CARECONTINUUM™

UTILIZATION MANAGEMENT MEDICAL POLICY

POLICY: Immune Disorders – Gene Therapy – Kresladi Utilization Management Medical Policy
- Kresladi® (marnetegragene autotemcel intravenous infusion – Rocket)

REVIEW DATE: 08/05/2026

OVERVIEW

Kresladi, an autologous hematopoietic stem cell (HSC)-based gene therapy, is indicated for the treatment of **severe leukocyte adhesion deficiency-I (LAD-I)**, in pediatric patients, due to biallelic variants in the integrin subunit beta 2 (*ITGB2*) gene without an available human leukocyte antigen (HLA)-matched sibling donor for allogeneic HSC transplant (HSCT).[1]

Kresladi is for autologous, one-time (per lifetime), single-dose intravenous use only.[1] Kresladi is composed of one or two infusion bags which contain 0.34 to 6.1 x 10^6 cells/mL suspended in a cryopreservation solution. Each infusion bag contains approximately 30 mL of Kresladi. Up to two drug product lots may be administered to meet the recommended dose. The minimum dose is 2.8 x 10^6 cells/kg.

Disease Overview

LAD-I is a rare, autosomal recessive inborn error of immunity characterized by defective leukocyte adhesion, migration, and tissue recruitment during infection and inflammation.[2,3] The estimated global prevalence of LAD-I is approximately 1 per 1 million individuals, although the true prevalence is likely underestimated due to the absence of routine newborn screening and variable clinical recognition, particularly in milder or atypical cases.[4] LAD-I most commonly presents in infancy or early childhood, especially in patients with severe disease. Historically, fewer than 400 cases had been reported worldwide prior to 2018.[3]

LAD-I is caused by pathogenic loss-of-function variants in the *ITGB2* gene, which encodes the beta 2 integrin subunit CD18, a critical component of leukocyte adhesion complexes.[2,3] Deficient or dysfunctional CD18 results in failure of neutrophil migration to sites of infection. Clinically, LAD-I is characterized by recurrent, severe bacterial and fungal infections, impaired wound healing, and the absence of pus at sites of infection, reflecting defective neutrophil recruitment.[2,3] Severe LAD-I is associated with high early mortality, with historical survival estimates indicating that only approximately 25% to 40% of untreated patients survive beyond 2 years of age. Importantly, survival past infancy or early childhood does not indicate disease attenuation, as patients with severe LAD-I continue to face persistent or increasing risks of life-threatening infections, inflammatory complications, and death without definitive therapy.[4] Patients with moderate LAD-I generally survive childhood but experience recurrent infections and chronic inflammatory disease, with substantial long-term morbidity and reduced life expectancy in the absence of curative treatment.[3]

Clinical Efficacy

The efficacy of Kresladi was evaluated in one Phase I/II study in pediatric patients with severe LAD-I (published) [n = 9].[2] Eligible patients were ≥ 3 months of age with a confirmed diagnosis of severe LAD-I.[2,5] Criteria included < 2% of CD18-expressing polymorphonuclear neutrophils (PMNs), as assessed by flow cytometry. Alternatively, patients with ≥ 2% of CD18-expressing PMNs could be enrolled if < 2% of the PMNs expressed CD11a or CD11b. All patients had pathogenic or likely pathogenic *ITGB2* variants. Patients with an eligible HLA-matched sibling donor were excluded. Kresladi was administered as a one-

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time intravenous infusion with a median cell dose of 4.3 x 10^6 cells/kg (range 2.8 x 10^6 cells/kg to 10 x 10^6 cells/kg).

Consensus Statement

Recent international expert consensus (2026) provides detailed guidance on the diagnosis, severity classification, and management of LAD-I, emphasizing integration of laboratory findings with clinical phenotype.[4] There is strong consensus that severe LAD-I is defined as meeting one of the following: 1) < 2% of expected PMN CD18 expression, or 2) ≥ 2% of expected PMN CD18 expression and < 2% of expected PMN CD11a and/or CD11b expression. Molecular genetic testing in conjunction with flow cytometry is considered ideal for confirmation of LAD-I diagnosis (strong consensus). In particular, the diagnostic criteria note that confirmatory *ITGB2* testing is mandatory before gene therapy (i.e., Kresladi); genetic testing is best practice but not mandatory prior to allogeneic HSCT. It is also remarked that it is ideal to diagnose severe LAD-I prior to clinical manifestations; definitive therapeutic modalities should be discussed without waiting for manifestations to occur.

POLICY STATEMENT

Prior Authorization is recommended for medical benefit coverage of Kresladi. Approval is recommended for those who meet the **Criteria** and **Dosing** for the listed indication. Because of the specialized skills required for evaluation and diagnosis of patients treated with Kresladi as well as the specialized training required for administration of Kresladi, approval requires Kresladi to be prescribed by a physician who specializes in the condition being treated. All approvals are provided for one-time (per lifetime) as a single dose. The approval duration is 1 year to allow for an adequate time frame to prepare and administer one dose of therapy. If claims history is available, verification is required for certain criteria, as noted by **[verification in claims history required]**. For dosing criteria, verification of the appropriate weight-based dosing is required by the Medical Director as noted by **[verification required]**.

All reviews (approvals and denials) will be forwarded to the Medical Director for evaluation. Some clients have elected Embarc Benefit Protection. For these clients, the Medical Director will coordinate with EviCore to ensure the Embarc Benefit Protection portion of the review has been completed. If the Embarc Benefit Protection portion of the review has not been completed, the Medical Director will route to Embarc@EviCore.com prior to completing the review.

Documentation: Documentation is required for use of Kresladi as noted in the criteria as **[documentation required]**. Documentation may include, but is not limited to, chart notes, laboratory tests, medical test results, claims records, prescription receipts, and/or other information. All documentation must include patient-specific identifying information.

Automation: None.

RECOMMENDED AUTHORIZATION CRITERIA

Coverage of Kresladi is recommended in those who meet the following criteria:

FDA-Approved Indication

1. **Leukocyte Adhesion Deficiency-I.** Approve a one-time (per lifetime) single dose if the patient meets ALL of the following (A, B, C, D, E, F, G, H, and I):
   A) Patient is < 18 years of age; AND

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B) Patient has not received Kresladi in the past **[verification in claims history required]**; AND
Note: If no claims for Kresladi is present (or if claims history is not available), the prescribing physician confirms that the patient has not previously received Kresladi.

C) According to the prescribing physician, hematopoietic stem cell transplantation (HSCT) is appropriate for the patient; AND

D) Patient meets ONE of the following (i or ii):
- **i.** Patient does not have a Human Leukocyte Antigen (HLA)-matched sibling donor; OR
- **ii.** Patient has an HLA-matched sibling donor, but the individual is not able or is not willing to donate; AND

E) Diagnosis of severe leukocyte adhesion deficiency-I is confirmed by BOTH of the following (i and ii):
- **i.** Documented biallelic pathogenic or likely pathogenic variants in the *ITGB2* gene **[documentation required]**; AND
- **ii.** Patient meets ONE of the following (a or b):
  - **a)** Patient has < 2% of normal CD18-expressing polymorphonuclear neutrophils as assessed by flow cytometry **[documentation required]**; OR
  - **b)** Patient meets BOTH of the following [(1) and (2)]:
    - **(1)** Patient has ≥ 2% of normal CD18-expressing polymorphonuclear neutrophils as assessed by flow cytometry **[documentation required]**; AND
    - **(2)** Patient has < 2% of normal CD11a- or CD11b-expressing polymorphonuclear neutrophils as assessed by flow cytometry **[documentation required]**; AND

F) According to the prescribing physician, patient does not have an active bloodstream infection or other serious, untreated infection; AND

G) The medication is prescribed by a hematologist, stem cell transplant physician, or pediatric immunologist with expertise in inborn errors of immunity; AND

H) Current patient body weight has been obtained within the past 30 days **[documentation required]**; AND

I) If criteria A through H are met, approve one dose of Kresladi by intravenous infusion to provide a one-time (per lifetime) single dose which contains a minimum of 2.8 x 10^6 CD34+ cells/kg of body weight **[verification required]**.

Dosing. The recommended dose of Kresladi is a one-time (per lifetime) single dose which contains a minimum of 2.8 x 10^6 CD34+ cells/kg of body weight administered by intravenous infusion.

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Coverage of Kresladi is not recommended in the following situations:

1. **Prior Receipt of Gene Therapy.** Kresladi has not been studied in patients who have undergone prior gene therapy.

2. **Leukocyte Adhesion Deficiency-II or -III.** Leukocyte adhesion deficiencies II and III are caused by genetic variants other than *ITGB2* and result in leukocyte migration defects unrelated to CD18; these conditions would not be expected to be responsive to Kresladi therapy.

3. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

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REFERENCES

1. Kresladi™ intravenous infusion [prescribing information]. Cranbury, NJ: Rocket; March 2026.
2. Booth C, Sevilla J, Almarza E, et al. Lentiviral gene therapy for severe leukocyte adhesion deficiency type 1. *N Engl J Med*. 2025;392(17):1698-1709.
3. Almarza Novoa E, Kasbekar S, Thrasher AJ, et al. Leukocyte adhesion deficiency-I: a comprehensive review of all published cases. *J Allergy Clin Immunol Pract*. 2018;6(4):1418-1420.
4. Heimall J, González-Granado LI, Booth C, et al. International clinical consensus on leukocyte adhesion deficiency-I: Modified Delphi analysis. *J Allergy Clin Immunol Glob*. 2026;5(3):100682.
5. Rocket Pharmaceuticals. A clinical trial to evaluate the safety and efficacy of RP-L201 in subjects with leukocyte adhesion deficiency-I. In: ClinicalTrials.gov [Internet]. Bethesda (MD): National Library of Medicine (US). 2000- [cited 2026 Aug 03]. Available at: https://clinicaltrials.gov/study/NCT03812263. NLM Identifier: NCT03812263.

HISTORY

Type of Revision	Summary of Changes	Review Date
New Policy	--	08/05/2026
Update	09/02/2026: No criteria changes. The following language was added to the policy statement: Some clients have elected Embarc Benefit Protection. For these clients, the Medical Director will coordinate with EviCore to ensure the Embarc Benefit Protection portion of the review has been completed. If the Embarc Benefit Protection portion of the review has not been completed, the Medical Director will route to Embarc@EviCore.com prior to completing the review.	NA

NA – Not applicable.

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