Blue Cross Blue Shield Blue Care Network of Michigan

Nonprofit corporations and independent licensees of the Blue Cross and Blue Shield Association

Medical benefit drug policies are a source for BCBSM and BCN medical policy information only. These documents are not to be used to determine benefits or reimbursement. Please reference the appropriate certificate or contract for benefit information. This policy may be updated and therefore subject to change.

Effective Date: 12/12/2024

Skysona® (elivaldogene autotemcel)

HCPCS: J3590

Policy:

Requests must be supported by submission of chart notes and patient specific documentation.

A. Coverage of the requested drug is provided when all the following are met:
   a. FDA approved indication
   b. FDA approved age
   c. Genetic testing confirming diagnosis of adenoleukodystrophy
   d. Must have the following:
      i. Magnetic resonance imaging (MRI) confirming cerebral involvement with abnormal demyelination in cerebral white matter
      ii. Early stage disease defined as a score on the cerebral adrenoleukodystrophy–specific neurologic function scale of 0 or 1 and a Loes score of 0.5 to 9.0
      iii. Elevated plasma very long chain fatty acids (VLCFA)
   e. Must not have the following:
      i. A prior hematopoietic stem cell transplant (HSCT) or currently be eligible for a HSCT with an HLA matched family donor
      ii. Presence of HIV-1, HIV-2, hepatitis B, hepatitis C, or human T lymphotrophic virus 1 (HTLV 1) infection
      iii. Hepatic compromise defined as any of the following:
         a) Aspartate transaminase (AST) greater than 2.5 times the upper limit of normal (ULN)
         b) Alanine transaminase (ALT) greater than 2.5 times the ULN
         c) Total bilirubin greater than 3.0 mg/dL
   f. Have not received prior treatment with any gene therapy or are being considered for treatment with any other gene therapy for cerebral adrenoleukodystrophy (CALD)
   g. The requesting physician attests to providing clinical outcome information within the Audaire Health™ provider portal as requested by BCBSM
   h. Trial and failure, intolerance, or a contraindication to the preferred products as specified in the BCBSM/BCN medical utilization management drug list

B. Quantity Limitations, Authorization Period and Renewal Criteria
   a. Quantity Limits: Align with FDA recommended dosing
   b. Authorization Period: 3 months

c. Renewal Criteria: Not applicable as no further authorization will be provided

***Note: Coverage and approval duration may differ for Medicare Part B members based on any applicable criteria outlined in Local Coverage Determinations (LCD) or National Coverage Determinations (NCD) as determined by Center for Medicare and Medicaid Services (CMS). See the CMS website at http://www.cms.hhs.gov/. Determination of coverage of Part B drugs is based on medically accepted indications which have supported citations included or approved for inclusion determined by CMS approved compendia.

Background Information:

- Cerebral adrenoleukodystrophy (CALD) is a rare, neurodegenerative. metabolic disorder caused by X-linked mutations in the ATP binding cassette subfamily D member 1 (ABCD1) gene that lead to impaired peroxisomal expression of adrenoleukodystrophy protein (ALDP). ALDP is needed to transport very long chain fatty acids (VLCFAs) into the peroxisome for degradation. The buildup of VLCFAs primarily affects the adrenal cortex through direct toxicity and brain white matter where perivascular infiltrates result in progressive inflammatory demyelination.

- The disease is heterogeneous, and the time course of clinical progression is highly variable. Boys typically present with inattention, hyperactivity, or academic challenges by 4 - 10 years of age. The disease progresses to neurologic dysfunction, disability, and ultimately to death by the second decade of life from complications of the disease without treatment. Many patients have primary adrenal insufficiency, which can cause fatigue and muscle weakness and lead to life-threatening adrenal crisis in the setting of illness or injury without treatment.

- The possibility of ALD may be raised by clinical signs or symptoms, family history of ALD, or a positive newborn screen. The VLCFA panel is highly sensitive for detecting ALD and is the appropriate first step in the diagnosis. If the VLCFA levels are elevated or if the ratios of VLCFA are abnormal, genetic testing for mutations of the ABCD1 gene should be performed to confirm the diagnosis. All individuals with confirmed ALD should undergo neuroimaging of the brain using MRI at the time of diagnosis. In symptomatic males with cerebral disease, MRI always demonstrates abnormal demyelination in cerebral white matter. Presymptomatic boys with CALD who initially have normal MRI should undergo follow-up imaging every 6 to 12 months. Since MRI changes precede neurologic signs, routine MRI surveillance allows for early detection of onset of cerebral involvement and may facilitate optimal early treatment.

- Skysona is a lentiviral vector (LVV) gene therapy indicated to slow the progression of neurologic dysfunction in boys 4 - 17 years of age with early, active CALD. Early, active CALD refers to asymptomatic or mildly symptomatic (neurologic function score, NFS ≤ 1) boys who have gadolinium enhancement on brain MRI and a Loes scores of 0.5 – 9. Skysona does not treat or prevent adrenal insufficiency and has not been studied in CALD secondary to head trauma. An immune response to Skysona may cause rapid loss of efficacy in patients with full deletions of the human adenosine triphosphate binding cassette, sub family D, member 1 (ABCD1) gene.

- Safety and efficacy of Skysona are being evaluated in the STARBEAM trial, a single-group, open-label, Phase II/III study of 32 patients 17 years of age or younger with CALD. Subjects were included if they had gadolinium enhancement on MRI due to CALD, a score on the cerebral adrenoleukodystrophy–specific neurologic function scale of 0 or 1, and a Loes score of 0.5 to 9.0. Patients who had an HLA-matched sibling who could donate cells for transplantation were excluded from the study. The primary endpoint was Major Functional Disabilities (MFD)-free survival, measuring the proportion of patients who did not have any of the six MFDs, were alive, did not receive a second allogenic HSCT or rescue cell administration, and had not withdrawn or been lost to follow-up at month 24. The MFDs are defined as: loss of communication, cortical blindness, requirement for tube feeding, total incontinence, wheelchair dependence, or complete loss of voluntary movement. Twenty-nine of the 32 patients remained free of major functional disabilities and had a score on the neurologic function scale of 0 or 1, indicating no or minimal clinical symptoms. Of the 3 patients who did not respond to therapy, 1 developed total incontinence at month 9 and subsequently died at month 22 and 2 subjects withdrew to receive rescue allo-HSCT at the investigator's discretion

due to progressive disease on brain MRI at months 13 and 17. Boys with CALD who had received Skysona therapy had generally stable disease or limited progression of disease on MRI of the head, as compared with the known rates of lesion progression among untreated boys (mean [±SD] increase in Loes score, 2.2 ± 0.55 and 2.3 ± 0.75 points per year for the posterior and anterior patterns, respectively).

- There are no other FDA approved treatments for CALD. Prior to Skysona's approval, allogeneic HSCT with an HLA-matched sibling donor was the standard of care. Retrospective studies have documented more favorable neurologic outcomes when allo-HSCT is performed early in the course of disease, prior to onset of significant neurologic dysfunction or radiographic disease burden. HSCT may increase rapidity of disease progression in patients with advanced cerebral disease and is not recommended in these patients. Disease progression may still occur for up to 12 – 24 months following HSCT, after which CALD appears to stabilize or progress more slowly. Because the disease may continue to progress following HSCT, treatment with HSCT should occur soon after diagnosis to prevent disability and death.

References:

1. Skysona [prescribing information]. Somerville, MA: Bluebird Bio, Inc.; April 2024.
2. Eichler F, Duncan C, Musolino PL, et al. Hematopoietic stem-cell gene therapy for cerebral adrenoleukodystrophy. NEJM. 2017 Oct 26; 377 (17): 1630 – 8.
3. Clinicaltrials.gov. A phase 3 study of Lenti-D drug product after myeloablative conditioning using busulfan and fludarabine in subjects ≤ 17 years of age with cerebral adrenoleukodystrophy (CALD). Available at: https://clinicaltrials.gov/ct2/show/NCT03852498?intr=%22Lenti-D%22+OR+%22Elivaldogene+Autotemcel%22+OR+%22eli-cel%22&draw=2&rank=3. Accessed on September 19, 2022.
4. Mahmood A, Dubey P, Moser HW, at al. X-linked adrenoleukodystrophy: therapeutic approaches to distinct phenotypes. Pediatr Transplant. 2005; 9 (Suppl 7): 55 – 62.

<table>
<tr><td colspan="3">Policy History</td></tr>
<tr><td>#</td><td>Date</td><td>Change Description</td></tr>
<tr><td>1.3</td><td>Effective Date: 12/12/2024</td><td>Annual review of criteria was performed - no changes were made</td></tr>
<tr><td>1.2</td><td>Effective Date: 12/14/2023</td><td>Annual review of criteria was performed - no changes were made</td></tr>
<tr><td>1.1</td><td>Effective Date: 12/01/2022</td><td>New policy</td></tr>
<tr><td>1.0</td><td>Effective Date: 10/20/2022</td><td>UM medical management system update for BCBS and BCN
<table>
<tr><th>Line of Business</th><th>PA Required in Medical Management System (Yes/No)</th></tr>
<tr><td>BCBS</td><td>Yes</td></tr>
<tr><td>BCN</td><td>Yes</td></tr>
<tr><td>MAPPO</td><td>No</td></tr>
<tr><td>BCNA</td><td>No</td></tr>
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** The prescribing information for a drug is subject to change. To ensure you are reading the most current information it is advised that you reference the most updated prescribing information by visiting the drug or manufacturer website or http://dailymed.nlm.nih.gov/dailymed/index.cfm.*

Blue Cross Blue Shield/Blue Care Network of Michigan
Medication Authorization Request Form
Skysona® (elivaldogene autotemcel)
HCPCS CODE: J3490/J3590

Blue Cross Blue Shield Blue Care Network of Michigan

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This form is to be used by participating physicians to obtain coverage for Skysona. For commercial members only, please complete this form and submit via fax to 1-877-325-5979. If you have any questions regarding this process, please contact BCBSM Provider Relations and Servicing or the Medical Drug Helpdesk at 1-800-437-3803 for assistance.

PATIENT INFORMATION		PHYSICIAN INFORMATION
Name		**Name**
ID Number		**Specialty**
D.O.B.	☐Male ☐Female	**Address**
Diagnosis		**City /State/Zip**
Drug Name	☐ Skysona	**Phone/Fax: P**: ( ) - **F**: ( ) -
Dose and Quantity		**NPI**
Directions		**Contact Person**
Date of Service(s)		**Contact Person Phone / Ext.**

STEP 1: DISEASE STATE INFORMATION

1. Is this for initiation or continuation of therapy?
   ☐ Initiation ☐ Continuation *Date patient started therapy*: _____
2. Please provide the NPI number for the place of administration: _____
3. Please specify the location of administration (e.g. name of facility):
   _____
4. Has the clinical outcome information been provided within the Audaire Health provider portal as requested by BCBSM?
   ☐ Yes ☐ No Comment: _____
5. **Initiation AND Continuation of therapy:**
   a. What is the patient's diagnosis?
      ☐ Early active cerebral adrenoleukodystrophy (CALD)
      ☐ Other – *please specify diagnosis:* _____
   b. Genetic testing to confirm diagnosis of adrenoleukodystrophy: _____ (Please attach any tests confirming diagnosis)
   c. Does the patient have a MRI confirming cerebral involvement with abnormal demyelination in cerebral white matter? (Please attach MRI test)
      ☐ Yes ☐ No ☐ Unknown
   d. What is the patient's cerebral adrenoleukodystrophy-specific neurologic function scale?
      ☐ 0 ☐ 1 ☐ Unknown ☐ Other, What is the score? _____
   e. What is the patient's Loes score? Please specify: _____
   f. Does the patient have elevated plasma very long chain fatty acids (VLCFA)?
      ☐ Yes, Please specify: _____ ☐ No ☐ Unknown
   g. Does the patient have any of the following?
      ☐ A prior hematopoietic stem cell transplant (HSCT)
      ☐ Currently eligible for a HSCT with an HLA matched family donor
      ☐ Presence of HIV-1 or HIV-2 infection
      ☐ Presence of Hepatitis B
      ☐ Presence of Hepatitis C
      ☐ Presence of human T lymphotrophic virus 1 (HTLV 1) infection
      ☐ Advanced liver disease is defined as:
         ☐ Aspartate transaminase (AST) greater than 2.5 times the upper limit of normal (ULN)
         ☐ Alanine transaminase (ALT) greater than 2.5 times the ULN
         ☐ Total bilirubin greater than 3.0 mg/dL
      ☐ None of the above
   h. Has the patient received prior treatment with any gene therapy, or is being considered for treatment with any other gene therapy for cerebral adrenoleukodystrophy (CALD)? ☐ Yes ☐ No Comment: _____
6. **Continuation of therapy** - *Please include rationale for continuation of therapy*_____
7. *Please add any other supporting medical information necessary for our review*

Coverage will not be provided if the prescribing physician's signature and date are not reflected on this document.

☐ Request for expedited review: I certify that applying the standard review time frame may seriously jeopardize the life or health of the member or the member's ability to regain maximum function

Physician's Name	Physician Signature	Date
Step 2: Checklist	☐ Form Completely Filled Out ☐ Attached necessary chart notes	☐ Important laboratory results
Step 3: Submit	**By Fax: BCBSM Specialty Pharmacy Mailbox** **1-877-325-5979**	**By Mail: BCBSM Specialty Pharmacy Program** **P.O. Box 312320, Detroit, MI 48231-2320**