Medical Policy

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

Title: Skysona

Professional / Institutional
Original Effective Date: November 15, 2022
Latest Review Date: January 8, 2026
Current Effective Date: January 8, 2026

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

Indication	Dose
Cerebral Adrenoleukodystrophy (CALD)	Skysona is provided as a single dose for infusion containing a suspension of CD34+ cells in one or two infusion bags. The minimum recommended dose is 5.0 x 10^6 CD34+ cells/kg. The dose is calculated based on the patient's weight prior to first apheresis. **Mobilization and Apheresis** • Patients are required to undergo hematopoietic stem cell (HSC) mobilization followed by apheresis to obtain CD34+ cells for product manufacturing. Weigh the patient prior to the first apheresis collection. Collect a minimum target number of CD34+ cells of 12 x 10^6 CD34+ cells/kg. • A back-up collection of CD34+ cells of ≥ 1.5 x 10^6 CD34+ cells/kg (if collected by apheresis) or ≥ 1.0 x 10^8 TNC/kg (Total Nucleated Cells, if

Indication	Dose
	collected by bone marrow harvest) is required. These cells must be collected from the patient and cryopreserved prior to initiating conditioning and infusion with Skysona. The back-up collection may be needed for rescue treatment if there is: ○ Compromise of Skysona after initiation of conditioning and before Skysona infusion ○ Primary engraftment failure ○ Loss of engraftment after infusion with Skysona • Note: G-CSF with or without plerixafor were used for mobilization **Myeloablative and Lymphodepleting Conditioning** • Full myeloablative and lymphodepleting conditioning must be administered before infusion of Skysona. Consult prescribing information for the conditioning agent(s) prior to treatment. • Do not begin conditioning until Skysona has been received and stored at the treatment center and the availability of the back-up collection of CD34+ cells is confirmed. After completion of conditioning, allow a minimum of 48 hours of washout before Skysona infusion. • Note: Busulfan was used for myeloablative conditioning, and cyclophosphamide or fludarabine was used for lymphodepletion
For autologous use only. For intravenous use only. – Before infusion, confirm that the patient's identity matches the unique patient identifiers on the Skysona infusion bag(s). The total number of infusion bags to be administered should also be confirmed with the Lot Information Sheet. – Do not use an in-line blood filter or an infusion pump. – Administer each infusion bag of Skysona via intravenous infusion (drip) by gravity flow over a period of less than 60 minutes. Product must be administered within 4 hours after thawing. – Do not sample, alter, irradiate, or refreeze Skysona.	

PRIOR AUTHORIZATION CLINICAL CRITERIA FOR APPROVAL

I. Length of Authorization [1]

Coverage will be provided for one treatment course (1 dose of Skysona) and may NOT be renewed.

II. Dosing Limits

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

- A single dose of Skysona containing a minimum of 5.0 x 10^6 CD34+ cells/kg of body weight, in one or more infusion bags

III. Initial Approval Criteria [1,2,6]

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 in the following conditions:

- Patient is a male at least 4 years of age and less than 18 years of age; **AND**
- Patient has been screened for hepatitis B virus (HBV), hepatitis C virus (HCV), human immunodeficiency virus 1 & 2 (HIV-1/HIV-2), and human T-lymphotrophic virus 1 & 2 (HTLV-1/HTLV-2) in accordance with clinical guidelines prior to collection of cells for manufacturing; **AND**
- Patient does not have an active infection, including clinically important localized infections; **AND**
- Patient will be administered prophylaxis for infection according to best clinical practices and guidelines; **AND**
- Vaccinations will not be administered within the 6 weeks prior to the start of myeloablative conditioning and until hematological recovery following treatment; **AND**
- Patient is up to date with all age-appropriate vaccinations, in accordance with current vaccination guidelines, prior to initiating therapy; **AND**
- Used as single agent therapy (not applicable to lymphodepleting or bridging therapy while awaiting manufacture); **AND**
- Patient will receive periodic life-long monitoring for hematological malignancies (e.g., myelodysplastic syndrome [MDS] and acute myeloid leukemia [AML]); **AND**
- Patient does not have a full *ABCD1* gene deletion; **AND**
- Patient will avoid concomitant therapy with anti-retroviral medications for at least one month prior to initiating medications for stem cell mobilization and for the expected duration for elimination of the medications, and until all cycles of apheresis are completed *(Note: if a patient requires anti-retroviral for HIV prophylaxis, confirm a negative test for HIV before beginning mobilization)*; **AND**
- Patient does not have disease secondary to head trauma; **AND**
- Therapy will not be used to prevent the development of or treat adrenal insufficiency due to adrenoleukodystrophy; **AND**
- Patient is eligible**§** to undergo hematopoietic stem cell transplant (HSCT) and has not had a prior allogeneic-HSCT; **AND**

- Males capable of fathering a child and their female partners of childbearing potential should use an effective method of contraception (e.g., intra-uterine device or combination of hormonal and barrier contraception) from start of mobilization through at least 6 months after administration of Skysona; **AND**

Cerebral Adrenoleukodystrophy (CALD) † Φ [1-6]

- Patient has a documented diagnosis of cerebral adrenoleukodystrophy (CALD)***** as defined by the following:
  - Elevated very long chain fatty acids (VLCFA) as confirmed by the following:
    - Plasma C26:0-lysophosphatidylcholine (C26:0-LPC) level; **OR**
    - Fasting plasma VLCFA levels: C26:0, ratio of C24:0 to C22:0, AND ratio of C26:0 to C22:0; **AND**
  - Pathogenic variants in the *ABCD1* gene as detected by genetic testing; **AND**
- Patient has active central nervous system (CNS) disease established by central radiographic review of brain magnetic resonance imaging (MRI) demonstrating both of the following:
  - Loes score between 0.5 and 9 (inclusive) on the 34-point scale; **AND**
  - Gadolinium enhancement on MRI of demyelinating lesions; **AND**
- Neurologic Function Score (NFS) ≤ 1 (asymptomatic or mildly symptomatic disease)

**Note: Patients with isolated pyramidal tract disease will be reviewed on a case-by-case basis*

§ *Eligibility criteria for allogeneic HCT are not absolute and vary by center. In general, patients are considered eligible for allogeneic HCT if they meet certain criteria like functional capacity, organ function, social support, etc.*

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

IV. Renewal Criteria [1]

Duration of authorization has not been exceeded *(refer to Section I)*.

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(s):

J3387 – Injection, elivaldogene autotemcel, per treatment

C9399 – Unclassified drugs or biologicals *(hospital outpatient use ONLY)*

NDC:

- Skysona up to 2 infusion bags, 20 mL/infusion bag, overwrap, and metal cassette: 73554-2111-xx

REVISIONS	
Posted: 10-15-2022 Effective: 11-15-2022	New medical policy added to the bcbsks.com web site. Policy is maintained by Prime Therapeutics LLC.
07-25-2023	Policy reviewed by Prime Therapeutics with non-clinical edits
05-14-2024	Policy reviewed by Prime Therapeutics with non-clinical edits
02-04-2025	Policy reviewed by Prime Therapeutics with non-clinical edits
Posted: 12-09-2025 Effective: 01-08-2026	Updated Clinical Rationale Section Update Clincial Criteria For Approval ▪ Removed: Evaluation Target Agent(s) will be approved when ALL of the following are met: 1. The patient has a diagnosis of active cerebral adrenoleukodystrophy (ALD) as defined by BOTH of the following: A. Elevated very long chain fatty acids (VLCFA) values AND B. Active central nervous system (CNS) disease established by central radiographic review of brain magnetic resonance imaging (MRI) demonstrating: 1. Loes score between 0.5 and 9 (inclusive) on the 34-point scale AND 2. Gadolinium enhancement on MRI of demyelinating lesions AND 2. The patient has a Neurologic Function Score (NFS) less than or equal to 1 AND 3. ONE of the following: A. The patient's sex is male OR B. The requested agent is medically appropriate for the patient's sex AND 4. If the patient has an FDA labeled indication, then ONE of the following: 1. The patient 's age is within FDA labeling for the requested indication for the requested agent OR 2. There is support for the use of the requested agent for the patient's age for the requested indication 5. The patient has NOT had an allogeneic hematopoietic stem cell transplant AND

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	6. The patient does NOT have availability of a willing 10/10 HLA-matched sibling donor (excluding female heterozygotes) AND 7. The patient does NOT have any of the following indicators of hematological compromise: A. Peripheral blood absolute neutrophil count (ANC) less than 1500 cells/mm^3 B. Platelet count less than 100,000 cells/mm^3 C. Hemoglobin less than 10 g/dL D. Uncorrected bleeding disorder AND 8. The patient does NOT have any of the following indicators of hepatic compromise: A. Aspartate transaminase (AST) value greater than 2.5 X the upper limit of normal (ULN) B. Alanine transaminase (ALT) value greater than 2.5 X ULN C. Total bilirubin value greater than 3.0 mg/dL unless the patient has a diagnosis of Gilbert's Syndrome and is otherwise stable AND 9. The patient does NOT have hepatitis B AND 10. The patient is NOT HIV positive AND 11. ONE of the following: A. The patient's hepatitis C virus (HCV) antibody is negative OR B. The patient's HCV antibody is positive AND the patient's HCV RNA is negative AND 12. The patient does NOT have another active infection AND 13. The patient has NOT had previous gene therapy for any diagnosis Length of Approval: 1 course per lifetime ▪ Added: Initial Approval Criteria 1,2,6 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 in the following conditions: • Patient is a male at least 4 years of age and less than 18 years of age; AND • Patient has been screened for hepatitis B virus (HBV), hepatitis C virus (HCV), human immunodeficiency virus 1 & 2 (HIV-1/HIV-2), and human T-lymphotrophic virus 1 & 2 (HTLV-1/HTLV-2) in accordance with clinical guidelines prior to collection of cells for manufacturing; AND • Patient does not have an active infection, including clinically important localized infections; AND • Patient will be administered prophylaxis for infection according to best clinical practices and guidelines; AND • Vaccinations will not be administered within the 6 weeks prior to the start of myeloablative conditioning and until hematological recovery following treatment; AND • Patient is up to date with all age-appropriate vaccinations, in accordance with current vaccination guidelines, prior to initiating therapy; AND • Used as single agent therapy (not applicable to lymphodepleting or bridging therapy while awaiting manufacture); AND • Patient will receive periodic life-long monitoring for hematological malignancies (e.g., myelodysplastic syndrome [MDS] and acute myeloid leukemia [AML]); AND • Patient does not have a full ABCD1 gene deletion; AND • Patient will avoid concomitant therapy with anti-retroviral medications for at least one month prior to initiating medications for stem cell mobilization and for the expected duration for elimination of the medications, and until all cycles of apheresis are completed (Note: if a patient requires anti-retroviral for HIV prophylaxis, confirm a negative test for HIV before beginning mobilization); AND • Patient does not have disease secondary to head trauma; AND • Therapy will not be used to prevent the development of or treat adrenal insufficiency due to adrenoleukodystrophy; AND • Patient is eligible§ to undergo hematopoietic stem cell transplant (HSCT) and has not had a prior allogeneic-HSCT; AND • Males capable of fathering a child and their female partners of childbearing potential should use an effective method of contraception (e.g., intra-uterine device or combination of hormonal and barrier contraception) from start of mobilization through at least 6 months after administration of Skysona; AND Cerebral Adrenoleukodystrophy (CALD) † Φ 1-6 • Patient has a documented diagnosis of cerebral adrenoleukodystrophy (CALD)* as defined by the following: o Elevated very long chain fatty acids (VLCFA) as confirmed by the following: · Plasma C26:0-lysophosphatidylcholine (C26:0-LPC) level; OR · Fasting plasma VLCFA levels: C26:0, ratio of C24:0 to C22:0, AND ratio of C26:0 to C22:0; AND o Pathogenic variants in the ABCD1 gene as detected by genetic testing; AND • Patient has active central nervous system (CNS) disease established by central radiographic review of brain magnetic resonance imaging (MRI) demonstrating both of the following:

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	o Loes score between 0.5 and 9 (inclusive) on the 34-point scale; AND o Gadolinium enhancement on MRI of demyelinating lesions; AND • Neurologic Function Score (NFS) ≤ 1 (asymptomatic or mildly symptomatic disease) *Note: Patients with isolated pyramidal tract disease will be reviewed on a case-by-case basis § Eligibility criteria for allogeneic HCT are not absolute and vary by center. In general, patients are considered eligible for allogeneic HCT if they meet certain criteria like functional capacity, organ function, social support, etc. † FDA Approved Indication(s); ‡ Compendia Recommended Indication(s); Φ Orphan Drug IV. Renewal Criteria 1 Duration of authorization has not been exceeded (refer to Section I).
	Updated Coding Section ▪ Removed J3590 ▪ Added New Code J3387 (eff. 01-01-2026)
	Policy maintained by Prime Therapeutics LLC

REFERENCES

1. Skysona [package insert]. Somerville, MA; bluebird bio, Inc.; April 2024. Accessed December 2024.
2. Raymond GV, Moser AB, Fatemi A. X-Linked Adrenoleukodystrophy. Initial Posting: March 26, 1999; Last Update: April 6, 2023. GeneReviews® [Internet]. Seattle (WA): University of Washington, Seattle; 1993-2024. Available from: https://www.ncbi.nlm.nih.gov/books/NBK1315/. Accessed December 2024.
3. Eichler F, Duncan C, Musolino PL, et al. Hematopoietic Stem-Cell Gene Therapy for Cerebral Adrenoleukodystrophy. N Engl J Med. 2017 Oct 26;377(17):1630-1638. doi: 10.1056/NEJMoa1700554. Epub 2017 Oct 4.
4. Moser HW, Loes DJ, Melhem ER, et al (2000) X-Linked adrenoleukodystrophy: overview and prognosis as a function of age and brain magnetic resonance imaging abnormality. A study involving 372 patients. Neuropediatrics 31:227–39. doi: 10.1055/s-2000-9236
5. Moser HW, Loes DJ, Melhem ER, et al. A Phase 2/3 Study of the Efficacy and Safety of Hematopoietic Stem Cells Transduced With Lenti-D Lentiviral Vector for the Treatment of Cerebral Adrenoleukodystrophy (CALD) – Clinical Trial Protocol. EudraCT No. 2011-001953-10. Registry name identifier: NCT01896102. Available at: https://clinicaltrials.gov/ProvidedDocs/02/NCT01896102/Prot_000.pdf
6. Engelen M, van Ballegoij WJC, Mallack EJ, et al. International Recommendations for the Diagnosis and Management of Patients With Adrenoleukodystrophy: A Consensus-Based Approach. Neurology 2022; 99:940.