Skysona® (elivaldogene autotemcel)
(Intravenous)

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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

A. Quantity Limit (max daily dose) [NDC 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.

B. 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]

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:

Use for indications outside of FDA-approved labeled indications does NOT meet medical criteria for coverage and will be considered investigational, thus will NOT be covered.

- 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 therapy and will not be administered concurrently while on therapy 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**
- Provider attests that informed consent was obtained from the patient/family, including potential risk for hematologic malignancy; **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 has not had a prior allogenic-HSCT; **AND**
- Patient is eligible**§** to undergo hematopoietic stem cell transplant; **AND**
- There is no known/available sibling-donor match for 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 one or more of 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; **OR**
    - 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]

Coverage may NOT be renewed.

V. Dosage/Administration [1]

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. **<u>Mobilization and Apheresis</u>** • 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 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 conditioning must be administered before infusion of Skysona. Consult prescribing information for the myeloablative 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.	

VI. Billing Code/Availability Information

HCPCS Code(s):

- J3590 – Unclassified biologics
- 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

VII. References

1. Skysona [package insert]. Somerville, MA; Bluebird bio, Inc.; September 2022. Accessed January 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 January 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.

Appendix 1 – Covered Diagnosis Codes

ICD-10	ICD-10 Description
E71.511	Neonatal adrenoleukodystrophy
E71.520	Childhood cerebral X-linked adrenoleukodystrophy
E71.521	Adolescent X-linked adrenoleukodystrophy
E71.528	Other X-linked adrenoleukodystrophy
E71.529	X-linked adrenoleukodystrophy, unspecified type

Appendix 2 – Centers for Medicare and Medicaid Services (CMS)

The preceding information is intended for non-Medicare coverage determinations. Medicare coverage for outpatient (Part B) drugs is outlined in the Medicare Benefit Policy Manual (Pub. 100-2), Chapter 15, §50 Drugs and Biologicals. In addition, National Coverage Determinations (NCDs) and/or Local Coverage Determinations (LCDs) may exist and compliance with these policies is required where applicable. Local Coverage Articles (LCAs) may also exist for claims payment purposes or to clarify benefit eligibility under Part B for drugs which may be self-administered. The following link may be used to search for NCD, LCD, or LCA documents: https://www.cms.gov/medicare-coverage-database/search.aspx. Additional indications, including any preceding information, may be applied at the discretion of the health plan..

Medicare Part B Covered Diagnosis Codes (applicable to existing NCD/LCD/LCA): N/A

Medicare Part B Administrative Contractor (MAC) Jurisdictions		
Jurisdiction	**Applicable State/US Territory**	**Contractor**
E (1)	CA, HI, NV, AS, GU, CNMI	Noridian Healthcare Solutions, LLC

Medicare Part B Administrative Contractor (MAC) Jurisdictions		
Jurisdiction	**Applicable State/US Territory**	**Contractor**
F (2 & 3)	AK, WA, OR, ID, ND, SD, MT, WY, UT, AZ	Noridian Healthcare Solutions, LLC
5	KS, NE, IA, MO	Wisconsin Physicians Service Insurance Corp (WPS)
6	MN, WI, IL	National Government Services, Inc. (NGS)
H (4 & 7)	LA, AR, MS, TX, OK, CO, NM	Novitas Solutions, Inc.
8	MI, IN	Wisconsin Physicians Service Insurance Corp (WPS)
N (9)	FL, PR, VI	First Coast Service Options, Inc.
J (10)	TN, GA, AL	Palmetto GBA, LLC
M (11)	NC, SC, WV, VA (excluding below)	Palmetto GBA, LLC
L (12)	DE, MD, PA, NJ, DC (includes Arlington & Fairfax counties and the city of Alexandria in VA)	Novitas Solutions, Inc.
K (13 & 14)	NY, CT, MA, RI, VT, ME, NH	National Government Services, Inc. (NGS)
15	KY, OH	CGS Administrators, LLC