Corporate Medical Policy: Elivaldogene autotemcel (Skysona®) **"Notification"** **POLICY EFFECTIVE APRIL 1, 2026**

Restricted Product(s):

- elivaldogene autotemcel (Skysona®) intravenous infusion for administration by a healthcare professional

FDA Approved Use:

- 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 ≤ 1) boys who have gadolinium enhancement on brain magnetic resonance imaging (MRI) and Loes scores of 0.5-9
- Limitations of use:
  - 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)
  - Not for the treatment or prevention of adrenal insufficiency
  - Not studied in CALD secondary to head trauma
  - 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
  - Due to 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 appropriateness and treatment timing for each boy, especially for the treatment of boys with isolated pyramidal tract disease as clinical manifestations do not usually occur until adulthood

Criteria for Medical Necessity:

The restricted product(s) may be considered medically necessary when the following criteria are met:

1. The patient is male AND 4 to 17 years of age; **AND**
2. The patient has a diagnosis of active **cerebral adrenoleukodystrophy (CALD) [medical record documentation required]**; **AND**
3. The diagnosis has been confirmed by BOTH of the following:
   a. Elevated very long chain fatty acids (VLCFA) values **[medical record documentation required]**; **AND**
   b. Active central nervous system (CNS) disease established by central radiographic review of brain magnetic resonance imaging (MRI) demonstrating **[medical record documentation required]**:
      i. Loes score between 0.5 and 9 (inclusive) on the 34-point scale; **AND**
      ii. Gadolinium enhancement on MRI of demyelinating lesions; **AND**
4. The patient has a Neurologic Function Score (NFS) less than or equal to 1 **[medical record documentation required]**; **AND**

5. The patient has NOT had an allogeneic hematopoietic stem cell transplantation (HSCT) **[medical record documentation required]**; **AND**
6. The patient does NOT have availability of a human leukocyte antigen (HLA)-matched allogeneic hematopoietic stem cell (allo-HSC) donor **[medical record documentation required]**; **AND**
7. The patient does NOT have any of the following indicators of hematological compromise **[medical record documentation required]**:
    a. Peripheral blood absolute neutrophil count (ANC) less than 1500 cells/mm^3; **OR**
    b. Platelet count less than 100,000 cells/mm^3; **OR**
    c. Hemoglobin less than 10 g/dL; **OR**
    d. Uncorrected bleeding disorder; **AND**
8. The patient does NOT have any of the following indicators of hepatic compromise **[medical record documentation required]**:
    a. Aspartate transaminase (AST) value greater than 2.5 times the upper limit of normal (ULN); **OR**
    b. Alanine transaminase (ALT) value greater than 2.5 times ULN; **OR**
    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 **[medical record documentation required]**; **AND**
10. The patient is NOT HIV positive **[medical record documentation required]**; **AND**
11. ONE of the following **[medical record documentation required]**:
    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 any other active infection **[medical record documentation required]**; **AND**
13. The patient has NOT had previous gene therapy for any diagnosis **[medical record documentation required]**; **AND**
14. The requested dose is within FDA labeled dosing for the requested indication **[medical record documentation required]**.

Duration of Approval: 180 days (one treatment course per lifetime)

Please note, for certain identified gene and cellular therapies such as elivaldogene autotemcel (Skysona®), when coverage is available and the individual meets medically necessary criteria, distribution from a specialty pharmacy provider due to cost (distribution channel restriction) may be required in order for coverage to be provided. **Please contact Blue Cross NC to coordinate this therapy.

FDA Label Reference				
Medication	**Indication**	**Dosing**	**HCPCS**	**Maximum Units***
elivaldogene autotemcel (Skysona®) intravenous (IV) infusion	Early, active cerebral adrenoleukodystrophy (CALD) in male patients 4-17 years of age	Dosing is based on the number of CD34+ cells in the infusion bag(s) per kg of body weight. The minimum recommended dose is 5.0 x 10^6 CD34+ cells/kg.	J3387	**1**

***Maximum units allowed for duration of approval**

Other revenue codes that may be applicable to this policy: 0891, 0892

Loes Score: MRI severity scale scoring system. A severity score (0 to 34) is calculated for each MRI scan based on a point system derived from location and extent of involvement and the presence of focal and/or global atrophy.

- Parieto-occipital white matter (maximum 4)
- Anterior temporal white matter (maximum 4)
- Frontal white matter (maximum 4)
  - Periventricular
  - Central
  - Subcortical
  - Local atrophy
- Corpus callosum (maximum 5)
  - Splenium
  - Genu
  - Body
  - Splenium atrophy
  - Genu atrophy
- Global atrophy (maximum 4)
  - Mild
  - Moderate
  - Severe
  - Brainstem

- Basal ganglia (maximum 1)
- Visual pathway (maximum 4)
    - Optic radiations
    - Meyer's loop
    - Lateral geniculate body
- Auditory pathway (maximum 4)
    - Medial geniculate body
    - Brachium of inferior colliculus
    - Lateral lemniscus
    - Pons
- Cerebellum (maximum 2)
    - White matter
    - Atrophy
- Projection fibers (maximum 2)
    - Internal capsule
    - Brain stem

Cerebral Adrenoleukodystrophy Neurologic Function Scale: To evaluate gross clinical neurologic status.

Hearing/auditory processing problems	1
Aphasia/apraxia	1
Loss of communication	3
Vision impairment/fields cut	1
Cortical blindness	2
Swallowing difficulty or other central nervous system dysfunction	2
Tube feeding	2
Running difficulties/hyperreflexia	1

Walking difficulties/spasticity/spastic gait (no assistance)	1
Spastic gait (needs assistance)	2
Wheelchair required	2
No voluntary movement	3
Episodes of urinary or fecal incontinency	1
Total urinary or fecal incontinency	2
Nonfebrile seizures	1
Possible total score	25

References: all information referenced is from FDA package insert unless otherwise noted below.

1. 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.
2. Loes DJ, Hite S, Moser H, et al. Adrenoleukodystrophy: a scoring method for brain MR observations. *AJNR Am J Neuroradiol*. 1994 Oct;15:1761-1766.
3. Miller WP, Mantovani LF, Muzic J, et al. Intensity of MRI gadolinium enhancement in cerebral adrenoleukodystrophy: a biomarker for inflammation and predictor of outcome following transplantation in higher risk patients. *AJNR Am J Neuroradiol*. 2016 Feb;37(2):367-372.

Policy Implementation/Update Information: Criteria and treatment protocols are reviewed annually by the Blue Cross NC P&T Committee, regardless of change. This policy is reviewed in Q4 annually.

April 2026: Coding change: Added the following applicable revenue codes associated with policy HCPCS code(s): 0891 (Special Processed Drugs – FDA Approved Cell Therapy) and 0892 (Special Processed Drugs – FDA Approved Gene Therapy). **Policy notification given 2/1/2026 for effective date 4/1/2026**.
January 2026: Coding change: Added HCPCS code J3387 (1 unit per treatment) to dosing reference table effective 1/1/2026; deleted C9399, J3490, and J3590 termed 12/31/2025.

October 2025: Criteria change: Updated indication to include without an available HLA-matched allo-HSC donor to reflect FDA label changes and adjusted wording throughout criteria to align. Added Gene/Cellular Therapy distribution channel management language according to benefit booklet for clarity.
October 2022: Original medical policy criteria issued.