Clinical Policy: Voriconazole (Vfend)

Reference Number: AZ.CP.PMN.1003
Effective Date: 11.16.16
Last Review Date: 11.20
Line of Business: Arizona Medicaid (AzCH-CCP and Care1st) Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

Description

Voriconazole (Vfend®) is an azole antifungal drug.

FDA approved indication

Vfend is indicated for treatment of:

- Invasive aspergillosis
- Serious infections caused by *Scedosporium apiospermum* and *Fusarium spp*., including *Fusarium solani*, in patients intolerant of, or refractory to, other therapy
- Candidemia (nonneutropenics) and disseminated candidiasis in skin, abdomen, kidney, bladder wall, and wounds
- Esophageal candidiasis

Policy/Criteria

Provider must submit documentation (which may include office chart notes and lab results) supporting that member has met all approval criteria

It is the policy of health plans affiliated with Arizona Complete Health-Complete Care Plan and Care 1st that Vfend is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Susceptible Fungal Infections

1. Request meets one of the following:
   a. Authorization is requested by an infectious disease (ID), transplant, or oncology specialist physician;
   b. Discharge from hospital-continuation of therapy;
   c. Definitive diagnosis of invasive aspergillosis;
   d. Empiric therapy of aspergillosis in febrile neutropenic transplant patients (usually bone marrow);
   e. Prophylaxis therapy for preventing aspergillosis in patients receiving chemotherapy for acute myeloid leukemia or in allogeneic hematopoietic cell transplant (HCT) recipients;
   f. Definitive diagnosis or a strong clinical suspicion of infection caused by *Aspergillis* species, *Fusarium* species or *Scedosporium apiospermum*;
   g. For candidemia in nonneutropenic patients and the following *Candida* infections: disseminated infections in skin and infections in abdomen, kidney, bladder wall, and wounds, and patient must have tried and failed or been intolerant to a course

of fluconazole (or caspofungin if *C. glabrata* is suspected) unless culture and sensitivity tests dictate otherwise;

h. For esophageal candidiasis, member must have tried and failed or been intolerant to a course of fluconazole;

2. Dose does not exceed 400 mg every 12 hours.

Approval duration: Up to 12 weeks

B. Other diagnoses/indications

1. Refer to AZ.CP.PMN.53 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized)

II. Continued Therapy

A. Susceptible Fungal Infections(must meet all)**:**

1. Currently receiving medication via a health plan affiliated with Arizona Complete Health Complete Care Plan or member has previously met initial approval criteria;
2. Documentation of positive response to therapy [labs, sign/symptom reduction, etc.];
3. If request is for a dose increase, new dose does not exceed 400 mg every 12 hours

Approval duration: Up to 12 weeks

B. Other diagnoses/indications (must meet 1 or 2)**:**

1. Currently receiving medication via Arizona Complete Health Complete Care Plan benefit and documentation supports positive response to therapy.
   Approval duration: Duration of request or 12 months (whichever is less); or
2. Refer to AZ.CP.PMN.53 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

III. Diagnoses/Indications for which coverage is NOT authorized:

A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off-label use policy – AZ.CP.PMN.53 or evidence of coverage documents;

B. Patient currently on rifampin, rifabutin, carbamazepine and long-acting barbiturates, sirolimus, terfenadine, astemizole, cisapride, pimozide, efavirenz, ritonavir, quinidine, St. John's Wort, or ergot alkaloids

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

N/A

Appendix B: General Information

- Definitive diagnosis of invasive aspergillosis depends upon the demonstration of the organism in tissue. In the appropriate clinical setting of pulmonary infiltrates in a patient who is neutropenic or immunosuppressed, visualization of the characteristic

fungi is commonly performed using Gomori methenamine silver stain, Calcofluor or a positive culture from sputum, needle biopsy, or bronchoalveolar lavage (BAL) fluid.

- After bone marrow transplantation a positive *Aspergillus* culture from sputum has a 95% positive predictive value for invasive disease.
- Pulmonary or infectious disease consultation in patients suspected of having invasive aspergillosis or chronic necrotizing *Aspergillus* pneumonia may be helpful in obtaining a diagnosis.
- Visual disturbances have been reported in up to 18.7% of study patients. The effect of VFEND is not known if treatment continues after 28 days; if necessary visual monitoring should occur.
- Efficacy and safety studies have not been performed in patients less than 2 years of age.
- Voriconazole can cause fetal harm when administered to fetal women.
- Severe cutaneous adverse reactions (SCARs), such as Stevens-Johnson syndrome (SJS), toxic epidermal necrolysis (TEN), and drug reaction with eosinophilia and systemic symptoms (DRESS), which can be life-threatening or fatal, have been reported during treatment with VFEND. If a patient develops a severe cutaneous adverse reaction, VFEND should be discontinued.
- Use half the maintenance dose in patients with **mild to moderate hepatic impairment**
- Avoid IV administration in patients with **moderate to severe renal impairment** (CrCl < 50 mL/min

Appendix C: Therapeutic Alternatives

Drug	Dosing Regimen	Dose/Limit/Maximum Dose
Treatment of Aspergillosis		
Amphotericin B	Amphotericin: 0.5-1.5 mg/kg/d Abelcet: 5 mg/kg/d AmBisome: 3-5 mg/kg/d Inhaled amphotericin for *Aspergillus* prophylaxis or colonization: 50 mg/d preceded by albuterol	
Cresemba® (isavuconazole)	Loading dose: 372 mg IV or 2 capsules (372 mg) PO every 8 hours for 6 doses (48 hours) Maintenance dose (start 12 to 24 hours after the last loading dose): 372 mg IV or 2 capsules (372 mg) PO once daily	1116 mg/day
Noxafil® (posaconazole)	Oral: Suspension: 200mg 3 times daily	

	Tablet: 200mg twice daily for 1 day then 300mg daily IV: 200mg twice daily for 1 day then 300mg daily	
Prophylaxis for Aspergillosis		
Noxafil® (posaconazole)	Oral: Suspension: 200mg 3 times daily Tablet: 200mg twice daily for 1 day then 300mg daily IV: 200mg twice daily for 1 day then 300mg daily	
Treatment of esophageal candidiasis		
Diflucan® (fluconazole)	Esophageal candidiasis: 200 mg Day 1 followed by 100 mg daily for 14-21 days and 2 weeks after resolution of symptoms	400 mg/day
Sporanox (itraconazole)	Oral suspension: 100-200 mg/day on an empty stomach for 2-4 weeks	Limited data beyond 6 months

Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) when the drug is available by both brand and generic.

Appendix D: Contraindications/Boxed Warnings

- Hypersensitivity to voriconazole or its excipients
- Coadministration with cisapride, pimozide or quinidine, sirolimus due to risk of serious adverse reactions
- Coadministration with rifampin, carbamazepine, long-acting barbiturates, efavirenz, ritonavir, rifabutin, ergot alkaloids, and St. John's Wort due to risk of loss of efficacy

V. Dosage and Administration

Indication	Dosing Regimen IV	Dosing Regimen PO	Maximum Dose
Invasive Aspergillosis	6 mg/kg q 12 hrs x 24 hrs. Then 4 mg/kg q 12 hrs	200 mg q 12 hrs	Loading: 6 mg/kg x 2 doses Maintenance 4 mg/kg
Aspergillis Prophylaxis	6 mg/kg q 12 hrs x 24 hrs. Then 4 mg/kg q 12 hrs	200 mg q 12 hrs	Loading: 6 mg/kg x 2 doses Maintenance 4 mg/kg

Candidemia in non-neutropenics and other deep tissue *Candida* infections	6 mg/kg q 12 hrs x 24 hrs. Then 3-4 mg/kg q 12 hrs	200 mg q 12 hrs	Loading: 6 mg/kg x 2 doses Maintenance 4 mg/kg
Scedosporiosis and Fusariosis	6 mg/kg q 12 hrs x 24 hrs. Then 4 mg/kg q 12 hrs	200 mg q 12 hrs	Loading: 6 mg/kg x 2 doses Maintenance 4 mg/kg
Esophageal Candidiasis	Not evaluated	200 mg q 12 hrs	400 mg daily

Adults and pediatric patients weighing less than 40 kg: PO maintenance dose 100 or 150 mg q 12 hrs

VI. Product Availability

Drug	Availability
Voriconazole	Tablets: 50 and 200 mg
Voriconazole	Suspension: 40 mg/ml
Voriconazole	Injection: 200 mg
Vfend I.V.	Powder for IV Soln: 200 mg
Vfend	Powder for oral suspension: 40 mg
Vfend	Tablets: 50 and 200 mg

VII. References

1. Vfend. Prescribing information, Pfizer. September, 2020.
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6. Stevens DA, Kan VL, Judson MA: Practice guidelines for diseases caused by Aspergillus. Infectious Diseases Society of America. Clin Infect Dis 2000 Apr; 30(4): 696-709
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9. Galgiani JN, Ampel NM, Catanzaro A, et al: 2016 Infectious Diseases Society of America (IDSA) Clinical practice guidelines for the treatment of coccidioidomycocis. Clin Infect Dis 2105 September; 63(6): e112-146.
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12.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Converted to new template; minor changes to verbiage and grammar. References updated.	07.08.17	11.17
Updated references with addition of IDSA treatment guidelines	09.11.18	
Updated section III to include additional meds from the package insert. Removed prophylaxis of fungal infection from section III so that prophylaxis therapy is allowed. Updated therapeutic alternatives for aspergillosis. Updated references. Updated section IA to include prophylaxis therapy. Contraindications added. Policy renumbered from AZ.CP.PHAR.32 to AZ.CP.PMN.1003	08.29.19	
Updated references and added to general information section Appendix B the following: Severe cutaneous adverse reactions (SCARs), such as Stevens-Johnson syndrome (SJS), toxic epidermal necrolysis (TEN), and drug reaction with eosinophilia and systemic symptoms (DRESS), which can be life-threatening or fatal, have been reported during treatment with VFEND. If a patient develops a severe cutaneous adverse reaction, VFEND should be discontinued.	09.19.20	10.20
Added Care1st logo. Added verbiage to specify that criteria also applies to Care1st.	5.10.21	04.21

Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in

developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. "Health Plan" means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan's affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

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Note: For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence.

Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.

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