

eladocagene exuparvovec-tneq (Kebilidi™)

Policy # 00948

Original Effective Date: 12/01/2025

Current Effective Date: 12/01/2025

Applies to all products administered or underwritten by Blue Cross and Blue Shield of Louisiana and its subsidiary, HMO Louisiana, Inc. (collectively referred to as the "Company"), unless otherwise provided in the applicable contract. Medical technology is constantly evolving, and we reserve the right to review and update Medical Policy periodically.

When Services May Be Eligible for Coverage

Coverage for eligible medical treatments or procedures, drugs, devices or biological products may be provided only if:

- *Benefits are available in the member's contract/certificate, and*
- *Medical necessity criteria and guidelines are met.*

Based on review of available data, the Company may consider the use of eladocagene exuparvovec-tneq (Kebilidi™)[‡] for the treatment of aromatic L-amino acid decarboxylase (AADC) deficiency to be **eligible for coverage**** when patient selection criteria are met.

Patient Selection Criteria

Coverage eligibility for the use of eladocagene exuparvovec-tneq (Kebilidi) will be considered when ALL of the following criteria are met:

- Patient is ≥ 16 months of age; AND
*(Note: This specific patient selection criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met).*
- Patient has reached skull maturity based on neuroimaging (documentation must be submitted); AND
- Patient has a genetically confirmed diagnosis of AADC deficiency confirmed by BOTH of the following:
 - Identification of biallelic pathogenic mutations in the *DDC* gene; AND
 - Decreased AADC enzyme activity in plasma; AND
- Patient is experiencing the classic clinical characteristics of severe AADC deficiency (e.g., oculogyric crises, hypotonia, developmental delay); AND
*(Note: This specific patient selection criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met).*
- According to the prescriber, the patient has continued symptoms of AADC deficiency affecting motor milestones (e.g., sitting, standing, independent ambulation) despite the use of at least one standard medication therapy. Note: standard medications used for AADC deficiency include dopamine agonists (e.g., pramipexole, ropinirole, rotigotine), monoamine oxidase inhibitors (e.g., tranylcypromine, selegiline), pyridoxine, and other forms of vitamin B6; AND
*(Note: This specific patient selection criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met).*

Policy # 00948

Original Effective Date: 12/01/2025

Current Effective Date: 12/01/2025

- Patient does not have other significant medical or neurological conditions that would create an unacceptable operative or anesthetic risk; AND
*(Note: This specific patient selection criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met).*
- Patient does NOT have pyridoxine-5'-phosphate oxidase or tetrahydrobiopterin (BH4) deficiency; AND
*(Note: This specific patient selection criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met).*
- Patient does NOT have an anti-adenovirus-associated virus, serotype 2 (anti-AAV2) antibody titer higher than 1:1200 or > 1 optical density value by enzyme-linked immunosorbent assay (ELISA); AND
- Patient does NOT have a clinically active infection; AND
- Patient has not received previous treatment with Kebilidi or any other gene therapy; AND
*(Note: This specific patient selection criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met).*
- Dose will not exceed 1.8×10^{11} vector genomes (0.32 mL) administered during a single stereotactic neurosurgical procedure.

When Services Are Considered Not Medically Necessary

Based on review of available data, the Company considers the use of eladocogene exuparvovec-tneq (Kebilidi) in patients younger than 16 months of age, who are not experiencing classic clinical characteristics of severe AADC deficiency despite the use of at least one standard medication therapy, who have other significant medical or neurological conditions, who have pyridoxine-5'-phosphate oxidase or BH4 deficiency, or who have received prior Kebilidi or other gene therapy treatment to be **not medically necessary**.**

When Services Are Considered Investigational

Coverage is not available for investigational medical treatments or procedures, drugs, devices or biological products.

Based on review of available data, the Company considers the use of eladocogene exuparvovec-tneq (Kebilidi) when patient selection criteria are not met (except those denoted to be **not medically necessary****) to be **investigational**.*

Background/Overview

Kebilidi is an adeno-associated virus (AAV) vector-based gene therapy indicated for the treatment of adult and pediatric patients with aromatic L-amino acid decarboxylase (AADC) deficiency. It must be administered directly into the putamen of the brain via stereotactic neurosurgery at a medical center that specializes in stereotactic neurosurgery. It is a one-time treatment that works by delivering a functional copy of the human *DDC* gene into the putamen of the brain.

Policy # 00948

Original Effective Date: 12/01/2025

Current Effective Date: 12/01/2025

Aromatic L-amino acid decarboxylase (AADC) deficiency (also known as dopa decarboxylase [DDC] deficiency) is an ultra-rare condition that is estimated to affect slightly over 100 patients globally with fewer than 50 diagnosed patients in the United States. It is caused by mutations in the *DDC* gene that result in abnormally low production of vital neurotransmitters, including dopamine, serotonin, norepinephrine, and epinephrine. This affects a wide range of body systems. Neurological development is slowed, leading to a delay or inability to reach developmental milestones including sitting up, crawling, walking, and talking at appropriate ages. AADC deficiency is also linked to autonomic dysfunction, leading to improper regulation of heart rate, body temperature, and gastrointestinal function. Other manifestations include movement disorders (e.g. dystonia, chorea, athetosis), and failure to thrive. Manifestations of the disease can be mild to severe with roughly 5% of cases classified as mild (ambulatory), 15% as moderate (non-ambulatory but not bedbound), and 80% as severe. More severe manifestations may include hypotonia and oculogyric crises.

There are no treatments for AADC deficiency, and therapy consists of symptom control. Symptom management may include supplements (e.g. vitamin B6 or pyridoxine), agents to mimic the dopamine response (e.g., dopamine receptor agonists), and agents that inhibit the breakdown of neurotransmitters (e.g., monoamine oxidase inhibitors). Some patients with AADC deficiency may also benefit from non-drug treatments such as physiotherapy, occupational therapy, or speech therapy.

FDA or Other Governmental Regulatory Approval

U.S. Food and Drug Administration (FDA)

Kebilidi was approved in November 2024 for the treatment of adult and pediatric patients with aromatic L-amino acid decarboxylase (AADC) deficiency.

Prior to its U.S. approval, eladocagene exuparvovec received marketing authorization in Europe, Great Britain, and Israel, as the brand name Upstaza, for patients 18 months of age and older with AADC deficiency.

Rationale/Source

This medical policy was developed through consideration of peer-reviewed medical literature generally recognized by the relevant medical community, U.S. Food and Drug Administration approval status, nationally accepted standards of medical practice and accepted standards of medical practice in this community, technology evaluation centers, reference to regulations, other plan medical policies, and accredited national guidelines.

The efficacy of Kebilidi was evaluated in one open-label, single arm study. The study enrolled pediatric patients with genetically confirmed, severe AADC deficiency who had achieved skull maturity assessed with neuroimaging. The main efficacy outcome measure was gross motor milestone achievement evaluated at week 48 and assessed using the Peabody Developmental Motor

eladocogene exuparvovec-tneq (Kebilidi™)

Policy # 00948

Original Effective Date: 12/01/2025

Current Effective Date: 12/01/2025

Scale, Second Edition (PDMS-2). Patients treated with Kebilidi were compared to an external untreated natural history cohort of 43 pediatric patients with severe AADC deficiency who had at least one motor milestone assessment after 2 years of age.

A total of 13 patients received a single total dose of 1.8×10^{11} vg of Kebilidi given as four intraputaminial infusions in a single stereotactic neurosurgical procedure. Patient age ranged from 1.3 to 10.8 years and 12 of the 13 patients had the severe phenotype of AADC deficiency defined as having no motor milestone achievement at baseline and no clinical response to standard of care therapies. The one remaining patient had a “variant” of the severe disease phenotype, with the ability to sit with assistance but with lack of head control.

Gross motor milestone achievement at Week 48 was assessed in 12 of the 13 patients treated. One patient dropped out of the study prior to Week 48.

Eight (67%) of the 12 treated patients achieved a new gross motor milestone at week 48: 3 patients achieved full head control, 2 patients achieved sitting with or without assistance, 2 patients achieved walking backwards and the patient with the “variant” severe phenotype was able to sit unassisted. The two patients who achieved walking backwards at week 48 were treated before 2 years of age. The four patients who were unable to achieve new gross motor milestones at week 48 were treated between the ages of 2.8 and 10.8 years. In comparison, none of the 43 untreated patients with the severe phenotype had documented motor milestone achievement at last assessment at a median age of 7.2 years (range 2 to 19 years).

References

1. Kebilidi [package insert]. PTC Therapeutics, Inc. Warren, NJ. Updated November 2024.
2. Kebilidi New Drug Review. IPD Analytics. Updated December 2024.

Policy History

Original Effective Date: 12/01/2025

Current Effective Date: 12/01/2025

11/06/2025 Medical Policy Committee review

11/12/2025 Medical Policy Implementation Committee approval. New policy.

Next Scheduled Review Date: 11/2026

Coding

The five character codes included in the Louisiana Blue Medical Policy Coverage Guidelines are obtained from Current Procedural Terminology (CPT®)‡, copyright 2024 by the American Medical Association (AMA). CPT is developed by the AMA as a listing of descriptive terms and five character identifying codes and modifiers for reporting medical services and procedures performed by physician.

Policy # 00948

Original Effective Date: 12/01/2025

Current Effective Date: 12/01/2025

The responsibility for the content of Louisiana Blue Medical Policy Coverage Guidelines is with Louisiana Blue and no endorsement by the AMA is intended or should be implied. The AMA disclaims responsibility for any consequences or liability attributable or related to any use, nonuse or interpretation of information contained in Louisiana Blue Medical Policy Coverage Guidelines. Fee schedules, relative value units, conversion factors and/or related components are not assigned by the AMA, are not part of CPT, and the AMA is not recommending their use. The AMA does not directly or indirectly practice medicine or dispense medical services. The AMA assumes no liability for data contained or not contained herein. Any use of CPT outside of Louisiana Blue Medical Policy Coverage Guidelines should refer to the most current Current Procedural Terminology which contains the complete and most current listing of CPT codes and descriptive terms. Applicable FARS/DFARS apply.

CPT is a registered trademark of the American Medical Association.

Codes used to identify services associated with this policy may include (but may not be limited to) the following:

Code Type	Code
CPT	No codes
HCPCS	C9399, J3590
ICD-10 Diagnosis	All related diagnoses

*Investigational – A medical treatment, procedure, drug, device, or biological product is Investigational if the effectiveness has not been clearly tested and it has not been incorporated into standard medical practice. Any determination we make that a medical treatment, procedure, drug, device, or biological product is Investigational will be based on a consideration of the following:

- A. Whether the medical treatment, procedure, drug, device, or biological product can be lawfully marketed without approval of the U.S. Food and Drug Administration (FDA) and whether such approval has been granted at the time the medical treatment, procedure, drug, device, or biological product is sought to be furnished; or
- B. Whether the medical treatment, procedure, drug, device, or biological product requires further studies or clinical trials to determine its maximum tolerated dose, toxicity, safety, effectiveness, or effectiveness as compared with the standard means of treatment or diagnosis, must improve health outcomes, according to the consensus of opinion among experts as shown by reliable evidence, including:
 1. Consultation with technology evaluation center(s);
 2. Credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community; or
 3. Reference to federal regulations.

eladocogene exuparvovec-tneq (Kebilidi™)

Policy # 00948

Original Effective Date: 12/01/2025

Current Effective Date: 12/01/2025

****Medically Necessary (or “Medical Necessity”)** - Health care services, treatment, procedures, equipment, drugs, devices, items or supplies that a Provider, exercising prudent clinical judgment, would provide to a patient for the purpose of preventing, evaluating, diagnosing or treating an illness, injury, disease or its symptoms, and that are:

- A. In accordance with nationally accepted standards of medical practice;
- B. Clinically appropriate, in terms of type, frequency, extent, level of care, site and duration, and considered effective for the patient's illness, injury or disease; and
- C. Not primarily for the personal comfort or convenience of the patient, physician or other health care provider, and not more costly than an alternative service or sequence of services at least as likely to produce equivalent therapeutic or diagnostic results as to the diagnosis or treatment of that patient's illness, injury or disease.

For these purposes, “nationally accepted standards of medical practice” means standards that are based on credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community, Physician Specialty Society recommendations and the views of Physicians practicing in relevant clinical areas and any other relevant factors.

‡ Indicated trademarks are the registered trademarks of their respective owners.

NOTICE: If the Patient’s health insurance contract contains language that differs from the BCBSLA Medical Policy definition noted above, the definition in the health insurance contract will be relied upon for specific coverage determinations.

NOTICE: Medical Policies are scientific based opinions, provided solely for coverage and informational purposes. Medical Policies should not be construed to suggest that the Company recommends, advocates, requires, encourages, or discourages any particular treatment, procedure, or service, or any particular course of treatment, procedure, or service.

NOTICE: Federal and State law, as well as contract language, including definitions and specific contract provisions/exclusions, take precedence over Medical Policy and must be considered first in determining eligibility for coverage.