

Lenmeldy (atidarsagene autotemcel)

Disclaimer

Clinical guidelines are developed and adopted to establish evidence-based clinical criteria for utilization management decisions. Clinical guidelines are applicable according to policy and plan type. The Plan may delegate utilization management decisions of certain services to third parties who may develop and adopt their own clinical criteria.

Coverage of services is subject to the terms, conditions, and limitations of a member's policy, as well as applicable state and federal law. Clinical guidelines are also subject to in-force criteria such as the Centers for Medicare & Medicaid Services (CMS) national coverage determination (NCD) or local coverage determination (LCD) for Medicare Advantage plans. Please refer to the member's policy documents (e.g., Certificate/Evidence of Coverage, Schedule of Benefits, Plan Formulary) or contact the Plan to confirm coverage.

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Summary

Metachromatic leukodystrophy (MLD) is a rare (1 in 40,000 to 1 in 100,000 in northern European and North Americans) autosomal recessive metabolic disease (lipidoses) caused by deficient activity of the enzyme arylsulfatase A (ARSA), and occasionally variants in the PSAP gene (saposin B deficiency). This leads to toxic accumulation of sulfatides, causing progressive demyelination and neurodegeneration. MLD is classified based on age of symptom onset into late infantile (< 30 months), early juvenile (30 months to <7 years), and adult (≥ 17 years) forms. The late infantile and early juvenile subtypes are most common and severe, characterized by rapid motor and cognitive decline, leading to premature death.

Historically, treatment has been limited to supportive care. Hematopoietic stem cell transplantation (HCT) has been used with some benefit in early juvenile MLD but is associated with significant risks. Lenmeldy (atidarsagene autotemcel) is an autologous hematopoietic stem-cell based gene therapy indicated to treat metachromatic leukodystrophy (MLD) in pediatric individuals with pre-symptomatic late infantile MLD, pre-symptomatic early juvenile MLD, or early symptomatic early juvenile MLD.

- Lenmeldy (atidarsagene autotemcel) uses a lentiviral vector to introduce a functional copy of the arylsulfatase A (ARSA) gene into the individual's own hematopoietic stem cells (HSCs) ex vivo.
- Lenmeldy (atidarsagene autotemcel) is prepared from the individual's own HSCs, collected via apheresis procedures, and enriched with CD34 +cells prior to ex-vivo genetic modification to carry the modified ARSA gene.
- The genetically modified cells are then infused back into the affected individual after myeloablative conditioning, allowing sustained production of the deficient ARSA enzyme.
- Lenmeldy is administered as a one-time intravenous infusion at a specialized treatment center.

Definitions

"Biallelic pathogenic variants" are disease-causing mutations present in both copies (maternal and paternal) of a gene, in this case the ARSA gene.

"Documentation" refers to written information, including but not limited to:

- Up-to-date chart notes, relevant test results, and/or relevant imaging reports to support diagnoses; or
- Prescription claims records, and/or prescription receipts to support prior trials of formulary alternatives.

"Early juvenile MLD" is a subtype of MLD with symptom onset between 30 months and 7 years of age. Disease progresses rapidly once symptoms appear.

"Early symptomatic early juvenile MLD" refers to patients with onset of initial MLD-related motor and/or cognitive symptoms between 30 months and 7 years of age, but with relative preservation of function, defined as ability to walk independently (GMFC-MLD level 0-1) and IQ ≥ 85 .

"GMFC-MLD" is the Gross Motor Function Classification for MLD, a 6-level scale describing motor function, ranging from 0 (walking normally) to 6 (complete loss of motor function).

"Late infantile MLD" is a subtype of MLD characterized by symptom onset before 30 months of age and rapidly progressive disease course.

"Presymptomatic Late Infantile (PSLI) MLD" refers to the stage of MLD where children have an expected disease onset ≤ 30 months of age and an ARSA genotype consistent with late-infantile MLD.

Pre-symptomatic status is defined as the absence of neurological signs and symptoms of MLD.

Pre-symptomatic children may have abnormal reflexes or abnormalities on brain MRI and/or nerve conduction tests not associated with functional impairment (e.g., no tremor, no peripheral ataxia).

"Presymptomatic Early Juvenile (PSEJ) MLD" refers to the stage of MLD where children have an expected disease onset >30 months and 7 years of age and an ARSA genotype consistent with early-juvenile MLD. Pre-symptomatic status is defined as the absence of neurological signs and symptoms of MLD, or physical exam findings limited to abnormal reflexes and/or clonus.

"Presymptomatic MLD" refers to the stage at which a patient has a confirmed MLD diagnosis based on biochemical and genetic testing but has not yet developed overt clinical symptoms.

"[s]" indicates state mandates may apply.

Clinical Indications

Medical Necessity Criteria for Initial Clinical Review

Initial Indication-Specific Criteria

Metachromatic Leukodystrophy

The Plan considers Lenmeldy (atidarsagene autotemcel) medically necessary when ALL of the following criteria are met:

1. Prescribed by or in consultation with a neurologist or hematologist/oncologist experienced in the treatment of MLD; *AND*
2. The member is 18 years of age or younger; *AND*
3. The member has a diagnosis of metachromatic leukodystrophy (MLD) and evidence of ALL of the following:
 - a. Arylsulfatase A (ARSA) activity below the normal range in peripheral blood mononuclear cells or fibroblasts; *and*
 - b. Molecular genetic testing confirming presence of two disease-causing mutations in the ARSA gene; *and*

- c. IF a novel ARSA variant(s) is identified, elevated sulfatide levels in a 24-hour urine collection; *AND*
4. The member has **ONE** (1) of the following MLD subtypes:
 - a. Pre-symptomatic late-infantile (PSLI) MLD, defined as:
 - i. Age at expected disease onset ≤ 30 months; *and*
 - ii. Absence of neurological signs/symptoms (but may have abnormal reflexes or abnormalities on brain MRI and/or nerve conduction tests not associated with functional impairment such as tremor or peripheral ataxia); *or*
 - b. Pre-symptomatic early-juvenile (PSEJ) MLD, defined as:
 - i. Age at expected disease onset >30 months and <7 years; *and*
 - ii. Absence of neurological signs/symptoms **OR** only abnormal reflexes and/or clonus on exam; *or*
 - c. Early symptomatic early-juvenile (ESEJ) MLD, defined as:
 - i. Disease onset >30 months and <7 years of age; *and*
 - ii. Ability to walk independently (GMFC-MLD level 0 with ataxia or level 1); *and*
 - iii. Intelligence quotient (IQ) ≥ 70 on age-appropriate neurocognitive testing; *AND*
5. The member has not previously received treatment with allogeneic hematopoietic stem cell transplantation (HSCT) or gene therapy for MLD; *AND*
6. Lenmeldy (atidarsagene autotemcel) will be administered as a one-time single-dose treatment at a qualified treatment center **AND** within the minimum and maximum recommended doses based on the member's MLD subtype as specified in the product labeling.

If the above prior authorization criteria are met, Lenmeldy (atidarsagene autotemcel) will be authorized for one dose per lifetime, with an approval duration of 6 months.^[5]

Continued Care

Medical Necessity Criteria for Subsequent Clinical Review

Subsequent Medical Necessity Criteria

There are no medical necessity criteria for reauthorization of Lenmeldy (atidarsagene autotemcel). Based on its mechanism of action and available evidence, there is no established rationale for reauthorizing Lenmeldy (atidarsagene autotemcel) after the initial one-time infusion at this time. All coverage of Lenmeldy (atidarsagene autotemcel) under this policy is limited to a single, one-time treatment course, in line with the FDA-approved labeling. Reauthorization requests would be considered experimental/investigational and not medically necessary.

Experimental or Investigational or Unproven / Not Medically Necessary¹

Lenmeldy (atidarsagene autotemcel) for any other indication or use is considered not medically necessary by the Plan, as it is deemed to be experimental, investigational, unproven, or not medically necessary. Non-covered indications include, but are not limited to, the following:

- Re-administration of Lenmeldy after initial treatment.
- Treatment of late juvenile MLD (symptom onset 7 to <17 years of age). Lenmeldy (atidarsagene autotemcel) has not been studied in this population.
- Treatment of adult-onset MLD (symptom onset \geq 17 years of age). Lenmeldy (atidarsagene autotemcel) has not been studied in this population.
- Treatment of MLD caused by pathogenic variants in genes other than ARSA (e.g., PSAP). Lenmeldy (atidarsagene autotemcel) does not treat PSAP gene-related MLD.
- Treatment of other leukodystrophies or lysosomal storage disorders.

Applicable Billing Codes

Table 1	
CPT/HCPCS Codes for metachromatic leukodystrophy considered medically necessary if criteria are met:	
<i>Code</i>	<i>Description</i>
96365	Intravenous infusion, for therapy, prophylaxis, or diagnosis (specify substance or drug); initial, up to 1 hour
96366	Intravenous infusion, for therapy, prophylaxis, or diagnosis (specify substance or drug); each additional hour (List separately in addition to code for primary procedure)
J3391	Injection, atidarsagene autotemcel, per treatment

Table 2	
ICD-10 diagnostic codes considered medically necessary for metachromatic leukodystrophy with Table 1 (CPT/HCPCS) codes if criteria are met:	
<i>Code</i>	<i>Description</i>
E75.25	Metachromatic Leukodystrophy

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Clinical Guideline Revision / History Information

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