Drug Coverage Policy

Effective Date……6/1/2025
Coverage Policy Number……IP0306
Policy Title…… Voriconazole (Oral)

Antifungals – Voriconazole (Oral)

- Vfend® (voriconazole tablets and oral suspension - Roerig/Pfizer, generic)

INSTRUCTIONS FOR USE
The following Coverage Policy applies to health benefit plans administered by Cigna Companies. Certain Cigna Companies and/or lines of business only provide utilization review services to clients and do not make coverage determinations. References to standard benefit plan language and coverage determinations do not apply to those clients. Coverage Policies are intended to provide guidance in interpreting certain standard benefit plans administered by Cigna Companies. Please note, the terms of a customer's particular benefit plan document [Group Service Agreement, Evidence of Coverage, Certificate of Coverage, Summary Plan Description (SPD) or similar plan document] may differ significantly from the standard benefit plans upon which these Coverage Policies are based. For example, a customer's benefit plan document may contain a specific exclusion related to a topic addressed in a Coverage Policy. In the event of a conflict, a customer's benefit plan document always supersedes the information in the Coverage Policies. In the absence of a controlling federal or state coverage mandate, benefits are ultimately determined by the terms of the applicable benefit plan document. Coverage determinations in each specific instance require consideration of 1) the terms of the applicable benefit plan document in effect on the date of service; 2) any applicable laws/regulations; 3) any relevant collateral source materials including Coverage Policies and; 4) the specific facts of the particular situation. Each coverage request should be reviewed on its own merits. Medical directors are expected to exercise clinical judgment where appropriate and have discretion in making individual coverage determinations. Where coverage for care or services does not depend on specific circumstances, reimbursement will only be provided if a requested service(s) is submitted in accordance with the relevant criteria outlined in the applicable Coverage Policy, including covered diagnosis and/or procedure code(s). Reimbursement is not allowed for services when billed for conditions or diagnoses that are not covered under this Coverage Policy (see "Coding Information" below). When billing, providers must use the most appropriate codes as of the effective date of the submission. Claims submitted for services that are not accompanied by covered code(s) under the applicable Coverage Policy will be denied as not covered. Coverage Policies relate exclusively to the administration of health benefit plans. Coverage Policies are not recommendations for treatment and should never be used as treatment guidelines. In certain markets, delegated vendor guidelines may be used to support medical necessity and other coverage determinations.

OVERVIEW
Voriconazole, an azole antifungal, is indicated in patients ≥ 2 years of age for the following uses:[1]

- **Candidemia,** in non-neutropenic patients and other deep tissue *Candida* infections.
- **Esophageal candidiasis.**
- **Invasive aspergillosis.**

- ***Scedosporium apiospermum*** (asexual form of *Pseudallescheria boydii*) and ***Fusarium spp.*** (including *Fusarium solani*), in patients intolerant of, or refractory to, other therapy.

The duration of voriconazole therapy is varied, ranging from a median duration of 15 days for esophageal candidiasis to 76 days for invasive aspergillosis.[1]

Guidelines
The Infectious Diseases Society of America (IDSA) recommends voriconazole as a treatment option for the treatment or prevention of invasive aspergillosis (2016) and for candidemia and candidiasis.[2,3] Use of voriconazole for treatment of infections caused by *Candida* spp and *Aspergillus* spp are also noted in the National Comprehensive Cancer Network (NCCN) guidelines for the prevention and treatment of cancer-related infections (version 3.2024 – September 23, 2024).[4] The IDSA guidelines for management of candidiasis note voriconazole has demonstrated effectiveness for candidemia and candidiasis, including mucosal and invasive candidiasis (e.g., *Candida* intravascular infections, including endocarditis and infections of implantable cardiac devices; fluconazole-refractory oropharyngeal candidiasis; *Candida* endophthalmitis).[3] Voriconazole represents an option in the first-line treatment of infections due to *Scedosporium* spp and *Fusarium* spp.[5]

NCCN guidelines also notes voriconazole as a treatment option for the prevention of fungal infections in patients with significant graft-versus-host disease (GVHD) [especially grade 3/4] who are receiving immunosuppressive therapy; treatment should continue until resolution of significant GVHD.[4] Voriconazole is also a treatment option for these groups of patients with neutropenia: patients with myelodysplastic syndrome, patients with acute myeloid leukemia, and patients who are allogeneic hematopoietic cell transplant recipients; treatment should continue until resolution of neutropenia.

The IDSA guidelines for the management of blastomycosis (2008; archived) note voriconazole as an option for the treatment of central nervous system blastomycosis.[6]

The Guidelines for Prevention and Treatment of Opportunistic Infections in Adults and Adolescents with Human Immunodeficiency Virus (HIV) Infections (last updated December 2024) recommend voriconazole as a treatment option for the prophylaxis/treatment of various fungal infections (e.g., candidiasis, histoplasmosis, coccidioidomycosis, and talaromycosis) in patients with HIV.[7]

Coverage Policy

Prior Authorization is recommended for prescription benefit coverage of Vfend tablets and oral suspension and generic voriconazole tablets and oral suspension. When clinically appropriate, the patient is directed to try the generic voriconazole prior to brand Vfend. All approvals are provided for the duration noted below. In cases where the approval is authorized in months, 1 month is equal to 30 days.

Vfend/Voriconazole is considered medically necessary when the following criteria are met:

FDA-Approved Indications

1. ***Aspergillus* Infection – Treatment.** Approve for 3 months if the patient meets the following:
   A) Preferred product criteria are met for the product as listed in the below table.

2. ***Candida* (Systemic) Infection – Treatment.** Approve for 3 months if the patient meets the following:
   A) Preferred product criteria are met for the product as listed in the below table.

3. **Esophageal Candidiasis – Treatment.** Approve for 3 months if the patient meets the following:
   A) Preferred product criteria are met for the product as listed in the below table.

4. ***Fusarium* Infection – Treatment.** Approve for 3 months if the patient meets the following:
   A) Preferred product criteria are met for the product as listed in the below table.

5. ***Scedosporium apiospermum* Infection – Treatment.** Approve for 3 months if the patient meets the following:
   A) Preferred product criteria are met for the product as listed in the below table.

Other Uses with Supportive Evidence

6. ***Aspergillus* Infection – Prophylaxis.** Approve for 6 months if the patient meets the following:
   A) Preferred product criteria are met for the product as listed in the below table.

7. **Blastomycosis – Treatment.** Approve for 3 months if the patient meets the following:
   A) Preferred product criteria are met for the product as listed in the below table.

8. ***Candida* Endophthalmitis – Treatment.** Approve for 3 months if the patient meets the following:
   A) Preferred product criteria are met for the product as listed in the below table.

9. **Fungal Infection (Systemic) in a Patient with Cancer and Neutropenia – Prophylaxis.** Approve for 6 months if the patient meets the following:
   Note: Examples of cancers predisposing neutropenic patients to risk of fungal infections include: myelodysplastic syndrome, acute myeloid leukemia, patients post-allogeneic hematopoietic cell transplant
   A) Preferred product criteria are met for the product as listed in the below table.

10. **Fungal Infection (Systemic) in a Patient with Graft-versus-Host Disease - Prophylaxis**. Approve for 6 months if the patient meets the following:
    A) Preferred product criteria are met for the product as listed in the below table.

11. **Fungal Infection (Systemic) in a Patient with Human Immunodeficiency Virus (HIV) – Prophylaxis or Treatment.** Approve for 6 months if the patient meets the following:
    A) Preferred product criteria are met for the product as listed in the below table.

12. **Oropharyngeal Candidiasis (Fluconazole-Refractory) – Treatment.** Approve for 3 months if the patient meets the following:
    A) Preferred product criteria are met for the product as listed in the below table.

13. **Fungal Infection (Systemic) that is Susceptible to Voriconazole – Treatment.** Approve for 3 months if the patient meets the following:
    A) Preferred product criteria are met for the product as listed in the below table.

14. **Patient is Currently Receiving Voriconazole.** Approve for 3 months to complete the course of therapy if the patient meets the following:

A) Preferred product criteria are met for the product as listed in the below table.

Employer Plans:

Product	Criteria
Vfend (voriconazole tablets and oral suspension)	Patient meets **BOTH** of the following (1 and 2): 1. Patient has tried the corresponding generic voriconazole product (tablet or oral suspension); AND 2. Patient cannot take the generic voriconazole product due to a formulation difference in the inactive ingredient(s) [e.g., difference in dyes, fillers, preservatives] between the brand and the bioequivalent generic product, which per the prescriber, would result in a significant allergy or serious adverse reaction.

Individual and Family Plans:

Product	Criteria
Vfend (voriconazole tablets and oral suspension)	Patient meets **BOTH** of the following (1 and 2): 1. Patient has tried the corresponding generic voriconazole product (tablet or oral suspension); AND 2. Patient cannot take the generic voriconazole product due to a formulation difference in the inactive ingredient(s) [e.g., difference in dyes, fillers, preservatives] between the brand and the bioequivalent generic product, which per the prescriber, would result in a significant allergy or serious adverse reaction.

When coverage is available and medically necessary, the dosage, frequency, duration of therapy, and site of care should be reasonable, clinically appropriate, and supported by evidence-based literature and adjusted based upon severity, alternative available treatments, and previous response to therapy.

Receipt of sample product does not satisfy any criteria requirements for coverage.

Voriconazole for any other use is considered not medically necessary. Criteria will be updated as new published data are available.

References

1. Vfend® tablet and oral suspension [prescribing information]. New York, NY: Roerig/Pfizer; October 2022.
2. 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 Infect Dis.* 2016;63(4): e1-e60.
3. Pappas PG, Kauffman CA, Andes DR, et al. Clinical practice guidelines for the management of candidiasis: 2016 update by the Infectious Diseases Society of America. *Clin Infect Dis*. 2016;62(4): e1-50.
4. The NCCN Prevention and Treatment of Cancer-Related Infections Clinical Practice Guidelines in Oncology (version 3.2024 – September 23, 2024). ©2024 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on February 27, 2025.
5. Tortorano AM, Richardson M, Roilides E, et al. European Society for Clinical Microbiology and Infectious Diseases (ESCMID) and European Confederation of Medical Mycology (ECMM) joint

guidelines on diagnosis and management of hyalohyphomycosis: Fusarium spp., Scedosporium spp. and others. *Clin Microb Infect*. 2014;20(Suppl 3): 37-46.
6. Chapman SW, Dismukes WE, Proia LA, et al. Clinical practice guidelines for the management of blastomycosis: 2008 update by the Infectious Diseases Society of America (Archived). *Clin Infect Dis*. 2008; 46:1801-1812.
7. Panel on Opportunistic Infections in HIV-Infected Adults and Adolescents. Guidelines for the prevention and treatment of opportunistic infections in HIV-infected adults and adolescents: recommendations from the Centers for Disease Control and Prevention, the National Institutes of Health, and the HIV Medicine Association of the Infectious Diseases Society of America. Available at: https://clinicalinfo.hiv.gov/sites/default/files/guidelines/documents/adult-adolescent-oi/guidelines-adult-adolescent-oi.pdf. Last updated December 16, 2024. Accessed on February 27, 2025.

Revision Details

Type of Revision	Summary of Changes	Date
Annual Revision	**Policy Name: Updated** title **from** "Voriconazole (Oral)" **to** "Antifungals – Voriconazole (Oral)." **Added** the following indications with an initial treatment duration of 3 months: *Candida* (Systemic) Infection – Treatment, Esophageal Candidiasis – Treatment, Candida Endophthalmitis – Treatment, and Oropharyngeal Candidiasis (Fluconazole-Refractory) – Treatment, and Fungal Infection (Systemic) that is Susceptible to Voriconazole – Treatment. **Added** "Note: Examples of cancers predisposing neutropenic patients to risk of fungal infections include: myelodysplastic syndrome, acute myeloid leukemia, patients post-allogeneic hematopoietic cell transplant" under Fungal Infection (Systemic) in a Patient with Cancer and Neutropenia – Prophylaxis. **Added** preferred product requirement criteria table for all indications for both Employer Plans and Individual and Family Plans. **Updated** initial approval duration from 6 months to 3 months for the following indications: Aspergillus Infection – Treatment, *Fusarium* Infection – Treatment, *Scedosporium apiospermum* Infection – Treatment, Blastomycosis – Treatment. **Updated** "Continuation of Therapy for Individual Currently Receiving Intravenous Voriconazole or Oral Voriconazole (Tablets or Oral Suspension) to Complete a Course of Therapy" to "Patient is Currently Receiving Voriconazole." and updated the duration of therapy to 3 months for patients Currently Receiving Voriconazole. **Removed** the following indication: Treatment of Invasive or Severe *Candida* Infections (for example, abdomen, bladder wall, candidemia, endophthalmitis, esophageal, kidney,	11/01/2024

	oropharyngeal, or skin) when there is failure, intolerance, or contraindication to fluconazole. **Removed** the following indications: Treatment of Coccidioidomycosis, Histoplasmosis, or Cryptococcosis when there is failure, intolerance, or contraindication to either fluconazole or itraconazole.	
Early Annual Revision	No criteria changes.	6/1/2025

The policy effective date is in force until updated or retired.

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