Lenmeldy™ (atidarsagene autotemcel)
(Intravenous)

Document Number: IC-0751

Last Review Date: 04/07/2025
Date of Origin: 04/04/2024
Dates Reviewed: 04/2024, 04/2025

I. Length of Authorization

Coverage will be provided for one treatment course (1 dose) and may not be renewed.

II. Dosing Limits

Max Units (per dose and over time) [HCPCS Unit]:

- A single dose of Lenmeldy contains 2 to 11.8× 10^6 cells/mL (1.8 to 11.8 x 10^6 CD34+ cells/mL) suspended in one to eight patient-specific infusion bags

III. Initial Approval Criteria [1]

Submission of supporting clinical documentation (including but not limited to medical records, chart notes, lab results, and confirmatory diagnostics) related to the medical necessity criteria is REQUIRED on all requests for authorizations. Records will be reviewed at the time of submission as part of the evaluation of this request. Please provide documentation related to diagnosis, step therapy, and clinical markers (i.e., genetic, and mutational testing) supporting initiation when applicable. Please provide documentation via direct upload through the PA web portal or by fax. Failure to submit the medical records may result in the denial of the request due to inability to establish medical necessity in accordance with policy guidelines.

Coverage is provided for the following conditions:

- Patient is less than 18 years of age; **AND**
- Patient is screened and found to be negative for hepatitis B virus (HBV), hepatitis C virus (HCV), human T-lymphotropic virus 1 & 2 (HTLV-1/HTLV-2), human immunodeficiency virus 1 & 2 (HIV-1/HIV-2), and mycoplasma infection before collection of cells for manufacturing; **AND**
- Patient will not be administered vaccinations during the 6 weeks preceding the start of myeloablative conditioning, and until hematological recovery following treatment *(Note: Where feasible, administer childhood vaccinations prior to myeloablative conditioning)*; **AND**
- Patient risk factors for thrombosis as well as veno-occlusive disease have been evaluated prior to administration; **AND**
- Prophylaxis for infection will be followed according to standard institutional guidelines; **AND**
- Patient will be monitored for hematological malignancies periodically after treatment; **AND**

- Patients will not receive prophylactic HIV anti-retroviral therapy for at least one-month preceding mobilization *(Note: anti-retrovirals may interfere with manufacturing)*; **AND**
- Patient will have mobilization of stem cells using granulocyte-colony stimulating factor (G-CSF with or without plerixafor); **AND**
- Used as single agent therapy (Note: not inclusive of busulfan conditioning regimen); **AND**
- Patient has not received a prior allogeneic stem cell transplant *(or has, but is without evidence of residual donor cells present),* and is a candidate for autologous stem cell transplantation (e.g., adequate renal and hepatic function); **AND**
- Patient does not have a known and available suitable 10/10 human leukocyte antigen matched related donor willing to participate in an allogeneic HSCT; **AND**
- Patient has not received other gene therapy for MLD; **AND**

Metachromatic Leukodystrophy (MLD) † Φ

- Patient has a confirmed diagnosis of MLD *(also known as arylsulfatase A deficiency)* as evidenced by the following biochemical and molecular markers:
    - Arylsulfatase A (ARSA) enzyme activity below the normal range in peripheral blood leukocytes or fibroblasts OR increased urinary excretion of sulfatides; **AND**
    - Presence of biallelic *ARSA* pathogenic mutation of known or novel polymorphisms *(Note: For patients with novel mutation(s), a 24-hour urine collection must show elevated sulfatide levels)*; **AND**
- Patient has pre-symptomatic late infantile (PSLI), presymptomatic early juvenile (PSEJ) or early symptomatic early juvenile (ESEJ) disease *(Note: Requests for children with late juvenile form of the disease will be reviewed on a case-by-case basis)*

† FDA Approved Indication(s); **‡** Compendia Recommended Indication(s); **Φ** Orphan Drug

IV. Renewal Criteria

- Duration of authorization has not been exceeded (*refer to Section I*)

V. Dosage/Administration

<table>
<tr><th>Indication</th><th>Dose</th></tr>
<tr><td>Metachromatic Leukodystrophy (MLD)</td><td>• Lenmeldy is provided as a single dose for infusion containing a suspension of CD34+ cells in one to eight infusion bags. The minimum and maximum recommended dose is based on the MLD disease subtype.
<table>
<tr><th>MLD Subtype</th><th>Minimum Recommended Dose (CD34+ cells/kg)</th><th>Maximum Recommended Dose (CD34+ cells/kg)</th></tr>
<tr><td>Pre-symptomatic late infantile</td><td>4.2×10^6</td><td>30×10^6</td></tr>
<tr><td>Pre-symptomatic early juvenile</td><td>9×10^6</td><td>30×10^6</td></tr>
<tr><td>Early symptomatic early juvenile</td><td>6.6×10^6</td><td>30×10^6</td></tr>
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	• The dose administered is calculated based on the child's weight at time of Lenmeldy infusion using the information provided on the Lot Information Sheet. See the Lot Information Sheet provided with the product shipment for additional information pertaining to dose.
– *Lenmeldy is for autologous use only. The patient's identity must match the patient identifiers on the drug cassette(s) and infusion bag(s).* – *Mobilization, apheresis, and myeloablative conditioning are required prior to LENMELDY infusion. Before initiating these procedures, confirm that hematopoietic stem cell (HSC) gene therapy is appropriate for the child.* – *A collection of a minimum of 8.0 × 10^6 CD34+ cells/kg of autologous cells is required based on a weight at time of apheresis collection. Collection of the minimum number of CD34+ cells required for manufacture may be achieved using one or more cycles of mobilization. A collection of unmanipulated back-up CD34+ cells of at least 2.0 × 10^6 CD34+ cells/kg is required. These cells must be collected from the child and be cryopreserved prior to myeloablative conditioning.*	

VI. Billing Code/Availability Information

HCPCS Code:

- J3590 – Unclassified biologics
- C9399 – Unclassified drugs or biologicals (*for hospital outpatient use only*)

NDC(s):

- Lenmeldy containing 2 to 11.8× 10^6 cells/mL (1.8 to 11.8 x 10^6 CD34+ cells/ml) suspended in one to eight patient-specific infusion bags: 83222-0200-xx

VII. References

1. Lenmeldy [package insert]. Boston, MA; Orchard Therapeutics NA; March 2024. Accessed February 2025.
2. ClinicalTrials.gov. An Open Label, Non-randomized Trial to Evaluate the Safety and Efficacy of a Single Infusion of OTL-200 in Patients With Late Juvenile (LJ) Metachromatic Leukodystrophy (MLD). https://clinicaltrials.gov/study/NCT04283227?intr=Atidarsagene&rank=1.
3. Biffi A, Montini E, Lorioli L, et al. Lentiviral hematopoietic stem cell gene therapy benefits metachromatic leukodystrophy. Science. 2013;341(6148):1233158. doi:10.1126/science.1233158
4. Fumagalli F, Calbi V, Natali Sora MG, 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. doi:10.1016/S0140-6736(21)02017-1
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6. ClinicalTrials.gov. A Phase I/II Clinical Trial of Hematopoietic Stem Cell Gene Therapy for the Treatment of Metachromatic Leukodystrophy. https://clinicaltrials.gov/study/NCT01560182?intr=NCT01560182&rank=1.

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10. Bonkowsky JL. Metachromatic leukodystrophy. In: Firth HV, Dashe JF (Eds.). *UpToDate*. Last updated July 11, 2024. Available at: https://www.uptodate.com/contents/metachromatic-leukodystrophy. Accessed March 2025.
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Appendix 1 – Covered Diagnosis Codes

ICD-10	ICD-10 Description
E75.25	Metachromatic leukodystrophy

Appendix 2 – Centers for Medicare and Medicaid Services (CMS)

The preceding information is intended for non-Medicare coverage determinations. Medicare coverage for outpatient (Part B) drugs is outlined in the Medicare Benefit Policy Manual (Pub. 100-2), Chapter 15, §50 Drugs and Biologicals. In addition, National Coverage Determinations (NCDs) and/or Local Coverage Determinations (LCDs) may exist and compliance with these policies is required where applicable. Local Coverage Articles (LCAs) may also exist for claims payment purposes or to clarify benefit eligibility under Part B for drugs which may be self-administered. The following link may be used to search for NCD, LCD, or LCA documents: https://www.cms.gov/medicare-coverage-database/search.aspx. Additional indications, including any preceding information, may be applied at the discretion of the health plan.

Medicare Part B Covered Diagnosis Codes (applicable to existing NCD/LCD/LCA): N/A

Medicare Part B Administrative Contractor (MAC) Jurisdictions		
Jurisdiction	**Applicable State/US Territory**	**Contractor**
E (1)	CA, HI, NV, AS, GU, CNMI	Noridian Healthcare Solutions, LLC
F (2 & 3)	AK, WA, OR, ID, ND, SD, MT, WY, UT, AZ	Noridian Healthcare Solutions, LLC
5	KS, NE, IA, MO	Wisconsin Physicians Service Insurance Corp (WPS)
6	MN, WI, IL	National Government Services, Inc. (NGS)

Medicare Part B Administrative Contractor (MAC) Jurisdictions		
Jurisdiction	**Applicable State/US Territory**	**Contractor**
H (4 & 7)	LA, AR, MS, TX, OK, CO, NM	Novitas Solutions, Inc.
8	MI, IN	Wisconsin Physicians Service Insurance Corp (WPS)
N (9)	FL, PR, VI	First Coast Service Options, Inc.
J (10)	TN, GA, AL	Palmetto GBA
M (11)	NC, SC, WV, VA (excluding below)	Palmetto GBA
L (12)	DE, MD, PA, NJ, DC (includes Arlington & Fairfax counties and the city of Alexandria in VA)	Novitas Solutions, Inc.
K (13 & 14)	NY, CT, MA, RI, VT, ME, NH	National Government Services, Inc. (NGS)
15	KY, OH	CGS Administrators, LLC