Blue Cross Blue Shield Blue Care Network of Michigan

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Medical benefit drug policies are a source for BCBSM and BCN medical policy information only. These documents are not to be used to determine benefits or reimbursement. Please reference the appropriate certificate or contract for benefit information. This policy may be updated and therefore subject to change.

P&T Date: 02/13/2025

Ryoncil® (remestemcel-L)

HCPCS: J3590

Policy:

Requests must be supported by submission of chart notes and patient specific documentation.

A. Coverage of the requested drug is provided when all the following are met:
   a. FDA approved indication
   b. FDA approved age
   c. Member has demonstrated progression of disease by day 5 or nonresponse by day 7 while on corticosteroids.
   d. Trial and failure, contraindication, or intolerance to Jakafi® (ruxolitinib) when age appropriate per FDA labeling.
   e. The requesting physician attests to providing clinical outcome information within the appropriate provider portal as requested by BCBSM.
   f. Trial and failure, contraindication, OR intolerance to the preferred drugs as listed in BCBSM/BCN's utilization management medical drug list.

B. Quantity Limitations, Authorization Period and Renewal Criteria
   a. Quantity Limits: Align with FDA recommended dosing
   b. Authorization Period: Aligns with FDA recommended or guideline supported treatment duration and provided for at least 60 days and up to 6 months at a time
   c. Renewal Criteria: Clinical documentation must be provided to confirm that current criteria are met and that the medication is providing clinical benefit

***Note: Coverage and approval duration may differ for Medicare Part B members based on any applicable criteria outlined in Local Coverage Determinations (LCD) or National Coverage Determinations (NCD) as determined by Center for Medicare and Medicaid Services (CMS). See the CMS website at http://www.cms.hhs.gov/. Determination of coverage of Part B drugs is based on medically accepted indications which have supported citations included or approved for inclusion determined by CMS approved compendia.

Background Information:

- Ryoncil is an allogeneic bone marrow-derived mesenchymal stromal cell (MSC) therapy indicated for the treatment of steroid-refractory acute graft versus host disease (SR-aGvHD) in pediatric patients 2 months of age and older.

- Acute GVHD occurs in approximately 50% of patients who receive an allogeneic bone marrow transplant (BMT). Over 30,000 patients worldwide undergo an allogeneic BMT annually, primarily during treatment for blood cancers, including about 20% in pediatric patients. SR-aGVHD is associated with mortality as high as 90% and significant extended hospital stay costs. Prior to the approval of Ryoncil, there were no FDA-approved treatments in the US for children under 12 with SR-aGVHD. GVHD has been classically divided into acute and chronic variants based on the time of onset using a cutoff of 100 days. However, this conventional division has been challenged by the recognition that signs of acute and chronic GVHD may occur outside of these designated periods. Acute GVHD manifestations include: classic maculopapular rash, abdominal cramps with diarrhea, and rising serum bilirubin concentration. Patients who demonstrate progression of disease by day 5 or nonresponse by day 7 are considered to have corticosteroid resistance.

- The National Comprehensive Cancer Network (NCCN) Hematopoietic Cell Transplantation (HCT) guidelines Version 1.2023 recommend Jakafi as a category 1 option for patients with SR-aGVHD. At this time, Jakafi is only indicated for patients 12 years and older with SR-aGVHD. Per UpToDate for patients with aGVHD grade 2 or higher, systemic glucocorticoids are recommended.

- The safety and effectiveness of Ryoncil were evaluated in a multicenter, single-arm study in 54 pediatric study participants with SR-aGVHD after undergoing allogeneic hematopoietic stem cell transplantation (allo-HSCT). The study enrolled pediatric patients with SR-aGVHD Grade B to D (excluding Grade B skin alone) as per International Blood and Marrow Transplantation Registry Severity Index Criteria (IBMTR) after receiving allo-HSCT. SR-aGVHD was defined as aGVHD that progressed within 3 days or did not improve within 7 consecutive days of treatment with methylprednisolone 2 mg/kg/day or equivalent.

    - The main efficacy outcome measures were Day-28 overall response rate (complete response rate and partial response rate) and the duration of response.

    - The overall response rate was 70% with sixteen study participants (30%) having had a complete response to treatment 28 days after receiving Ryoncil, and 22 study participants (41%) having had a partial response.

        - Overall response rate at Day-28 by baseline disease severity is as follows: Grade B (3/6; 50%), Grade C (16/23; 70%), and Grade D (19/25; 76%).

    - The median duration of response, as calculated from Day-28 response to either progression (worsening by one stage in any organ without improvement in other organs in comparison to prior response assessment), new systemic therapy for aGVHD, or death from any cause, was 54 days.

References:

1. Ryoncil [prescribing information]. New York, NY. Mesoblast, Inc. December 2024
2. BioSpace. Press Release. Mesoblast's RYONCIL® is the First U.S. FDA-Approved Mesenchymal Stromal Cell (MSC) Therapy - BioSpace December 18, 2024
3. National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology. Hematopoietic Cell Transplantation (HCT) **(**Version 2.2024)– August 30, 2024. NCCN.org
4. Chao NJ. Clinical manifestations, diagnosis, and grading of chronic graft-versus-host-disease. UpToDate. https://www.uptodate.com/contents/clinical-manifestations-diagnosis-and-grading-of-chronic-graft-versus-host-disease accessed August 2021

<table>
<tr><th colspan="3">Policy History</th></tr>
<tr><th>#</th><th>Date</th><th>Change Description</th></tr>
<tr><td>1.5</td><td>Effective Date:
03/03/2025</td><td>UM medical management system update for MAPPO and BCNA
<table><tr><th>Line of Business</th><th>PA Required in Medical Management System (Yes/No)</th></tr><tr><td>BCBS</td><td>Yes</td></tr><tr><td>BCN</td><td>Yes</td></tr><tr><td>MAPPO</td><td>Yes</td></tr><tr><td>BCNA</td><td>Yes</td></tr></table></td></tr>
<tr><td>1.4</td><td>Effective Date:
03/31/2025

P&T Date:
02/13/2025</td><td>New policy.
This criteria replaces previously approved preliminary criteria.</td></tr>
<tr><td>1.3</td><td>Effective Date:
01/09/2025</td><td>UM medical management system update for BCBS and BCN
<table><tr><th>Line of Business</th><th>PA Required in Medical Management System (Yes/No)</th></tr><tr><td>BCBS</td><td>Yes</td></tr><tr><td>BCN</td><td>Yes</td></tr><tr><td>MAPPO</td><td>No</td></tr><tr><td>BCNA</td><td>No</td></tr></table></td></tr>
<tr><td>1.2</td><td>Effective Date:
12/12/2024</td><td>Updated authorization period to align with OncoHealth preferred verbiage.</td></tr>
<tr><td>1.1</td><td>Effective Date:
06/06/2024</td><td>Annual review of criteria was performed, no changes were made.</td></tr>
<tr><td>1.0</td><td>Effective Date:
06/08/2023</td><td>Preliminary drug review
<table><tr><th>Line of Business</th><th>PA Required in Medical Management System (Yes/No)</th></tr><tr><td>BCBS</td><td>No</td></tr><tr><td>BCN</td><td>No</td></tr><tr><td>MAPPO</td><td>No</td></tr><tr><td>BCNA</td><td>No</td></tr></table></td></tr>
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** The prescribing information for a drug is subject to change. To ensure you are reading the most current information it is advised that you reference the most updated prescribing information by visiting the drug or manufacturer website or http://dailymed.nlm.nih.gov/dailymed/index.cfm.*