

Title: Ryoncil (remestemcel-L)	Division: Medical Management Department: Utilization Management
Approval Date: 9/29/2026	LOB: Medicaid, SNP, HARP, CHP, QHP, EP, Gold, Goldcare, Medicare, Ultracare
Effective Date: 9/29/2026	Policy Number: UM-MP357
Review Date: 9/29/2027	Cross Reference Number:
Retired Date:	

1. POLICY DESCRIPTION:

Cellular Therapy – Ryoncil (remestemcel-L)

2. RESPONSIBLE PARTIES:

Medical Management Administration, Pharmacy Department, Utilization Management, Integrated Care Management, Claims Department

3. DEFINITIONS:

Ryoncil is a cellular therapy indicated for the treatment of steroid-refractory, acute, graft-versus-host disease (aGvHD). Ryoncil contains an active ingredient that is comprised of culture-expanded mesenchymal stromal cells isolated from the bone marrow of healthy human adult donors. The mechanism of action of Ryoncil is not clear but may be related to immunomodulatory effects through T-cell activation, measured by proliferation and secretion of proinflammatory cytokines.

4. POLICY:

Ryoncil will be considered medically necessary once the following coverage criteria is met. Approvals may be subject to dosing limits in accordance with FDA-approved labeling, accepted compendia, and/or evidence-based practice guidelines.

Chart notes must be submitted to confirm diagnosis and previous treatment(s).

INITIAL REQUEST:**1. Steroid Refractory, Acute Graft-Versus-Host-Disease (aGvHD):**

A. Member must be two months of age or older to 17 years of age;

AND

B. Member must have a diagnosis of steroid-refractory aGvHD, failure to respond to steroid treatment is defined by ONE of the following:

a. aGvHD that shows progression within 3 days of consecutive treatment with 2 mg/kg/day methylprednisolone or equivalent;

OR

b. aGvHD that show no improvement within 7 days of consecutive treatment with 2 mg/kg/day methylprednisolone or equivalent;

AND

- C. Prescribed by or in consultation with an board-certified oncologist, hematologist, or bone marrow transplant specialist;

AND

- D. Member must have a disease severity classified as ONE of the following using the International Blood and Marrow Transplantation Registry (IBMTR) Severity Index Criteria;;

- a. Grade B aGvHD involving the liver and/or GI tract, with or without concomitant skin disease;

OR

- b. Grade C or Grade D aGvHD involving the skin, liver, and/or GI tract;

AND

- E. Members who have had persistent GI GVHD manifested diarrhea with stool volume < 500 mL/kg/day (for participants >50 kg) or <30 mL/kg/day (for participants ≥50 kg) and the absence of nausea or vomiting are considered to have Grade B GVHD with both of the following:

- a. Other causes of diarrhea had been ruled out (eg, Clostridium difficile, adenovirus or cytomegalovirus [CMV] infection, or oral magnesium administration);

AND

- b. The low stool volume reflected the effects of fasting, narcotics, or antidiarrheal medications;

AND

- F. For members 12 years of age and older, member has tried and failed ruxolitinib or has a contraindication/intolerance to ruxolitinib;

AND

- G. Member must have adequate renal function defined by calculated creatinine clearance of >30 mL/min per 1.73 m² utilizing ONE of the following calculations:

- a. Members 1 to 17 years of age, renal function is determined using the Bedside Schwartz equation: Glomerular Filtration Rate (GFR, in mL/min per 1.73 m²) = (0.413 * height [cm])/serum creatinine (mg/dL);

OR

- b. Members under 1 year of age, renal function is determined using the Schwartz equation adjusted for this age group: Creatinine Clearance (mL/min per 1.73 m²) = (height [cm] * 0.45)/serum creatinine (mg/dL);

AND

- H. Member has a minimum Karnofsky/Lansky Performance Level of at least 30;

AND

- I. Female members of childbearing potential are required to use a medically accepted method of contraception;

AND

- J. Male members with partners of childbearing potential must agree to use adequate contraception;

AND

- K. Member must NOT have any of the following:

- a. Grade B aGvHD with only skin involvement;

AND

- b. Evidence of active pulmonary disease;

AND

- c. Underlying or current uncontrolled medical conditions that include but are not limited to infection, heart failure, or pulmonary hypertension that would interfere with treatment;

AND

- d. History of hematopoietic stem cell transplant (HSCT) for a solid tumor disease;

AND

- e. Evidence of active infection that include but are not limited to HIV and hepatitis B or C virus infection;

AND

- f. Any history of participation in clinical trial for aGvHD therapeutic agent;

AND

- g. Any history of no response to treatment with Ryoncil;

AND

- h. Known hypersensitivity to dimethyl sulfoxide (DMSO) or to murine, porcine, or bovine proteins;

AND

- L. Authorization is for no more than 8 doses of Ryoncil given 2 doses per week for 4 consecutive weeks.

CONTINUATION OF THERAPY:

1. Steroid Refractory, Acute Graft-Versus-Host-Disease (aGvHD):

- A. Initial conditions of coverage have been met;

AND

- B. Member has no evidence of unacceptable toxicity or disease progression while on the current regimen;

AND

- C. Member demonstrates a positive response to therapy defined by a partial or mixed response to therapy (TABLE 1);

AND

- D. Treatment cycles must be at least 28 days apart;

AND

- E. Authorization is for no more than 4 doses of Ryoncil given weekly for 4 consecutive weeks if member has had a partial or mixed response (for a total of 12 doses including the initial treatment);

TABLE 1:

Recommended Treatment Based on Day 28 Response		
Response	Definition	Recommendation
Complete Response (CR)	Resolution of all signs and symptoms of aGvHD in all involved organs, with all organ stages improving to 0	No further treatment with Ryoncil
Partial or Mixed Response	Organ improvement of at least one stage without worsening in any other organ	Repeat administration of Ryoncil once a week for 4 consecutive weeks (4 doses total)
No Response	No response to therapy	Consider alternative treatment
Recurrence of aGvHD after CR	aGvHD that occurs later after a complete response from previous treatment	Repeat administration of Ryoncil twice a week for an additional 4 consecutive weeks (8 doses total)

5. LIMITATIONS/ EXCLUSIONS:

Ryoncil will be considered experimental and investigational if prescribed for indications that have not been approved by the FDA and will not be covered under this policy.

Use of Ryoncil for more than 12 doses for one aGvHD episode is considered experimental and investigational and not covered under this policy.

6. APPLICABLE PROCEDURE CODES:

CPT	Description
D89.810	Acute Graft-Versus-Host Disease

7. APPLICABLE DIAGNOSIS CODES:

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

8. REFERENCES:

1. Ryoncil [package insert]. New York, NY; Mesoblast, Inc. September 2026. Accessed September 2026.
2. Mesoblast Ltd. Mechanisms of action [website]. Melbourne, VIC: Mesoblast; 2025. Available at: <https://www.mesoblast.com>. Accessed September, 2026.
3. 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.
4. IPD Analytics. ICD-10-CM CODES.

9. REVISION LOG:

REVISIONS	INITIAL	DATE
Creation date	JL	9/29/2026
Annual Review		

Approved:

Sanjiv Shah
MD

Digitally signed by Sanjiv
Shah MD
Date: 2026.10.21
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Dr. Sanjiv Shah, Chair
Chief Medical Officer

Medical Guideline Disclaimer:

Property of Metro Plus Health Plan. All rights reserved. The treating physician or primary care provider must submit MetroPlus Health Plan clinical evidence that the patient meets the criteria for the treatment or surgical procedure. Without this documentation and information, Metroplus Health Plan will not be able to properly review the request for prior authorization. The clinical review criteria expressed in this policy reflects how MetroPlus Health Plan determines whether certain services or supplies are medically necessary. MetroPlus Health Plan established the clinical review criteria based upon a review of currently available clinical information(including clinical outcome studies in the peer-reviewed published medical literature, regulatory status of the technology, evidence-based guidelines of public health and health research agencies, evidence-based guidelines and positions of leading national health professional organizations, views of physicians practicing in relevant clinical areas, and other relevant factors). MetroPlus Health Plan expressly reserves the right to revise these conclusions as clinical information changes, and welcomes further relevant information. Each benefit program defines which services are covered. The conclusion that a particular service or supply is medically necessary does not constitute a representation or warranty that this service or supply is covered and/or paid for by MetroPlus Health Plan, as some programs exclude coverage for services or supplies that MetroPlus Health Plan considers medically necessary. If there is a discrepancy between this guidelines and a member's benefits program, the benefits program will govern. In addition, coverage may be mandated by applicable legal requirements of a state, the Federal Government or the Centers for Medicare & Medicaid Services (CMS) for Medicare and Medicaid members. All coding and website links are accurate at time of publication. MetroPlus Health Plan has adopted the herein policy in providing management, administrative and other services to our members, related to health benefit plans offered by our organization.

