Drug Coverage Policy

Effective Date.....04/01/2026
Coverage Policy Number.....IP0732
Policy Title.....Ryoncil

Graft-Versus-Host Disease - Ryoncil

- Ryoncil® (remestemcel-L-rknd intravenous infusion - Mesoblast)

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

Ryoncil, an allogeneic bone marrow-derived mesenchymal stromal cell therapy indicated for the treatment of steroid-refractory acute graft-versus-host disease (GVHD) in pediatric patients ≥ 2 months of age.[1]

Disease Overview
Acute GVHD occurs when alloreactive donor-derived T cells within the donated tissue (graft) provoke an immunological response leading to systemic inflammation, cytotoxicity, and potential end organ damage.[2,3] This serious, life-threatening condition is a common complication of allogeneic hematopoietic stem cell transplantation. In 2021, over 8,000 allogeneic transplants were performed in the US. Approximately 20% to 80% of patients undergoing this type of transplant develop acute GVHD and around 50% of these patients do not respond to corticosteroids, which is the first-line treatment.

Dosing Information
The recommended dosage of Ryoncil is 2×10^6 mesenchymal stromal cells/kg body weight given as an intravenous (IV) infusion twice per week for 4 consecutive weeks for a total of 8 infusions.[1] Deliver the infusions at least 3 days apart. Evaluate for a response 28 ± 2 days after the first dose and administer further treatment as appropriate as described based on Day 28 response as follows: no further treatment with Ryoncil if patients have a complete response; repeat Ryoncil administration once a week for an additional 4 weeks (four infusions total) for patients with a partial or mixed response; for patients with no response, consider alternative treatments; and repeat Ryoncil administration twice a week for an additional 4 consecutive weeks (eight infusions total) for patients who experience a recurrence of GVHD following a complete response.

Guidelines
The National Comprehensive Cancer Network (NCCN) guidelines for Hematopoietic Cell Transplantation (version 3.2025 – September 24, 2025) do not address Ryoncil.[3] For patients with steroid-refractory acute GVHD, Jakafi® (ruxolitinib tablets) is the only category 1 recommended agent. Other alternative agents recommended by NCCN for acute GVHD (category 2A) include the following: Lemtrada® (alemtuzumab IV infusion), alpha-1 antitrypsin, anti-thymocyte globulin, Simulect® (basiliximab IV infusion), calcineurin inhibitors (e.g., tacrolimus, cyclosporine), Enbrel® (etanercept subcutaneous [SC] injection), extracorporeal photopheresis, infliximab, mTOR inhibitors (e.g., sirolimus), mycophenolate mofetil, pentostatin, tocilizumab, and Entyvio® (vedolizumab IV infusion and SC injection).

Coverage Policy

POLICY STATEMENT
Prior Authorization is required for benefit coverage of Ryoncil. Approval is recommended for those who meet the **Criteria** and **Dosing** for the listed indication. All approvals are provided for the duration noted below. Extended approvals are allowed if the patient continues to meet the Criteria and Dosing. Requests for doses outside of the established dosing documented in this policy will be considered on a case-by-case basis by a clinician (i.e., Medical Director or Pharmacist). Because of the specialized skills required for evaluation and diagnosis of patients treated with Ryoncil as well as the monitoring required for adverse events and long-term efficacy, approval requires Ryoncil to be prescribed by or in consultation with a physician who specializes in the condition being treated.

Ryoncil is considered medically necessary when the following are met:

FDA-Approved Indication

1. **Acute Graft-Versus-Host Disease.** Approve for up to twelve infusions per episode if the patient meets ALL of the following (A, B, and C):
   A) Patient is ≥ 2 months of age and < 18 years of age; AND
   B) Patient has steroid-refractory acute graft-versus-host disease; AND
   C) The medication is prescribed by or in consultation with a hematologist, oncologist, transplant specialist physician, or a physician associated with a transplant center.

   Dosing. Approve if the requested dosing meets BOTH of the following (A and B):
   A) Approve 2×10^6 mesenchymal stromal cells/kg body weight given by intravenous infusion; AND
   B) Infusions are administered twice weekly for 4 weeks, then once weekly for up to 4 additional weeks for a total of up to 12 infusions per episode.

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

Coding Information

1) This list of codes may not be all-inclusive.
2) Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement.

Considered Medically Necessary when criteria in the applicable policy statements listed above are met:

HCPCS Codes	Description
J3402	Injection, remestemcel-l-rknd, per therapeutic dose (Code effective 10/1/2025)
J3590	Unclassified biological (Code effective until 09/30/2025)

References

1. Ryoncil® intravenous infusion [prescribing information]. New York, NY: Mesoblast; December 2024.
2. Kurtzberg J, Abdel-Azim H, Carpenter P, et al, for the MSB-GCHD001/002 study group. A phase 3, single-arm, prospective study of remestemcel-L, ex vivo culture-expanded adult human mesenchymal stromal cells for the treatment of pediatric patients who failed to respond to steroid treatment for acute graft-versus-host disease. *Biol Blood Marrow Transplant*. 2020;26(5):845-854.
3. The NCCN Hematopoietic Cell Transplantation (HCT) Clinical Practice Guidelines in Oncology (version 3.2025 – September 24, 2025). © 2025 National Comprehensive Cancer Network, Inc. Available at: http://www.nccn.org. Accessed on January 15,2026.

Revision Details

Type of Revision	Summary of Changes	Date
New	New policy	05/15/2025
Annual Revision	No criteria changes.	04/01/2026

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