Harvard Pilgrim Health Care | TUFTS Health Plan

Medical Necessity Guidelines

Medical Benefit Drugs

LENMELDY™ (atidarsagene autotemcel)

Effective: July 1, 2026

Prior Authorization Required If REQUIRED, submit supporting clinical documentation pertinent to service request.	Yes ☒ No ☐

Applies to:

Commercial Products

☒ Harvard Pilgrim Health Care Commercial products; Fax 617-673-0988
☒ Tufts Health Plan Commercial products; Fax 617-673-0988

Public Plans Products

☒ Tufts Health Direct – A Massachusetts Qualified Health Plan (QHP) (a commercial product); Fax 617-673-0988
☐ Tufts Health Together – MassHealth Accountable Care Partnership Plans; Fax 617-673-0939
☒ Tufts Health RITogether – A Rhode Island Medicaid Plan; Fax 617-673-0939
☐ Tufts Health One Care-- A dual-eligible product; Fax 617-673-0956

Senior Products

☐ Tufts Health Plan Senior Care Options (SCO), (a dual-eligible product); Fax 617-673-0956
☐ Tufts Medicare Preferred HMO, (a Medicare Advantage product); Fax 617-673-0956
☐ Tufts Medicare Preferred PPO, (a Medicare Advantage product); Fax 617-673-0956

Note: While you may not be the provider responsible for obtaining prior authorization, as a condition of payment you will need to ensure that prior authorization has been obtained.

Overview

Metachromatic leukodystrophy (MLD) is a rare recessive genetic disorder caused by mutations in the arylsulfatase-A (ARSA) gene affecting the production of the enzyme ARSA. This results in a deficiency of ARSA leading to accumulation of sulfatides. MLD is one of the most common leukodystrophies, characterized by the damage of the myelin sheath that covers the nerve fibers of the central and peripheral nervous systems, resulting in progressive demyelination, neurodegeneration, loss of motor and cognitive function, and early death.

The clinical subtypes of MLD are characterized by age at onset. Late infantile (LI-MLD) (50-60% of patients) is the most common and aggressive subtype in which symptoms start before 30 months and children lose the ability to walk and swallow within 1-2 years. Juvenile MLD is divided into two subsets: early juvenile (30 months to 6 years) and late juvenile (7 – 16 years). In the early juvenile subtype (EJ-MLD), significant disability occurs within 3 years of symptom onset. Early symptoms of both subtypes include low motor tone, losing or failing to achieve motor and cognitive milestones, and behavioral and cognitive problems. Adult MLD occurs in patients exhibiting symptom onset ≥ 17 years of age. Progression of this disease leads to difficulty swallowing and breathing that may require gastrostomy tubes, suctioning, and ventilatory support. Survival rates differ and are based on subtype; LI-MLD survival rate is about 8 years; EJ-MLD survival rate is 10-20 years.

Food and Drug Administration (FDA) Approved Indications:

- LENMELDY (atidarsagene autotemcel) is an autologous hematopoietic stem cell-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).
- Treatment consists of a single intravenous infusion of Lenmeldy consisting of autologous CD34+ cells, containing hematopoietic stem cells (HSCs), transduced with a lentiviral vector (LVV) encoding the human arylsulfatase A (ARSA) gene, suspended in cryopreservation solution. Mobilization, apheresis, and myeloablative conditioning are required prior to Lenmeldy infusion.

  Myeloablative conditioning is performed to remove the native HSPCs that carry the defective ARSA gene. After Lenmeldy infusion, transduced HSPCs engraft in bone marrow, repopulate the hematopoietic compartment and their progeny produce

the ARSA enzyme. This functional ARSA enzyme assists in breaking down and preventing the harmful accumulation of sulfatides. Dosing of Lenmeldy is based on the number of CD34+ cells in the infusion bag(s) per kg of body weight. Minimum recommended dose is based on the MLD disease subtype.

Note: Lenmeldy can only be administered at a Lenmeldy Authorized Treatment Center (ATC). For information on locating an Authorized Treatment Center, please go to LENMELDY(TM) (atidarsagene autotemcel) – Now Available

Clinical Guideline Coverage Criteria

The Plan may cover a **one-time infusion** of Lenmeldy **per lifetime** for the treatment of children with metachromatic leukodystrophy (MLD) when **all** the following clinical criteria is met:

1. Diagnosis of metachromatic leukodystrophy (MLD) confirmed by **All**:
    a. Documentation of an arylsulfatase A (ARSA) genotype (biallelic ARSA pathogenic variant); **and**
    b. Biochemical testing, **both**:
        i. Deficient ARSA enzyme activity in leukocytes (ARSA activity below the normal range in peripheral blood mononuclear cells or fibroblasts); **and**
        ii. Elevated urinary excretion of sulfatides; **and**
2. **One** of the following forms of MLD:
    a. Pre-symptomatic* late infantile MLD (PSLI) with expected disease onset** at or before 30 months of age and an ARSA genotype consistent with LI MLD; **or**
    b. Pre-symptomatic* early juvenile (PSEJ) MLD with expected disease onset** > 30 months and < 7 years of age and an ARSA genotype consistent with EJ MLD, **One**:
        i. Absence of neurological signs and symptoms of MLD; **or**
        ii. Physical exam findings limited to abnormal reflexes and/or clonus; **or**
    c. Early symptomatic early juvenile (ESEJ) MLD with disease onset > 30 months of age and < 7 years of age and an ARSA genotype consistent with EJ MLD, **both**:
        i. GMFC-MLD score of 0 (walking independently) with ataxia or score of 1 with or without ataxia; **and**
        ii. Intelligence quotient (IQ) ≥ 85 on age-appropriate neurodevelopmental testing; **and**
3. Prescribed by or in consultation with a specialist prescriber (i.e. neurologist or hematologist/oncologist); **and**
4. The Provider attests that the Member will not receive anti-retroviral medications for at least one month prior to initiating medications for stem cell mobilization and for the expected duration of time needed for the elimination of the medication; **and**
5. The Provider attests that the Member will be screened to confirm negative serology tests for HIV-1/2, HTLV-1/2, HBV, HCV, and mycoplasma infection; **and**
6. Member has not received any prior gene therapy; **and**
7. Lenmeldy will be administered at an Authorized Treatment Center.

*Pre-symptomatic refers to absence of disease-related symptoms or neurological examination findings.

**Expected disease onset refers to a diagnosis of pre-symptomatic disease through testing of sibling(s) of a previously affected and diagnosed child or through newborn screening.

Note: Exceptions for impairments due to non-MLD comorbidities (e.g., motor impairments that may be due to comorbid neuromuscular disease) or patients close to the Intelligence Quotient (IQ) cutoff may be considered on an individual basis.

Gross Motor Function Classification (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

Limitations

- Lenmeldy will not be covered if the Member demonstrates clinical decompensation from time of authorization to time of infusion and no longer meets clinical coverage criteria and if attestation does not confirm negative serology test for HIV-1/2, HTLV-1/2, HBV, HCV, and mycoplasma infection.
- Lenmeldy is considered investigational in Members with late juvenile MLD or adult MLD.
- Any indications for Lenmeldy other than those outlined above are considered investigational and will not be covered.
- Presence of hepatic and renal impairment as Lenmeldy has not been studied in these conditions.
- Members who have had a hematopoietic stem cell transplantation (HSCT) within the past 6 months are excluded. Consideration may be given in certain situations for Member's who have had a previous HSCT.
- Repeat infusion of Lenmeldy is not covered as the safety and effectiveness of repeat administration has not been evaluated and FDA approval has not been given.

Codes

The following code(s) require prior authorization:

Table 1: HCPCS Codes

HCPCS Codes	Description
J3391	Injection, Atidarsagene Autotemcel, per treatment

References:

1. OTL-200 in patients with late juvenile metachromatic leukodystrophy (MLD). ClinicalTrials.gov identifier: NCT04283227. Updated November 22, 2022. https://clinicaltrials.gov/ct2/show/NCT04283227?term=OTL-200&draw=1&rank=1.
2. LENMELDY (atidarsagene autotemcel). [package insert]. Boston, MA: Orchard Therapeutics, Inc; April 2024.
3. Clinical Trials.gov. Gene Therapy for Metachromatic Leukodystrophy (MLD). PEV237823: 40Accessed at Study Details | Gene Therapy for Metachromatic Leukodystrophy (MLD) | ClinicalTrials.gov. Accessed May 16, 2024.
4. Clinical Trials.gov. A Safety and Efficacy Study of Cryopreserved OTL-200 for Treatment of Metachromatic Leukodystrophy (MLD). PEV255; 4; : 90Study Details | A Safety and Efficacy Study of Cryopreserved OTL-200 for Treatment of Metachromatic Leukodystrophy (MLD) | ClinicalTrials.gov. Accessed May 16, 2024.
5. Fumagalli F, Zambon AA, Rancoita PMV, et al. Metachromatic leukodystrophy: A single-center longitudinal study of 45 patients. J Inherit Metab Dis. 2021;44(5):1151-1164. doi:10.1002/jimd.12388.
6. Kehrer C, Elgün S, Raabe C, et al. Association of Age at Onset and First Symptoms With Disease Progression in Patients With Metachromatic Leukodystrophy. Neurology. 2021;96(2):e255-e266. doi:10.1212/WNL.0000000000011047.
7. New Drug Review: LENMELDY (atidarsagene autotemcel). IPD Analytics. March 2024.
8. Fumagalli F, Calbi V, Natali Sora MG, et al. Lentiviral hematopoietic 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
9. Armstrong N, Olaye A, Noake C, Pang F. A systematic review of clinical effectiveness and safety for historical and current treatment options for metachromatic leukodystrophy in children, including atidarsagene autotemcel. Orphanet J Rare Dis. 2023;18(1):248. Published 2023 Aug 29. doi:10.1186/s13023-023-02814-2
10. Metachromatic leukodystrophy. UpToDate.com/login [via subscription only]. Published October 17, 2025. Updated February 1, 2026. Accessed March 19, 2026.
11. National Institute for Health and Care Excellence (NICE). Atidarsagene autotemcel for treating metachromatic leukodystrophy [HST18]. URL: https://www.nice.org.uk/guidance/hst18. Published March 28, 2022. Accessed March 26, 2025.
12. Adang LA, Bonkowsky JL, Boelens JJ, et al. Consensus guidelines for the monitoring and management of metachromatic leukodystrophy in the United States. Cryotherapy. 2024;26(7):739-748. doi:10.1016/j.jcyt.2024.03.487
13. Asbreuk M. et. al.. Metachromatic Leukodystrophy: New Therapy Advancements and Emerging Research Directions. Neurology. 2025 Jul 22;105(2):e213817. doi: 10.1212/WNL.0000000000213817. Epub 2025 Jun 27. PMID: 40577679; PMCID: PMC12205745.
14. Fumagalli F, et. al. Long-Term Effects of Atidarsagene Autotemcel for Metachromatic Leukodystrophy. N Engl J Med. 2025 Apr 24;392(16):1609-1620. doi: 10.1056/NEJMoa2405727. PMID: 40267426.
15. Laugwitz L, et. al. Newborn screening in metachromatic leukodystrophy - European consensus-based recommendations on clinical management. Eur J Paediatr Neurol. 2024 Mar;49:141-154. doi: 10.1016/j.ejpn.2024.03.003. Epub 2024 Mar 9. PMID: 38554683.

Approval And Revision History

June 20, 2024: Reviewed by the Medical Policy Approval Committee (MPAC), effective August 1, 2024

Subsequent endorsement date(s) and changes made:

- July 22, 2024: Reviewed by MPAC, MA Together will move to the MassHealth unified formulary, effective October 1, 2024
- April 16, 2025: Reviewed by MPAC, references updated, effective May 16, 2025.
- May 13, 2025: Coding updated per AMA HCPCS, added code J3391 effective July 1, 2025.
- December 17, 2025: Reviewed by MPAC, revised both Criteria and Limitations section to add attestation language. Effective February 1, 2026.
- May 20, 2026: Reviewed by MPAC, renewed without changes effective July 1, 2026.

Background, Product and Disclaimer Information

Medical Necessity Guidelines are developed to determine coverage for benefits and are published to provide a better understanding of the basis upon which coverage decisions are made. We make coverage decisions using these guidelines, along with the Member's benefit document, and in coordination with the Member's physician(s) on a case-by-case basis considering the individual Member's health care needs.

Medical Necessity Guidelines are developed for selected therapeutic or diagnostic services found to be safe and proven effective in a limited, defined population of patients or clinical circumstances. They include concise clinical coverage criteria based on current literature review, consultation with practicing physicians in our service area who are medical experts in the particular field, FDA and other government agency policies, and standards adopted by national accreditation organizations. We revise and update Medical Necessity Guidelines annually, or more frequently if new evidence becomes available that suggests needed revisions.

For self-insured plans, coverage may vary depending on the terms of the benefit document. If a discrepancy exists between a Medical Necessity Guideline and a self-insured Member's benefit document, the provisions of the benefit document will govern. For Tufts Health Together (Medicaid), coverage may be available beyond these guidelines for pediatric members under age 21 under the Early and Periodic Screening, Diagnostic and Treatment (EPSDT) benefits of the plan in accordance with 130 CMR 450.140 and 130 CMR 447.000, and with prior authorization.

Treating providers are solely responsible for the medical advice and treatment of Members. The use of this guideline is not a guarantee of payment, or a final prediction of how specific claim(s) will be adjudicated. Claims payment is subject to eligibility and benefits on the date of service, coordination of benefits, referral/authorization, utilization management guidelines when applicable, and adherence to plan policies, plan procedures, and claims editing logic.