

Rezzayo (rezafungin)

Disclaimer

Clinical guidelines are developed and adopted to establish evidence-based clinical criteria for utilization management decisions. Clinical guidelines are applicable according to policy and plan type. The Plan may delegate utilization management decisions of certain services to third parties who may develop and adopt their own clinical criteria.

Coverage of services is subject to the terms, conditions, and limitations of a member's policy, as well as applicable state and federal law. Clinical guidelines are also subject to in-force criteria such as the Centers for Medicare & Medicaid Services (CMS) national coverage determination (NCD) or local coverage determination (LCD) for Medicare Advantage plans. Please refer to the member's policy documents (e.g., Certificate/Evidence of Coverage, Schedule of Benefits, Plan Formulary) or contact the Plan to confirm coverage.

Summary

Candidemia and invasive candidiasis (IC) are serious infections caused by the invasion of *Candida* species into the bloodstream and deep tissues. These infections predominantly affect immunocompromised individuals and those with significant comorbidities. Candidemia is associated with high morbidity and mortality rates, with a conservative estimate of approximately 70% all-cause mortality in patients receiving no or inadequate treatment.

The current standard of care for candidemia/IC involves the use of systemic antifungal therapy in combination with control of the infection source, whenever possible. Echinocandins, including caspofungin, micafungin, and anidulafungin, are considered the first-line initial therapy for these infections, except for certain cases involving the central nervous system, urinary tract, or eyes. These echinocandins are administered intravenously on a daily basis. Alternative treatment options include azole drugs and amphotericin B. Typically, patients receive intravenous antifungal therapy initially for 3 to 5 days, followed by a switch to an oral formulation upon clinical improvement. The total duration of

treatment usually extends for at least 2 weeks after the clearance of *Candida* species from the blood in the case of candidemia, or after achieving adequate source control and clinical response in the case of invasive candidiasis. However, most patients are transitioned to oral azole therapy once they become clinically stable. It is important to note that the only available oral stepdown therapies belong to the azole class of antifungals. Therefore, patients who are intolerant to azoles, have concomitant medications with significant drug-drug interactions, or are infected with azole-resistant *Candida* species must continue receiving daily intravenous antifungal therapy for the entire duration of treatment.

In the context of treating candidemia and invasive candidiasis, REZZAYO™ (rezafungin for injection) has emerged as a potential treatment option. It is an echinocandin antifungal indicated for patients 18 years of age or older who have limited or no alternative options for these infections.

- The approval of this indication is based on limited clinical safety and efficacy data specific to REZZAYO.
- It is important to note that REZZAYO has not been studied in patients with endocarditis, osteomyelitis, and meningitis caused by *Candida*.
- Prior to initiating antifungal therapy, it is recommended to obtain specimens for culture and other laboratory data, including histopathology and non-culture diagnostics. While therapy can be initiated before the test results are known, it is essential to adjust the antifungal treatment based on the results once they become available.

Definitions

“**Candidemia**” refers to the presence of *Candida* species, specifically yeast, in the bloodstream. It is a bloodstream infection caused by the invasion of *Candida* fungi.

“**Chorioretinitis**” is an inflammation of the choroid and retina, the tissues at the back of the eye. It can be caused by various factors, including infections such as *Candida*, leading to potential vision loss if left untreated.

“**Endocarditis**” is an inflammation of the inner lining of the heart chambers and heart valves, known as the endocardium. It is typically caused by a bacterial or fungal infection, including *Candida*, that affects the heart.

“**Endophthalmitis**” is a severe inflammation of the intraocular tissues, specifically the vitreous and aqueous humor of the eye. It can occur as a result of an infection, including fungal infections like *Candida*, and can lead to significant visual impairment or loss.

“**Invasive candidiasis**” refers to the invasion of Candida fungi into deep tissues and organs, beyond the bloodstream. It typically occurs in individuals with compromised immune systems and can affect various organs, leading to serious complications.

“**Meningitis**” is an inflammation of the protective membranes covering the brain and spinal cord, known as the meninges. It can be caused by different pathogens, including Candida, and is characterized by symptoms such as fever, headache, neck stiffness, and altered mental status.

“**Osteomyelitis**” is an infection of the bone and bone marrow, usually caused by bacteria but can also be caused by fungi like Candida. It results in inflammation, pain, and can lead to bone destruction if not treated promptly.

Clinical Indications

The Plan considers **Rezzayo (rezafungin)** medically necessary when **ALL** of the following criteria are met:

1. The medication is prescribed by or in consultation with an infectious disease specialist; **AND**
2. The member is 18 years of age or older; **AND**
3. Rezzayo (rezafungin) is being requested for **ONE** of the following:
 - a. empiric antifungal therapy of suspected invasive candidiasis for a critically ill non-neutropenic member meeting **BOTH** of the following:
 - i. with fever and no other known cause; **and**
 - ii. the member is unable to use **ANY** other IV echinocandin (anidulafungin, caspofungin, micafungin); **or**
 - b. treatment of candidemia **AND** the member meets **ONE** of the following criteria:
 - i. Non-neutropenic **AND** is unable to use **ANY** of the following options:
 1. Other IV echinocandin (anidulafungin, caspofungin, micafungin); **or**
 2. Fluconazole (IV or oral) if the member is not critically ill and is unlikely to have infections caused by fluconazole-resistant Candida; **or**
 3. IV amphotericin B (or its derivatives), IF **ONE** of the following is applicable:
 - a. echinocandin- and azole-resistant Candida are suspected; **or**
 - b. echinocandins and fluconazole cannot be used because of intolerance, limited availability, or resistance; **or**
 - ii. Neutropenic **AND** is unable to use **ANY** of the following options:

1. Other IV echinocandin (anidulafungin, caspofungin, micafungin); **or**
2. IV amphotericin B (or its derivatives); **or**
3. Fluconazole, **IF** one of the following is applicable:
 - a. for initial therapy and the member is not critically ill and have had no prior exposure to azole antifungals; **or**
 - b. for step-down therapy during neutropenia and the member is clinically stable and has fluconazole-susceptible isolates and documented bloodstream clearance; **or**
4. Voriconazole, **IF** one of the following is applicable:
 - a. for initial therapy when broader antifungal coverage is required; **or**
 - b. step-down therapy during neutropenia and the member is clinically stable and has voriconazole-susceptible isolates and documented bloodstream clearance; **or**
- c. The treating provider has indicated that rezafungin is the treatment of choice based on **BOTH** of the following:
 - i. the clinical status of patient, knowledge of species or antifungal susceptibility, relative drug toxicity, presence of organ dysfunction, available knowledge of the use of the drug in a given patient population and patient prior exposure to antifungal agents; **and**
 - ii. the member is unable to use **ANY** other IV echinocandin (anidulafungin, caspofungin, micafungin); **AND**
4. The member does **NOT** have known hypersensitivity to any echinocandin (i.e., rezafungin, caspofungin, micafungin, and anidulafungin).

If the above prior authorization criteria is met, the requested medication will be approved for up to 4 weekly doses.

Experimental or Investigational / Not Medically Necessary

Rezzayo (rezafungin) for any other indication or use is considered not medically necessary by the Plan, as it is deemed to be experimental, investigational, or unproven.

Applicable Billing Codes (HCPCS/CPT Codes)

Service(s) name	
CPT/HCPCS Codes considered medically necessary if criteria are met:	
<i>Code</i>	<i>Description</i>
96365	Intravenous infusion, for therapy, prophylaxis, or diagnosis (specify substance or drug); initial, up to 1 hour
96366	Intravenous infusion, for therapy, prophylaxis, or diagnosis (specify substance or drug); each additional hour (List separately in addition to code for primary procedure)
J0349	Injection, rezafungin, 1 mg
ICD-10 codes considered medically necessary if criteria are met:	
<i>Code</i>	<i>Description</i>
B37.0	Candidal stomatitis
B37.1	Pulmonary candidiasis
B37.41	Candidal cystitis and urethritis
B37.49	Other urogenital candidiasis
B37.7	Candidal sepsis
B37.81	Candidal esophagitis
B37.82	Candidal enteritis
B37.89	Other sites of candidiasis
B44.0	Invasive pulmonary aspergillosis
B44.1	Other pulmonary aspergillosis
B44.2	Tonsillar aspergillosis
B44.7	Disseminated aspergillosis
B44.89	Other forms of aspergillosis
B44.9	Aspergillosis, unspecified
D70.3	Neutropenia due to infection
D70.8	Other neutropenia

Z48.290	Encounter for aftercare following bone marrow transplant
Z94.81	Bone marrow transplant status
Z94.84	Stem cells transplant status

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Clinical Guideline Revision / History Information

Original Date: 06/29/2023

Reviewed/Revised: 10/27/2023