BlueCross BlueShield
Federal Employee Program
Blue Cross Blue Shield Association
750 9th St NW, Suite 900
Washington, D.C. 20001
1-800-624-5060
Fax 1-877-378-4727

5.21.198

Section:	Prescription Drugs	**Effective Date:**	January 1, 2025
Subsection:	Antineoplastic Agents	**Original Policy Date:**	December 30, 2022
Subject:	Rezlidhia	**Page:**	1 of 4

Last Review Date: December 13, 2024

Rezlidhia

Description

Rezlidhia (olutasidenib)

Background

Rezlidhia (olutasidenib) is a small-molecule inhibitor of mutated isocitrate dehydrogenase-1 (IDH1). In patients with acute myeloid leukemia (AML), susceptible IDH1 mutations are defined as those leading to increased levels of 2-hydroxyglutarate (2-HG) in the leukemia cells and where efficacy is predicted by clinically meaningful remissions with the recommended dose of Rezlidhia and/or inhibition of mutant IDH1 enzymatic activity at concentrations of Rezlidhia sustainable at the recommended dosage according to validated methods. The most common of such mutations in patients with AML are R132H and R132C substitutions (1).

Regulatory Status

FDA-approved indication: Rezlidhia is an isocitrate dehydrogenase-1 (IDH1) inhibitor indicated for the treatment of adult patients with relapsed or refractory acute myeloid leukemia (AML) with a susceptible IDH1 mutation as detected by an FDA-approved test (1).

Rezlidhia has a boxed warning for differentiation syndrome, which can be fatal if not treated. Differentiation syndrome is associated with rapid proliferation and differentiation of myeloid cells. Symptoms of differentiation syndrome in patients treated with Rezlidhia included leukocytosis, dyspnea, pulmonary infiltrates/pleuropericardial effusion, kidney injury, fever, edema, pyrexia, and weight gain. If differentiation syndrome is suspected, withhold Rezlidhia, initiate systemic corticosteroids and hemodynamic monitoring until symptom resolution (1).

Patients treated with Rezlidhia can develop hepatotoxicity, presenting as increased alanine aminotransferase (ALT), increased aspartate aminotransferase (AST), increased blood alkaline phosphatase, and/or elevated bilirubin. Liver function tests should be obtained at baseline and periodically during treatment with Rezlidhia (1).

The safety and effectiveness of Rezlidhia in pediatric patients less than 18 years of age have not been established (1).

Related policies
Idhifa, Tibsovo

Policy

This policy statement applies to clinical review performed for pre-service (Prior Approval, Precertification, Advanced Benefit Determination, etc.) and/or post-service claims.

Rezlidhia may be considered **medically necessary** if the conditions indicated below are met.

Rezlidhia may be considered **investigational** for all other indications.

Prior-Approval Requirements

Age 18 years of age or older

Diagnosis

Patient must have the following:

1. Relapsed or refractory acute myeloid leukemia (AML)

AND ALL of the following:

1. Susceptible isocitrate dehydrogenase-1 (IDH1) mutation as detected by an FDA-approved test
2. Prescriber agrees to monitor for signs and symptoms of differentiation syndrome
3. Prescriber agrees to monitor liver function tests (LFTs)

Prior – Approval *Renewal* Requirements

Age 18 years of age or older

Diagnosis

Patient must have the following:

1. Relapsed or refractory acute myeloid leukemia (AML)

AND ALL of the following:

1. **NO** disease progression or unacceptable toxicity
2. Prescriber agrees to monitor for signs and symptoms of differentiation syndrome
3. Prescriber agrees to monitor liver function tests (LFTs)

Policy Guidelines

Pre - PA Allowance

None

Prior - Approval Limits

Quantity 180 capsules per 90 days

Duration 12 months

Prior – Approval *Renewal* Limits

Same as above

Rationale

Summary

Rezlidhia is an isocitrate dehydrogenase-1 (IDH1) inhibitor indicated for the treatment of adult patients with relapsed or refractory acute myeloid leukemia (AML) with a susceptible IDH1 mutation as detected by an FDA-approved test. Rezlidhia has a boxed warning regarding differentiation syndrome. The safety and effectiveness of Rezlidhia in pediatric patients less than 18 years of age have not been established (1).

Prior authorization is required to ensure the safe, clinically appropriate, and cost-effective use of Rezlidhia while maintaining optimal therapeutic outcomes.

References

1. Rezlidhia [package insert]. Greenville, NC: Metrics Contract Services; April 2024.
2. NCCN Drugs & Biologics Compendium® Olutasidenib 2024. National Comprehensive

Cancer Network, Inc. Accessed on October 3, 2024.

Policy History

Date	Action
December 2022	Addition to PA
March 2023	Annual review and reference update
December 2023	Annual review and reference update
September 2024	Annual review and reference update
December 2024	Annual review and reference update

Keywords

This policy was approved by the FEP® Pharmacy and Medical Policy Committee on December 13, 2024 and is effective on January 1, 2025.