

## Clinical Policy: Elivaldogene Autotemcel (Skysona)

Reference Number: PA.CP.PHAR.556

Effective Date: 01/2023

Last Review Date: 10/2025

### Description

Elivaldogene autotemcel (Skysona<sup>®</sup>) is a genetically modified autologous CD34+ cell enriched population that contains hematopoietic stem cells transduced ex vivo with a lentiviral vector encoding *ABCD1* complementary deoxyribonucleic acid (cDNA) for human adrenoleukodystrophy protein.

### FDA Approved Indication(s)

Skysona is indicated to slow the progression of neurologic dysfunction in boys 4-17 years of age with early, active cerebral adrenoleukodystrophy (CALD) without an available human leukocyte antigen (HLA)-matched donor for allogeneic hematopoietic stem cell transplant. Early, active CALD refers to asymptomatic or mildly symptomatic (neurologic function score, NFS  $\leq 1$ ) boys who have gadolinium enhancement on brain magnetic resonance imaging (MRI) and Loes scores of 0.5-9.

This indication is approved under accelerated approval based on 24-month Major Functional Disability (MFD)-free survival. Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial(s).

Limitation(s) of use:

- Skysona does not treat or prevent adrenal insufficiency due to adrenoleukodystrophy.
- An immune response to Skysona may limit the persistence of descendent cells of Skysona, causing rapid loss of efficacy of Skysona in patients with full deletions of the human adenosine triphosphate binding cassette, sub family D, member (*ABCD1*) gene.
- Skysona has not been studied in CALD secondary to head trauma.
- Given the risk of hematologic malignancy with Skysona, and unclear long-term durability of Skysona and human adrenoleukodystrophy protein (ALDP) expression, careful consideration should be given to the timing of treatment for each boy and treatment of boys with isolated pyramidal tract disease since their clinical symptoms do not usually occur until adulthood.

### Policy/Criteria

*Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.*

All requests reviewed under this policy **require medical director review**.

It is the policy of PA Health & Wellness<sup>®</sup> that Skysona is **medically necessary** when the following criteria are met:

#### I. Initial Approval Criteria

*\*Only for initial treatment dose; subsequent doses will not be covered.*

##### A. Cerebral Adrenoleukodystrophy (must meet all):

1. Diagnosis of adrenoleukodystrophy with both of the following (a and b):
    - a. Genetic confirmation of *ABCD1* mutation;
    - b. Elevated levels of very long chain fatty acids (VLCFA);
  2. Prescribed by or in consultation with both of the following (a and b):
    - a. Neurologist;
    - b. Transplant specialist;
  3. Member is a biologic male;
  4. Age between 4 and 17 years;
  5. Early, active CNS disease established by brain MRI demonstrating both of the following (a and b):
    - a. Loes score  $\geq 0.5$  and  $\leq 9$  on the 34-point scale (*see Appendix D*);
    - b. Gadolinium enhancement of demyelinating lesions on MRI;
  6. Member has an NFS  $\leq 1$  (*see Appendix D*);
  7. Member has no available HLA-matched (i.e., full HLA-matching of all evaluated alleles) donor;
  8. Transplant specialist attestation that member is clinically stable and eligible to undergo myeloablative conditioning and HSCT;
  9. Member has not received prior allogeneic HSCT;
  10. Member has not received prior gene therapy;
  11. For members with CALD and isolated pyramidal tract disease: Hematology specialist attestation of both of the following (a and b):
    - a. Member understands the potential increased risk of malignancy associated with Skysona treatment;
    - b. Applicable hematology assessments have been performed (*see Appendix E for examples*);
  12. Member is not positive for the presence of HIV type 1 or 2;
  13. Dose contains a minimum of  $5 \times 10^6$  CD34+ cells/kg.
- Approval duration: 3 months (one time infusion per lifetime)**

**B. Other diagnoses/indications**

1. Refer to the off-label use policy if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): PA.CP.PMN.53

**II. Continued Therapy**

**A. Cerebral Adrenoleukodystrophy** Continued therapy will not be authorized as Skysona is indicated to be dosed one time only.

**Approval duration: Not applicable**

**B. Other diagnoses/indications (must meet 1 or 2):**

1. Currently receiving medication via PA Health & Wellness benefit and documentation supports positive response to therapy or the Continuity of Care policy (PA.PHARM.01) applies.

**Approval duration: Duration of request or 6 months (whichever is less); or**

2. Refer to the off-label use policy if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): PA.CP.PMN.53

**III. Diagnoses/Indications for which coverage is NOT authorized:**

- A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policies – PA.CP.PMN.53.

**IV. Appendices/General Information**

*Appendix A: Abbreviation/Acronym Key*

*ABCD1*: adenosine triphosphate binding cassette, sub family D, member 1  
ALDP: adrenoleukodystrophy protein  
CALD: cerebral adrenoleukodystrophy  
cDNA: complementary deoxyribonucleic acid  
FDA: Food and Drug Administration  
HLA: human leukocyte antigen

HSCT: hematopoietic stem cell transplantation  
MFD: major functional disability  
MRI: magnetic resonance imaging  
NFS: neurologic function score  
VLCFA: very long chain fatty acids

*Appendix B: Therapeutic Alternatives*

Not applicable

*Appendix C: Contraindications/Boxed Warnings*

- Contraindication(s): none
- Boxed warning(s): hematologic malignancy

*Appendix D: General Information*

- The Loes score is a rating of the severity of abnormalities in the brain found on MRI. It ranges from 0 to 34, based on a point system derived from the location and extent of disease and the presence of atrophy in the brain, either localized to specific points or generally throughout the brain. A score of 0 indicates a normal MRI, and higher scores indicate increased severity of cerebral lesions.
- The CALD NFS is a 25-point score used to evaluate the severity of gross neurologic dysfunction across 15 symptoms in six categories. An NFS of 0 indicates that there is no observed impairment in the neurologic functions that are assessed on the 25-point scale, and higher scores correspond to increasing severity of functional deficits.
- Hematologic malignancies, including life-threatening cases of myelodysplastic syndrome (MDS) and acute myeloid leukemia (AML), have developed in patients treated with Skysona in clinical studies between 14 months and 10 years after Skysona administration, and the cancers appear to be related to treatment with Skysona. Death related to treatment for malignancy and relapse of malignancy have occurred..

*Appendix E: Baseline Hematologic Assessments for CALD with isolated pyramidal tract disease*

- Complete blood count with differential
- Hematopathology review of peripheral blood smear
- Hematopathology review of bone marrow biopsy (core and aspirate) with flow cytometry, conventional karyotyping, and next generation sequencing (NGS) with a

molecular panel appropriate for age and including coverage for gene mutations expected in myeloid and lymphoid malignancies

- Testing for germline mutations that are associated with hematologic malignancy

**V. Dosage and Administration**

Indication	Dosing Regimen	Maximum Dose
CALD	Minimum recommended dose: $5.0 \times 10^6$ CD34+ cells/kg	None

**VI. Product Availability**

Single-dose cell suspension: up to two infusion bags of genetically modified autologous cells enriched for CD34+ cells labeled for the specific recipient

**VII. References**

1. Skysona Prescribing Information. Somerville, MA: bluebird bio, Inc.; August 2025. Available at: [https://www.bluebirdbio.com/-/media/bluebirdbio/Corporate%20COM/Files/SKYSONA/SKYSONA\\_prescribing\\_information.pdf](https://www.bluebirdbio.com/-/media/bluebirdbio/Corporate%20COM/Files/SKYSONA/SKYSONA_prescribing_information.pdf). Accessed August 8, 2025.
2. ClinicalTrials.gov. 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). Available at: <https://clinicaltrials.gov/ct2/show/NCT01896102>. Accessed August 8, 2025.
3. ClinicalTrials.gov. A clinical study to assess the efficacy and safety of gene therapy for the treatment of cerebral adrenoleukodystrophy (CALD). Available at <https://clinicaltrials.gov/ct2/show/NCT03852498>. Accessed August 7, 2024.
4. 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(21):940-951.
5. Engelen M, Kemp S, de Visser M, et al. X-linked adrenoleukodystrophy (X-ALD): clinical presentation and guidelines for diagnosis, follow-up and management. *Orphanet Journal of Rare Diseases* 2012;7:51.
6. Zhu J, Eichler F, Biffi A, et al. The changing face of adrenoleukodystrophy. *Endocr Rev*. 2020 August;41(4):577-593.
7. ALD Info. Diagnosis of ALD. Available at: <https://adrenoleukodystrophy.info/clinical-diagnosis/diagnosis-of-ald>. Accessed August 7, 2025.

**Coding Implications**

Codes referenced in this clinical policy are for informational purposes only. Inclusion or exclusion of any codes does not guarantee coverage. Providers should reference the most up-to-date sources of professional coding guidance prior to the submission of claims for reimbursement of covered services.

HCPCS Codes	Description
J3590	Unclassified biologics
C9399	Unclassified drugs or biologicals

<b>Reviews, Revisions, and Approvals</b>	<b>Date</b>
Policy created	01/2023
4Q 2023 annual review: no significant changes; references reviewed and updated.	10/2023
4Q 2024 annual review: removed Appendix E VLCFA lab reference ranges; added hematologic malignancy information to Appendix D; references reviewed and updated.	10/2024
4Q 2025 annual review: RT4: updated FDA-approved indication to include lack of an available HLA-matched donor for allogeneic HSCT; removed criterion option for having an HLA-matched donor and its accompanying criteria per PI; references reviewed and updated.	10/2025