09-J4000-08

Original Effective Date: 11/01/21

Reviewed: 10/09/24

Revised: 11/15/24

Subject: Belumosudil (Rezurock™) tablets

THIS MEDICAL COVERAGE GUIDELINE IS NOT AN AUTHORIZATION, CERTIFICATION, EXPLANATION OF BENEFITS, OR A GUARANTEE OF PAYMENT, NOR DOES IT SUBSTITUTE FOR OR CONSTITUTE MEDICAL ADVICE. ALL MEDICAL DECISIONS ARE SOLELY THE RESPONSIBILITY OF THE PATIENT AND PHYSICIAN. BENEFITS ARE DETERMINED BY THE GROUP CONTRACT, MEMBER BENEFIT BOOKLET, AND/OR INDIVIDUAL SUBSCRIBER CERTIFICATE IN EFFECT AT THE TIME SERVICES WERE RENDERED. THIS MEDICAL COVERAGE GUIDELINE APPLIES TO ALL LINES OF BUSINESS UNLESS OTHERWISE NOTED IN THE PROGRAM EXCEPTIONS SECTION.

DESCRIPTION:

Belumosudil (Rezurock) is FDA-approved for the treatment of adult and pediatric patients 12 years of age and older with chronic graft-versus-host disease (cGVHD) after failure of at least two prior lines of systemic therapy. Chronic GVHD is associated with significant morbidity in patients following allogeneic hematopoietic stem cell transplantation (HSCT). Belumosudil reduces inflammation and fibrosis in affected organs by inhibiting a protein kinase signaling pathway.

The efficacy of belumosudil was evaluated in an open-label, randomized, multicenter trial, which enrolled patients with cGVHD who had received 2–5 previous lines of systemic therapy, including patients who had previously received ibrutinib (32%) and ruxolitinib (31%). Combined therapy with ibrutinib and ruxolitinib was not permitted although other standard treatment could be continued if the patient was on a stable dose for at least 2 weeks prior to study. Treatment with supportive care therapies was permitted during the study. Patients were randomized to receive either belumosudil 200 mg once or twice daily (n = 66 in each treatment group). The primary endpoint was overall response which included complete or partial response according to the 2014 NIH Response Criteria. The overall response rate (ORR) was achieved in 75% of patients taking belumosudil once daily after 6 months and a similar response was achieved in the twice daily treatment group. In patients achieving a response, no death or use of a new systemic therapy occurred in 62% of patients for at least 12 months since the response. Many patients were able reduce their dose of corticosteroids (65%) and/or calcineurin inhibitors (47%). In addition, there were 60% of patients who experienced a clinically meaningful improvement in a Quality of Life assessment (Lee Symptom Scale). The most common (≥ 20%) adverse reactions included infections, asthenia, nausea, diarrhea, dyspnea, cough, edema, hemorrhage, abdominal pain, musculoskeletal pain, headache, phosphate decreased, gamma glutamyl transferase increased, lymphocytes decreased, and hypertension.

The NCCN guidelines for hematopoietic stem cell transplant (HSCT) provide guidance of the use of belumosudil for chronic graft-versus-host disease (GVHD) as additional therapy in conjunction with systemic corticosteroids following failure (steroid-refractory disease) to two or more prior lines of systemic therapy.

POSITION STATEMENT:

Comparative Effectiveness

The FDA has deemed the drug(s) or biological product(s) in this coverage policy to be appropriate for self-administration or administration by a caregiver (i.e., not a healthcare professional). Therefore, coverage (i.e., administration) in a provider-administered setting such as an outpatient hospital, ambulatory surgical suite, physician office, or emergency facility is not considered medically necessary.

Initiation of belumosudil (Rezurock™) **meets the definition of medical necessity** for the following indications when all of the associated criteria are met:

1. Chronic graft-versus-host disease (cGVHD)
    a. The member is diagnosed with cGVHD following an allogeneic hematopoietic stem cell transplant
    b. Member's disease is refractory to an adequate trial of at least two systemic agents for the treatment of cGVHD (e.g., corticosteroids, tacrolimus, cyclosporine, mycophenolate mofetil, ibrutinib, ruxolitinib, methotrexate, sirolimus, axatilimab)
2. Dosage does not exceed 200 mg per day*

Approval duration: 6 months

Continuation of belumosudil (Rezurock™) **meets the definition of medical necessity** when **ALL** of the following criteria are met:

1. An authorization or reauthorization for belumosudil (Rezurock™) has been previously approved by Florida Blue or another health plan in the past 2 years for the treatment of cGVHD, **OR** the member has previously met **ALL** indication-specific criteria.
2. The member has a beneficial response to treatment with belumosudil (e.g., improvement in cGVHD symptoms) – documentation must be submitted
3. Dosage does not exceed 200 mg per day*

Approval duration: 12 months

*Note: Dose may be increased to 200 mg twice daily if member requires continued use of a chronic proton pump inhibitor or strong CYP3A inducer (e.g. rifampin, carbamazepine) and no alternative treatment is available – documentation and rationale for use must be provided

DOSAGE/ADMINISTRATION:

THIS INFORMATION IS PROVIDED FOR INFORMATIONAL PURPOSES ONLY AND SHOULD NOT BE USED AS A SOURCE FOR MAKING PRESCRIBING OR OTHER MEDICAL DETERMINATIONS. PROVIDERS SHOULD REFER TO THE MANUFACTURER'S FULL

PRESCRIBING INFORMATION FOR DOSAGE GUIDELINES AND OTHER INFORMATION RELATED TO THIS MEDICATION BEFORE MAKING ANY CLINICAL DECISIONS REGARDING ITS USAGE.

FDA-approved

- Treatment of adult and pediatric patients 12 years and older with chronic graft versus-host disease (chronic GVHD) after failure of at least two prior lines of systemic therapy
- 200 mg given orally once daily until progression of chronic GVHD that requires new systemic therapy
- Treatment has not been studied in patients with pre-existing severe renal impairment. For patients with pre-existing severe renal impairment, consider the risks and potential benefits before initiating treatment. Avoid use in patients with moderate or severe hepatic impairment without liver GVHD.
- Monitor total bilirubin, aspartate aminotransferase (AST), and alanine aminotransferase (ALT) at least monthly

Dose Adjustments

- Monitor or discontinue treatment for Grade 3 or higher adverse reactions. See prescribing information.
- Increase the dosage to 200 mg twice daily when coadministered with strong CYP3A inducers (rifampin)
- Increase the dosage to 200 mg twice daily when coadministered with proton pump inhibitors

Drug Availability

- 200 mg tablet

PRECAUTIONS:

Boxed Warning

- None

Contraindications

- None

Precautions/Warnings

- Embryo-Fetal Toxicity: Can cause fetal harm. Advise females of reproductive potential of the potential risk to a fetus and to use effective contraception.

BILLING/CODING INFORMATION:

The following codes may be used to describe:

HCPCS Coding

J8499	Prescription drug, oral, non-chemotherapeutic, not otherwise specified

ICD-10 Diagnosis Codes That Support Medical Necessity

D89.811	Chronic graft-versus-host disease

REIMBURSEMENT INFORMATION:

Refer to section entitled **POSITION STATEMENT**.

PROGRAM EXCEPTIONS:

Federal Employee Program (FEP): Follow FEP guidelines.

State Account Organization (SAO): Follow SAO guidelines.

Medicare Part D: Florida Blue has delegated to Prime Therapeutics authority to make coverage determinations for the Medicare Part D services referenced in this guideline.

Medicare Advantage: No National Coverage Determination (NCD) and/or Local Coverage Determination (LCD) were found at the time of the last guideline review date.

DEFINITIONS:

None

RELATED GUIDELINES:

Immune Globulin Therapy, 09-J0000-06

Rituximab products, 09-J0000-59

Ibrutinib (Imbruvica), 09-J2000-09

Axatilimab (Niktimvo), 09-J4000-98

OTHER:

REFERENCES:

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2. DRUGDEX® System [Internet]. Greenwood Village (CO): Thomson Micromedex; Updated periodically [cited 2024 Oct 1].
3. Jagasia MH, Greinix HT, Arora M et al. National Institutes of Health Consensus Development Project on Criteria for Clinical Trials in Chronic Graft-versus-Host disease. Biol Blood Marrow Transplant. 2015 Mar; 21 (3): 389-401.

4. National Comprehensive Cancer Network. Cancer Guidelines. Cancer Guidelines and Drugs and Biologics Compendium. [cited 2024 Oct 1]
5. National Comprehensive Cancer Network. Clinical Practice Guidelines in Oncology. Version 2.2024. Hematopoietic cell transplantation (HCT). Available from http://www.nccn.org/professionals/physician_gls/PDF/hct.pdf.
6. Orphan Drug Designations and Approval [Internet]. Silver Spring (MD): US Food and Drug Administration; 2024 [2024 Oct 1]. Available from: http://www.accessdata.fda.gov/scripts/opdlisting/oopd/index.cfm/.
7. Rezurock (belumosudil)[package insert]. Kadmon Pharmaceuticals, Inc. Warrendale, PA. Nov 2023.

COMMITTEE APPROVAL:

This Medical Coverage Guideline (MCG) was approved by the Florida Blue Pharmacy Policy Committee on 10/09/24.

GUIDELINE UPDATE INFORMATION:

11/01/21	New Medical Coverage Guideline.
01/15/23	Review and revision to guideline; consisting of updating the references.
11/15/24	Review and revision to guideline; consisting of updating the continuation criteria, dosing and references.