Clinical Policy: Atidarsagene Autotemcel (Lenmeldy)

Reference Number: CP.PHAR.602
Effective Date: 03.18.24
Last Review Date: 02.25
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

Atidarsagene autotemcel (Lenmeldy™) is an autologous hematopoietic stem cell-based gene therapy.

FDA Approved Indication(s)

Lenmeldy is indicated for the treatment of children with pre-symptomatic late infantile (PSLI), pre-symptomatic early juvenile (PSEJ), or early symptomatic early juvenile (ESEJ) metachromatic leukodystrophy (MLD).

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.

All requests reviewed under this policy **require medical director review**.

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

I. Initial Approval Criteria

A. Metachromatic Leukodystrophy* (must meet all)**:**

**Only for initial treatment dose; subsequent doses will not be covered.*

1. Diagnosis of MLD confirmed by both of the following (a and b):
   a. Arylsulfatase A (ARSA) activity below the normal range in peripheral blood mononuclear cells or fibroblasts;
   b. Presence of two disease-causing mutations of either known or novel alleles, and:
      i. If novel alleles are identified, elevated sulfatide levels in a 24-hour urine collection;
2. Prescribed by or in consultation with a medical geneticist, neurologist, or physician specialized in bone marrow transplantation (e.g., hematologist/oncologist);
3. One of the following (a or b):
   a. Age < 7 years;
   b. Age between 7 to 17 years, and age at onset of symptoms was < 7 years;
4. Member has one of the following forms of MLD (a, b, or c) (*see Appendix D*):
   a. PSLI;
   b. PSEJ;
   c. ESEJ, and member is able to walk independently (i.e., without support) and does not have cognitive decline (i.e., intelligence quotient [IQ] ≥ 85);

5. Member has not previously received hematopoietic stem cell gene therapy;
6. If member has previously received allogeneic hematopoietic stem cell transplant, both of the following (a and b):
   a. It has been > 6 months since the transplant;
   b. There is no evidence of residual cells of donor origin;
7. Dose is at least one of the following (a, b, or c):
   a. PSLI: 4.2×10^6 $CD34^+$ cells/kg;
   b. PSEJ: 9×10^6 $CD34^+$ cells/kg;
   c. ESEJ: 6.6×10^6 $CD34^+$ cells/kg;
8. Dose does not exceed 30×10^6 $CD34^+$ cells/kg.

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

B. Other diagnoses/indications (must meet 1 or 2)**:**

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

A. Metachromatic Leukodystrophy

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

Approval duration: Not applicable

B. Other diagnoses/indications (must meet 1 or 2)**:**

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.

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

ARSA: arylsulfatase A
ENG: electroneurography
ESEG: early symptomatic early juvenile
FDA: Food and Drug Administration
GMFC: gross motor function classification
IQ: intelligence quotient
MLD: metachromatic leukodystrophy
PSEJ: pre-symptomatic early juvenile
PSLI: pre-symptomatic late infantile

Appendix B: Therapeutic Alternatives

Not applicable

Appendix C: Contraindications/Boxed Warnings

None reported

Appendix D: General Information

- The MLD disease spectrum can present in a variety of clinical forms, primarily based on the age of onset of the first symptoms of the disease. To date, Lenmeldy has only demonstrated efficacy in the late infantile and early juvenile forms. There is an ongoing study in the late juvenile form with estimated study completion in March 2031.
- In clinical studies, the late infantile and early juvenile MLD forms were defined as follows:
  - PSLI: Late infantile – pre-symptomatic, and 2 out of the following 3 criteria must be met:
    - Age at onset of symptoms in the older sibling(s) ≤ 30 months
    - 2 null (0) mutant ARSA alleles
    - Peripheral neuropathy at electroneurography (ENG) study

- PSEJ, ESEJ: Early juvenile – pre- or early-symptomatic, and 2 out of the following 3 criteria must be met:
  - Age at onset of symptoms (in the patient or in the older sibling) between 30 months and 6 years (had not celebrated their 7th birthday)
  - 1 null (0) and 1 residual (R) mutant ARSA allele(s)
  - Peripheral neuropathy at ENG study with null (0) or residual (R) alleles referring to either known or novel mutations
- Pre-symptomatic clinical status was defined as patients without neurological impairment (disease-related symptoms). Pre-symptomatic children were permitted to have abnormal reflexes or abnormalities on brain magnetic resonance imaging and/or nerve conduction tests not associated with functional impairment (e.g., no tremor, no peripheral ataxia).
- Early-symptomatic clinical status was defined as patients meeting the following 2 criteria: IQ ≥ 85 and the ability to walk independently (gross motor function classification for MLD [GMFC-MLD] Level 0 with ataxia or GMFC-MLD Level 1).

- GMFC-MLD:
  - Level 0 = walking without support quality of performance normal for age
  - Level 1 = walking without support but with reduced quality of performance
  - Level 2 = walking with support, walking without support not possible
  - Level 3 = sitting without support and locomotion such as crawling or rolling, walking without support not possible
  - Level 4 = sitting without support but no locomotion or sitting without support not possible but locomotion such as crawling or rolling
  - Level 5 = no locomotion nor sitting without support but head control is possible
  - Level 6 = loss of any locomotion as well as loss of any head and trunk control

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
MLD	One time IV infusion of a minimum dose as described below, up to a maximum dose of 30×10^6 $CD34^+$ cells/kg • PSLI: 4.2×10^6 $CD34^+$ cells/kg • PSEJ: 9×10^6 $CD34^+$ cells/kg • ESEJ: 6.6×10^6 $CD34^+$ cells/kg	30×10^6 $CD34^+$ cells/kg

VI. Product Availability

Single-dose cell suspension for intravenous infusion. Lenmeldy is composed of one to eight infusion bags which contain 2 to 11.8×10^6 cells/mL (1.8 to 11.8 x 10^6 $CD34^+$ cells/mL) suspended in cryopreservation solution.

VII. References

1. Lenmeldy Prescribing Information. Boston, MA: Orchard Therapeutics; March 2024. Available at: www.lenmeldy.com. Accessed October 31, 2024.
2. Orchard Therapeutics. Gene therapy for metachromatic leukodystrophy (MLD). ClinicalTrials.gov. Available at: https://clinicaltrials.gov/ct2/show/NCT01560182. Accessed October 31, 2024.

3. Orchard Therapeutics. A safety and efficacy study of cryopreserved OTL-200 for treatment of metachromatic leukodystrophy. ClinicalTrials.gov. Available at: https://classic.clinicaltrials.gov/ct2/show/NCT03392987. Accessed October 31, 2024.
4. Sessa M, Lorioli L, Fumgalli F, et al. Lentiviral haemopoietic stem-cell gene therapy in early-onset metachromatic leukodystrophy: an ad-hoc analysis of a non-randomised, open-label, phase 1/2 trial. Lancet. 2016; 388(10043): 476-487.
5. Fumagalli F, Calbi V, Sora MGN, et al. Lentiviral haematopoietic stem-cell gene therapy for early-onset metachromatic leukodystrophy: long-term results from a non-randomised, open-label, phase 1/2 trial and expanded access. Lancet. 2022; 399(10322): 372-383.
6. Lin G, Suh K, Fahim SM, et al. Atidarsagene autotemcel for metachromatic leukodystrophy. Institute for Clinical and Economic Review, October 30, 2023. Available at: https://icer.org/assessment/metachromatic-leukodystrophy-2023. Accessed October 31, 2024.

Coding Implications

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
J3391	Injection, atidarsagene autotemcel, per treatment

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy created pre-emptively	09.06.22	02.23
1Q 2024 annual review: no significant changes as drug is not yet FDA-approved; references reviewed and updated.	11.02.23	02.24
RT1: drug is now FDA approved – criteria updated per FDA labeling: clarified diagnostic criteria to only require 24-hour urine collection if novel alleles are identified, added coverage for children between 7 to 17 years of age as long as onset of symptoms began before age 7, revised MLD forms to align with terminology used in the PI, clarified that walking independently means without support and modified IQ requirement from 70 to 85, updated dosing to include minimum and maximum recommendations; added physician specialized in bone marrow transplantation as a prescriber option per specialist feedback; added allowance for prior receipt of allogeneic hematopoietic stem cell transplant in alignment with study protocol; references reviewed and updated.	05.07.24	08.24
1Q 2025 annual review: no significant changes; references reviewed and updated.	10.31.24	02.25
HCPCS code added [J3391] and removed codes [J3590, C9399].	05.16.25	

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.