Lenmeldy™ (atidarsagene autotemcel)

(Intravenous)

Effective Date: 11/01/2024
Review Date: 08/28/2024
Scope: Medicaid, Commercial, Medicare-Medicaid Plan (MMP)

I. Length of Authorization

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

II. Dosing Limits

- **Quantity Limit (max daily dose) [NDC Unit]:**
  - A single dose of Lenmeldy contains 2 to 11.8 x 10^6 cells/mL (1.8 to 11.8 x 10^6 CD34+ cells/mL) suspended in one or more patient-specific infusion bags
- **Max Units (per dose and over time) [HCPCS Unit]:**
  - A single dose of Lenmeldy contains 2 to 11.8 x 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. Summary of Evidence

Lenmeldy is an autologous hematopoietic stem cell (HSC)-based gene therapy 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). The clinical efficacy and safety of Lenmeldy was established in two single-arm, open-label clinical trials (NCT01560182 and NCT03392987) and a European Union expanded access program. The motor function and overall survival of participants treated with Lenmeldy (N=37) were compared to an external untreated natural history cohort of children with late-infantile (N=28) and early juvenile MLD (N=21). All of the 17 children with the late-infantile form of MLD treated with Lenmeldy and followed until at least 5 years of age remained event free, with an event defined as the first occurrence of loss of locomotion and loss of sitting without support (Gross Motor Function Classification (GMFC)-MLD level ≥ 5) or death, compared to 0% of untreated children with late-infantile MLD. Treatment with Lenmeldy significantly extended overall survival compared with untreated natural history group; all Lenmeldy-treated children with PSLI MLD were alive at 6 years from birth, and 10 children in the natural history group had died (42%). The results for PSEJ MLD indicated that all 3 children with evaluable motor outcomes retained normal gait. The results for ESEJ MLD indicated that 3/10 children showed decline for motor and cognitive outcomes and 2/10 children treated with Lenmeldy died. The most common adverse reactions associated with treatment include febrile

neutropenia, stomatitis, respiratory tract infection, rash, device-related infections, other viral infections, pyrexia, gastroenteritis, and hepatomegaly. Common laboratory abnormalities reported with Lenmeldy use include elevated D-dimer, neutropenia, and elevated liver enzymes.

IV. Initial Approval Criteria [1]

Submission of medical records (chart notes) related to the medical necessity criteria is REQUIRED on all requests for authorizations. Records will be reviewed at the time of submission. Please provide documentation related to diagnosis, step therapy, and clinical markers (i.e. genetic and mutational testing) supporting initiation when applicable.

Coverage is provided for the following conditions:

- Patient age is less than 18 years; **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 a 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 10/10 human leukocyte antigen matched related donor willing to participate in an allogenic HSCT; **AND**

- Patient has not received other gene therapy for MLD; **AND**
- Lenmeldy is required to be prescribed by or in consultation with a neurologist, geneticist, hematologist, or oncologist; **AND**
- Patient will undergo treatment at a manufacturer approved Qualified Treatment Center (QTC); **AND**
- MMP members who have previously received this medication within the past 365 days are not subject to Step Therapy Requirements; **AND**

Metachromatic Leukodystrophy (MLD):

- Patient has documented 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 mononuclear cells-leukocytes or fibroblasts OR increased urinary excretion of sulfatides; **AND**
    - Presence of biallelic ARSA pathogenic mutation of known polymorphisms *(Note: Patients with novel mutations, a 24-hour urine collection must show elevated sulfatide levels),* **AND**
- Patient has pre-symptomatic late infantile (PSLI), pre-symptomatic early juvenile (PSEJ), or early symptomatic early juvenile (ESEJ) disease by meeting one of the following criteria:
    - Documentation of diagnosis of the PSLI subtype of MLD confirmed by both of the following:
        - Absence of disease-related symptoms; **AND**
        - Two out of three of the following:
            - Age at onset of symptoms in the older sibling(s) ≤30 months; **AND/OR**
            - Two null (0) mutant ARSA alleles; **AND/OR**
            - Peripheral neuropathy as determined by electroneurographic or electronystagmography study; **OR**
    - Documentation of diagnosis of the PSEJ subtype of MLD confirmed by both of the following:
        - Absence of disease-related symptoms or physical examination findings limited to clonus and/or abnormal reflexes not associated with functional impairment (e.g., no tremor, no peripheral ataxia); **AND**
        - Documentation of two out of three of the following:
            - Age at onset of symptoms (in the patient or in the older sibling(s)) between 30 months and <7 years; **AND/OR**
            - One null (0) and one residual (R) mutant ARSA allele(s); **AND/OR**
            - Peripheral neuropathy as determined by electroneurographic or electronystagmography study; **OR**
    - Documentation of diagnosis of the ESEJ subtype of MLD confirmed by all of the following:

- Gross Motor Function Classification (GMFC)-MLD score of ≤1; **AND**
- IQ ≥85 on age-appropriate neurodevelopmental testing; **AND**
- Documentation of two out of three of the following:
  - Age at onset of symptoms (in the patient or in the older sibling(s)) between 30 months and <7 years; **AND/OR**
  - One null (0) and one residual (R) mutant ARSA allele(s); **AND/OR**
  - Peripheral neuropathy as determined by electroneurographic or electronystagmography study

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

V. Renewal Criteria

Coverage cannot be renewed.

VI. Dosage/Administration

Indication	Dose
Metachromatic Leukodystrophy (MLD)	• 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. **MLD Subtype** / **Minimum Recommended Dose (CD34+ cells/kg)** / **Maximum Recommended Dose (CD34+ cells/kg)** **Pre-symptomatic late infantile** / **4.2×10^6** / **30×10^6** **Pre-symptomatic early juvenile** / **9×10^6** / **30×10^6** **Early symptomatic early juvenile** / **6.6×10^6** / **30×10^6** • 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.*	

VII. Billing Code/Availability Information

HCPCS Code:

- J3590 – Unclassified biologics

NDC(s):

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

VIII. References

1. Amtagvi [package insert]. Philadelphia, PA; Iovance Biotherapeutics Manufacturing, LLC; February 2024. Accessed February 2024.
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confirmation and management of presymptomatic individuals. ACMG Standards and Guidelines. Genet Med. 2011;13:457-84.

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10. Bonkowsky JL (Mar 2024). Metachromatic leukodystrophy. In Patterson MC, Firth HV, Dashe JF (Eds.). *UpToDate*. Accessed March 20, 2024. Available from: https://www.uptodate.com/contents/metachromatic-leukodystrophy?search=Metachromatic%20Leukodystrophy%20&source=search_result&selectedTitle=1%7E33&usage_type=default&display_rank=1#H6
11. Page KM, Stenger, EO, Connelly JA, et al. Hematopoietic Stem Cell Transplantation to Treat Leukodystrophies: Clinical Practice Guidelines from the Hunter's Hope Leukodystrophy Care Network. Biol Blood Marrow Transplant. 2019 Dec;25(12):e363-e374.

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 additions, 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,	Noridian Healthcare Solutions, LLC

	AZ	
5	KS, NE, IA, MO	Wisconsin Physicians Service Insurance Corp (WPS)
6	MN, WI, IL	National Government Services, Inc. (NGS)
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, LLC
M (11)	NC, SC, WV, VA (excluding below)	Palmetto GBA, LLC
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

Policy Rationale:

Lenmeldy was reviewed by the Neighborhood Health Plan of Rhode Island Pharmacy & Therapeutics (P&T) Committee. Neighborhood adopted the following clinical coverage criteria to ensure that its members use Lenmeldy according to Food and Drug Administration (FDA) approved labeling and/or relevant clinical literature. Neighborhood worked with network prescribers and pharmacists to draft these criteria. These criteria will help ensure its members are using this drug for a medically accepted indication, while minimizing the risk for adverse effects and ensuring more cost-effective options are used first, if applicable and appropriate. For INTEGRITY (Medicare-Medicaid Plan) members, these coverage criteria will only apply in the absence of National Coverage Determination (NCD) or Local Coverage Determination (LCD) criteria. Neighborhood will give individual consideration to each request it reviews based on the information submitted by the prescriber and other information available to the plan.