Harvard Pilgrim Health Care | TUFTS Health Plan

Medical Necessity Guidelines
Medical Benefit Drugs
Ryoncil (remestemcel-L)

Effective: February 1, 2026

Prior Authorization Required If REQUIRED, submit supporting clinical documentation pertinent to service request.	Yes ☒ No ☐

Applies to:

Commercial Products

☒ Harvard Pilgrim Health Care Commercial products; Fax 617-673-0988
☒ Tufts Health Plan Commercial products; Fax 617-673-0988

Public Plans Products

☒ Tufts Health Direct – A Massachusetts Qualified Health Plan (QHP) (a commercial product); Fax 617-673-0988
☐ Tufts Health Together – MassHealth Accountable Care Partnership Plans; Fax 617-673-0939
☒ Tufts Health RITogether – A Rhode Island Medicaid Plan; Fax 617-673-0939
☐ Tufts Health One Care-- A dual-eligible product; Fax 617-673-0956

Senior Products

☐ Tufts Health Plan Senior Care Options (SCO), (a dual-eligible product); Fax 617-673-0956
☐ Tufts Medicare Preferred HMO, (a Medicare Advantage product); Fax 617-673-0956
☐ Tufts Medicare Preferred PPO, (a Medicare Advantage product); Fax 617-673-0956

Note: While you may not be the provider responsible for obtaining prior authorization, as a condition of payment you will need to ensure that prior authorization has been obtained.

Overview

Graft-versus-host disease (GVHD) occurs after an allogeneic hematopoietic stem cell transplant (aHSCT) when the transplanted cells from the donor (graft) induce an immune response in the recipient (host), causing the host's immune system to attack and reject the newly transplanted cells. GVHD has been typically divided into acute and chronic variants based on the time of onset using a cutoff of 100 days post-transplant. Common manifestations include skin rash, gastrointestinal (GI) distress, and liver abnormalities. Acute GVHD can occur in up to 50% of patients receiving hematopoietic stem cell transplantation from an HLA-matched sibling. Corticosteroids remain the most commonly used treatment. Steroid-refractory acute graft-versus-host disease (SR-aGVHD) following HSCT is associated with significantly poor, potentially fatal, health outcomes and extended hospital stays. The occurrence is typically higher in unmatched donors. Each year, more than 8500 U.S. patients undergo an aHSCT, primarily during treatment for blood cancer, 1,500 of whom are children. Acute GVHD continues to be a major cause of morbidity and mortality after allogeneic hematopoietic cell transplant (HCT) in pediatric patients.

Food and Drug Administration (FDA) Approved Indications:

- 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.

The recommended dosage of Ryoncil is 2×10^6 MSC/kg body weight per intravenous infusion given twice per week for 4 consecutive weeks. Infusions should be administered at least 3 days apart. Assess the response 28 ± 2 days after the first dose and administer further treatment as appropriate as described below. Monitor for hypersensitivity reactions during infusion. Premedicate patients with corticosteroids and antihistamines 30-60 minutes prior to administration.

Table 1: Recommended Treatment Based on Day 28 Response

Response	Recommendation
Complete Response (CR)	No further treatment
Partial or Mixed Response*	Repeat administration once a week for additional 4 weeks (4 infusions total)

No Response	Consider alternative treatments
Recurrence of GVHD after CR	Repeat administration twice a week for an additional 4 consecutive weeks (8 infusions total)

*Partial response defined as organ improvement of at least one stage without worsening in any other organ, whereas mixed response was 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.

Clinical Guideline Coverage Criteria

The Plan may cover Ryoncil when all the following clinical criteria is met:

1. The Member has a diagnosis of steroid-refractory acute graft-versus-host disease (SR-aGVHD) following an allogeneic hematopoietic stem cell transplant; **and**
2. The Member's disease severity is classified as Grade B, C, or D according to the International Blood and Marrow Transplantation Registry (IBMTR) Severity Index Criteria[13]; **and**
3. The Member had an inadequate response to methylprednisolone 2 mg/kg/day or equivalent defined as disease progression within 3 days of treatment or no improvement within 7 consecutive days of treatment; **and**
4. The Member is 2 months to 17 years of age at the time of treatment; **and**
5. The Member has adequate renal function; **and**
6. The Member has no positive laboratory test result indicating infection with the human immunodeficiency virus (HIV) at any time and/or active Hepatitis B or C virus infection within 3 months prior to planned Ryoncil therapy; **and**
7. The Prescriber is an oncologist, hematologist, or transplant specialist.

Note: Initial authorization duration: 1 month

Reauthorization/Continuation of Therapy

The plan may consider continuation of Ryoncil for the Member requesting reauthorization when **all** the following criteria are met:

1. Initial criteria continues to be met; and
2. When **either** of the following criteria is met:
    a. Partial or mixed response; there is an improvement in symptoms while on the current regimen (maximum of 4 infusions); or
    b. Recurrence of SR-aGVHD following complete response (maximum of 8 infusions total).

Limitations

The plan will not cover Ryoncil (remestemcel-L) under any of the following conditions:

- The Member has hypersensitivity to dimethyl sulfoxide (DMSO) or Porcine and Bovine proteins.
- The Member is pregnant, lactating, or planning a pregnancy.
- The Member received an HSCT transplant for a solid tumor disease.

Codes

The following code(s) require prior authorization:

Table 1: CPT/HCPCS Codes

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

References:

1. Ryoncil (remestemcel-L). [package insert]. New York, NY: Mesoblast, Inc. Dec 2024
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3. Kurtzberg J, Prockop S, Chaudhury S, et al. Study 275: Updated Expanded Access Program for Remestemcel-L in

Steroid-Refractory Acute Graft-versus-Host Disease in Children. *Biol Blood Marrow Transplant*. 2020;26(5):855-864. doi:10.1016/j.bbmt.2020.01.026
4. Kurtzberg J, Prockop S, Teira P, et al. Allogeneic human mesenchymal stem cell therapy (remestemcel-L, Prochymal) as a rescue agent for severe refractory acute graft-versus-host disease in pediatric patients. *Biol Blood Marrow Transplant*. 2014;20(2):229-235. doi:10.1016/j.bbmt.2013.11.001
5. New Drug Review; Ryoncil (remestemcel-L-rkind). IPD Analytics. Available at https://www.ipdanalytics.com/ [subscription required]. January 2025.
6. A Prospective Study of Remestemcel-L, Ex-vivo Cultured Adult Human Mesenchymal Stromal Cells, for the Treatment of Pediatric Participants Who Have Failed to Respond to Steroid Treatment for Acute Graft-Versus-Host Disease (aGVHD); NCT02336230. Accessed @ https://clinicaltrials.gov/study/NCT02336230. Accessed March 3, 2025/
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8. 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(4):855-864. doi:10.1046/j.1365-2141.1997.1112925.x
9. Zhang M, Cai J, Gulati V, Khoshpouri P, Orsi M. Acute Graft-versus-Host Disease. Radiographics. 2024;44(7):e230238. doi:10.1148/rg.230238
10. Justiz Vaillant AA, Modi P, Mohammadi O. Graft-Versus-Host Disease. In: StatPearls. Treasure Island (FL): StatPearls Publishing; June 7, 2024.
11. Avenoso D, et. al. Healthcare Resource Utilization and Associated Costs in Patients With Chronic Graft-Versus-Host Disease Post-Allogeneic Hematopoietic Stem Cell Transplantation in England. Transplant Cell Ther. 2024 Dec;30(12):1207.e1-1207.e11. doi: 10.1016/j.jtct.2024.10.002. Epub 2024 Oct 9. PMID: 39389467.
12. Etra A, Ferrara JLM, Levine JE. Remestemcel-L-rknd (Ryoncil): the first approved cellular therapy for steroid-refractory acute GVHD. Blood. 2025 Oct 16;146(16):1897-1901. doi: 10.1182/blood.2025028553. PMID: 40845051; PMCID: PMC12543205.
13. Rowlings PA, et. al. IBMTR Severity Index for grading acute graft-versus-host disease: retrospective comparison with Glucksberg grade. Br J Haematol. 1997 Jun;97(4):855-64. doi: 10.1046/j.1365-2141.1997.1112925.x. PMID: 9217189.

Approval And Revision History

December 17, 2025: Reviewed by the Medical Policy Approval Committee (MPAC). Effective date February 1, 2026.

Background, Product and Disclaimer Information

Medical Necessity Guidelines are developed to determine coverage for benefits and are published to provide a better understanding of the basis upon which coverage decisions are made. We make coverage decisions using these guidelines, along with the Member's benefit document, and in coordination with the Member's physician(s) on a case-by-case basis considering the individual Member's health care needs.

Medical Necessity Guidelines are developed for selected therapeutic or diagnostic services found to be safe and proven effective in a limited, defined population of patients or clinical circumstances. They include concise clinical coverage criteria based on current literature review, consultation with practicing physicians in our service area who are medical experts in the particular field, FDA and other government agency policies, and standards adopted by national accreditation organizations. We revise and update Medical Necessity Guidelines annually, or more frequently if new evidence becomes available that suggests needed revisions.

For self-insured plans, coverage may vary depending on the terms of the benefit document. If a discrepancy exists between a Medical Necessity Guideline and a self-insured Member's benefit document, the provisions of the benefit document will govern. For Tufts Health Together (Medicaid), coverage may be available beyond these guidelines for pediatric members under age 21 under the Early and Periodic Screening, Diagnostic and Treatment (EPSDT) benefits of the plan in accordance with 130 CMR 450.140 and 130 CMR 447.000, and with prior authorization.

Treating providers are solely responsible for the medical advice and treatment of Members. The use of this guideline is not a guarantee of payment or a final prediction of how specific claim(s) will be adjudicated. Claims payment is subject to eligibility and benefits on the date of service, coordination of benefits, referral/authorization, utilization management guidelines when applicable, and adherence to plan policies, plan procedures, and claims editing logic.