Medical Policy

BlueCross BlueShield Kansas
An Independent licensee of the
Blue Cross Blue Shield Association

Title: Lenmeldy (atidarsagene autotemcel)

Professional / Institutional
Original Effective Date: September 1, 2024
Latest Review Date: December 23, 2024
Current Effective Date: December 23, 2024

State and Federal mandates and health plan member contract language, including specific provisions/exclusions, take precedence over Medical Policy and must be considered first in determining eligibility for coverage. To verify a member's benefits, contact Blue Cross and Blue Shield of Kansas Customer Service.

The BCBSKS Medical Policies contained herein are for informational purposes and apply only to members who have health insurance through BCBSKS or who are covered by a self-insured group plan administered by BCBSKS. Medical Policy for FEP members is subject to FEP medical policy which may differ from BCBSKS Medical Policy.

The medical policies do not constitute medical advice or medical care. Treating health care providers are independent contractors and are neither employees nor agents of Blue Cross and Blue Shield of Kansas and are solely responsible for diagnosis, treatment and medical advice.

If your patient is covered under a different Blue Cross and Blue Shield plan, please refer to the Medical Policies of that plan.

POLICY AGENT SUMMARY – MEDICAL PRIOR AUTHORIZATION

<table>
<tr><th>Indication</th><th>Dose</th></tr>
<tr><td>Metachromatic Leukodystrophy (MLD)</td><td>
Lenmeldy is provided as a single dose for infusion containing a suspension of CD34+ cells in one to eight infusion bags. The minimum and maximum recommended dose is based on the MLD disease subtype.
<table>
<tr><th>MLD Subtype</th><th>Minimum Recommended Dose (CD34+ cells/kg)</th><th>Maximum Recommended Dose (CD34+ cells/kg)</th></tr>
<tr><td>Pre-symptomatic late infantile</td><td>4.2×10^6</td><td>30×10^6</td></tr>
<tr><td>Pre-symptomatic early juvenile</td><td>9×10^6</td><td>30×10^6</td></tr>
<tr><td>Early symptomatic early juvenile</td><td>6.6×10^6</td><td>30×10^6</td></tr>
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Indication	Dose
	• The dose administered is calculated based on the child's weight at time of Lenmeldy infusion using the information provided on the Lot Information Sheet. See the Lot Information Sheet provided with the product shipment for additional information pertaining to dose.
– Lenmeldy is for autologous use only. The patient's identity must match the patient identifiers on the drug cassette(s) and infusion bag(s). *– Mobilization, apheresis, and myeloablative conditioning are required prior to LENMELDY infusion. Before initiating these procedures, confirm that hematopoietic stem cell (HSC) gene therapy is appropriate for the child.* *–A collection of a minimum of 8.0 × 10^6 CD34+ cells/kg of autologous cells is required based on a weight at time of apheresis collection. Collection of the minimum number of CD34+ cells required for manufacture may be achieved using one or more cycles of mobilization. A collection of unmanipulated back-up CD34+ cells of at least 2.0 × 10^6 CD34+ cells/kg is required. These cells must be collected from the child and be cryopreserved prior to myeloablative conditioning.*	

PRIOR AUTHORIZATION CLINICAL CRITERIA FOR APPROVAL

I. Length of Authorization

One treatment course (1 dose) and cannot be renewed.

II. Dosing Limits

A. Quantity Limit (max daily dose) [NDC Unit]:

- A single dose of Lenmeldy contains 2 to 11.8× 10^6 cells/mL (1.8 to 11.8 x 10^6 CD34+ cells/mL) suspended in one or more patient-specific infusion bags

B. Max Units (per dose and over time) [HCPCS Unit]:

- A single dose of Lenmeldy contains 2 to 11.8× 10^6 cells/mL (1.8 to 11.8 x 10^6 CD34+ cells/mL) suspended in one to eight patient-specific infusion bags

III. Initial Approval Criteria [1]

o Submission of medical records (chart notes) related to the medical necessity criteria is REQUIRED on all requests for authorizations. Records will be reviewed at the time of submission. Please provide documentation related to diagnosis, step therapy, and clinical markers (i.e. genetic and mutational testing) supporting initiation when applicable. Please provide documentation via direct upload through the PA web portal or by fax.

Coverage is provided for the following conditions:

- Patient age is less than 18 years; **AND**
- Patient is screened and found to be negative for hepatitis B virus (HBV), hepatitis C virus (HCV), human T-lymphotrophic virus 1 & 2 (HTLV-1/HTLV-2), human immunodeficiency virus 1 & 2 (HIV-1/HIV-2), and mycoplasma infection before collection of cells for manufacturing; **AND**
- Patient will not be administered vaccinations during the 6 weeks preceding the start of myeloablative conditioning, and until hematological recovery following treatment *(Note: Where feasible, administer childhood vaccinations prior to myeloablative conditioning)*; **AND**
- Patient risk factors for thrombosis as well as veno-occlusive disease have been evaluated prior to administration; **AND**
- Prophylaxis for infection will be followed according to standard institutional guidelines; **AND**
- Patient will be monitored for hematological malignancies periodically after treatment; **AND**
- Patients will not receive prophylactic HIV anti-retroviral therapy for at least one-month preceding mobilization *(Note: anti-retrovirals may interfere with manufacturing)*; **AND**
- Patient will have mobilization of stem cells using granulocyte-colony stimulating factor (G-CSF with or without plerixafor); **AND**
- Used as single agent therapy (Note: not inclusive of busulfan conditioning regimen); **AND**
- Patient has not received a prior allogeneic stem cell transplant *(or has, but is without evidence of residual donor cells present),* and is a candidate for autologous stem cell transplantation (e.g., adequate renal and hepatic function); **AND**
- Patient has not received other gene therapy for MLD; **AND**

Metachromatic Leukodystrophy (MLD)

- Patient has a confirmed diagnosis of MLD *(also known as arylsulfatase A deficiency)* as evidenced by the following biochemical and molecular markers:
    - Arylsulfatase A (ARSA) enzyme activity below the normal range in peripheral blood mononuclear cells-leukocytes or fibroblasts OR increased urinary excretion of sulfatides; **AND**
    - Presence of biallelic ARSA pathogenic mutation of known polymorphisms *(Note: Patients with novel mutations, a 24-hour urine collection must show elevated sulfatide levels)*; **AND**
- Patient has pre-symptomatic late infantile (PSLI), presymptomatic, early juvenile (PSEJ) or early symptomatic early juvenile (ESEJ) disease *(Note: Requests for children with late juvenile form of the disease will be reviewed on a case-by-case basis)*

† FDA Approved Indication(s); ‡ Compendia Recommended Indication(s); Φ Orphan Drug

IV. Renewal Criteria

Coverage cannot be renewed.

Please refer to the member's contract benefits in effect at the time of service to determine coverage or non-coverage of these services as it applies to an individual member.

CLINICAL RATIONALE

See package insert for FDA preshttps://dailymed.nlm.nih.gov/dailymed/index.cfm

CODING

The following codes for treatment and procedures applicable to this policy are included below for informational purposes. This may not be a comprehensive list of procedure codes applicable to this policy.

Inclusion or exclusion of a procedure, diagnosis or device code(s) does not constitute or imply member coverage or provider reimbursement. Please refer to the member's contract benefits in effect at the time of service to determine coverage or non-coverage of these services as it applies to an individual member.

The code(s) listed below are medically necessary ONLY if the procedure is performed according to the "Policy" section of this document.

HCPCS Code:

- J3590 – Unclassified biologics

NDC(s):

- Lenmeldy containing 2 to 11.8× 10^6 cells/mL (1.8 to 11.8 x 10^6 CD34+ cells/ml) suspended in one or eight patient-specific infusion bags: 83222-0200-xx

REFERENCES

1. Lenmeldy [package insert]. Boston, PA; Orchard Therapeutics NA; April 2024. Accessed April 2024.
2. ClinicalTrials.gov. An Open Label, Non-randomized Trial to Evaluate the Safety and Efficacy of a Single Infusion of OTL-200 in Patients With Late Juvenile (LJ) Metachromatic Leukodystrophy (MLD). https://clinicaltrials.gov/study/NCT04283227?intr=Atidarsagene&rank=1.
3. Biffi A, Montini E, Lorioli L, et al. Lentiviral hematopoietic stem cell gene therapy benefits metachromatic leukodystrophy. Science. 2013;341(6148):1233158. doi:10.1126/science.1233158
4. Fumagalli F, Calbi V, Natali Sora MG, et al. Lentiviral haematopoietic stem-cell gene therapy for early-onset metachromatic leukodystrophy: long-term results from a non-randomised, open-label, phase 1/2 trial and expanded access. Lancet. 2022;399(10322):372-383. doi:10.1016/S0140-6736(21)02017-1
5. 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(10043):476-487. doi:10.1016/S0140-6736(16)30374-9

6. ClinicalTrials.gov. A Phase I/II Clinical Trial of Hematopoietic Stem Cell Gene Therapy for the Treatment of Metachromatic Leukodystrophy. https://clinicaltrials.gov/study/NCT01560182?intr=NCT01560182&rank=1.
7. Gomez-Ospina N. Arylsulfatase A deficiency. In: GeneReviews, Adam MP, Feldman J, Mirzaa GM, et al. (Eds), University of Washington, Seattle 2020. Available at: https://www.ncbi.nlm.nih.gov/books/NBK1130/ (Accessed on March 2024).
8. Wang RY, Bodamer OA, Watson MS, et al. Lysosomal storage diseases: Diagnostic confirmation and management of presymptomatic individuals. ACMG Standards and Guidelines. Genet Med. 2011;13:457-84.
9. Schoenmakers DH, Mochel F, Adang LA, et al. Inventory of current practices regarding hematopoietic stem cell transplantation in metachromatic leukodystrophy in Europe and neighboring countries. Orphanet J Rare Dis 2024; 19:46.
10. Bonkowsky JL (Mar 2024). Metachromatic leukodystrophy. In Patterson MC, Firth HV, Dashe JF (Eds.). *UpToDate*. Accessed March 20, 2024. Available from: https://www.uptodate.com/contents/metachromatic-leukodystrophy?search=Metachromatic%20Leukodystrophy%20&source=search_result&selectedTitle=1%7E33&usage_type=default&display_rank=1#H6
11. Page KM, Stenger, EO, Connelly JA, et al. Hematopoietic Stem Cell Transplantation to Treat Leukodystrophies: Clinical Practice Guidelines from the Hunter's Hope Leukodystrophy Care Network. Biol Blood Marrow Transplant. 2019 Dec;25(12):e363-e374.

REVISIONS	
Posted 07-23-2024 Effective 09-01-2024	Policy added to the bcbsks.com web site.
12-23-2024	Updated Approval Criteria: • Removed requirement that patient does not have a known 10/10 human leukocyte antigen matched related donor willing to participate in HSCT per trade
	Medical policy reviewed and maintained by Prime Therapeutics