CARECONTINUUM™

UTILIZATION MANAGEMENT MEDICAL POLICY

POLICY: Graft-Versus-Host Disease – Ryoncil Utilization Management Medical Policy
- Ryoncil® (remestemcel-L-rknd intravenous infusion – Mesoblast)

REVIEW DATE: 01/29/2025

OVERVIEW

Ryoncil, is 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 and older.[1,2]

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.[3] This serious, life-threatening condition is a more 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 per intravenous (IV) infusion given 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 2.2024 – August 30, 2024) 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, mammalian target of rapamycin inhibitors (e.g., tacrolimus), mycophenolate mofetil, pentostatin, tocilizumab, and Entyvio® (vedolizumab IV infusion and SC injection).

POLICY STATEMENT

Prior Authorization is recommended for medical 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.

Automation: None.

RECOMMENDED AUTHORIZATION CRITERIA

Coverage of Ryoncil is recommended in those who meet the following criteria:

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.

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Coverage of Ryoncil is not recommended in the following situations:

1. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

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 2.2024 – August 30, 2024). © 2024 National Comprehensive Cancer Network, Inc. Available at: http://www.nccn.org. Accessed on January 1, 2024.

HISTORY

Type of Revision	Summary of Changes	Review Date
New Policy	--	01/29/2025