Preemptive policy: This is a P&T approved policy and can be used after the drug is FDA approved until it is superseded by an updated policy

CENTENE® Corporation

Clinical Policy: RP-L201

Reference Number: CP.PHAR.599
Effective Date: FDA Approval Date
Last Review Date: 02.23
Line of Business: Commercial, HIM, Medicaid

Coding Implications
Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

Description

RP-L201 is a gene therapy product consisting of autologous CD34+ enriched hematopoietic stem cells transduced with a Chim-CD18-WPRE lentiviral vector carrying a functional copy of the integrin beta-2 (*ITGB2)* gene.

FDA Approved Indication(s) [Pending]

RP-L201 is proposed for the treatment of severe leukocyte adhesion deficiency type 1 (LAD-I) disorder.

Policy/Criteria

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

It is the policy of health plans affiliated with Centene Corporation® that RP-L201 is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria*

**Criteria will mirror the clinical information from the prescribing information once FDA-approved*

A. Leukocyte Adhesion Deficiency Type 1 (must meet all)**:**

1. Confirmed diagnosis of LAD-I as demonstrated by flow cytometry indicating one of the following (a or b):*
   a. CD18 expression on < 2% neutrophils (polymorphonuclear neutrophils [PMNs]);
   b. CD18 expression on ≥ 2% PMNs concurrently with all of the following (i, ii, and iii):
      i. CD11a or CD11b expression on < 2% PMNs;
      ii. Genetic testing showing *ITGB2* gene mutation;
      iii. Clinical history consistent with LAD-I or a known family history (*see Appendix D for examples*);
2. Prescribed by or in consultation with both of the following (a and b):*
   a. Transplant specialist;
   b. One of the following (i-iv):
      i. Hematologist;
      ii. Oncologist;
      iii. Immunologist;
      iv. Infectious disease specialist;

3. Age ≥ 3 months;*
4. For members without documented family history of LAD-I: ≥ 1 prior significant bacterial or fungal infection (*see Appendix D for examples*);*
5. One of the following (a or b):*
   a. Member has no available human leukocyte antigen (HLA)-matched sibling donors;
   b. Member has an available HLA-matched sibling donor, and both of the following (i and ii):
      i. Provider submits medical rationale that stem cell collection is not feasible (e.g., donor is in utero, is a newborn from whom cord blood was not collected, or is unable to undergo donation procedure because of medical impairments);
      ii. Member/caregiver understands the risks and benefits of alternative therapeutic options such as allogeneic hematopoietic stem cell transplantation (HSCT);
6. Transplant specialist attestation that member is clinically stable and eligible to undergo myeloablative conditioning and HSCT;*
7. Dose is at least 2 x 10^6 total CD34+ cells/kg.*

Approval duration: 3 months (one time infusion per lifetime)*

B. Other diagnoses/indications:

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

II. Continued Therapy*

**Criteria will mirror the clinical information from the prescribing information once FDA-approved*

A. Leukocyte Adhesion Deficiency Type 1

1. Continued therapy will not be authorized as RP-L201 is indicated to be dosed one time only.

Approval duration: Not applicable

B. Other diagnoses/indications:

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):

a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or
b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; or

2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 2 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

III. Diagnoses/Indications for which coverage is NOT authorized:

A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off-label use policies – CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

CD: cluster of differentiation
FDA: Food and Drug Administration
HLA: human leukocyte antigen
HSCT: hematopoietic stem cell transplantation
ITGB2: integrin beta-2
LAD-I: leukocyte adhesion deficiency type 1
PMNs: polymorphonuclear neutrophils

Appendix B: Therapeutic Alternatives

Not applicable

Appendix C: Contraindications/Boxed Warnings

- Contraindication(s): pending
- Boxed warning(s): pending

Appendix D: General Information

- Clinical history consistent with LAD-I includes as a hallmark symptom a delay in the detachment of the umbilical cord after birth (≥ 3 weeks) with frequent progression to inflammation of the umbilical cord stump and surrounding tissues (omphalitis); inflammation of the skin and mucous membranes (lining of the nose, mouth, gums); lack of pus formation at the sites of infection; and delayed wound healing due to impaired immune response.
- Significant bacterial and fungal infections are characterized as systemic, persistent, recurrent, severe, or progressing to large areas of the body. The infections most often affect the soft tissues such as skin, mucous membranes of the nose and the mouth causing gingivitis (inflammation of the gums), periodontitis (inflammation of the tissues around

the teeth) but may also develop in other sites and cause chronic middle ear infections (otitis media), pneumonia, peritonitis, and deep abscesses. The infections develop shortly after birth and throughout infancy and may cause life-threatening complications in many cases if not addressed in a timely manner.

V. Dosage and Administration [Pending]

Indication	Dosing Regimen	Maximum Dose
LAD-I*	Pending	Pending

VI. Product Availability [Pending]

Pending

VII. References

1. ClinicalTrials.gov. Gene Therapy for Leukocyte Adhesion Deficiency-I (LAD-I): A phase I/II clinical trial to evaluate the safety and efficacy of the infusion of autologous hematopoietic stem cells transduced with a lentiviral vector encoding the *ITGB2* gene. Last updated November 22, 2021. Available at: https://clinicaltrials.gov/ct2/show/NCT03812263. Accessed August 8, 2022.
2. McKusick, VA, Kniffin, CL. Leukocyte adhesion deficiency, type I; LAD-I. OMIM – Online Mendelian Inheritance in Man, Johns Hopkins University, 23 Aug. 2022. Available at: https://omim.org/entry/116920?search=%22lad%20deficiency%22&highlight=%22lad%20deficiency%22. Accessed September 3, 2022.
3. National Library of Medicine: MedlinePlus. Leukocyte adhesion deficiency type 1. April 1, 2014. Available at: https://medlineplus.gov/genetics/condition/leukocyte-adhesion-deficiency-type-1/#frequency. Accessed August 8, 2022.
4. National Organization for Rare Disorders. Leukocyte adhesion deficiency syndromes. 2018. Available at: https://rarediseases.org/rare-diseases/leukocyte-adhesion-deficiency-syndromes. Accessed August 8, 2022.

Coding Implications [Pending]

Codes referenced in this clinical policy are for informational purposes only. Inclusion or exclusion of any codes does not guarantee coverage. Providers should reference the most up-to-date sources of professional coding guidance prior to the submission of claims for reimbursement of covered services.

HCPCS Codes	Description
Pending	Pending

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy created pre-emptively	10.25.22	02.23

Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted

standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. "Health Plan" means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan's affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

This clinical policy is the property of the Health Plan. Unauthorized copying, use, and distribution of this clinical policy or any information contained herein are strictly prohibited. Providers, members and their representatives are bound to the terms and conditions expressed herein through the terms of their contracts. Where no such contract exists, providers, members and their representatives agree to be bound by such terms and conditions by providing services to members and/or submitting claims for payment for such services.

Note:
For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.