Mass General Brigham
Health Plan

Lenmeldy (atidarsagene autotemcel)

Policy Number: 080

	Commercial and Qualified Health Plans	MassHealth	Medicare Advantage
Authorization Required	X	X	X
No Prior Authorization			

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
        - Mbr is ≤30 mos 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 w/ 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)
        - Mbr is <7 yrs of age
        - Absence of neurological signs and symptoms of MLD or physical exam findings limited to abnormal reflexes and/or clonus except for abnormal reflexes or abnormalities on brain MRI and/or nerve conduction tests not associated w/ 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 >30 mos and <7 yrs of age
        - Mbr is <18 yrs of age
        - IQ ≥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. 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 HBV, HCV, or HIV; and

b. Hepatic and/or renal impairment; and

4. The member is a candidate for allogeneic HSC 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.

Medicaid variation
Mass General Brigham Health Plan uses the MassHealth Drug List for coverage determinations for members of the MGB ACO. Criteria for Lenmeldy are found in the MassHealth Drug List.

Medicare Variation
Mass General Brigham Health Plan uses guidance from the Centers for Medicare and Medicaid Services (CMS) for coverage 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 coverage determinations. When there is no guidance from CMS for the requested service, Mass General Brigham Health Plan's medical policies are used for coverage determinations. **At the time of Mass General Brigham Health Plan's most recent policy review, Medicare does not have an NCD/LCD for Lenmeldy.**

Codes

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

This list of codes applies to Commercial and MassHealth only:

Authorized Code	Code Description
J3590	Unclassified biologic administered other than oral method or a chemotherapy drug.

Effective
October 2024: Effective date.

References

Batzios SP, Zafeiriou DI. Developing treatment options for metachromatic leukodystrophy. Mol Genet Metab 2012; 105:56.

Biffi A, Montini E, Lorioli L, et al. Lentiviral hematopoietic stem cell gene therapy benefits metachromatic leukodystrophy. Science. 2013 Aug 23;341(6148):1233158. doi: 10.1126/science.1233158. Epub 2013 Jul 11. PMID: 23845948.

Bonkowsky JL. (2024). Metachromatic leukodystrophy. JA Dashe (Ed.), *UpToDate*. Retrieved April 23, 2024, from Metachromatic leukodystrophy - UpToDate.

European Medicines Agency (October 14, 2021). Retrieved April 2024, from Libmeldy | European Medicines Agency (europa.eu).

Fumagalli F, Calbi V, Sora MGN, et al. Lentiviral haematopoietic stem-cell gene therapy for early-onset metachromatic leukodystrophy: long-term results from a non-randomized, open-label, phase 1/2 trial and expanded access. Lancet. 2022;399:372-83.

Hayes Inc. (March 20, 2024). Emerging technology report: atidarsagene autotemcel (Lenmeldy, Orchard Therapeutics) for metachromatic leukodystrophy. Retrieved April 2024, from Hayes Knowledge Center | symplr (hayesinc.com).

Jensen TL, Gøtzsche CR, Woldbye DPD. Current and Future Prospects for Gene Therapy for Rare Genetic Diseases Affecting the Brain and Spinal Cord. Front Mol Neurosci 2021; 14:695937.

Sessa M, Lorioli L, Fumagalli F, et al. Lentiviral haemopoietic stem-cell gene therapy in early-onset metachromatic leukodystrophy: an ad-hoc analysis of a non-randomised, open-label, phase 1/2 trial. Lancet 2016; 388:476.

Stansfield N. (February 9, 2024). Orchard Therapeutics' Arsa-cel restores ARSA enzyme activity in patients with late juvenile MLD. Retrieved April 2024, from Orchard Therapeutics' Arsa-cel Restores ARSA Enzyme Activity in Patients With Late Juvenile MLD (cgtlive.com).

US Food and Drug Administration (March 18, 2024). FDA approves first gene therapy for children with metachromatic leukodystrophy. Retrieved April 2024, from FDA Approves First Gene Therapy for Children with Metachromatic Leukodystrophy | FDA.