatment failure. Alternative treatments for this include compounded products, such as boric acid suppositories, and intravaginal flucytosine or amphotericin B cream.
- Clinical failure should be investigated fully to assess other possible reasons or pathogens, and if azole resistance suspected, should prompt a culture to assess fluconazole susceptibility. If feasible, treatment should be guided specifically to fluconazole resistant isolates. If this cannot be done in a timely manner, a culture should still be done to guide future treatments, even if treatment is to be started prior to culture results.
- Ibrexafungerp is a new class of antifungal, and the first non-azole medication to be approved by vulvovaginal candidiasis.
    - The data is limited in that neither phase 3 trial used an active comparator, so efficacy compared to topical products or oral fluconazole is not known. Data against species other than *C.albicans* is largely limited to *C.glabrata*, and while preliminary, responses to this pathogen may be lower.
    - Diarrhea and other GI side effects are common, and are dose dependent.
    - Due to teratogenic effects in animals, it is CONTRAINDICATED in pregnancy, and is impacted by drug-drug interactions.
    - IBX cannot be given with moderate to strong CYP3A inducers, and requires dose adjustment in those on CYP3A inhibitors
- IBX currently may have a role as a treatment of acute, moderate-severe VVC in non-pregnant adult females with azole-resistant organisms, and in those who may have a contraindication to the use of topical or oral azole antifungals.
    - **The pregnancy status in female patients of reproductive potential should be verified prior to the initiation of ibrexafungerp. Female patients of reproductive potential should use effective contraception while on ibrexafungerp and for 4 days after the last dose.**
- Clinical trials assessing the use of ibrexafungerp for prevention of recurrent VVC are currently in progress.
- Studies are also ongoing evaluating IBX as a treatment for invasive fungal infections (invasive candidiasis and invasive aspergillosis), but additional data is needed to assess the benefit of IBX in these types of infections and the tolerability, given GI tolerability limited the treatment dose used in the VANISH trials.

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