

# 5.60.055

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<b>Subsection:</b>	Central Nervous System Drugs	<b>Original Policy Date:</b>	January 1, 2023
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**Last Review Date:** March 6, 2026

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## Skysona

### Description

#### Skysona (elivaldogene autotemcel)

##### Background

Cerebral adrenoleukodystrophy (CALD) is a genetic disorder caused by a mutation in the *ABCD1* gene. It is the childhood-onset form of ALD and leads to the accumulation of very long chain fatty acids in the brain and adrenal glands. This can cause damage to the myelin sheaths in the brain and spine which is required for normal functioning. CALD is an X-linked condition and as a result mainly affects males while females are often carriers with no or very mild symptoms (1).

Skysona (elivaldogene autotemcel) adds functional copies of the *ABCD1* cDNA into patients' hematopoietic stem cells (HSCs) through transduction of autologous CD34+ cells with Lenti-D LVV. After Skysona infusion, transduced CD34+ HSCs engraft in the bone marrow and differentiate into various cell types, including monocytes capable of production functional adrenoleukodystrophy protein (ALDP). Functional ALDP can then participate in the local degradation of very long chain fatty acids, which is believed to slow or possibly prevent inflammation and demyelination (2).

##### Regulatory Status

FDA-approved indication: Skysona 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) without an available human leukocyte antigen (HLA)-matched donor for allogeneic hematopoietic stem cell transplant. Early, active

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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 (2).

#### Limitations of Use: (2)

- Skysona does not treat or prevent adrenal insufficiency.
- An immune response to Skysona may cause rapid loss of efficacy of Skysona in patients with full deletions of the human adenosine triphosphate binding cassette, sub family D, member 1 (*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 ALDP expression, careful consideration should be given to the timing of treatment for each boy and treatment of boys with isolated pyramidal tract disease as clinical manifestations do not usually occur until adulthood.

Skysona has a boxed warning regarding hematologic malignancy. Hematologic malignancy, including life-threatening cases of myelodysplastic syndrome and acute myeloid leukemia, has occurred in patients treated with Skysona. The cancers appear to be the result of the Skysona lentiviral vector, Lenti-D, integration in proto-oncogenes. Monitor patients closely for evidence of malignancy through complete blood counts at least every 3 months and through assessments for evidence for clonal expansion or predominance at least twice in the first year and annually thereafter; consider bone marrow evaluations as clinically indicated (2).

Skysona also contains warnings for serious infections, prolonged cytopenias, delayed platelet engraftment, and risk of neutrophil engraftment failure, hypersensitivity reactions, anti-retroviral use, and laboratory test interference (2).

Skysona was not studied in combination with other treatments to lower very-long-chain fatty acid (VLFCA) levels (e.g., statins, Lorenzo's Oil, or dietary regimens). Caution is advised regarding the continuation of VLFCA lowering treatments after Skysona administration (2).

The safety and effectiveness of Skysona in pediatric patients less than 4 years of age have not been established (2).

#### **Related policies**

[Policy](#)

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*This policy statement applies to clinical review performed for pre-service (Prior Approval, Precertification, Advanced Benefit Determination, etc.) and/or post-service claims.*

Skysona may be considered **medically necessary** if the conditions indicated below are met.

Skysona may be considered **investigational** for all other indications.

## Prior-Approval Requirements

**Age** 4 to 17 years of age

### Diagnosis

Patient must have the following:

1. Cerebral adrenoleukodystrophy (CALD)

**AND ALL** of the following:

- a. Asymptomatic or mildly symptomatic (neurologic function score, NFS  $\leq 1$ )
- b. Elevated very-long-chain fatty acids (VLCFAs)
- c. Gadolinium enhancement (GdE+) on brain MRI and Loes score of 0.5 to 9
- d. Confirmed mutation in the *ABCD1* gene
- e. Fertile patients will be advised to use effective contraception during treatment from the start of mobilization and for 6 months after Skysona administration

**AND NONE** of the following:

- a. Prior gene therapy or allogenic hematopoietic stem cell transplant
- b. Absolute neutrophil count (ANC)  $< 1500$  cells /cubic millimeter
- c. Platelet count  $< 100,000$  cells / cubic millimeter
- d. Uncorrected bleeding disorder
- e. Hemoglobin  $< 10$  grams per deciliter
- f. Aspartate transaminase (AST) and alanine transaminase (ALT)  $> 2.5$  times the upper limit of normal (ULN)
- g. Total bilirubin values  $> 3.0$  milligram per deciliter, except if patient is diagnosed with Gilbert's Syndrome and is otherwise stable
- h. Left ventricular ejection fraction (LVEF)  $< 40\%$
- i. Estimated glomerular filtration rate (eGFR)  $< 70$  ml/min/1.73m<sup>2</sup>
- k. Immediate family member (i.e., parent or siblings) with a known history of hematological malignancy, including myelodysplastic syndrome

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- l. Clinically significant uncontrolled, active bacterial, viral, fungal, parasitic, or prion associated infection
- m. Positive for human immunodeficiency virus (HIV1 or HIV-2) or human T lymphotropic virus 1 (HTLV-1)
- n. Active hepatitis B virus or hepatitis C virus infection
- o. Contraindication to continued MRI studies
- p. Contraindication to the use of Granulocyte colony-stimulating factor (G-CSF) or plerixafor during the mobilization of hematopoietic stem cells
- q. Contraindications to the use of busulfan or fludarabine

## **Prior – Approval *Renewal* Requirements**

None

### **Policy Guidelines**

## **Pre – PA Allowance**

None

## **Prior - Approval Limits**

**Quantity**      One infusion (only one PA approval for one infusion per lifetime)

### **Rationale**

#### **Summary**

Skysona is indicated to slow the progression of neurologic dysfunction in boys 4-17 years of age with early, active cerebral adrenoleukodystrophy (CALD). CALD is a genetic neurological disorder in which there is a buildup of very long chain fatty acids in the brain and adrenal glands, causing damage to myelin sheaths. Skysona has a boxed warning regarding hematologic malignancy. Skysona is for autologous use only (1-2).

Prior approval is required to ensure the safe, clinically appropriate, and cost-effective use of Skysona while maintaining optimal therapeutic outcomes.

#### **References**

1. Cerebral Adrenoleukodystrophy. Child Neurology Foundation. July 2021. Accessed from <https://www.childneurologyfoundation.org/disorder/cerebral-adrenoleukodystrophy/>.

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2. Skysona [package insert]. Somerville, MA: Bluebird Bio, Inc.; August 2025.

## Policy History

Date	Action
January 2023	Addition to PA. Per Association policy, removed the following requirements: male gender; patient cannot continue to use statins, Lorenzo's Oil or dietary regimens used to lower VLCFA levels after administration of Skysona; availability of human leukocyte antigen-matched donor
March 2023	Annual review
March 2024	Annual editorial review. Per Association policy, changed requirement for immediate family member to not have a history of a hematological malignancy
March 2025	Annual editorial review and reference update
March 2026	Annual editorial review and reference update

## Keywords

**This policy was approved by the FEP® Pharmacy and Medical Policy Committee on March 6, 2026 and is effective on April 1, 2026.**