Ryoncil® (remestemcel-L-rknd)
(Intravenous)

Effective Date: 06/01/2025
Dates Reviewed: 05/14/2025
Medical Scope: Medicaid, Commercial, MMP

I. Length of Authorization

Coverage will be provided for 1 month and may be renewed once (up to 16 total doses).

II. Dosing Limits

A. Max Units (per dose and over time) [HCPCS Unit]:

- 225 million MSC twice a week for 4 weeks (up to 16 total doses)

III. Summary of Evidence

Ryoncil (remestemcel-L-rknd) 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. The MSB-GVHD001 trial that led to Ryoncil's approval was a Phase 3, open-label, single-arm study with 54 pediatric patients aged 7 months to 17 years (median age 7 years) with SR-aGVHD, 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. Patients with skin-only grade B aGVHD were excluded. The primary outcome of Day-28 overall response rate (both complete response rate and partial response rate) was achieved in 38 patients (70% [95% CI: 56.4%, 82%]), with 16 of those patients achieving a complete response (30% [95% CI: 18.0%, 43.6%]. The median duration of response was 54 days (range: 7, 159+), which was 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. The most common

adverse reactions (incidence ≥20%) with Ryoncil were infections, pyrexia, hemorrhage, edema, abdominal pain, and hypertension.

IV. Initial Approval Criteria

Submission of medical records (chart notes) related to the medical necessity criteria is REQUIRED on all requests for authorizations. Records will be reviewed at the time of submission. Please provide documentation related to diagnosis, step therapy, and clinical markers (i.e., genetic, and mutational testing) supporting initiation when applicable. Please provide documentation via direct upload through the PA web portal or by fax.

Coverage is provided for treatment in the following conditions:

- MMP members who have previously received this medication within the past 365 days are not subject to Step Therapy Requirements; **AND**
- Patient is at least 2 months of age to 17 years old; **AND**
- The medication is prescribed by or in consultation with a hematologist, oncologist, or physician experienced in the management of transplant patients

Acute Graft-Versus-Host Disease (aGVHD) † Φ [1-7]

- Patient has steroid-refractory disease *(defined as disease that shows progression within 3 days, or no improvement within 7 days of consecutive treatment with 2 mg/kg/day methylprednisolone or equivalent)*; **AND**
- Patient has Grade C or D aGVHD involving the skin, liver and/or gastrointestinal (GI) tract or Grade B aGVHD involving the liver and/or GI tract, with or without concomitant skin disease [International Bone Marrow Transplant Registry (IBMTR) grading].
- Patient does not have skin-only involvement or evidence of encephalopathy or diffuse alveolar hemorrhage or other active pulmonary disease; **AND**
- Patient does not have a known hypersensitivity to dimethyl sulfoxide (DMSO) or porcine and bovine proteins; **AND**
- Patient is post-allogeneic stem cell transplant *(Note: Symptoms of aGVHD typically appear before day 100)*
- If patient is 12-17 years of age, medical rationale has been provided for why treatment with Jakafi (ruxolitinib) is not appropriate

† FDA Approved Indication(s); ‡ Compendia Recommended Indication(s); **Φ** Orphan Drug

V. Renewal Criteria [1]

Coverage can be renewed based on the following criteria:

- Patient continues to meet the universal and other indication-specific relevant criteria identified in section IV; **AND**
- Absence of unacceptable toxicity from the drug. Examples of unacceptable toxicity include: severe infusion related reactions, hypersensitivity reactions, etc.; **AND**
    - Patient has experienced at minimum a partial response (defined as organ improvement of at least 1 stage without worsening in any other organ) OR a mixed response (defined as improvement in at least 1 evaluable organ with worsening in another organ); **AND**
        - Patient will require treatment with four additional (weekly) doses; **OR**
    - Patient is experiencing an aGVHD flare after achieving a complete response [CR]); **AND**
        - Patient will require treatment with eight additional (twice weekly) doses

Note: Patients who experience a complete response (defined as resolution of aGVHD in all involved organs) OR no response, may not renew coverage and will be reviewed on a case-by-case basis.

VI. Dosage/Administration [1,3,7,21-23,25]

Indication	Dose
aGVHD	• The recommended dosage of Ryoncil is 2×10^6 mesenchymal stromal cell (MSC)/kg body weight per intravenous infusion given twice a week for 4 consecutive weeks for a total of 8 infusions. Administer infusions at least 3 days apart. • Assess response 28 ± 2 days after the first dose and administer further treatment as appropriate as described below based on Day 28 response. o CR – no further treatment o PR or mixed response – repeat once weekly for 4 weeks (4 infusions total) o No response – consider alternative treatments o Recurrence after CR – repeat twice weekly for 4 week (8 infusions total)
- *Ryoncil is shipped directly to the clinical facility in a liquid nitrogen dry shipper maintained at a temperature of ≤ -135°C.* - *Ryoncil must remain frozen at ≤ -135°C in liquid nitrogen vapor phase until thawed immediately prior to administration.* - *Patient infusion must occur within 5 hours from the start time of first vial(s) of RYONCIL thaw. Administer using an infusion pump, under the supervision of a qualified health professional experienced in the management of SR-aGvHD.*	

VII. Billing Code/Availability Information

HCPCS Code:

- J3590 — Unclassified biologics

NDC:

- Ryoncil target 25 x 10^6 MSCs in 3.8 mL in a single-dose vial: 73648-0154-xx

VIII. References

1. Ryoncil [package insert]. New York, NY; Mesoblast, Inc. December 2025. Accessed December 2025.
2. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) for remestemcel-L. National Comprehensive Cancer Network, 2025. The NCCN Compendium® is a derivative work of the NCCN Guidelines®. NATIONAL COMPREHENSIVE CANCER NETWORK®, NCCN®, and NCCN GUIDELINES® are trademarks owned by the National Comprehensive Cancer Network, Inc. To view the most recent and complete version of the Compendium, go online to NCCN.org. Accessed January 2025.
3. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) for Hematopoietic Cell Transplantation (HCT) Version 1.2025. National Comprehensive Cancer Network, 2025. The NCCN Compendium® is a derivative work of the NCCN Guidelines®. NATIONAL COMPREHENSIVE CANCER NETWORK®, NCCN®, and NCCN GUIDELINES® are trademarks owned by the National Comprehensive Cancer Network, Inc. To view the most recent and complete version of the Compendium, go online to NCCN.org. Accessed January 2025.
4. ClinicalTrials.gov. **NCT02336230**. A Single-arm, Prospective Study of Remestemcel-L, Ex-vivo Culture-Expanded Adult Human Mesenchymal Stromal Cells, for the Treatment of Pediatric Patients Who Have Failed to Respond to Steroid Treatment for Acute GVHD. | ClinicalTrials.gov.
5. ClinicalTrials.gov. **NCT00366145**. A Phase III, Randomized, Double Blind, Placebo-Controlled Study to Evaluate the Efficacy and Safety of Prochymal® (Ex-vivo Cultured Adult Human Mesenchymal Stem Cells) Infusion for the Treatment of Patients Who Have Failed to Respond to Steroid Treatment for Acute GVHD. | ClinicalTrials.gov.
6. Kurtzberg J, Abdel-Azim H, Carpenter P, et al; MSB-GVHD001/002 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 May;26(5):845-854. doi: 10.1016/j.bbmt.2020.01.018. Epub 2020 Feb 1
7. Kebriaei P, Hayes J, Daly A, et al. A Phase 3 Randomized Study of Remestemcel-L versus Placebo Added to Second-Line Therapy in Patients with Steroid-Refractory Acute Graft-versus- Host Disease. Biol Blood Marrow Transplant. 2020 May;26(5):835-844. doi: 10.1016/j.bbmt.2019.08.029. Epub 2019 Sep 7. PMID: 31505228; PMCID: PMC7060124..

Appendix 1 – Covered Diagnosis Codes

ICD-10	ICD-10 Description
D89.810	Acute graft-versus-host disease

Appendix 2 – Centers for Medicare and Medicaid Services (CMS)

The preceding information is intended for non-Medicare coverage determinations. Medicare coverage for outpatient (Part B) drugs is outlined in the Medicare Benefit Policy Manual (Pub. 100-2), Chapter 15, §50 Drugs and Biologicals. In addition, National Coverage Determinations (NCDs) and/or Local Coverage Determinations (LCDs) may exist and compliance with these policies is required where applicable. Local Coverage Articles (LCAs) may also exist for claims payment purposes or to clarify benefit eligibility under Part B for drugs which may be self-administered. The following link may be used to search for NCD, LCD, or LCA documents: https://www.cms.gov/medicare-coverage-database/search.aspx. Additional indications, including any preceding information, may be applied at the discretion of the health plan.

Medicare Part B Covered Diagnosis Codes (applicable to existing NCD/LCA/LCD): N/A

Medicare Part B Administrative Contractor (MAC) Jurisdictions		
Jurisdiction	**Applicable State/US Territory**	**Contractor**
E (1)	CA, HI, NV, AS, GU, CNMI	Noridian Healthcare Solutions, LLC
F (2 & 3)	AK, WA, OR, ID, ND, SD, MT, WY, UT, AZ	Noridian Healthcare Solutions, LLC
5	KS, NE, IA, MO	Wisconsin Physicians Service Insurance Corp (WPS)
6	MN, WI, IL	National Government Services, Inc. (NGS)
H (4 & 7)	LA, AR, MS, TX, OK, CO, NM	Novitas Solutions, Inc.
8	MI, IN	Wisconsin Physicians Service Insurance Corp (WPS)
N (9)	FL, PR, VI	First Coast Service Options, Inc.
J (10)	TN, GA, AL	Palmetto GBA
M (11)	NC, SC, WV, VA (excluding below)	Palmetto GBA
L (12)	DE, MD, PA, NJ, DC (includes Arlington & Fairfax counties and the city of Alexandria in VA)	Novitas Solutions, Inc.
K (13 & 14)	NY, CT, MA, RI, VT, ME, NH	National Government Services, Inc. (NGS)
15	KY, OH	CGS Administrators, LLC

Policy Rationale:

Ryoncil was reviewed by the Neighborhood Health Plan of Rhode Island Pharmacy & Therapeutics (P&T) Committee. Neighborhood adopted the following clinical coverage criteria to ensure that its members use Ryoncil according to Food and Drug Administration (FDA) approved labeling and/or relevant clinical literature. Neighborhood worked with network prescribers and pharmacists to draft these criteria. These criteria will help ensure its members are using this drug for a medically accepted indication, while minimizing the risk for adverse effects and ensuring more cost-effective options are used first, if applicable and appropriate. For INTEGRITY (Medicare-Medicaid Plan) members, these coverage criteria will only apply in the absence of National Coverage Determination (NCD) or Local Coverage Determination (LCD) criteria. Neighborhood will give individual consideration to each request it reviews based on the information submitted by the prescriber and other information available to the plan.