PROVIDER POLICIES & PROCEDURES

LENMELDY® (ATIDARSAGENE AUTOTEMCEL)

The primary purpose of this document is to assist providers enrolled in the Connecticut Medical Assistance Program (CMAP) with the information needed to support a medical necessity determination for Lenmeldy (atidarsagene autotemcel). By clarifying the information needed for prior authorization of services, HUSKY Health hopes to facilitate timely review of requests so that individuals obtain the medically necessary care they need as quickly as possible.

Metachromatic leukodystrophy (MLD) is a rare autosomal recessive lysosomal disease that causes progressive central and peripheral nervous system demyelination. MLD is caused by deficient activity of the lysosomal enzyme arylsulfatase A (ARSA). The age at disease onset primarily distinguishes the three major subtypes of MLD: late-infantile onset (age six months to two years), juvenile onset (age 3 to <16 years), and less commonly, adult onset (age ≥16).

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 in pediatric and adult patients. Lenmeldy works by inserting one or more functional copies of the human ARSA complementary deoxyribonucleic acid (cDNA) into the patients' own stem cells.

CLINICAL GUIDELINE

Coverage guidelines for the use of Lenmeldy will be made in accordance with the DSS definition of Medical Necessity. The following criteria are guidelines *only*. Coverage guidelines are based on an assessment of the individual and their unique clinical needs. If the guidelines conflict with the definition of Medical Necessity, the definition of Medical Necessity shall prevail. The guidelines are as follows:

Initial Requests

Lenmeldy (atidarsagene autotemcel) may be considered medically necessary for individuals with MLD when the following criteria are met:

A. Medical record documentation confirming ALL the following:
   a. The individual has a diagnosis of MLD as confirmed by ALL of the following:
      i. Biochemical testing demonstrating ARSA activity below the normal range; **AND**
      ii. Presence of two disease-causing ARSA mutations of either known or novel alleles confirmed by genetic testing; **AND**
      iii. Presence of sulfatides in a 24-hour urine collection to exclude MLD carriers and patients with ARSA pseudodeficiency; **AND**
   b. The individual has ONE of the following subtypes of MLD:

i. Pre-symptomatic late infantile (PSLI) metachromatic leukodystrophy as defined by ALL of the following:
    1. Disease onset ≤ 30 months of age; **AND**
    2. ARSA genotype consistent with LI MLD; **AND**
    3. Pre-symptomatic status defined as the absence of neurological signs and symptoms of MLD; **OR**

ii. Pre-symptomatic early juvenile (PSEJ) metachromatic leukodystrophy as defined by ALL of the following:
    1. Disease onset > 30 months and <7 years of age; **AND**
    2. ARSA genotype consistent with EJ MLD; **AND**
    3. Pre-symptomatic status defined as the absence of neurological signs and symptoms of MLD or physical exam findings limited to abnormal reflexes and/or clonus; **OR**

iii. Early symptomatic early juvenile (ESEJ) metachromatic leukodystrophy as defined by ALL of the following:
    1. Disease onset > 30 months and <7 years of age; **AND**
    2. ARSA genotype consistent with EJ MLD
    3. Early symptomatic status defined as walking independently (GMFC-MLD Level 0 with ataxia or GMFC-MLD Level 1) and IQ ≥ 85; **AND**

B. Lenmeldy is prescribed by or in consultation with a hematologist or a physician who specializes in the treatment of metachromatic leukodystrophy; **AND**

C. The treating provider attests to ALL of the following:

a. The individual has been screened for and does not have evidence of ANY of the following infections:
    i. Hepatitis B virus (HBV); **AND**
    ii. Hepatitis C virus (HCV); **AND**
    iii. Human T-lymphotrophic virus 1 & 2 (HTLV-1/HTLV-2); **AND**
    iv. Human immunodeficiency virus 1 & 2 (HIV-1/HIV-2); **AND**
    v. Cytomegalovirus (CMV); **AND**
    vi. Mycoplasma infection; **AND**

b. The individual has been evaluated for risk factors for BOTH the following, provided prophylaxis as clinically indicated, and will continue to be monitored after infusion:
    i. Thrombosis and thromboembolic events; **AND**
    ii. Veno-occlusive disease; **AND**

c. The individual will not receive any vaccinations during the 6 weeks preceding the start of myeloablative conditioning, and until hematological recovery following treatment as outlined in the FDA-approved labeling for Lenmeldy; **AND**

d. The individual is considered to be an eligible candidate for a hematopoietic stem-cell (HSC) gene therapy; **AND**

e. ONE of the following apply:
    i. The individual has not previously received an allogenic hematopoietic stem cell transplant; **OR**
    ii. If the individual has previously received an allogenic hematopoietic stem cell transplant, at least 6 months have passed and there is no evidence of residual cells of donor origin; **AND**

f. The individual has not previously received Lenmeldy or any other gene therapy; **AND**

g. The treating provider will follow all FDA recommendations for usage, dosage, preparation, administration, monitoring and patient education

Reauthorization Requests
N/A

Investigational and Not Medically Necessary
Lenmeldy (atidarsagene autotemcel) is an autologous gene therapy intended for one-time single-dose intravenous use only, repeat administration with Lenmeldy is considered investigational and not medically necessary.

Lenmeldy for any other disease state or subtype of MLD is considered investigational and not medically necessary.

NOTE: EPSDT Special Provision
Early and Periodic Screening, Diagnosis, and Treatment (EPSDT) is a federal Medicaid requirement that requires the Connecticut Medical Assistance Program (CMAP) to cover services, products, or procedures for Medicaid enrollees under 21 years of age where the service or good is medically necessary health care to correct or ameliorate a defect, physical or mental illness, or a condition identified through a screening examination. The applicable definition of medical necessity is set forth in Conn. Gen. Stat. Section 17b-259b (2011) [ref. CMAP Provider Bulletin PB 2011-36].

PROCEDURE
Prior authorization of Lenmeldy is required. Coverage determinations will be based upon a review of requested and/or submitted case-specific information.

The following information is needed to review requests for Lenmeldy:

1. Fully completed State of Connecticut, Department of Social Services HUSKY Health Lenmeldy Prior Authorization Request form (to include physician's order and signature);
2. Clinical documentation supporting the medical necessity of treatment with Lenmeldy should include the following:
    a. Clinical test results including ALL of the following:
        i. Biochemical testing demonstrating ARSA activity below the normal range; **AND**
        ii. 24-hour urine collection confirming presence of sulfatides; **AND**
        iii. Genetic testing results confirming presence of two disease-causing ARSA mutations of either known or novel alleles; **AND**
    b. Medical record documentation confirming:
        i. A diagnosis of MLD with ONE of the following subtypes as defined above:
            1. Pre-symptomatic late infantile (PSLI) metachromatic leukodystrophy; **OR**
            2. Pre-symptomatic early juvenile (PSEJ) metachromatic leukodystrophy; **OR**
            3. Early symptomatic early juvenile (ESEJ) metachromatic leukodystrophy; **AND**
    c. Signed provider attestation confirming the following:
        i. Absence of infection with ALL of the following:
            1. Hepatitis B virus (HBV); **AND**
            2. Hepatitis C virus (HCV); **AND**
            3. Human T-lymphotrophic virus 1 & 2 (HTLV-1/HTLV-2); **AND**
            4. Human immunodeficiency virus 1 & 2 (HIV-1/HIV-2); **AND**
            5. Cytomegalovirus (CMV); **AND**
            6. Mycoplasma infection; **AND**

ii. The individual has been evaluated for risk factors for BOTH the following, provided prophylaxis as clinically indicated, and will continue to be monitored after infusion:
    1. Thrombosis and thromboembolic events; **AND**
    2. Veno-occlusive disease; **AND**
iii. The individual will not receive any vaccinations during the 6 weeks preceding the start of myeloablative conditioning, and until hematological recovery following treatment; **AND**
iv. The individual is considered to be an eligible candidate for a hematopoietic stem-cell (HSC) gene therapy; **AND**
v. If the individual has previously received an allogenic hematopoietic stem cell transplant, at least 6 months have passed and there is no evidence of residual cells of donor origin; **AND**
vi. The individual has not previously received Lenmeldy or any other gene therapy; **AND**

3. Other information as requested.

Initial Authorization
If approved, authorization will be given for a one-time, single-dose intravenous infusion of Lenmeldy, per lifetime.

Reauthorization
N/A

EFFECTIVE DATE
This Policy for the prior authorization of Lenmeldy for individuals covered under the HUSKY Health Program is effective August 1, 2025.

LIMITATIONS
Not Applicable

CODE:

Code	Definition
J3391	Injection, atidarsagene autotemcel, per treatment

DEFINITIONS

1. **Current Procedural Terminology (CPT):** The most recent edition of a listing, published by the American Medical Association, of descriptive terms and identifying codes for reporting medical services performed by providers.
2. **HUSKY A**: Connecticut children and their parents or a relative caregiver; and pregnant women may qualify for HUSKY A (also known as Medicaid). Income limits apply.
3. **HUSKY B**: Uninsured children under the age of 19 in higher income households may be eligible for HUSKY B (also known as the Children's Health Insurance Program) depending on their family income level. Family cost-sharing may apply.
4. **HUSKY C**: Connecticut residents who are age 65 or older or residents who are ages 18-64 and who are blind, or have another disability, may qualify for Medicaid coverage under HUSKY C (this includes

Medicaid for Employees with Disabilities (MED-Connect), if working). Income and asset limits apply.

5. **HUSKY D**: Connecticut residents who are ages 19-64 without dependent children and who: (1) do not qualify for HUSKY A; (2) do not receive Medicare; and (3) are not pregnant, may qualify for HUSKY D (also known as Medicaid for the Lowest-Income populations).
6. **HUSKY Health Program**: The HUSKY A, HUSKY B, HUSKY C, HUSKY D and HUSKY Limited Benefit programs, collectively.
7. **HUSKY Limited Benefit Program or HUSKY, LBP**: Connecticut's implementation of limited health insurance coverage under Medicaid for individuals with tuberculosis or for family planning purposes and such coverage is substantially less than the full Medicaid coverage.
8. **Medically Necessary or Medical Necessity**: (as defined in Connecticut General Statutes § 17b-259b) Those health services required to prevent, identify, diagnose, treat, rehabilitate or ameliorate an individual's medical condition, including mental illness, or its effects, in order to attain or maintain the individual's achievable health and independent functioning provided such services are: (1) Consistent with generally-accepted standards of medical practice that are defined as standards that are based on (A) credible scientific evidence published in peer-reviewed medical literature that is generally recognized by the relevant medical community, (B)recommendations of a physician-specialty society, (C) the views of physicians practicing in relevant clinical areas, and (D) any other relevant factors; (2) clinically appropriate in terms of type, frequency, timing, site, extent and duration and considered effective for the individual's illness, injury or disease; (3) not primarily for the convenience of the individual, the individual's health care provider or other health care providers; (4) not more costly than an alternative service or sequence of services at least as likely to produce equivalent therapeutic or diagnostic results as to the diagnosis or treatment of the individual's illness, injury or disease; and (5) based on an assessment of the individual and his or her medical condition.
9. **Prior Authorization**: A process for approving covered services prior to the delivery of the service or initiation of the plan of care based on a determination by CHNCT as to whether the requested service is medically necessary.

ADDITIONAL RESOURCES AND REFERENCES:

- A Safety and Efficacy Study of Cryopreserved OTL-200 for Treatment of Metachromatic Leukodystrophy (MLD). ClinicalTrials.gov identifier: NCT03392987. Updated January 27, 2025. Accessed May 29. 2025. https://clinicaltrials.gov/study/NCT03392987
- Bonkowsky J. Metachromatic leukodystrophy. In: UpToDate. Firth HV and Dashe JF (Eds). Wolters Kluwer. Updated May 19, 2025. Accessed May 29, 2025.
- Fahim SM, Lin G, Suh K, et al. Atidarsagene autotemcel for metachromatic leukodystrophy. J *Manag Care Spec Pharm*. 2024;30(2):201-205. doi:10.18553/jmcp.2024.30.2.201
- Fumagalli F, Calbi V, Gallo V, et al. Long-Term Effects of Atidarsagene Autotemcel for Metachromatic Leukodystrophy. *N Engl J Med*. 2025;392(16):1609-1620. doi:10.1056/NEJMoa2405727
- 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
- Gene Therapy for Metachromatic Leukodystrophy (MLD). ClinicalTrials.gov identifier: NCT01560182. Updated November 24, 2023. Accessed May 29, 2025. https://clinicaltrials.gov/study/NCT01560182
- Lenmeldy [package insert]. Boston, MA: Orchard Therapeutics North America. Revised May 2024.

- OTL-200 in Patients With Late Juvenile Metachromatic Leukodystrophy (MLD). ClinicalTrials.gov identifier: NCT04283227. Updated January 18, 2024. Accessed May 29, 2025. https://clinicaltrials.gov/study/NCT04283227

PUBLICATION HISTORY

Status	Date	Action Taken
Original publication	June 2025	Approved at the June 11, 2025 CHNCT Medical Reviewer meeting. Approved by the CHNCT Clinical Quality Subcommittee on June 16, 2025. Approved by DSS on July 9, 2025.