Ryoncil (remestemcel-L-rknd)

Humana

Medicaid Medical Coverage Policy

Original Effective Date: 05/06/2025
Effective Date: 06/13/2025
Review Date: 05/06/2025
Policy Number: HUM-2263-000
Line of Business: Medicaid
State(s): FL

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Description

Allogeneic (donor) hematopoietic cell transplantation (HCT) is a conventional and potentially curative treatment for childhood blood cancers, as well as nonmalignant inherited blood disorders such as beta thalassemia and sickle cell disease. The procedure involves transferring hematopoietic (blood-forming) stem cells from healthy donors to an individual whose own stem cells have been destroyed by disease or intensive treatments (eg, high-dose chemotherapy and/or radiation therapy). These donated stem cells can come from either a related or unrelated donor. After being infused into the receiver's bloodstream, the transplanted stem cells migrate to the bone marrow and start engraftment (producing new blood cells). To minimize the risk of the individual's immune system rejecting the donor cells and ensure successful engraftment, recipients can receive immunosuppressive therapy before the transplantation.[2]

Acute graft-versus-host disease (aGVHD) is a complication of an allogeneic HCT, that typically appears in the early post-transplantation period. The donor's immune cells (the graft) identify the recipient's body (the host) as foreign and triggers an immune response, where the GI tract, liver and skin are the organs primarily affected.[10] Although the incidence of aGVHD varies depending on the type of transplant and the source of the donor cells, *severe* aGVHD is linked to the highest risk of primary treatment failure and the highest transplant-related mortality.[5] Overall, aGVHD can occur in up to 50% of individuals receiving stem cells from a human leukocyte antigen (HLA)-matched sibling, with higher incidence rates when the stem cells come

from HLA-unmatched donors. The risk of developing aGVHD is greater in the older population compared to younger, with approximately 20% of pediatric individuals who undergo allogeneic HCT develop aGVHD.[2]

Treatment for aGVHD is based on the specific organs involved, the severity (or grade) of the disease and whether the GI tract is affected.[10] Steroid therapy is the primary first-line treatment and may be supplemented with additional medications.[2] Some individuals can develop **steroid-resistant (SR) aGVHD**, which is characterized by disease progression by day 5 or a lack of response to treatment by day 7.[10] An estimated 35% to 60% of individuals develop SR-aGVHD, with mortality rates as high as 90% in both the pediatric and adult population.[2]

Ryoncil (remestemcel-L-rknd) is an allogeneic bone marrow-derived mesenchymal stromal cell (MSC) therapy, approved by the US Food and Drug Administration (FDA) for the treatment of SR-aGVHD in pediatric individuals 2 months of age and older.[11] MSCs are versatile, nonhematopoietic cells with the ability to suppress the immune system, and when administered intravenously, they elicit minimal to no immune response from the host. Ryoncil (remestemcel-L-rknd) is reputed to reduce inflammation in SR-aGVHD by inhibiting the growth of donor white blood cells.[2] The recommended dosage per intravenous infusion is given twice per week for 4 consecutive weeks. Infusions should be administered at least 3 days apart.[11]

Requests for Ryoncil (remestemcel-L-rknd) require review by a medical director.

Coverage Determination

Humana members may be eligible under the Plan for **Ryoncil (remestemcel-L-rknd)** when the following criteria are met:

- Absence of limitations; **AND**
- Individual is 2 months to 17 years of age[5,11]; **AND**
- Individual is diagnosed with Grade B-D aGVHD (using grading scale, International Bone Marrow Transplant Registry [IBMTR]) requiring corticosteroid systemic therapy[11]; **AND**
- Individual has failed to respond to steroid treatment (failure to respond defined as any Grade B-D IBMTR) that shows progression within 3 days, or no improvement within 7 days of consecutive treatment with 2 mg/kg/day methylprednisolone or equivalent[5,11]; **AND**
- Individual has had persistent GI GVHD manifested by diarrhea with stool volume less than 500 mL/kg/day (for participants greater than 50 kg) or less than 30 mL/kg/day (for participants less than or equal to 50 kg)[5]. In the absence of nausea or vomiting, individuals could have been considered to have Grade B GVHD if one of the following applies:
    - Other causes of diarrhea had been ruled out (eg, Clostridium difficile, adenovirus or cytomegalovirus [CMV] infection, or oral magnesium administration)**; OR**

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

- Individual has adequate renal function (defined by a calculated creatinine clearance of greater than 30 mL/min per 1.73 m^2)[5]; **AND**
- Individual has 30 or greater score on the Karnofsky/Lansky performance status scale[5]

For repeat/subsequent infusions[11]:

- Assess response 28 plus/minus 2 days after the first dose and administer further treatment as appropriate as described in Appendix B

Coverage Limitations

Humana members may **NOT** be eligible under the Plan for **Ryoncil (remestemcel-L-rknd)** for any indications other than those listed above including, but may not be limited to[5,11]:

- Individual has a known hypersensitivity to dimethyl sulfoxide (DMSO) or to bovine, murine or porcine proteins; **OR**
- Individual is pregnant or breastfeeding

A review of the current medical literature shows that there is **no evidence** to determine that this service is standard medical treatment. There is an absence of current, widely-used treatment guidelines or acceptable clinical literature examining benefit and long-term clinical outcomes establishing the value of this service in clinical management for these indications.

Coding Information

Any codes listed on this policy are for informational purposes only. Do not rely on the accuracy and inclusion of specific codes. Inclusion of a code does not guarantee coverage and/or reimbursement for a service or procedure.

CPT® Code(s)	Description	Comments
No code(s) identified		
CPT® Category III Code(s)	**Description**	**Comments**
No code(s) identified		
HCPCS Code(s)	**Description**	**Comments**
J3590	Unclassified biologics	

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10. UpToDate, Inc. Treatment of acute graft-versus-host disease. https://uptodate.com. Updated January 17, 2025.

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Appendix

Appendix A

Severity of aGVHD is commonly graded using the IBMTR Severity Index[4]

Grade	Description
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)

Appendix B

Dosage administration - Recommended Treatment Based on Day 28 Response[11]

Response	Recommendation
Complete Response (CR)	No further treatment with Ryoncil
Partial or Mixed Response	Repeat administration of Ryoncil once a week for additional 4 weeks (4 infusions total)
No Response	Consider alternative treatments
Recurrence of GVHD after CR	Repeat administration of Ryoncil twice a week for an additional 4 consecutive weeks (8 infusions total)

Appendix C

Karnofsky performance status[8]

Condition	Percentage	Comments
Able to carry on normal activity and to work. No special care is needed.	100	Normal, no complaints, no evidence of disease
	90	Able to carry on normal activity, minor signs or symptoms of disease
	80	Normal activity with effort, some signs or symptoms of disease
Unable to work. Able to live at home, care for most personal needs. A varying degree of assistance is needed	70	Cares for self, unable to carry on normal activity or to do active work
	60	Requires occasional assistance, but is able to care for most of his needs
	50	Requires considerable assistance and frequent medical care
Unable to care for self. Requires equivalent of institutional or hospital care. Disease may be progressing rapidly	40	Disabled, requires special care and assistance. (In bed more than 50% of the time)
	30	Severely disabled, hospitalization is indicated although death not imminent. (Almost completely bedfast)
	20	Hospitalization necessary, very sick, active supportive treatment necessary. (Totally bedfast and requiring extensive nursing care by professionals and/or family)
	10	Moribund, fatal processes progressing rapidly. (Comatose or barely arousable)
	0	Dead

Change Summary

05/06/2025 New Policy.