Antifungals Prior Authorization with Quantity Limit Program Summary

This program applies to Medicaid.

The BCBS MN Step Therapy Supplement also applies to this program for Medicaid.

Requests for an oral liquid form of a drug must be approved if BOTH of the following apply:

1) the indication is FDA approved AND

2) the patient is using an enteral tube for feeding or medication administration

POLICY REVIEW CYCLE

Effective Date	**Date of Origin**
02-01-2024	07-01-2019

FDA APPROVED INDICATIONS AND DOSAGE

Agent(s)	FDA Indication(s)	Notes	Ref#
Brexafemme® (ibrexafungerp) Tablets	Treatment in adult and post-menarchal pediatric females for: • Vulvovaginal candidiasis (VVC) • Reduction in the incidence of recurrent vulvovaginal candidiasis (RVVC)		14
Cresemba® (isavuconazonium) Capsules Injection	Treatment of invasive aspergillosis and invasive mucormycosis		1
Noxafil® (posaconazole) Oral suspension* Delayed-release tablet* Solution for injection* PowderMix Kit	Treatment of invasive aspergillosis in adults and pediatric patients 13 years of age and older (injection and tablets only) Prophylaxis against invasive *Aspergillus* and *Candida* in patients who are at high risk of developing these infections due to being severely immunocompromised Treatment of oropharyngeal candidiasis, including oropharyngeal candidiasis refractory to itraconazole or fluconazole (oral suspension only) Noxafil injection: Adults and pediatric patients 2 years of age and older who weigh greater than 40kg Noxafil tablets: Adults and pediatric patients 2 years of age and older who weigh greater than 40 kg. Oral suspension: Adults and patients 13 years of age and older. Noxafil delayed-release tablets and oral suspension are not interchangeable	*generic available	2

Agent(s)	FDA Indication(s)	Notes	Ref#
Vfend® (voriconazole) Tablets* Oral suspension* Injection*	Treatment of adults and pediatric patients 2 years of age and older with: • Invasive aspergillosis • Candidemia in non-neutropenics and other deep tissue *Candida* infections • Esophageal candidiasis • Serious fungal infections caused by *Scedosporium apiospermum* and *Fusarium* species, including *Fusarium solani*, in patients intolerant of, or refractory to, other therapy	*generic available	3
Vivjoa® (oteseconazole) Capsules	Treatment to reduce the incidence of recurrent vulvovaginal candidiasis (RVVC) in females with a history of RVVC who are NOT of reproductive potential		17

See package insert for FDA prescribing information: https://dailymed.nlm.nih.gov/dailymed/index.cfm

CLINICAL RATIONALE

Esophageal candidiasis and candidemia	Infectious Diseases Society of America (IDSA) guidelines recommend fluconazole as the first line oral therapy for esophageal candidiasis and candidemia in nonneutropenic patients. Fluconazole is also recommended for prophylaxis against esophageal candidiasis in at risk patients. For patients with fluconazole-refractory disease, guidelines recommend itraconazole or voriconazole. Voriconazole has demonstrated effectiveness for both mucosal and invasive candidiasis, but offers little advantage over fluconazole as initial therapy. Its clinical use has been primarily for step-down oral therapy in patients with infection due to C. krusei and fluconazole-resistant, voriconazole-susceptible C. glabrata.(4)
Vulvovaginal candidiasis	For the treatment of uncomplicated vulvovaginal candidiasis, the IDSA guidelines recommend any topical antifungal agent, with no one agent superior to the other, or a single 150mg oral dose of fluconazole as a first line therapy. In severe cases, guidelines recommend fluconazole 150mg given every 72 hours for a total of 2 or 3 doses. For recurring vulvovaginal candidiasis, defined as four or more episodes of symptomatic infection within one year, treatment consists of 10 to 14 days of induction therapy with a topical agent or oral fluconazole, followed by fluconazole weekly for 6 months. For *C. glabrata* vulvovaginitis that is unresponsive to oral azoles, topical intravaginal boric acid capsules or nystatin intravaginal suppositories have a strong recommendation but the quality of evidence is low.(4) *Efficacy* Brexafemme is FDA approved and was evaluated for use in post-menarchal females with vulvovaginal candidiasis (VVC) in two randomized placebo-controlled clinical trials (Trial 1, NCT03734991 and Trial 2, NCT03987620). The trials had a similar design and 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 VVC. In both trials, statistically significantly greater percentages of patients experienced a complete clinical response at TOC, negative culture at TOC, and complete clinical response at follow-up treatment with Brexafemme compared to placebo.(14)
Oropharyngeal candidiasis	First line therapy for oropharyngeal candidiasis includes clotrimazole troches or nystatin suspension for mild or moderate disease or fluconazole for severe disease. Guidelines recommend posaconazole or itraconazole for fluconazole-refractory disease.(4)

Recurrent vulvovaginal candidiasis	Vulvovaginal candidiasis is considered recurrent when at least four discrete episodes occur in one year or at least three episodes occur in one year and are not related to antibiotic therapy. Recurrent vulvovaginal candidiasis is distinguished from persistent infection by the presence of a symptom-free interval.(18) Treatment for recurrent vulvovaginal candidiasis (RVVC), consists of 10 to 14 days of induction therapy with a topical agent or oral fluconazole, followed by fluconazole weekly for 6 months. For C. glabrata vulvovaginitis that is unresponsive to oral azoles, topical intravaginal boric acid capsules or nystatin intravaginal suppositories have a strong recommendation but the quality of evidence is low.(4) Newer agents, Brexafemme and Vivjoa, do not have current IDSA guideline recommendations for treatment of RVVC. Patients who may benefit from with Brexafemme or Vivjoa, include those who are allergic to fluconazole and other triazoles, do not tolerate fluconazole or other triazoles, and/or have candida infections that are resistant to fluconazole.(16,17) *Efficacy* Brexafemme is also FDA approved for use in post-menarchal females with recurrent vulvovaginal candidiasis (RVVC). A randomized placebo-controlled clinical trial (Trial 3, NCT04029116) was conducted to evaluate the safety and efficacy of Brexafemme 300 mg (two 150 mg tablets) administered approximately 12 hours apart for one day, for a total daily dosage of 600 mg (four 150 mg tablets) administered once monthly for six months. 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. 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. Clinical Success at Week 24 and 36 was greater for Brexafemme compared to placebo.(14) Vivjoa is indicated to reduce the incidence of recurrent vulvovaginal candidiasis (RVVC) in females with a history of RVVC who are NOT of reproductive potential. A total of 656 adults and post-menarchal pediatric females with RVVC (defined as greater than or equal to 3 episodes of vulvovaginal candidiasis (VVC) in a 12-month period. Both trials consisted of two phases: an open-label induction phase and an 11-week maintenance phase. Patients received three sequential doses of 150 mg of fluconazole on Days, 1, 4 and 7 during the induction phase. Patients returned 14 days after the first dose of fluconazole and if the acute VVC episode was resolved (signs and symptoms score < 3) they were randomized (2:1) to receive either 150 mg of Vivjoa or placebo for 7 days followed by 11 weekly doses in the maintenance phase. Vivjoa was superior to placebo in patients through Week 48, with acute VVC episodes, or who took medication known to treat VVC during the Maintenance Phase through Week 48.(17) A third trial, was a randomized, double-blind trial evaluating the efficacy and safety of Vivjoa versus fluconazole and placebo in adults and post-menarchal pediatric females with RVVC. During the induction phase, patients received 1050 mg of Vivjoa over two days (4x150mg) on Day 1 and (3x150mg) on Day 2 or three sequential doses of 150 mg of fluconazole on Days, 1, 4 and 7. Patients returned 14 days after the first dose and moved to the maintenance phase if the acute VVC episode was resolved. During the maintenance phase, patients received 150 mg Vivjoa weekly or placebo weekly for 11 weeks with an additional post randomization phase through Week 50. Vivjoa was superior to fluconazole/placebo in all groups of patients.(17)
Aspergillus	IDSA guidelines recommend posaconazole for prophylaxis against aspergillus in hematopoietic stem cell transplant (HSCT) recipients with graft versus host disease (GVHD) at high risk, acute myeloid leukemia (AML), or myelodysplastic syndrome at high risk. Voriconazole or posaconazole are recommended for prophylaxis against invasive aspergillosis in patients with prolonged neutropenia at high risk for infection. IDSA guidelines recommend voriconazole for treatment of invasive pulmonary aspergillosis. Liposomal amphotericin B and isavuconazole are possible alternative therapies. An individualized approach should be used for refractory or progressive

	aspergillosis, but can include amphotericin B, micafungin, caspofungin, posaconazole, or itraconazole.(5)
Rare fungal infections	The European Confederation of Medical Mycology (ECMM), together with the Mycoses Study Group Education & Research Consortium guidelines for the diagnosis and management of mucormycosis recommend diagnosis of mucormycosis using biopsy, direct microscopy, histopathology, culture and molecular-based methods. First-line treatment with liposomal amphotericin is strongly supported across all patterns of organ involvement. Isavuconazole is recommended with moderate strength for the first-line treatment of mucormycosis. The group marginally supports use of posaconazole oral suspension, and moderately supports posaconazole delayed release tablets and infusion for first-line treatment. Invasive mucormycosis is a serious and rare disease in which active controlled clinical trials are not feasible. At the time the guideline was written, the only antifungal drug approved for this indication was amphotericin B, which is associated with several adverse events and also has limitations with regard to use in patients with renal impairment.(6) Isavuconazonium has shown activity against Mucorales such as *Rhizopus oryzae* and Mucormycetes species.(1) *Scedosporoium* species are typically resistant to polyenes (amphotericin B) as well as fluconazole and echinocandins (micafungin, casprofungin, and anidulafungin). Most international guidelines recommend voriconazole as first-line therapy; however, antifungal combination therapy has emerged as a promising option. In vitro data suggests isavuconazole may have good activity against *Scedosporoium*. *Fusarium* are some of the more difficult fungi to treat, due to high levels of resistance to antifungal agents. Itraconazole, voriconazole, isavuconazole and posaconazole are all treatment possibilities.(7)
Blastomycosis	IDSA guidelines recommend itraconazole as the first line oral agent for the treatment of mild to moderate pulmonary or disseminated extrapulmonary blastomycosis. Itraconazole is also recommended in patients as a step down from amphotericin B for more severe cases of these infections. Fluconazole and voriconazole are considered alternatives for the treatment of blastomycosis.(8)
Solid Organ Transplant Patients	Transplant patients have a significant risk of invasive fungal disease. Infection is caused mainly by Candida, Aspergillus, and Cryptocpoccus.(9) The 2013 guidelines from the American Society of Transplantation recommend amphotericin B, itraconazole, fluconazole, voriconazole, posaconazole, and/or an echinocandin, depending on the specific situation.(11,12) The 2016 IDSA Aspergillus treatment guidelines suggest use of voriconazole or itraconazole for aspergillus prophylaxis after lung transplant.(5)
Hematopoietic Stem Cell Transplant (HSCT) Recipients	Patients undergoing hematopoietic stem cell transplants are at an increased risk of infection with infection being the primary cause of death in 8% of autologous HSCT patients and 17%-20% of allogeneic HCT recipients. Risk factors for fungal infection in this population includes mucositis, neutropenia, and GVHD. Additionally, allogeneic transplant recipients are at a significantly higher risk for fungal infection than those receiving autologous marrow stem cells. Guidelines recommend fluconazole as the drug of choice for the prophylaxis of invasive candidiasis though there is increasing resistance to fluconazole.(13) The IDSA guidelines for treatment of Aspergillosis, recommend posaconazole for antifungal prophylaxis in HSCT recipients with GVHD at high risk of infection. Itraconazole may be an alternative but its utility is limited by tolerability issues.(5) Voriconazole has demonstrated efficacy in secondary prophylaxis of invasive aspergillosis.(5,13)
Safety (1-3, 14,16,17)	Brexafemme carries the following contraindications: • Pregnancy • Hypersensitivity to ibrexafungerp Cresemba carries the following contraindications: • Hypersensitivity to isavuconazonium • Coadministration with string CYP3A4 inhibitors, such as ketoconazole or high-dose ritonavir

	• Coadministration with strong CYP3A4 inducers, such as rifampin, carbamazepine, St. John's wort, or long acting barbiturates
	• Use in patients with familial short QT syndrome
	
	Noxafil carries the following contraindications:
	
	• Hypersensitivity to posaconazole, any component of Noxafil product, or other azole antifungal agents
	• Concomitant administration with:
	  ○ Sirolimus
	  ○ CYP3A4 substrates that prolong the QT interval (pimozide, quinidine)
	  ○ HMG-CoA reductase inhibitors primarily metabolized through CYP3A4 (atorvastatin, lovastatin, simvastatin)
	
	Vfend carries the following contraindications:
	
	• Hypersensitivity to voriconazole or its excipients
	• Concomitant administration with:
	  ○ Terfenadine, astemizole, cisapride, pimozide or quinidine (drugs leading to QT prolongation or rare occurrences of torsade de pointes
	  ○ Sirolimus
	  ○ Rifampin, carbamazepine, long-acting barbiturates
	  ○ Ritonavir, high-dose (400 mg every 12 hours)
	  ○ Rifabutin
	  ○ Ergot alkaloids (ergotamine, dihydroergotamine)
	  ○ St. John's Wort
	  ○ Efavirenz doses of 400 mg every 24 hours or higher
	
	Vivjoa carries the following contraindications:
	
	• Females of reproductive potential
	• Pregnant and lactating women
	• Hypersensitivity to oteseconazole

REFERENCES

Number	Reference
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3	Vfend prescribing information. Pfizer. October 2022.
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5	Patterson TF, Thompson GR, Denning DW, et al. Practice Guidelines for the Diagnosis and Management of Aspergillosis: 2016 Update by the Infectious Diseases Society of America. *Clin Infec Dis.* 2016;63(4):e1-e60.
6	Cornely OA, Alastruey-Izquierdo A, Arenz D et al. Global Guideline for the Diagnosis and Management of Murcormycosis: An Initiative of the European Confederation of Medical Mycology in cooperation with the Mycoses Study Group Education and Research Consortium. The Lancet Infections Diseases 2019; 19:12, E405-421. https://www.thelancet.com/journals/laninf/article/PIIS1473-3099(19)30312-3/fulltext.
7	McCarthy MW, Katragkou A, Iosifidis E, et. al. Recent Advances in the Treatment of Scedosporiosis and Fusariosis. *J. Fungi* (basel) 2018;4. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6023441/.

Number	Reference
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12	Singh NM, Husain S. Aspergillosis in solid organ transplantation. *Am J Transplant.* 2013;13:228-241. . https://onlinelibrary.wiley.com/doi/epdf/10.1111/ajt.12115.
13	Tomblyn M, Chiller T, Einele H et al. Guidelines for preventing infectious complications among hematopoietic cell transplantation recipients: a global perspective. Biol Blood Marrow Transplant. 2009;15(10):1143-238. https://www.bbmt.org/article/S1083-8791(09)00300-0/fulltext.
14	Brexafemme prescribing information. Scynexis, Inc. November 2022.
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16	Sobel, J. Candida vulvovaginitis: Treatment. UpToDate. Literature review current through June 2022. Last updated February 2022.
17	Vivjoa prescribing information. Mycovia Pharmaceuticals, Inc. April 2022.
18	Ringdahl, E M.D. Treatment of Recurrent Vulvovaginal Candidiasis. Am Fam Physician. 2000;61(11):3306-3312

POLICY AGENT SUMMARY PRIOR AUTHORIZATION

Target Brand Agent(s)	Target Generic Agent(s)	Strength	Targeted MSC	Available MSC	Final Age Limit	Preferred Status
Brexafemme	ibrexafungerp citrate tab	150 MG	M ; N ; O ; Y	N		
Cresemba	isavuconazonium sulf for iv sol	372 MG	M ; N ; O ; Y	N		
Cresemba	isavuconazonium sulfate cap	186 MG ; 74.5 MG	M ; N ; O ; Y	N		
Vivjoa	oteseconazole cap therapy pack	150 MG	M ; N ; O ; Y	N		
Noxafil	posaconazole for delayed release susp packet	300 MG	M ; N ; O ; Y	N		
Noxafil	posaconazole iv soln	300 MG/16.7ML	M ; N ; O ; Y	O ; Y		
Noxafil	posaconazole susp	40 MG/ML	M ; N ; O ; Y	O ; Y		
Noxafil	posaconazole tab delayed release	100 MG	M ; N ; O ; Y	O ; Y		
Vfend iv	voriconazole for inj	200 MG	M ; N ; O ; Y	M ; O ; Y		
Vfend	voriconazole for susp	40 MG/ML	M ; N ; O ; Y	O ; Y		
Vfend	voriconazole tab	200 MG ; 50 MG	M ; N ; O ; Y	O ; Y		

POLICY AGENT SUMMARY QUANTITY LIMIT

Target Brand Agent Name(s)	Target Generic Agent Name(s)	Strength	QL Amount	Dose Form	Day Supply	Duration	Addtl QL Info	Allowed Exceptions	Targeted NDCs When Exclusions Exist
Brexafemme	Ibrexafungerp Citrate Tab	150 MG	4	Tablets	90	DAYS			
Vivjoa	Oteseconazole Cap Therapy Pack	150 MG	18	Capsules	180	DAYS			

CLIENT SUMMARY – PRIOR AUTHORIZATION

Target Brand Agent Name(s)	Target Generic Agent Name(s)	Strength	Client Formulary
Brexafemme	ibrexafungerp citrate tab	150 MG	Medicaid
Cresemba	isavuconazonium sulf for iv sol	372 MG	Medicaid
Cresemba	isavuconazonium sulfate cap	186 MG ; 74.5 MG	Medicaid
Noxafil	posaconazole for delayed release susp packet	300 MG	Medicaid
Noxafil	posaconazole iv soln	300 MG/16.7ML	Medicaid
Noxafil	posaconazole susp	40 MG/ML	Medicaid
Noxafil	posaconazole tab delayed release	100 MG	Medicaid
Vfend	voriconazole for susp	40 MG/ML	Medicaid
Vfend	voriconazole tab	200 MG ; 50 MG	Medicaid
Vfend iv	voriconazole for inj	200 MG	Medicaid
Vivjoa	oteseconazole cap therapy pack	150 MG	Medicaid

CLIENT SUMMARY – QUANTITY LIMITS

Target Brand Agent Name(s)	Target Generic Agent Name(s)	Strength	Client Formulary
Brexafemme	Ibrexafungerp Citrate Tab	150 MG	Medicaid
Vivjoa	Oteseconazole Cap Therapy Pack	150 MG	Medicaid

PRIOR AUTHORIZATION CLINICAL CRITERIA FOR APPROVAL

Module	Clinical Criteria for Approval
Brexafemme	**Brexafemme (ibrexafungerp)** will be approved when BOTH of the following are met 1. ONE of the following: A. BOTH of the following: 1. The patient is an adult or post-menarchal pediatric patient AND ONE of the following: A. The requested agent will be used for the treatment of vulvovaginal candidiasis (VVC) **OR** B. BOTH of the following: 1. The patient is using the requested agent to reduce the incidence of recurrent vulvovaginal candidiasis (RVVC) **AND** 2. The patient has experienced greater than or equal to 3 episodes of vulvovaginal candidiasis (VVC) in a 12 months period **AND** 2. ONE of the following: A. The patient's medication history includes fluconazole AND ONE of the following: 1. The patient has had an inadequate response to fluconazole **OR**

Module	Clinical Criteria for Approval
	2. The prescriber has submitted an evidence-based and peer-reviewed clinical practice guideline supporting the use of the requested agent over to fluconazole **OR** B. The patient has an intolerance or hypersensitivity to fluconazole **OR** C. The patient has an FDA labeled contraindication to fluconazole **OR** D. The patient is currently being treated with the requested agent as indicated by ALL of the following: 1. A statement by the prescriber that the patient is currently taking the requested agent **AND** 2. A statement by the prescriber that the patient is currently receiving a positive therapeutic outcome on requested agent **AND** 3. The prescriber states that a change in therapy is expected to be ineffective or cause harm **OR** E. The prescriber has provided documentation that fluconazole cannot be used due to a documented medical condition or comorbid condition that is likely to cause an adverse reaction, decrease ability of the patient to achieve or maintain reasonable functional **OR** B. The patient has another FDA approved indication for the requested agent and route of administration **AND** 2. The patient does NOT have any FDA labeled contraindications to the requested agent **Compendia Allowed:** CMS Approved Compendia **Length of Approval:** 3 months for treatment of vulvovaginal candidiasis, 6 months for recurrent vulvovaginal candidiasis and all other indications NOTE: If Quantity Limit applies, please refer to Quantity Limit Criteria.
Cresemba	**Initial Evaluation** **Cresemba (isavuconazole)** will be approved when BOTH of the following are met: 1. ONE of the following: A. The patient has a diagnosis of invasive aspergillosis **OR** B. The patient has a diagnosis of invasive mucormycosis **OR** C. The patient has another FDA approved indication for the requested agent and route of administration **AND** 2. The patient does NOT have any FDA labeled contraindications to the requested agent **Compendia Allowed:** CMS Approved Compendia **Length of Approval:** 6 months **Renewal Evaluation** **Cresemba (isavuconazole)** will be approved when ALL of the following are met: 1. The patient has been previously approved for the requested agent through the plan's Prior Authorization review process **AND** 2. ONE of the following: A. BOTH of the following: 1. The patient has a diagnosis of invasive aspergillosis **AND** 2. The patient has continued indicators of active disease (e.g., continued radiologic findings, positive cultures, positive serum galactomannan assay) **OR**

Module	Clinical Criteria for Approval
	B. BOTH of the following: 1. The patient has a diagnosis of invasive mucormycosis **AND** 2. The patient has continued indicators of active disease (e.g., continued radiologic findings, direct microscopy findings, histopathology findings, positive cultures, positive serum galactomannan assay) **OR** C. BOTH of the following: 1. The patient has another FDA approved indication or another indication that is supported in compendia for the requested agent and route of administration **AND** 2. The prescriber has submitted information supporting continued use of the requested agent for the requested indication **AND** 3. The patient does NOT have any FDA labeled contraindications to the requested agent **Compendia Allowed:** CMS Approved Compendia **Length of Approval:** 6 months
Noxafil	**Initial Evaluation** **Noxafil (posaconazole)** will be approved when ONE of the following are met: 1. ALL of the following: A. ONE of the following: 1. The patient has a diagnosis of oropharyngeal candidiasis AND ONE of the following: A. The patient's medication history includes itraconazole or fluconazole AND ONE of the following: 1. The patient has had an inadequate response to itraconazole or fluconazole **OR** 2. The prescriber has submitted an evidence-based and peer-reviewed clinical practice guideline supporting the use of the requested agent over itraconazole or fluconazole **OR** B. The patient has an intolerance or hypersensitivity to itraconazole or fluconazole **OR** C. The patient has an FDA labeled contraindication to BOTH fluconazole AND itraconazole **OR** D. The patient is currently being treated with the requested agent as indicated by ALL of the following: 1. A statement by the prescriber that the patient is currently taking the requested agent **AND** 2. A statement by the prescriber that the patient is currently receiving a positive therapeutic outcome on requested agent **AND** 3. The prescriber states that a change in therapy is expected to be ineffective or cause harm **OR** E. The prescriber has provided documentation that BOTH fluconazole AND itraconazole cannot be used due to a documented medical condition or comorbid condition that is likely to cause an adverse reaction, decrease ability of the patient to achieve or maintain reasonable functional ability in performing daily activities or cause physical or mental harm **OR** 2. BOTH of the following: A. The requested agent is prescribed for prophylaxis of invasive Aspergillus or Candida **AND** B. The patient is severely immunocompromised (e.g., hematopoietic stem cell transplant (HSCT) recipients, a hematologic malignancy with prolonged neutropenia from chemotherapy), or is a high-risk solid organ (lung, heart-lung, heart, pancreas, liver, kidney, small bowel) transplant patient **OR** 3. The patient has an infection caused by Scedosporium or Zygomycetes **OR**

Module	Clinical Criteria for Approval
	4. The patient has a diagnosis of invasive Aspergillus AND ONE of the following: A. The patient's medication history includes voriconazole, amphotericin B, or isavuconazole AND ONE of the following: 1. The patient has had an inadequate response to voriconazole, amphotericin B, or isavuconazole **OR** 2. The prescriber has submitted an evidence-based and peer-reviewed clinical practice guideline supporting the use of the requested agent over voriconazole, amphotericin B, or isavuconazole **OR** B. The patient has an intolerance or hypersensitivity to voriconazole, amphotericin B, or isavuconazole **OR** C. The patient has an FDA labeled contraindication to voriconazole, amphotericin B, AND isavuconazole **OR** D. The patient is currently being treated with the requested agent as indicated by ALL of the following: 1. A statement by the prescriber that the patient is currently taking the requested agent **AND** 2. A statement by the prescriber that the patient is currently receiving a positive therapeutic outcome on requested agent **AND** 3. The prescriber states that a change in therapy is expected to be ineffective or cause harm **OR** E. The prescriber has provided documentation that voriconazole, amphotericin B, AND isavuconazole cannot be used due to a documented medical condition or comorbid condition that is likely to cause an adverse reaction, decrease ability of the patient to achieve or maintain reasonable functional ability in performing daily activities or cause physical or mental harm **OR** 5. The patient has another FDA approved indication for the requested agent and route of administration **OR** 6. The patient has another indication that is supported in compendia for the requested agent and route of administration **AND** B. If the patient has an FDA approved indication, then ONE of the following: 1. The patient's age is within FDA labeling for the requested indication for the requested agent **OR** 2. The prescriber has provided information in support of using the requested agent for the patient's age for the requested indication **AND** C. The patient does NOT have any FDA labeled contraindications to the requested agent **OR** 2. If the request is for an oral liquid form of a medication, then BOTH of the following: A. The patient has an FDA approved indication **AND** B. The patient uses an enteral tube for feedings or medication administration **Compendia Allowed:** CMS Approved Compendia **Length of Approval:** 1 month for oropharyngeal candidiasis, 6 months for all other indications **Renewal Evaluation** **Noxafil (posaconazole)** will be approved when BOTH of the following are met: 1. The patient has been previously approved for the requested agent through the plan's Prior Authorization review process (NOTE: See initial criteria for a diagnosis of oropharyngeal candidiasis) **AND** 2. ONE of the following: A. BOTH of the following: 1. ONE of the following: A. BOTH of the following:

Module	Clinical Criteria for Approval
	1. The requested agent is being prescribed for prophylaxis of invasive Aspergillus or Candida **AND** 2. The patient continues to be severely immunocompromised (e.g., hematopoietic stem cell transplant (HSCT) recipients, a hematologic malignancy with prolonged neutropenia from chemotherapy), or is a high-risk solid organ (lung, heart-lung, heart, pancreas, liver, kidney, small bowel) transplant patient **OR** B. BOTH of the following: 1. The patient has a serious infection caused by Scedosporium or Zygomycetes **AND** 2. The patient has continued indicators of active disease (e.g., continued radiologic findings, positive cultures, positive serum galactomannan assay for Aspergillus) **OR** C. BOTH of the following: 1. The patient has a diagnosis of invasive Aspergillus **AND** 2. The patient has continued indicators of active disease (e.g., continued radiologic findings, positive cultures, positive serum galactomannan assay for Aspergillus) **OR** D. BOTH of the following: 1. The patient has another FDA approved indication or another indication that is supported in compendia for the requested agent and route of administration **AND** 2. The prescriber has submitted information supporting continued use of the requested agent for the requested indication **AND** 2. The patient does NOT have any FDA labeled contraindications to the requested agent **OR** B. If the request is for an oral liquid form of a medication, then BOTH of the following: 1. The patient has an FDA approved indication **AND** 2. The patient uses an enteral tube for feedings or medication administration **Compendia Allowed:** CMS Approved Compendia **Length of Approval:** 6 months
Vfend	**Initial Evaluation** **Vfend (voriconazole)** will be approved when ONE of the following are met: 1. ALL of the following: A. ONE of the following: 1. The patient has a diagnosis of invasive Aspergillus **OR** 2. BOTH of the following: A. The requested agent is being prescribed for prophylaxis of invasive Aspergillus or Candida **AND** B. The patient is severely immunocompromised (e.g., hematopoietic stem cell transplant (HSCT) recipients, a hematologic malignancy with prolonged neutropenia from chemotherapy), or is a high-risk solid organ (lung, heart-lung, heart, pancreas, liver, kidney, small bowel) transplant patient **OR** 3. The patient has a diagnosis of esophageal candidiasis, candidemia, or other deep tissue Candida infection AND ONE of the following: A. The patient's medication history includes fluconazole AND ONE of the following: 1. The patient has had an inadequate response to fluconazole **OR**

Module	Clinical Criteria for Approval
	2. The prescriber has submitted an evidence-based and peer-reviewed clinical practice guideline supporting the use of the requested agent over fluconazole **OR** B. The patient has an intolerance or hypersensitivity to fluconazole **OR** C. The patient has an FDA labeled contraindication to fluconazole **OR** D. The patient is currently being treated with the requested agent as indicated by ALL of the following: 1. A statement by the prescriber that the patient is currently taking the requested agent **AND** 2. A statement by the prescriber that the patient is currently receiving a positive therapeutic outcome on requested agent **AND** 3. The prescriber states that a change in therapy is expected to be ineffective or cause harm **OR** E. The prescriber has provided documentation that fluconazole cannot be used due to a documented medical condition or comorbid condition that is likely to cause an adverse reaction, decrease ability of the patient to achieve or maintain reasonable functional ability in performing daily activities or cause physical or mental harm **OR** 4. The patient has a serious infection caused by Scedosporium or Fusarium species **OR** 5. The patient has a diagnosis of blastomycosis AND ONE of the following: A. The patient's medication history includes itraconazole AND ONE of the following: 1. The patient has had an inadequate response to itraconazole **OR** 2. The prescriber has submitted an evidence-based and peer-reviewed clinical practice guideline supporting the use of the requested agent over itraconazole **OR** B. The patient has an intolerance or hypersensitivity to itraconazole **OR** C. The patient has an FDA labeled contraindication to itraconazole **OR** D. The patient is currently being treated with the requested agent as indicated by ALL of the following: 1. A statement by the prescriber that the patient is currently taking the requested agent **AND** 2. A statement by the prescriber that the patient is currently receiving a positive therapeutic outcome on requested agent **AND** 3. The prescriber states that a change in therapy is expected to be ineffective or cause harm **OR** E. The prescriber has provided documentation that itraconazole cannot be used due to a documented medical condition or comorbid condition that is likely to cause an adverse reaction, decrease ability of the patient to achieve or maintain reasonable functional ability in performing daily activities or cause physical or mental harm **OR** 6. The patient has another FDA approved indication for the requested agent and route of administration **OR** 7. The patient has another indication that is supported in compendia for the requested agent and route of administration **AND** B. If the patient has an FDA labeled indication, then ONE of the following: 1. The patient's age is within FDA labeling for the requested indication for the requested agent **OR** 2. The prescriber has provided information in support of using the requested agent for the patient's age for the requested indication **AND** C. The patient does NOT have any FDA labeled contraindications to the requested agent **OR** 2. If the request is for an oral liquid form of a medication, then BOTH of the following:

Module	Clinical Criteria for Approval
	A. The patient has an FDA approved indication **AND** B. The patient uses an enteral tube for feedings or medication administration **Compendia Allowed:** CMS Approved Compendia **Length of Approval:** 1 month for esophageal candidiasis, 6 months for all other indications **Renewal Evaluation** **Vfend (voriconazole)** will be approved when BOTH of the following are met: 1. The patient has been previously approved for the requested agent through the plan's Prior Authorization review process **AND** 2. ONE of the following: A. ALL of the following: 1. ONE of the following: A. BOTH of the following: 1. The patient has a diagnosis of invasive Aspergillus **AND** 2. The patient has continued indicators of active disease (e.g., continued radiologic findings, positive cultures, positive serum galactomannan assay for Aspergillus) **OR** B. BOTH of the following: 1. The requested agent is being prescribed for prophylaxis of invasive Aspergillus or Candida **AND** 2. The patient is severely immunocompromised (e.g., hematopoietic stem cell transplant (HSCT) recipients, a hematologic malignancy with prolonged neutropenia from chemotherapy), or is a high-risk solid organ (lung, heart-lung, heart, pancreas, liver, kidney, small bowel) transplant patient **OR** C. BOTH of the following: 1. The patient has a diagnosis of esophageal candidiasis, candidemia, or other deep tissue Candida infection **AND** 2. The patient has continued indicators of active disease (e.g., continued radiologic findings, positive cultures, positive serum galactomannan assay for Aspergillus) **OR** D. BOTH of the following: 1. The patient has a serious infection caused by Scedosporium or Fusarium species **AND** 2. The patient has continued indicators of active disease (e.g., continued radiologic findings, positive cultures, positive serum galactomannan assay for Aspergillus) **OR** E. BOTH of the following: 1. The patient has a diagnosis of blastomycosis **AND** 2. The patient has continued indicators of active disease (e.g., continued radiologic findings, positive cultures, positive serum galactomannan assay for Aspergillus) **OR** F. BOTH of the following: 1. The patient has another FDA approved indication or another indication that is supported in compendia for the requested agent and route of administration **AND** 2. The prescriber has submitted information supporting continued use of the requested agent for the intended diagnosis **AND** 2. The patient does NOT have any FDA labeled contraindications to the requested agent **OR** B. If the request is for an oral liquid form of a medication, then BOTH of the following:

Module	Clinical Criteria for Approval
	1. The patient has an FDA approved indication **AND** 2. The patient uses an enteral tube for feedings or medication administration **Compendia Allowed:** CMS Approved Compendia **Length of Approval:** 1 month for esophageal candidiasis, 6 months for all other indications
Vivjoa	**Vivjoa (oteseconazole)** will be approved when BOTH of the following are met: 1. ONE of the following: A. ALL of the following: 1. The patient has a diagnosis of recurrent vulvovaginal candidiasis **AND** 2. The patient has experienced greater than or equal to 3 episodes of vulvovaginal candidiasis (VVC) in a 12 months period **AND** 3. ONE of the following: A. The patient's medication history includes fluconazole for the current infection AND ONE of the following: 1. The patient has had an inadequate response to fluconazole for the current infection **OR** 2. The prescriber has submitted an evidence-based and peer-reviewed clinical practice guideline supporting the use of the requested agent over to fluconazole for the current infection **OR** B. The patient has an intolerance or hypersensitivity to fluconazole **OR** C. The patient has an FDA labeled contraindication to fluconazole **OR** D. The patient will be using fluconazole as part of the combination dosing (fluconazole with Vivjoa) for the current infection **OR** E. The patient is currently being treated with the requested agent as indicated by ALL of the following: 1. A statement by the prescriber that the patient is currently taking the requested agent **AND** 2. A statement by the prescriber that the patient is currently receiving a positive therapeutic outcome on requested agent **AND** 3. The prescriber states that a change in therapy is expected to be ineffective or cause harm **OR** F. The prescriber has provided documentation that fluconazole cannot be used due to a documented medical condition or comorbid condition that is likely to cause an adverse reaction, decrease ability of the patient to achieve or maintain reasonable functional **OR** B. The patient has another FDA approved indication for the requested agent and route of administration **OR** C. The patient has another indication that is supported in compendia for the requested agent and route of administration **AND** 2. The patient does NOT have any FDA labeled contraindications to the requested agent **Compendia Allowed:** CMS Approved Compendia **Length of Approval:** 4 months NOTE: If Quantity Limit applies, please refer to Quantity Limit Criteria.

QUANTITY LIMIT CLINICAL CRITERIA FOR APPROVAL

Module	Clinical Criteria for Approval
Brexafemme, Vivjoa	**Quantity Limit for the Target Agent(s)** will be approved when ONE of the following is met: 1. The requested quantity (dose) does NOT exceed the program quantity limit **OR**

Module	Clinical Criteria for Approval
	2. ALL of the following: A. The requested quantity (dose) exceeds the program quantity limit **AND** B. The requested quantity (dose) does NOT exceed the maximum FDA labeled dose for the requested indication **AND** C. The requested quantity (dose) cannot be achieved with a lower quantity of a higher strength that does NOT exceed the program quantity limit **OR** 3. ALL of the following: A. The requested quantity (dose) exceeds the program quantity limit **AND** B. The requested quantity (dose) exceeds the maximum FDA labeled dose for the requested indication **AND** C. The prescriber has provided information in support of therapy with a higher dose for the requested indication **Length of Approval**: Brexafemme: 3 months for treatment of vulvovaginal candidiasis; 6 months for recurrent vulvovaginal candidiasis; 6 months for all other indications Vivjoa: 4 months