BlueCross BlueShield
Federal Employee Program
Blue Cross Blue Shield Association
750 9th St NW, Suite 900
Washington, D.C. 20001
1-800-624-5060
Fax 1-877-378-4727

5.99.032

Section:	Prescription Drugs	**Effective Date:**	July 1, 2025
Subsection:	Miscellaneous Products	**Original Policy Date:**	April 25, 2025
Subject:	Ryoncil	**Page:**	1 of 4

Last Review Date: June 12, 2025

Ryoncil

Description

Ryoncil (remestemcel-L-rknd)

Background
Ryoncil (remestemcel-L-rknd) is an allogenic bone marrow-derived mesenchymal stromal cell (MSC) therapy indicated for the treatment of steroid-refractory acute graft versus host disease (SR-aGvHD). The mechanism of action for Ryoncil is not clear but may be related to immunomodulary effects. Data from in vitro studies demonstrate that MSCs inhibit T cell activation as measured by proliferation and secretion of pro-inflammatory cytokines. Acute GvHD occurs when alloreactive donor-derived T cells within donated tissue (graft) trigger and immunological response, and alloreactive donor-derived T cells play a role in mediating the systemic inflammation, cytotoxicity and potential end organ damage associated with aGvHD (1).

Regulatory Status
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 (1).

Ryoncil is contraindicated in patients with known hypersensitivity to dimethyl sulfoxide (DMSO) or porcine and bovine proteins (1).

Treatment with Ryoncil has been associated with hypersensitivity/acute infusion reactions, transmission of infectious agents, and ectopic tissue formation. Premedicate patients with an antihistamine and corticosteroids and monitor closely for signs and symptoms of hypersensitivity or acute infusion reactions. Infusion should be interrupted if a hypersensitivity or infusion reaction occurs. Do not administer Ryoncil in patients who experience serious or life-threatening reactions.

Ryoncil contains cells from human donors and has possible risks of transmitting infectious disease or agents despite screening and testing for many communicable diseases associated with xenotransplantation. Ectopic tissue formation may occur following treatment due to the ability of human mesenchymal stromal cells to differentiate into mesenchymal lineage cells such as bone, cartilage and fat cells (1).

The safety and effectiveness of Ryoncil in patients less than 2 months of age have not been established (1).

Related policies

Policy

This policy statement applies to clinical review performed for pre-service (Prior Approval, Precertification, Advanced Benefit Determination, etc.) and/or post-service claims.

Ryoncil may be considered **medically necessary** if the conditions indicated below are met.

Ryoncil may be considered **investigational** for all other indications.

Prior-Approval Requirements

Age 2 months through 17 years

Diagnosis

Patient must have the following:

1. Acute graft-versus-host disease (GVHD)
    a. Patient is steroid-refractory (progressed within 3 days or no improvement within 7 consecutive days of treatment with methylprednisolone 2 mg/kg/day or equivalent)

Prior – Approval *Renewal* Requirements

Age 2 months through 17 years

Diagnosis

Patient must have the following:

1. Acute graft-versus-host disease (GVHD)

AND ONE of the following:
   a. Partial or mixed response
   b. Recurrence of GVHD after complete response
      i. Patient is steroid-refractory

Policy Guidelines

Pre - PA Allowance

None

Prior - Approval Limits

Quantity 8 infusions

Duration 28 days

Prior – Approval *Renewal* Limits

Response	Quantity	Dosing
Partial or Mixed Response	4 infusions	1 infusion per week
Recurrence of GVHD after complete response	8 infusions	2 infusions per week

Duration 28 days*

*__ONE__ renewal __ONLY__

Rationale

Summary

Ryoncil (remestemcel-L-rknad) 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). Treatment with Ryoncil has been associated with hypersensitivity/acute infusion reactions, transmission of infectious agents, and ectopic tissue formation. The safety and effectiveness of Ryoncil in patients less than 2 months of age have not been established (1).

Prior authorization is required to ensure the safe, clinically appropriate, and cost-effective use of Ryoncil while maintaining optimal therapeutic outcomes.

References

1. Ryoncil [package insert]. New York, NY: Mesoblast, Inc.; January 2025.

Policy History

Date	Action
April 2025	Addition to PA
June 2025	Annual review

Keywords

This policy was approved by the FEP® Pharmacy and Medical Policy Committee on June 12, 2025 and is effective on July 1, 2025.