EVH Clinical Guideline 5106.CC for Ryoncil® (remestemcel-L-rknd)

Guideline Number: EVH_CG_5106.CC	Applicable Codes	
"Evolent" refers to Evolent Health LLC and Evolent Specialty Services, Inc.		
Original Date: March 2026	**Last Revised Date:** January 2026	**Implementation Date:** March 2026

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STATEMENT

General Information

- *It is the policy of the Health Plan to maintain a prior authorization process that promotes appropriate utilization of specific drugs with potential for misuse or limited indications. This process involves a review using Food and Drug Administration (FDA) criteria to make a determination of Medical Necessity, and approval by the Medical Policy Committee.*
- *If the established criteria are not met, the request is referred to a Medical Director for review, if required for the plan and level of request.*

Purpose

The purpose of this guideline is to define the prior authorization process for the following drug: Ryoncil® (remestemcel-L-rknd).

Scope

This guideline applies to all practitioners who are involved in providing the requested drug. This guideline is specific to the Health Plan's medical benefit.

INITIAL REVIEW CRITERIA

The request must meet all of the criteria listed below.

- Must be age 2 months to 17 years old
- Must be prescribed by or in consultation with an oncologist, hematologist, or transplant specialist
- Must have a diagnosis of acute graft versus host disease (aGvHD) following an allogeneic hematopoietic stem cell transplantation (HSCT)
- Must have chart documentation to support grade B to D severity aGvHD, per International Bone Marrow Transplant Registry (IBMTR) grading scale (see **Appendix 1**)
- Must have tried systemic steroids with an inadequate response OR have an intolerance or contraindication to systemic steroids
    - Inadequate response is defined as use of methylprednisolone or equivalent at 2mg/kg/day with disease progression within 3 days or no improvement within 7 days of consecutive treatment
- Must be prescribed at a dose within the manufacturer's dosing guidelines (based on diagnosis, weight, etc.) listed in the FDA approved labeling
    - *NOTE:* Only one course of Ryoncil will be approved initially (8 total infusions). Further infusions are subject to reauthorization criteria.
- Must have documentation or an attestation from the provider for all the following:

- Member must not have received any second line therapy to treat aGVHD (e.g., mycophenolate mofetil, etanercept, sirolimus, extracorporeal photopheresis, bretuximab, anti-thymocyte globulin)
- Member does not have a known hypersensitivity to dimethyl sulfoxide (DMSO) or to murine, porcine, or bovine proteins

REAUTHORIZATION CRITERIA

All prior authorization renewals are reviewed to determine the Medical Necessity for continuation of therapy. The request must meet all of the criteria listed under the specific member's situation below.

Members with NO RESPONSE to prior Ryoncil injections will not be eligible for reauthorization.

Partial or Mixed Response

- Must have recent chart note documentation showing the member experienced either a partial or mixed response to the prior 8 infusions of Ryoncil
  - Partial response is defined as organ improvement of at least one stage without worsening in any other organ
  - Mixed response is defined as improvement of at least one evaluable organ with worsening in another organ as per International Blood and Marrow Transplantation Registry Severity Index Criteria grading system (see **Appendix 1**)
- Must be prescribed at a dose within the manufacturer's dosing guidelines (based on diagnosis, weight, etc.) listed in the FDA approved labeling

Recurrence After Complete Response

- Must have recent chart note documentation showing the member previously had a complete response to Ryoncil and now has a recurrence of GvHD
- Must be prescribed at a dose within the manufacturer's dosing guidelines (based on diagnosis, weight, etc.) listed in the FDA approved labeling

APPROVAL DURATIONS

Initial Authorization	Up to 6 months
Reauthorization	Same as initial

APPENDIX

International Bone Marrow Transplant Registry Severity Index[3]

Grade A	• Stage 1 skin involvement (extent of rash, less than 25%) • No liver or GI involvement
Grade B	• Stage 2 skin involvement (extent of rash, 25% to 50%) **OR** • Stage 1-2 liver involvement (total bilirubin, 34-102 µmol/l) **OR** • Stage 1-2 GI involvement (volume of diarrhea, 550-1500 mL/day)
Grade C	• Stage 3 skin involvement (extent of rash, greater than 50%) **OR** • Stage 3 liver involvement (total bilirubin, 103-255 µmol/l) **OR** • Stage 3 GI involvement (volume of diarrhea, greater than 1500 mL/day)
Grade D	• Stage 4 skin involvement (bullae) **OR** • Stage 4 liver involvement (total bilirubin, greater than 255 µmol/l) **OR** • Stage 4 GI involvement (severe pain and ileus)

CODING AND STANDARDS

Codes

Code	Brand	Description
J3402	Ryoncil	Injection, remestemcel-l-rknd, per therapeutic dose

Applicable Lines of Business

☐	CHIP (Children's Health Insurance Program)
☐	Commercial
☐	Exchange/Marketplace
☒	Medicaid
☐	Medicare Advantage

BACKGROUND

Ryoncil 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.

POLICY HISTORY

Date	Summary
January 2026	• New Guideline

LEGAL AND COMPLIANCE

Guideline Approval

Committee

Reviewed / Approved by Evolent Administrative Services Medical Policy Committee

Disclaimer

Evolent Clinical Guidelines do not constitute medical advice. Treating health care professionals are solely responsible for diagnosis, treatment, and medical advice. Evolent uses Clinical Guidelines in accordance with its contractual obligations to provide utilization management. Coverage for services varies for individual members according to the terms of their health care coverage or government program. Individual members' health care coverage may not utilize some Evolent Clinical Guidelines. Evolent clinical guidelines contain guidance that requires prior authorization and service limitations. A list of procedure codes, services or drugs may not be all inclusive and does not imply that a service or drug is a covered or non-

covered service or drug. Evolent reserves the right to review and update this Clinical Guideline in its sole discretion. Notice of any changes shall be provided as required by applicable provider agreements and laws or regulations. Members should contact their Plan customer service representative for specific coverage information.

REFERENCES

1. RYONCIL (remestemcel-L-rknd) [prescribing information]. New York, New York: Mesoblast
2. Kurtzberg J, Abdel-Azim H, Carpenter P, Chaudhury S, Horn B, Mahadeo K, Nemecek E, Neudorf S, Prasad V, Prockop S, Quigg T, Satwani P, Cheng A, Burke E, Hayes J, Skerrett D; 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. PMID: 32018062; PMCID: PMC8322819.
3. Rowlings PA, Przepiorka D, Klein JP, et al. IBMTR Severity Index for grading acute graft-versus-host disease: retrospective comparison with Glucksberg grade. Br J Haematol. 1997;97:855–864