Oscar Clinical Guideline: Lenmeldy (atidarsagene autotemcel) (CG117, Ver. 3)

Lenmeldy (atidarsagene autotemcel)

Summary

Metachromatic leukodystrophy (MLD) is a rare (1 in 40,000 to 1 in 100,000 in northern European and North Americans) genetic neurodegenerative disorder caused by deficient activity of the enzyme arylsulfatase A (ARSA) (and occasionally variants in the PSAP gene). This leads to toxic accumulation of sulfatides, causing progressive demyelination and neurologic deterioration. 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.

"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 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.

Medical Necessity Criteria for Initial Authorization

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 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; *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.

<u>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.</u>

Medical Necessity Criteria for Reauthorization

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 / Not Medically Necessary

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, or unproven. 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).

- Treatment of adult-onset MLD (symptom onset ≥17 years of age).
- 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 (HCPCS/CPT Codes)

Service(s) name	
CPT/HCPCS Codes considered medically necessary if criteria are met:	
Code	*Description*
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
ICD-10 codes considered medically necessary if criteria are met:	
Code	*Description*
E75.25	Metachromatic Leukodystrophy

References

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Clinical Guideline Revision / History Information

Original Date: 06/27/2024

Reviewed/Revised: 10/01/2025, 11/01/2025