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

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I. Length of Authorization

- Initial: Prior authorization validity will be provided initially for 1 month.
- Renewal: Prior authorization validity may be renewed every month thereafter (*Refer to Section IV & V for recurrence therapy criteria*).

II. Dosing Limits

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

- 1 billable unit (1 dose) twice a week for 4 weeks (up to 16 total doses)

III. Initial Approval Criteria [1]

Submission of supporting clinical documentation (including but not limited to medical records, chart notes, lab results, and confirmatory diagnostics) related to the medical necessity criteria is REQUIRED on all requests for authorizations. Records will be reviewed at the time of submission as part of the evaluation of this request. 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**.** Failure to submit the medical records may result in the denial of the request due to inability to establish medical necessity in accordance with policy guidelines.

Prior authorization validity is provided for treatment of the following conditions:

- Patient is at least 2 months of age; **AND**

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 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);* **AND**
- For patients 12 years and older, patient has had an inadequate response to an adequate trial of, or contraindication or intolerance to ruxolitinib

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

IV. Renewal Criteria [1,5]

Prior authorization validity can be renewed based on the following criteria:

- Patient continues to meet the universal and other indication-specific relevant criteria identified in section III; **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); **AND**
    - Patient will require treatment with four additional (weekly) doses; **OR**
  - Patient is experiencing an aGVHD recurrence after achieving a complete response [CR]); **AND**
    - Patient will require treatment with eight additional (twice weekly) doses

Note: *For patients who experience a complete response (defined as resolution of aGVHD in all involved organs) OR no response, prior authorization validity may not be renewed, and exceptions will be reviewed on a case-by-case basis.*

V. Dosage/Administration [1,3,7]

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. ○ Complete Response – no further treatment

Indication	Dose
	○ Partial Response or mixed response – repeat once weekly for 4 weeks (4 infusions total) ○ No response – consider alternative treatments ○ Recurrence after Complete Response – 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.*	

VI. Billing Code/Availability Information

HCPCS Code:

- J3402 – Injection, remestemcel-l-rknd, per therapeutic dose; 1 billable unit = 1 therapeutic dose

NDC(s):

- Ryoncil Kit Sizes:

Patient Weight (kg)	Kit contents (single infusion)			
	4-vial cartons	1-vial cartons	Total Cartons	NDC Number
<12.5	0	1	1	73648-111-01
12.5 to <25	0	2	2	73648-112-02
25 to <37.5	0	3	3	73648-113-03
37.5 to <50	1	0	1	73648-114-01
50 to <62.5	1	1	2	73648-115-02
62.5 to <75	1	2	3	73648-116-03
75 to <87.5	1	3	4	73648-117-04
87.5 to <100	2	0	2	73648-118-02
100 to <112.5	2	1	3	73648-119-03
112.5 to <125	2	2	4	73648-120-04
125 to <137.5	2	3	5	73648-121-05
137.5 to <150	3	0	3	73648-122-03

VII. References

1. Ryoncil [package insert]. New York, NY; Mesoblast, Inc. September 2025. Accessed October 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

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3. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) for Hematopoietic Cell Transplantation (HCT) Version 3.2025. 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 October 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 A – Non-Quantitative Treatment Limitations (NQTL) Factor Checklist

Non-quantitative treatment limitations (NQTLs) refer to the methods, guidelines, standards of evidence, or other conditions that can restrict how long or to what extent benefits are provided under a health plan. These may include things like utilization review or prior authorization. The utilization management NQTL applies comparably, and not more stringently, to mental health/substance use disorder (MH/SUD) Medical Benefit Prescription Drugs and medical/surgical (M/S) Medical Benefit Prescription Drugs. The table below lists the factors that were considered in designing and applying prior authorization to this drug/drug group, and a summary of the conclusions that Prime's assessment led to for each.

Factor	Conclusion
Indication	Yes: Consider for PA
Safety and efficacy	No: PA not a priority

Potential for misuse/abuse	No: PA not a priority
Cost of drug	Yes: Consider for PA

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/LCD/LCA): 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