Mass General Brigham
Health Plan

Medical Policy
Lenmeldy (atidarsagene autotemcel)

Policy Number: 080

	Commercial and Qualified Health Plans*	Mass General Brigham ACO**	Medicare Advantage	One Care	Senior Care Options (SCO)
Authorization Required	X	X	X	X	X
No Prior Authorization					

**Prior authorization for Lenmeldy for Commercial and Qualified Health Plan members is managed by Prime Therapeutics. See Prime Therapeutics policy for Lenmeldy for medical necessity criteria.*

***Prior authorization for Lenmeldy for Mass General Brigham ACO members is managed by the MassHealth Drug Utilization Review Program. See the MassHealth Variation below for more information.*

Overview

This document describes the guidelines Mass General Brigham Health Plan utilizes to determine medical necessity for infusion of Lenmeldy (atidarsagene autotemcel), a gene therapy treatment for metachromatic leukodystrophy (MLD).

Coverage Guidelines

Mass General Brigham Health Plan considers Lenmeldy **medically necessary** for the treatment of MLD when ALL of the following criteria are met:

1. The member must have a diagnosis of ONE of the following:
    a. Pre-symptomatic late infantile (PSLI) MLD, as defined by ALL of the following:
        - 2 null mutant ARSA alleles
        - Member is up to 30 months of age
        - Absence of neurological signs and symptoms of MLD except for abnormal reflexes or abnormalities on brain MRI and/or nerve conduction tests not associated with functional impairment (e.g., no tremor, no peripheral ataxia)
        - Peripheral neuropathy as determined by electroneurographic study

    b. Pre-symptomatic early juvenile (PSEJ) MLD, as defined by ALL of the following:
        - 1 null and 1 R mutant ARSA allele(s)
        - Member is less than 7 years of age
        - Absence of neurological signs and symptoms of MLD or physical examination findings limited to abnormal reflexes and/or clonus except for abnormal reflexes or abnormalities on brain MRI and/or nerve conduction tests not associated with functional impairment (e.g., no tremor, no peripheral ataxia).
        - Peripheral neuropathy as determined by electroneurographic study

c. Early symptomatic early juvenile (ESEJ) MLD, as defined by ALL of the following:
    - 1 null and 1 R mutant ARSA allele(s)
    - Disease onset after 30 months and before 7 years of age
    - Member is less than 18 years of age
    - IQ is at least 85 on age-appropriate neurodevelopmental testing
    - Gross Motor Function Classification in metachromatic leukodystrophy (GMFC-MLD) level 0 w/ ataxia OR GMFC-MLD level 1

2. Diagnosis was confirmed by BOTH of the following:
    a. Arylsulfatase A (ARSA) enzyme activity below the normal range; and
    b. A 24-hour urine collection showing elevated sulfatide levels; and
3. Absence of BOTH of the following:
    a. Clinically significant and active bacterial, fungal, parasitic, severe concomitant disease or viral infection including Hepatitis B, Hepatitis C, or HIV; and
    b. Hepatic and/or renal impairment; and
4. The member is a candidate for allogeneic hematopoiestic stem cell transplantation but there is no available matched donor; and
5. The member has not received a prior allogeneic stem cell transplant (or if they have, there is no evidence of residual donor cells present); and
6. The member has not received Lenmeldy or any other gene therapy previously; and
7. The medication is prescribed by or in consultation with a physician who specializes in the treatment of MLD

Exclusions
All other indications are considered experimental, investigational, or unproven.

Medicare Variation
Mass General Brigham Health Plan uses guidance from the Centers for Medicare and Medicaid Services (CMS) for medical necessity determinations for its Medicare Advantage plan members. National Coverage Determinations (NCDs), Local Coverage Determinations (LCDs), Local Coverage Articles (LCAs), and documentation included in the Medicare manuals are the basis for medical necessity determinations. When there is no guidance from CMS for the requested service, Mass General Brigham Health Plan's medical policies are used for medical necessity determinations. **At the time of Mass General Brigham Health Plan's most recent policy review, Medicare had:**

- **Medicare Benefit Policy Manual Chapter 15: Covered Medical and Other Health Services**

Medicaid Variation
Prior authorization requests for Lenmeldy for Mass General Brigham ACO members should be submitted to the MassHealth Drug Utilization Review Program. Criteria for Lenmeldy are found in the Table 72: Agents Not Otherwise Classified on the MassHealth Drug List.

One Care and SCO Variation

Mass General Brigham Health Plan uses guidance from CMS for medical necessity determinations for its One Care and SCO plan members. NCDs, LCDs, LCAs, and documentation included in the Medicare manuals are the basis for medical necessity determinations. When there is no guidance from CMS for the requested service, Mass General Brigham Health Plan uses medical necessity guidelines from MassHealth. When there is no guidance from CMS or from MassHealth, Mass General Brigham Health Plan's medical policies are used for medical necessity determinations.

Codes

The following codes are included below for informational purposes only; inclusion of a code does not constitute or imply coverage or reimbursement.

Authorized Code	Code Description
J3391	Injection, atidarsagene autotemcel, per treatment.

Summary of Evidence

The groundbreaking studies by Sessa et al. (2016), Biffi et al. (2013), and Fumagalli et al. (2022) used a non-randomized, open-label, phase 1/2 clinical trial design to evaluate lentiviral hematopoietic stem cell (HSC) gene therapy for early-onset Metachromatic Leukodystrophy (MLD). These trials were uniquely structured as expanded access programs, allowing patients who could not participate in traditional randomized trials to receive potentially life-altering treatment. The patient population was carefully selected, targeting individuals with early-onset MLD characterized by severe neurological symptoms before age 2, specifically those diagnosed with ARSA enzyme deficiency.

The studies implemented rigorous inclusion and exclusion criteria to ensure patient safety and treatment efficacy. Patients were selected based on having significant disease progression but still within the early stages before major irreversible neurological damage occurred. Exclusion criteria included advanced stage MLD, previous irreversible neurological damage, severe immunodeficiency, autoimmune diseases, active infections, previous stem cell transplants, and contraindications to chemotherapy. This strategic patient selection was designed to maximize potential treatment benefits while minimizing potential risks.

The primary endpoint of these trials focused on the restoration of ARSA enzyme activity, with a critical emphasis on neurodegeneration stabilization. The results were remarkably promising. Patients receiving the lentiviral HSC gene therapy exhibited significant improvements in ARSA enzyme levels, increasing from negligible baseline levels to 20-50% of normal activity (Fumagalli et al. 2022). This enzyme level restoration was considered clinically meaningful, with levels approaching or exceeding 10% of normal activity deemed sufficient to prevent neurodegeneration.

Neurological Function and Developmental Preservation: One of the most compelling aspects of the study was the preservation of neurological function. In the Fumagalli et al. (2022) study, over 80% of treated patients demonstrated significant preservation of neurological function, with statistical significance noted in long-term follow-ups. Patients exhibited minimal to no cognitive decline over 3-6 years post-treatment, a stark contrast to the rapid cognitive regression typically observed in untreated MLD patients. Motor function assessments (Sessa et al., 2016), including clinical scales like GMFM-88, showed stabilized gross motor skills, with some children maintaining critical developmental milestones such as independent walking for up to 3 years post-treatment.

The long-term survival data presented a transformative narrative. Multiple studies, including those by Fumagalli et al. (2022) and Sessa et al. (2016), indicated significantly improved survival rates approaching those of age-matched controls. While untreated MLD patients historically experienced median survival of less than 5 years

after symptom onset, treated patients showed markedly improved survival rates at 5-6 years post-treatment. This represents a substantial advancement in managing this devastating genetic disorder.

The safety profile of Lenmeldy was carefully documented across multiple studies including Biffi et al. (2013). Fumagalli et al. (2022) noted transient immune reactions but importantly found no long-term adverse effects such as insertional mutagenesis. Adverse events were closely monitored, with some patients experiencing mild, transient effects like cytokine release syndrome. Serious adverse events were rare and primarily related to immunologic responses. Immunosuppressive therapy was employed in select cases to prevent immune rejection.

Based on the studies above, Mass General Brigham Health Plan considers Lenmeldy to be medically necessary for members with PSLI, PSEJ, or ESEJ MLD who meet criteria derived from the inclusion criteria for the pivotal trials by Sessa et al. (2016) and Fumagalli et al. (2022).

Effective
January 2026: Ad hoc update. Updated prior authorization table and added variation for One Care and SCO members.
October 2025: Annual update. Fixed code disclaimer. Updated link to the specific table in the MassHealth Drug List. Fixed heading and typos. Updated code list.
April 2025: Ad hoc update. MassHealth variation updated to include new prior authorization process.
March 2025: Ad hoc update. Summary of evidence added.
October 2024: Effective date.

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