PROVIDER POLICIES & PROCEDURES

RYONCIL® (REMESTEMCEL-L-RKND)

The primary purpose of this document is to assist providers enrolled in the Connecticut Medical Assistance Program (CMAP) with the information needed to support a medical necessity determination for RYONCIL (remestemcel-L-rknd). By clarifying the information needed for prior authorization of services, HUSKY Health hopes to facilitate timely review of requests so that individuals obtain the medically necessary care they need as quickly as possible.

Graft-versus-host disease (GVHD) is a complication of allogeneic hematopoietic cell transplantation (HCT) that occurs when immune cells transplanted from a non-identical donor (the graft) recognize the transplant recipient (the host) as foreign, thereby triggering an immune response resulting in disease in the transplant recipient. When this occurs in the early post-transplantation period it is referred to as *acute graft-versus-host disease (aGVHD).* Systemic corticosteroids are primarily used in the treatment of more severe forms of GVHD, however when individuals have disease that progresses by day 5 or no response to treatment by day 7 this is termed *steroid-refractory acute graft versus host disease (SR-aGvHD).*

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.

CLINICAL GUIDELINE
Coverage guidelines for the use of Ryoncil will be made in accordance with the DSS definition of Medical Necessity. The following criteria are guidelines *only*. Coverage guidelines are based on an assessment of the individual and their unique clinical needs. If the guidelines conflict with the definition of Medical Necessity, the definition of Medical Necessity shall prevail. The guidelines are as follows:

Initial Requests

An initial 4-week course of treatment with RYONCIL (remestemcel-L-rknd) may be considered medically necessary for pediatric patients with SR-aGvHD when the following criteria are met:

A. The individual is between 2 months and 17 years of age; **AND**
B. The individual has been diagnosed with grades B-D aGvHD (excluding skin-only grade B) as defined by the International Blood and Marrow Transplantation Registry (IBMTR) severity index criteria; **AND**
C. The individual has failed to respond to steroid treatment, with failure to respond defined as any grade B-D aGvHD that shows progression within 3 days, or no improvement within 7 days of consecutive treatment with 2 mg/kg/day methylprednisolone or equivalent; **AND**
D. The medication is prescribed by or in consultation with a hematologist, oncologist, or a provider specializing in transplant medicine; **AND**
E. The individual has adequate renal function as defined by a calculated creatinine clearance of >30 mL/min per 1.73 m^2; **AND**

F. The individual has a Karnofsky/Lansky Performance Level ≥30; **AND**
G. The individual does not have any of the following:
    a. A known hypersensitivity to dimethyl sulfoxide (DMSO) or Porcine and Bovine proteins; **OR**
    b. Evidence of diffuse alveolar hemorrhage or other active pulmonary disease; **OR**
    c. An HSCT transplant for a solid tumor disease; **OR**
    d. Prior treatment with MSCs, including remestemcel-L-rknd; **OR**
    e. Evidence of severe hepatic veno-occlusive disease or sinusoidal obstruction; **OR**
    f. Evidence of encephalopathy, as defined by a change in mental status since the onset of aGVHD; **OR**
    g. Current pregnancy; **OR**
    h. Current treatment for a solid tumor malignancy; **AND**
H. The treating provider will follow all FDA-approved labeling for dosing, administration, and additional monitoring for Ryoncil.

Reauthorization Requests

Reauthorization for an additional 4-week treatment course with RYONCIL (remestemcel-L-rknd) in individuals who completed an initial 4-week treatment course may be considered medically necessary for pediatric patients with SR-aGvHD when the following criteria are met:

The individual has demonstrated one of the following after an initial 28-day course of treatment with Ryoncil:
A. Partial response: organ improvement of at least one stage without worsening of any other organ; **OR**
B. Mixed response: improvement of at least one evaluable organ with worsening in another organ per International Blood and marrow Transplantation Registry Severity Index criteria grading system.

Note: Requests for individuals who are experiencing a recurrence of SR-aGvHD after complete response to Ryoncil will be reviewed as an initial authorization request.

Investigational and Not Medically Necessary

Ryoncil for all other indications is considered investigational and not medically necessary.

Repeat treatment with Ryoncil is considered not medically necessary when the initial treatment has resulted in no response.

NOTE: EPSDT Special Provision
Early and Periodic Screening, Diagnosis, and Treatment (EPSDT) is a federal Medicaid requirement that requires the Connecticut Medical Assistance Program (CMAP) to cover services, products, or procedures for Medicaid enrollees under 21 years of age where the service or good is medically necessary health care to correct or ameliorate a defect, physical or mental illness, or a condition identified through a screening examination. The applicable definition of medical necessity is set forth in Conn. Gen. Stat. Section 17b-259b (2011) [ref. CMAP Provider Bulletin PB 2011-36].

PROCEDURE

Prior authorization of Ryoncil is required. Coverage determinations will be based upon a review of requested and/or submitted case-specific information.

The following information is needed to review requests for Ryoncil:

1. Fully completed State of Connecticut, Department of Social Services HUSKY Health Program Ryoncil Prior Authorization Request form (to include physician's order and signature);
2. Clinical documentation supporting the medical necessity of treatment with Ryoncil should include the following:
    a. Medical record documentation confirming:
        i. Diagnosis of grades B-D SR-aGvHD (Note: failure to respond to steroid treatment is defined as any grade B-D aGvHD that shows progression within 3 days, or no improvement within 7 days of consecutive treatment with 2 mg/kg/day methylprednisolone or equivalent); **AND**
    b. Signed provider attestation confirming the following:
        i. The individual has adequate renal function as defined by a calculated creatinine clearance of >30 mL/min per 1.73 m^2 ; **AND**
        ii. The individual has a Karnofsky/Lansky Performance Level ≥30; **AND**
        iii. The individual does not have any of the following:
            1. A known hypersensitivity to dimethyl sulfoxide (DMSO) or Porcine and Bovine proteins; **OR**
            2. Evidence of diffuse alveolar hemorrhage or other active pulmonary disease; **OR**
            3. An HSCT transplant for a solid tumor disease; **OR**
            4. Prior treatment with MSCs, including remestemcel-L-rknd; **OR**
            5. Evidence of severe hepatic veno-occlusive disease or sinusoidal obstruction; **OR**
            6. Evidence of encephalopathy, as defined by a change in mental status since the onset of aGvHD; **OR**
            7. Current pregnancy; **OR**
            8. Current treatment for a solid tumor malignancy; **AND**
        iv. The provider will follow all FDA-approved labeling for dosing, administration, and additional monitoring for Ryoncil
3. Other information as requested.

Initial Authorization

If the above criteria are met, authorization will be given for one four-week course of treatment (twice per week for four weeks).

Reauthorization

If the above criteria are met, reauthorization will be given for one additional course of treatment as follows:

In individuals with partial or mixed response:

- An additional four-week course of Ryoncil to be administered once per week for four weeks

EFFECTIVE DATE

This Policy for the prior authorization of Ryoncil for individuals covered under the HUSKY Health Program is

effective February 01, 2026.

LIMITATIONS
Not Applicable

CODE:

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

DEFINITIONS

1. **Current Procedural Terminology (CPT):** The most recent edition of a listing, published by the American Medical Association, of descriptive terms and identifying codes for reporting medical services performed by providers.
2. **HUSKY A**: Connecticut children and their parents or a relative caregiver; and pregnant women may qualify for HUSKY A (also known as Medicaid). Income limits apply.
3. **HUSKY B**: Uninsured children under the age of 19 in higher income households may be eligible for HUSKY B (also known as the Children's Health Insurance Program) depending on their family income level. Family cost-sharing may apply.
4. **HUSKY C**: Connecticut residents who are age 65 or older or residents who are ages 18-64 and who are blind, or have another disability, may qualify for Medicaid coverage under HUSKY C (this includes Medicaid for Employees with Disabilities (MED-Connect), if working). Income and asset limits apply.
5. **HUSKY D**: Connecticut residents who are ages 19-64 without dependent children and who: (1) do not qualify for HUSKY A; (2) do not receive Medicare; and (3) are not pregnant, may qualify for HUSKY D (also known as Medicaid for the Lowest-Income populations).
6. **HUSKY Health Program**: The HUSKY A, HUSKY B, HUSKY C, HUSKY D and HUSKY Limited Benefit programs, collectively.
7. **HUSKY Limited Benefit Program or HUSKY, LBP**: Connecticut's implementation of limited health insurance coverage under Medicaid for individuals with tuberculosis or for family planning purposes and such coverage is substantially less than the full Medicaid coverage.
8. **Medically Necessary or Medical Necessity**: (as defined in Connecticut General Statutes § 17b-259b) Those health services required to prevent, identify, diagnose, treat, rehabilitate or ameliorate an individual's medical condition, including mental illness, or its effects, in order to attain or maintain the individual's achievable health and independent functioning provided such services are: (1) Consistent with generally-accepted standards of medical practice that are defined as standards that are based on (A) credible scientific evidence published in peer-reviewed medical literature that is generally recognized by the relevant medical community, (B)recommendations of a physician-specialty society, (C) the views of physicians practicing in relevant clinical areas, and (D) any other relevant factors; (2) clinically appropriate in terms of type, frequency, timing, site, extent and duration and considered effective for the individual's illness, injury or disease; (3) not primarily for the convenience of the individual, the individual's health care provider or other health care providers; (4) not more costly than an alternative service or sequence of services at least as likely to produce equivalent therapeutic or diagnostic results as to the diagnosis or treatment of the individual's illness, injury or disease; and (5) based on an assessment of the individual and his or her medical condition.
9. **Prior Authorization**: A process for approving covered services prior to the delivery of the service or initiation of the plan of care based on a determination by CHNCT as to whether the requested

service is medically necessary.

ADDITIONAL RESOURCES AND REFERENCES:

- 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). ClinicalTrials.gov identifier: NCT02336230.Updated March 17, 2022. https://clinicaltrials.gov/study/NCT02336230
- Chao NJ. Clinical manifestations, diagnosis, and grading of acute graft-versus-host disease. In: UpToDate, Negrin RS, Rosmarin AG (Eds.). Wolters Kluwer. Updated August 27, 2024. Accessed October 29, 2025.
- 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. doi:10.1016/j.bbmt.2020.01.018
- Mahat U, Przepiorka D, Fashoyin-Aje LA. Remestemcel-L-rknd for Steroid-Refractory Acute Graft-vs-Host Disease in Pediatric Patients. *JAMA.* 2025;334(1):81–82. doi:10.1001/jama.2025.6179
- Ryoncil [package insert]. New York, NY; Mesoblast, Inc.; Revised January 2025.
- Zeiser R. Treatment of acute graft-versus-host disease. In: UpToDate, Negrin RS, Chao NJ, Rosmarin AG (Eds.). Wolters Kluwer. Updated May 16, 2025. Accessed October 29, 2025

PUBLICATION HISTORY

Status	Date	Action Taken
Original publication	November 2025	Approved at the November 12, 2025 CHNCT Medical Reviewer meeting. Approved by the CHNCT Clinical Quality Subcommittee on December 15, 2025. Approved by DSS on 12/29/2025.