Corporate Medical Policy: Remestemcel-L-rknd (Ryoncil®) **"Notification"** **POLICY EFFECTIVE APRIL 1, 2026**

Restricted Product(s):

- remestemcel-L-rknd (Ryoncil®) intravenous infusion for administration by a healthcare professional

FDA Approved Use:

- For the treatment of steroid-refractory acute graft versus host disease (SR-aGVHD) in pediatric patients 2 months of age and older

Criteria for Medical Necessity:

The restricted product(s) may be considered medically necessary when the following criteria are met:

Initial Criteria for Approval:

1. The patient is 2 months to less than 18 years of age; **AND**
2. The patient has a diagnosis of **steroid-refractory acute graft versus host disease (SR-aGVHD) [medical record documentation required]**; **AND**
    a. The patient's disease severity is classified as grade B, C, or D per the International Blood and Marrow Transplantation Registry Severity Index Criteria (IBMTR) **[medical record documentation required]**; **AND**
    b. The patient has symptoms involving the skin, liver, and/or gastrointestinal tract **[medical record documentation required]**; **AND**
    c. The patient does NOT have grade B aGVHD with skin-only involvement **[medical record documentation required]**; **AND**
3. The patient has failed to respond to first-line systemic steroid treatment, defined as disease progression within 3 days or no improvement within 7 days of consecutive treatment with methylprednisolone 2 mg/kg/day or equivalent **[medical record documentation required]**; **AND**
4. The patient is post-allogeneic hematopoietic stem cell transplantation (HSCT) **[medical record documentation required]**; **AND**
5. For patients 12 to less than 18 years of age, ONE of the following:
    a. The patient has tried and had an inadequate response to ruxolitinib (Jakafi®) **[medical record documentation required]**; **OR**
    b. The patient has an intolerance, FDA labeled contraindication, or hypersensitivity to ruxolitinib (Jakafi®) **[medical record documentation required]**; **AND**
6. The patient does NOT have evidence of encephalopathy, or diffuse alveolar hemorrhage or other active pulmonary disease **[medical record documentation required]**; **AND**
7. The patient does NOT have a known hypersensitivity to dimethyl sulfoxide (DMSO) or to murine, porcine, or bovine proteins **[medical record documentation required]**; **AND**

8. The prescriber is a specialist in the area of the patient's diagnosis (e.g., oncologist, hematologist, transplant specialist) or has consulted with a specialist in the area of the patient's diagnosis **[medical record documentation required]**; **AND**
9. The requested dose is within FDA labeled dosing for the requested indication, and the requested quantity does NOT exceed the maximum units allowed for the duration of approval (see table below) **[medical record documentation required]**; **AND**
10. The patient will NOT receive more than 8 infusions total for initial treatment **[medical record documentation required]**.

Duration of Approval: 30 days (1 month)
8 infusions total per initial authorization; Maximum of 16 infusions total per lifetime

Continuation Criteria for Approval:

1. The patient was approved through Blue Cross NC initial criteria for approval; **OR**
2. The patient would have met initial criteria for approval at the time they started therapy **[medical record documentation required]**; **AND**
3. The patient is less than 18 years of age; **AND**
4. The patient does NOT have any unacceptable toxicity from the requested agent (e.g., severe infusion-related reactions, hypersensitivity reactions, etc.) **[medical record documentation required]**; **AND**
5. The patient has ONE of the following responses following the initial treatment of 8 infusions with the requested agent **[medical record documentation required]**:
    a. Partial response (PR), defined as organ improvement of at least one stage without worsening in any other organ per the International Blood and Marrow Transplantation Registry (IBMTR) Severity Index Criteria **[medical record documentation required]**; **AND**
        i. The patient will require treatment with 4 additional (weekly) infusions over four consecutive weeks **[medical record documentation required]**; **AND**
        ii. The patient will start their 9th infusion within 7 days of completing their 8th initial infusion **[medical record documentation required]**; **OR**
    b. Mixed response (MR), defined as improvement of at least one evaluable organ stage with worsening in another organ per the IBMTR Severity Index Criteria **[medical record documentation required]**; **AND**
        i. The patient will require treatment with 4 additional (weekly) infusions over four consecutive weeks **[medical record documentation required]**; **AND**
        ii. The patient will start their 9th infusion within 7 days of completing their 8th initial infusion **[medical record documentation required]**; **OR**
    c. Recurrence of grade B, C, or D aGVHD after achieving complete resolution of aGVHD in all involved organs **[medical record documentation required]**; **AND**

i. The patient will require treatment with 8 additional (twice weekly) infusions over four consecutive weeks **[medical record documentation required]**; **AND**

6. The patient does NOT have evidence of encephalopathy, or diffuse alveolar hemorrhage or other active pulmonary disease **[medical record documentation required]**; **AND**
7. The prescriber is a specialist in the area of the patient's diagnosis (e.g., oncologist, hematologist, transplant specialist) or has consulted with a specialist in the area of the patient's diagnosis **[medical record documentation required]**; **AND**
8. The requested dose is within FDA labeled dosing for the requested indication, and the requested quantity does NOT exceed the maximum units allowed for the duration of approval (see table below) **[medical record documentation required]**; **AND**
9. The patient has NOT received more than 16 infusions total **[medical record documentation required]**.

Duration of Approval: 30 days (1 month)
Partial or mixed response: 4 infusions total; Maximum of 16 infusions total per lifetime
Recurrence following complete response: 8 infusions total; Maximum of 16 infusions total per lifetime

** Please note, for certain identified gene and cellular therapies such as remestemcel-L-rknd (Ryoncil®), when coverage is available and the individual meets medically necessary criteria, distribution from a specialty pharmacy provider due to cost (distribution channel restriction) may be required in order for coverage to be provided. **Please contact Blue Cross NC** to coordinate this therapy.

FDA Label Reference				
Medication	**Indication**	**Dosing**	**HCPCS**	**Maximum Units***
remestemcel-L-rknd (Ryoncil®) intravenous (IV) infusion	SR-aGVHD in pediatric patients ≥ 2 months of age	IV: 2 × 10^6 mesenchymal stromal cell (MSC)/kg body weight per infusion • Initial treatment: twice weekly (at least 3 days apart) for 4 consecutive weeks for **8 infusions total** • Assess response 28 ± 2 days after first dose and give further treatment as appropriate based on day 28 response as follows: ○ Complete response: no further Ryoncil treatment ○ Partial or mixed response: repeat Ryoncil treatment once weekly for an additional 4 consecutive weeks (**4 infusions total**) ○ No response: consider alternative treatments	J3402	Initial: 8 infusions Continuation: Partial or mixed response: 4 infusions Recurrence following complete response: 8 infusions

FDA Label Reference				
Medication	**Indication**	**Dosing**	**HCPCS**	**Maximum Units***
		○ Recurrence of GVHD after complete response: repeat Ryoncil treatment twice weekly for an additional 4 consecutive weeks (**8 infusions total**)		

***Maximum units allowed for duration of approval**

Other revenue codes that may be applicable to this policy: 0891, 0892

References: all information referenced is from FDA package insert unless otherwise noted below.

1. 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 Graft-versus-Host Disease. *Biol Blood Marrow Transplant*. 2020;26(5):845-854.

Policy Implementation/Update Information: Criteria and treatment protocols are reviewed annually by the Blue Cross NC P&T Committee, regardless of change. This policy is reviewed in Q2 annually.

April 2026: Coding change: Added the following applicable revenue codes associated with policy HCPCS code(s): 0891 (Special Processed Drugs – FDA Approved Cell Therapy) and 0892 (Special Processed Drugs – FDA Approved Gene Therapy). Added Gene/Cellular Therapy distribution channel management language according to benefit booklet for clarity. **Policy notification given 2/1/2026 for effective date 4/1/2026**.
October 2025: Coding change: Added HCPCS code J3402 (1 unit per therapeutic dose) to dosing reference table effective 10/1/2025; deleted C9399, J3490, J3590, and J9999 termed 9/30/2025.
October 2025: Criteria change: Removed Site of Care medical necessity criteria.
May 2025: Original medical policy criteria issued.