Neighborhood Health Plan OF RHODE ISLAND™
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Skysona® (elivaldogene autotemcel)
(Intravenous)

Effective Date: 5/01/2023
Dates Reviewed: 3/30/2023, 12/07/2023, 01/04/2024, 9/03/2025
Scope: Medicaid, Commercial, Medicare

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

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

III. Summary of Evidence

Skysona (elivaldogene autotemcel) is an autologous hematopoietic stem cell-based gene therapy indicated to slow the progression of neurologic dysfunction in boys 4-17 years of age with early, active cerebral adrenoleukodystrophy (CALD). Early, active CALD refers to asymptomatic or mildly symptomatic (neurologic function score, NFS ≤1) boys who have gadolinium enhancement on brain magnetic resonance imaging (MRI) and Loes scores of 0.5 – 9. It carries warnings of serious infections, prolonged cytopenias, delayed platelet engraftment, a risk of neutrophil engraftment failure, and black box warning for hematologic malignancy. Common adverse reactions include mucositis, N/V/D, febrile neutropenia, alopecia, decreased appetite, constipation, pyrexia, headache, and rash. The safety and efficacy of Skysona were assessed in two 24-month, open-label, single-arm studies in patients with early, active CALD as defined by Loes score between 0.5 – 9 and gadolinium enhancement (GdE+) on MRI, as well as a neurologic function score (NFS) ≤ 1, indicating limited changes in neurologic function. The primary endpoints of Study 1 (N = 32) were the percentage of patients who are alive and have none of the 6 MFDs at Month 24 and without allo-HSCT or rescue cell administration as well as the proportion of patients who experienced either acute or chronic graft versus host disease (GVHD) by Month 24. The primary endpoints of Study 2 were the percentage of patients who are alive and have none of the 6 MFDs at Month 24 and the percentage of patients with neutrophil engraftment after drug product infusion. The efficacy of Skysona was compared to an external natural history control. Skysona demonstrated slower progression to MFD or death from time of symptom onset in patients with early, active CALD compared to a similar natural history of disease. Kaplan-Meier estimated KFD-free survival

at Month 24 from time of first NFS ≥ 1 were 72% (95% CI: 35%, 90%) for the symptomatic Skysona cohort and 43% (95% CI: 10%, 73%) for the Natural History Population.

IV. 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:

- Skysona must be prescribed by or in consultation with a physician who specializes in the treatment of adrenoleukodystrophy (ALD).
- 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 T-lymphotrophic virus 1 & 2 (HTLV-1/HTLV-2), and human immunodeficiency virus 1 &2 (HIV-1/HIV-2) in accordance with clinical guidelines prior to collection of cells (leukapheresis); **AND**
- Patient does not have an active infection, including clinically important localized infections; **AND**
- Prophylaxis for infection will be followed according to standard institutional 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**
- Patient will receive periodic life-long monitoring for hematological malignancies *(Myelodysplastic syndrome [MDS] has developed in patients treated in clinical studies with a varied clinical presentation)*; **AND**
- Patient does not have a full *ABCD1*-gene deletion *(Note: Rapid loss of efficacy due to immune response may result)*; **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 head trauma induced disease; **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**

- Patient has no known or available 10/10 HLA-matched family hematopoietic stem cell donor; **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

Cerebral Adrenoleukodystrophy (CALD) † Φ [1-5]

- 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 *ABCD*1 gene detected by molecular 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 indications; **‡** Compendia Recommended Indication(s); **Φ** Orphan Drug

V. Renewal Criteria [1]

Coverage cannot be renewed.

VI. Dosage/Administration [1]

Indication	Dose
Cerebral Adreno-leukodystrophy (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 5.0×10^6 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 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 12×10^6 CD34+ cells/kg. – A back-up collection of CD34+ cells of $\geq 1.5 \times 10^6$ CD34+ cells/kg (if collected by apheresis) or $> 1.0 \times 10^8$ TNC/kg (Total Nucleated Cells, if collected by bone marrow harvest) is required. These cells must be collected from the patient and be cryopreserved prior to myeloablative conditioning. The back-up collection may be needed for rescue treatment if there is: o Compromise of hematopoietic stem cells or Skysona before infusion o Primary engraftment failure o Loss of engraftment after infusion with Skysona – Note: G-CSF +/- plerixafor were used for mobilization **Myeloablative & 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 for lymphodepletion **Administration** – Verify that the patient's identity matches the unique patient identification information on the Skysona infusion bag(s) prior to infusion. – Do not sample, alter, irradiate, or refreeze Skysona. – Do not use an in-line blood filter or an infusion pump. – Administer each infusion bag of Skysona via intravenous infusion over a period of less than 60 minutes. Product must be administered within 4 hours after thawing.
For autologous use only. For intravenous use only. – Match the identity of the patient with the patient identifiers on the metal cassette(s), infusion bag(s), and Lot Information Sheet upon receipt. Keep the infusion bag(s) in the metal cassette(s) and store in the vapor phase of liquid nitrogen at less than or equal to -140°C (≤ -220°F) until ready for thaw and administration. Thaw prior to infusion, do not re-freeze after thawing. Do not irradiate as this could lead to inactivation.	

VII. Billing Code/Availability Information

HCPCS Code:

- J3590 – Unclassified biologics

NDC:

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

Note: Medicare members who have previously received this medication within the past 365 days are not subject to Step Therapy Requirements.

VIII. References

1. Skysona [package insert]. Somerville, MA; Bluebird bio, Inc: August 2025. Accessed August 2025.
2. Raymond GV, Moser AB, Fatemi A. X-Linked Adrenoleukodystrophy. 1999 Mar 26 [Updated 2018 Feb 15]. GeneReviews® [Internet]. Seattle (WA): University of Washington, Seattle; 1993-2022. Available from: https://www.ncbi.nlm.nih.gov/books/NBK1315/. Accessed September 2022.
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

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)

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 Determination (NCD), Local Coverage Determinations (LCDs), and Local Coverage Articles (LCAs) may exist and compliance with these policies is required where applicable. They can be found at: https://www.cms.gov/medicare-coverage-database/search.aspx. Additional indications may be covered 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
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

Policy Rationale:

Skysona was reviewed by the Neighborhood Health Plan of Rhode Island Pharmacy & Therapeutics (P&T) Committee. Neighborhood adopted the following clinical coverage criteria to ensure that its members use Skysona according to Food and Drug Administration (FDA) approved labeling and/or relevant clinical literature. Neighborhood worked with network prescribers and pharmacists to draft these criteria. These criteria will help ensure its members are using this drug for a medically accepted indication, while minimizing the risk for adverse effects and ensuring more cost-effective options are used first, if applicable and appropriate. For Medicare members, these coverage criteria will only apply in the absence of National Coverage Determination (NCD) or Local Coverage Determination (LCD) criteria. Neighborhood will give individual consideration to each request it reviews based on the information submitted by the prescriber and other information available to the plan.