# Clinical Policy: Atidarsagene Autotemcel (Lenmeldy)

Reference Number: PA.CP.PHAR.602
Effective Date: 08/2024
Last Review Date: 01/2026

**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 PA Health & Wellness® 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: $4.2 \times 10^6$ $CD34^+$ cells/kg;
   b. PSEJ: $9 \times 10^6$ $CD34^+$ cells/kg;
   c. ESEJ: $6.6 \times 10^6$ $CD34^+$ cells/kg;
8. Dose does not exceed $30 \times 10^6$ $CD34^+$ cells/kg.

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

**B. Other diagnoses/indications**

1. Refer to the off-label use policy if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): PA.CP.PMN.53

## 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. Currently receiving medication via PA Health & Wellness benefit and documentation supports positive response to therapy or the Continuity of Care policy (PA.PHARM.01) applies.

   **Approval duration: Duration of request or 12 months (whichever is less)**; or
2. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): PA.CP.PMN.53

## 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 – PA.CP.PMN.53

## 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 7$^{th}$ 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 $30 \times 10^6$ $CD34^+$ cells/kg<br>• PSLI: $4.2 \times 10^6$ $CD34^+$ cells/kg | $30 \times 10^6$ $CD34^+$ cells/kg |

| | | |
|---|---|---|
| | • PSEJ: $9 \times 10^6$ $CD34^+$ cells/kg<br>• ESEJ: $6.6 \times 10^6$ $CD34^+$ 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 $11.8 \times 10^6$ 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 24, 2025.
2. Orchard Therapeutics. Gene therapy for metachromatic leukodystrophy (MLD). ClinicalTrials.gov. Available at: https://clinicaltrials.gov/ct2/show/NCT01560182. Accessed November 5, 2025.
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 November 5, 2025.
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 November 5, 2025.
7. Adang LA, Bonkowsky JL, Boelens JJ, et al. Consensus guidelines for the monitoring and management of metachromatic leukodystrophy in the United States. Cytotherapy. 2024; 26(7): 739-748.

## 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 |
|---|---|
| Policy created | 07/2024 |
| 1Q 2025 annual review: no significant changes; references reviewed and updated. | 01/2025 |

| Reviews, Revisions, and Approvals | Date |
|---|---|
| 1Q 2026 annual review: no significant changes; HCPCS code added [J3391] and removed codes [J3590, C9399]; references reviewed and updated. | 01/2026 |