

Clinical Policy: Remestemcel-L-rknd (Ryoncil)

Reference Number: LA.PHAR.474

Effective Date:

Last Review Date: 09.17.25

Line of Business: Medicaid

[Coding Implications](#)

[Revision Log](#)

See [Important Reminder](#) at the end of this policy for important regulatory and legal information.

****Please note: This policy is for medical benefit****

Description

Remestemcel-L-rknd (Ryoncil®) is an allogeneic bone marrow-derived mesenchymal stem cell (MSC) therapy.

FDA Approved Indication(s)

Ryoncil is indicated for the treatment of steroid-refractory acute graft versus host disease (GVHD) in pediatric patients 2 months of age and older.

Policy/Criteria

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

It is the policy of Louisiana Healthcare Connections that Ryoncil is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Acute Graft Versus Host Disease (must meet all):

1. Diagnosis of grade II to IV (*see Appendix F*) acute GVHD following hematopoietic cell transplantation;
2. Disease is steroid-refractory as evidenced by any of the following (a, b, or c):
 - a. Progression of acute GVHD within 3 to 5 days of therapy onset with ≥ 2 mg/kg per day of prednisone or dose equivalent corticosteroid (*see Appendix D and E*);
 - b. Failure to improve within 5 to 7 days of treatment initiation with ≥ 2 mg/kg per day of prednisone or dose equivalent corticosteroid (*see Appendix D and E*);
 - c. Partial response after > 28 days of immunosuppressive treatment including ≥ 2 mg/kg per day of prednisone or dose equivalent corticosteroid (*see Appendix B, D, and E*);
3. Prescribed by or in consultation with an oncologist, hematologist, or bone marrow transplant specialist;
4. Age 2 months to ≤ 17 years;
5. Documentation of member's current body weight in kg;
6. Request meets one of the following (a or b):*
 - a. Dose does not exceed 2×10^6 MSC/kg (1 dose) two times per week;

- b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

**Prescribed regimen must be FDA-approved or recommended by NCCN*

Approval duration: 1 month (8 doses)

B. Other diagnoses/indications (must meet 1 or 2):

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to LA.PMN.255
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy LA.PMN.53.

II. Continued Therapy

A. Acute Graft Versus Host Disease (must meet all):

1. Currently receiving medication via Louisiana Healthcare Connections, or documentation supports that member is currently receiving Ryoncil for acute GVHD and has received this medication for at least 28 days;
2. For requests extending beyond 28 days, one of the following (a or b):
 - a. Member has demonstrated evidence of a partial or mixed response but not yet a complete response (*see Appendix E*);
 - b. GVHD has recurred following a complete response (*see Appendix E*);
3. Member has not received more than 16 doses of Ryoncil;
4. If request is for a dose increase, documentation of member's current body weight in kg;
5. Request meets one of the following (a, b, or c):*
 - a. For members with partial or mixed response: Dose does not exceed 2×10^6 MSC/kg (1 dose) per week;
 - b. For recurrence of GVHD after complete response, or for requests to complete the first 28 days of treatment: Dose does not exceed 2×10^6 MSC/kg (1 dose) two times per week;
 - c. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

**Prescribed regimen must be FDA-approved or recommended by NCCN*

Approval duration: 1 month

Members requesting completion of the first 28 days of treatment: up to 8 doses

Members with partial or mixed response: 4 additional doses, up to a total of 12 doses

Members experiencing recurrence of GVHD after complete response: 8 additional doses, up to a total of 16 doses

B. Other diagnoses/indications (must meet 1 or 2):

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to LA.PMN.255
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy LA.PMN.53.

III. Diagnoses/Indications for which coverage is NOT authorized:

- A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policy LA.PMN.53 **Appendices/General Information**

Appendix A: Abbreviation/Acronym Key

FDA: Food and Drug Administration

NCCN: National Comprehensive Cancer Network

GVHD: graft-versus-host disease

MSC: mesenchymal stem cells

Appendix B: Therapeutic Alternatives

This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may not be a formulary agent and may require prior authorization.

| Drug Name | Dosing Regimen | Dose Limit/ Maximum Dose |
|---|---|--|
| Examples of corticosteroids for acute GVHD | | |
| betamethasone, dexamethasone, prednisone, prednisolone, methylprednisone* | Dose recommendations per NCCN based on organ involvement: Upper GI only: 0.5-1 mg/kg/day methylprednisolone (or prednisone dose equivalent) Skin/lower GI/liver: 1-2 mg/kg/day methylprednisolone (or prednisone dose equivalent) | Corticosteroid dosage must be individualized and is highly variable depending on the nature and severity of the disease, route of treatment, and on patient response |

Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) when the drug is available by both brand and generic.

*Off-label

Appendix C: Contraindications/Boxed Warnings

- Contraindication(s): known hypersensitivity to dimethyl sulfoxide (DMSO) or porcine and bovine proteins
- Boxed warning(s): none reported

Appendix D: Equivalent Corticosteroid Dosages

| Acute Steroid-Refractory GVHD: Equivalent Corticosteroid Dosages | |
|---|------------|
| Prednisolone | 5 mg PO |
| Prednisone | 5 mg PO |
| Methylprednisolone | 4 mg PO |
| Dexamethasone | 0.75 mg PO |
| Betamethasone | 0.75 mg PO |

Appendix E: Measurement of Response to Therapy

| Response Definitions per Pivotal Study and Prescribing Information | |
|---|---|
| Complete response | Resolution of acute GVHD in all involved organs |

| Response Definitions per Pivotal Study and Prescribing Information | |
|--|--|
| Partial response | Organ improvement of at least 1 stage without worsening of any other organs |
| Mixed response | Improvement in at least 1 evaluable organ with worsening in another |
| No response | No change in any organ stage in any organ system and no improvement in organ stage |
| Progression | Deterioration in at least 1 organ system by 1 stage or more with no improvement in any other organ |

Appendix F: General Information

- Acute GVHD refers to an allogeneic inflammatory response occurring in three organs: the skin, the liver, and the gastrointestinal tract. A grading system is used to assess the severity of disease based on clinical manifestations and the extent of organ involvement. There are a number of different grading systems available (e.g., Glucksberg, modified Glucksberg, Keystone, International Bone Marrow Transplantation Registry [IBMTR], Mount Sinai Acute GvHD International Consortium [MAGIC]), none of which has been shown to be superior in predicting survival. While there are no standardized definitions for each grade across these systems, all consider grade I disease to involve only the skin. Grade II, III, and IV disease go beyond the skin and additionally involve the liver and/or gastrointestinal tract.

IV. Dosage and Administration

| Indication | Dosing Regimen | Maximum Dose |
|-------------------------------|--|--------------|
| Steroid-refractory acute GVHD | <p>2 x 10⁶ MSC/kg IV twice weekly (at least 3 days apart) for 4 consecutive weeks (8 infusions)</p> <p>Assess response 28 ± 2 days after the first dose, and administer further treatment if appropriate as described below:</p> <ul style="list-style-type: none"> If complete response, no further treatment with Ryoncil If partial or mixed response, repeat administration of Ryoncil once a week for additional 4 weeks (i.e., 4 additional infusions) If no response, consider alternative treatments If GVHD recurs after complete response, repeat administration of Ryoncil twice a week for an additional 4 consecutive weeks (i.e., 8 additional infusions) | See regimen |

V. Product Availability

Cell suspension for intravenous infusion in a target concentration of 6.68 x 10⁶ MSCs per mL in 3.8 mL contained in a 6 mL cryovial

VI. References

1. Ryoncil Prescribing Information. New York, NY: Mesoblast, Inc.; December 2024. Available at: <https://www.fda.gov/media/184603/download>. Accessed January 8, 2025.
2. National Comprehensive Cancer Network. Hematopoietic Cell Transplantation (HCT): Pre-Transplant Recipient Evaluation and Management of Graft-Versus-Host Disease Version 2.2024. Available at: https://www.nccn.org/professionals/physician_gls/pdf/hct.pdf. Accessed January 8, 2025.
3. Kurtzberg J, Abdel-Azim H, Carpenter P et al. 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 GVHD. Biol Blood Marrow Transplant. 2020 May; 26(5): 845-854.
4. Clinical Pharmacology [database online]. Philadelphia, PA: Elsevier; 2025. Available at: <https://www.clinicalkey.com/pharmacology/>. Accessed January 8, 2025.
5. Schoemans HM, Lee SJ, Ferrara JL, et al. EBMT-NIH-CIBMTR Task Force position statement on standardized terminology & guidance for graft-versus-host disease assessment. Bone Marrow Transplant. 2018;53(11):1401–1415.
6. Oncologic Drugs Advisory Committee briefing document: Remestemcel-L for treatment of steroid refractory acute graft versus host disease in pediatric patients. Published August 13, 2020.

Coding Implications

Codes referenced in this clinical policy are for informational purposes only. Inclusion or exclusion of any codes does not guarantee coverage. Providers should reference the most up-to-date sources of professional coding guidance prior to the submission of claims for reimbursement of covered services.

| HCPCS Codes | Description |
|--------------------|-----------------------------------|
| J3590 | Unclassified biologics |
| C9399 | Unclassified drugs or biologicals |

| Reviews, Revisions, and Approvals | Date | LDH Approval Date |
|--|-------------|--------------------------|
| Converted corporate to local policy. | 09.17.25 | |

Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. LHCC makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved.

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