Policy and Procedure	
PHARMACY PRIOR AUTHORIZATION POLICY AND CRITERIA ORPTCHEM041.1024	**HEMATOLOGICAL AGENTS** **LENMELDY®** (atidarsagene autotemcel suspension)
Effective Date: 1/1/2025	**Review/Revised Date**:
Original Effective Date: 01/25	**P&T Committee Meeting Date**: 10/24
Approved by: Oregon Region Pharmacy and Therapeutics Committee	

SCOPE:
Providence Health Plan and Providence Health Assurance as applicable (referred to individually as "Company" and collectively as "Companies").

APPLIES TO:
Commercial
Medicare Part B
Medicaid

POLICY CRITERIA:

COVERED USES:
All Food and Drug Administration (FDA)-Approved Indications

REQUIRED MEDICAL INFORMATION:
For authorization, all the following criteria must be met:

1. Diagnosis of metachromatic leukodystrophy (MLD) as evidence by all the following (a and b):
    a. Arylsulfatase A (ARSA) activity below the normal range in peripheral blood mononuclear cells or fibroblasts
    b. Identification of two disease-causing ARSA alleles, either known or novel mutations
        i. If a novel ARSA variant is identified, documentation of presence of elevated sulfatides in a 24-hour urine collection
2. Documentation of one of the following MLD subtypes (a, b, or c):
    a. Pre-symptomatic late-infantile (PSLI) MLD with absence of neurological signs/symptoms and one of the following:
        i. The recipient has an older sibling with a diagnosis of MLD whose age at symptoms onset was equal to or less than six years of age (had not celebrated their seveth birthday)
        ii. Age at expected disease onset less than or equal to 30 months
    b. Pre-symptomatic early juvenile MLD and both of the following (i and ii):
        i. Age at expected disease onset greater than 30 months and less than seven years of age

ii. Absence of neurological signs/symptoms or only abnormal reflexes and/or clonus on exam

c. Early-symptomatic early juvenile MLD and all the following (i, ii, and iii):
   i. Disease onset greater than 30 months and less than seven years of age
   ii. Ability to walk independently, defined by a gross motor function classification for MLD (GMFC MLD) level 0 with ataxia, or GMFC MLD level 1
   iii. IQ equal to or greater than 85 on age-appropriate neurocognitive testing

EXCLUSION CRITERIA:
- Previous use of atidarsagene autotemcel (Lenmeldy®) or any other gene therapy previously
- Concurrent use in combination with other autologous genome edited hematopoietic stem cell-based gene therapies
- Positive test result for HIV or for hepatitis C or B

AGE RESTRICTIONS:
May be approved for patients aged 18 years and less

PRESCRIBER RESTRICTIONS:
Must be prescribed by, or in consultation with, a neurologist or hematologist/oncologist or physician experienced in the treatment of metachromatic leukodystrophy (MLD).

COVERAGE DURATION:
Authorization will be approved for six months (limited to a one-time single-dose intravenous treatment per lifetime).

QUANTITY LIMIT:
one-time single-dose intravenous treatment per lifetime

Requests for indications that were approved by the FDA within the previous six (6) months may not have been reviewed by the health plan for safety and effectiveness and inclusion on this policy document. These requests will be reviewed using the New Drug and or Indication Awaiting P&T Review; Prior Authorization Request ORPTCOPS047.

Requests for a non-FDA approved (off-label) indication requires the proposed indication be listed in either the American Hospital Formulary System (AHFS), Drugdex, or the National Comprehensive Cancer Network (NCCN) and is considered subject to evaluation of the prescriber's medical rationale, formulary alternatives, the available published evidence-based research and whether the proposed use is determined to be experimental/investigational.

Coverage for Medicaid is limited to a condition that has been designated a covered line item number by the Oregon Health Services Commission listed on the Prioritized List of Health Care Services.

Coverage decisions are made on the basis of individualized determinations of medical necessity and the experimental or investigational character of the treatment in the individual case.

INTRODUCTION:
Atidarsagene autotemcel (Lenmeldy®) is the first FDA-approved gene therapy for metachromatic leukodystrophy (MLD).

FDA APPROVED INDICATIONS:
Atidarsagene autotemcel (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).

POSITION STATEMENT:
Metachromatic leukodystrophy (MLD) is a rare, autosomal recessive lysosomal storage disorder which may be caused by mutations in the arylsulfatase A (ARSA) or the sphingolipid activator protein B (PSAP) genes. To date, approximately 260 ARSA variants and 60 PSAP variants have been identified and associated with MLD; most cases of MLD are related to pathogenic ARSA variants. Enzymatic deficiencies caused by these mutations result in the accumulation of sulfatides which produce microglial damage, progressive demyelination, and neurodegeneration. These effects are observed throughout the body, but particularly in the central and peripheral nervous systems. Disease manifestations of MLD include progressive loss of motor and cognitive function, ultimately leading to death. Signs and symptoms of MLD may include regression in speech and developmental milestones, behavioral/cognitive problems, seizures, balance difficulties, trouble swallowing, and gait abnormalities. Across all MLD subtypes, life expectancy is shortened and many pediatric patients with MLD do not reach adulthood.[4]

The clinical spectrum of MLD varies between patients; three clinical forms are described in the literature and are differentiated by the age of symptom onset: late infantile, juvenile, and adult. In general, earlier age at symptom onset is associated with more severe disease and more rapid disease progression.[4]

- Symptoms of late infantile-onset MLD (LI-MLD) are observed before 30 months of age (mean, 16-18 months old). LI-MLD accounts for 50-60% of all cases of MLD. Patients with this form of the condition typically lose the ability to walk and swallow within 1-2 years of symptom onset, and survive less than eight years after symptom onset.[4]
- Juvenile-onset MLD, which accounts for 20-35% of all MLD cases, is further subdivided into early juvenile (EJ-MLD; onset between 30 months and six years

old) and late juvenile (LJ-MLD; onset between 7-16 years old) forms. The mean age at symptom onset ranged between 6-10 years and survival after symptom onset is in the range of 10-20 years.[4]
- Adult-onset MLD is initially noted in patients >17 years old, often between 17-35 years old. Decline with this form of MLD is slow and sometimes imperceptible. Death occurs around 25 years a er symptoms first manifest.[4]

Atidarsagene autotemcel (Lenmeldy®) is the first FDA-approved gene therapy for this disease. MLD treatment prior to atidarsagene focused on supportive care and symptom management. Atidarsagene is approved for autologous use only for a one-time single-dose intravenous use only. Atidarsagene has moderate quality evidence based on two single-arm, open-label clinical trials in 37 children who received atidarsagene that showing a reduction in risk of severe motor impairment or death. Eligible patients had a molecular and biochemical diagnosis of MLD, which was classified as either pre-symptomatic late infantile (PSLI), pre-symptomatic early juvenile (PSEJ), or early symptomatic early juvenile (ESEJ). The primary efficacy endpoint for the trials was severe motor impairment-free survival, defined as the interval from birth to the first occurrence of loss of locomotion and loss of sitting without support or death. This was compared to children in natural history cohort. All children with pre-symptomatic late infantile MLD who were treated with atidarsagene were alive at 6 years of age, compared to only 58% of children in the natural history group. At 5 years of age, 71% of treated children were able to walk without assistance. Eighty-five percent of treated children had normal language and performance IQ scores (not reported in untreated children). Children with pre-symptomatic early juvenile and early symptomatic early juvenile MLD showed slowing of motor and/or cognitive disease.[1,2,3,4]

ICER's review of atidarsagene noted the following:[5]
- For children with presymptomatic late infantile MLD:
  - All panelists (13-0) found that current evidence is adequate to demonstrate a net health benefit for atidarsagene autotemcel (arsa-cel) when compared to usual care.
- For children with presymptomatic early juvenile MLD:
  - All panelists (13-0) found that current evidence is adequate to demonstrate a net health benefit for atidarsagene autotemcel (arsa-cel) when compared to usual care.
- For children with symptomatic early juvenile MLD:
  - A majority of panelists (12-1) found that current evidence is adequate to demonstrate a net health benefit for atidarsagene autotemcel (arsa-cel) when compared to usual care.

REFERENCE/RESOURCES:

1. Lenmeldy Package insert. Boston, MA. Orchard Therapeutics. April 2024.
2. Lenmeldy In: DRUGDEX® System [Internet database]. Greenwood Village, Colo: Thomson Reuters (Healthcare) Inc. Updated periodically. Accessed July 8, 2024.
3. Lenmeldy In: Lexi-Drugs Online [Internet database]. Hudson, OH: Lexi-Comp, Inc. Updated periodically. Accessed July 8, 2024.
4. Lenmeldy (atidarsagene autotemcel) suspension for intravenous infusion). Prime therapeutics monograph. March 2024.
5. Atidarsagene autotemcel for metachromatic leukodystrophy. Final Evidence Report. *ICER*. October 30, 2023. Available at: chrome-extension://efaidnbmnnnibpcajpcglclefindmkaj/https://icer.org/wp-content/uploads/2023/10/MLD-Final-Evidence-Report_For-Publication_10302023.pdf.