**09-J5000-06**

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**Revised: 01/15/26**

# Subject: Eladocagene exuparvovec-tneq (Kebilidi) Suspension for Intraputaminal Infusion

**THIS MEDICAL COVERAGE GUIDELINE IS NOT AN AUTHORIZATION, CERTIFICATION, EXPLANATION OF BENEFITS, OR A GUARANTEE OF PAYMENT, NOR DOES IT SUBSTITUTE FOR OR CONSTITUTE MEDICAL ADVICE. ALL MEDICAL DECISIONS ARE SOLELY THE RESPONSIBILITY OF THE PATIENT AND PHYSICIAN. BENEFITS ARE DETERMINED BY THE GROUP CONTRACT, MEMBER BENEFIT BOOKLET, AND/OR INDIVIDUAL SUBSCRIBER CERTIFICATE IN EFFECT AT THE TIME SERVICES WERE RENDERED. THIS MEDICAL COVERAGE GUIDELINE APPLIES TO ALL LINES OF BUSINESS UNLESS OTHERWISE NOTED IN THE PROGRAM EXCEPTIONS SECTION.**


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## DESCRIPTION:

Aromatic L-amino acid decarboxylase (AADC) deficiency is a rare autosomal recessive genetic disease caused by variations in the human dopa decarboxylase (DDC) gene, which results in decreased synthesis of dopamine and serotonin from their precursor molecules as well as subsequent synthesis of epinephrine and norepinephrine from dopamine. AADC deficiency is estimated to affect 300 to 350 patients worldwide and is prevalent among certain Asian populations such as those from China, Japan, and Taiwan. The clinical presentation of AADC deficiency occurs within the first six months of life and includes developmental delays, abnormal movements (e.g., dystonia, hypokinesia), and autonomic nervous system dysfunction (e.g., ptosis, miosis, inappropriate or impaired sweating, drooling, temperature dysregulation, hypotension, hypoglycemia, and abnormal heart rhythms). Long-term complications include cardiac decompensation, orthopedic complications, and infections. Until recently treatment has been symptomatic management with non-ergot derived dopamine agonists (e.g., pramipexole, ropinirole, rotigotine), monoamine oxidase (MAO) inhibitors, anticholinergic agents, and pyridoxine (vitamin B6).

On November 13, 2024, the FDA approved eladocagene exuparvovec-tneq (Kebilidi), which is a recombinant adeno-associated virus serotype 2 (rAAV2) based gene therapy designed to deliver a copy of the DDC gene, which encodes the AADC enzyme. Intraputaminal infusion of eladocagene exuparvovec-tneq (Kebilidi) results in AADC enzyme expression and subsequent production of dopamine in the putamen.

According to the manufacturer prescribing information, the efficacy of eladocagene exuparvovec-tneq (Kebilidi) was evaluated in one open-label, single arm study (NCT04903288). The study enrolled pediatric patients with genetically confirmed, severe AADC deficiency with documented decreased plasma AADC

enzyme activity who had achieved skull maturity assessed with neuroimaging and persistent neurological defects despite standard medical therapy (e.g., dopamine agonists, monoamine oxidase inhibitor, pyridoxine or other forms of vitamin B6). Patients were excluded if they had other enzyme deficiencies such as pyridoxine 5'-phosphate oxidase or tetrahydrobiopterin (BH4) deficiency, anti-adeno-associated virus, serotype 2 (anti-AAV2) antibody titer higher than 1:1200 or >1 optical density value by enzyme-linked immunosorbent assay, or evidence of a clinically active infection. The main efficacy outcome measure was gross motor milestone achievement evaluated at week 48 and assessed using the Peabody Developmental Motor Scale, Second Edition (PDMS-2). Patients treated with eladocagene exuparvovec-tneq (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 $1.8\times10^{11}$ vg of eladocagene exuparvovec-tneq (Kebilidi) given as four intraputaminal infusions in a single stereotactic neurosurgical procedure. The demographic characteristics of the population were as follows: the median age was 2.8 years (1.3 to 10.8 years), 7 patients (54%) were female, 10 patients (77%) were Asian, 2 patients (15%) were Caucasian, and 1 patient was of "other" race. Twelve 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 in the study; 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 in the historical control with the severe phenotype had documented motor milestone achievement at last assessment with a median age of 7.2 years (range 2 to 19 years).

As outline in the eladocagene exuparvovec-tneq (Kebilidi) prescribing information, the most common adverse reactions (incidence ≥15%) were dyskinesia, pyrexia, hypotension, anemia, salivary hypersecretion, hypokalemia, hypophosphatemia, insomnia, hypomagnesemia, and procedural complications.

## POSITION STATEMENT:

The administration of eladocagene exuparvovec-tneq (Kebilidi) **meets the definition of medical necessity** when **ALL** of the following are met:

1. Diagnosis of severe aromatic L-amino acid decarboxylase (AADC) deficiency at the time of treatment
2. Member does **NOT** have any other enzyme deficiencies such as pyridoxine 5'-phosphate oxidase or tetrahydrobiopterin (BH4) deficiency
3. Genetic test demonstrating biallelic mutations in the human dopa decarboxylase (DDC) gene – Laboratory documentation of the genetic testing results must be submitted

4. Documentation of decreased plasma AADC enzyme activity – Laboratory documentation must be submitted
5. Documentation that skull maturity has been achieved based on neuroimaging – Medical record documentation must be submitted
6. Member experiences persistent neurological defects despite standard medical therapy (e.g., dopamine agonists, monoamine oxidase inhibitor, pyridoxine or other forms of vitamin B6) – Medical documentation must be submitted
7. Anti-adeno-associated virus, serotype 2 (anti-AAV2) antibody titer is **NOT** higher than 1:1200 or >1 optical density value by enzyme-linked immunosorbent assay – Laboratory documentation must be submitted
8. Member does **NOT** have a clinically active infection
9. Member is clinically stable and able to undergo intraputaminal infusions as part of a stereotactic neurosurgical procedure in the opinion of the treating physician
10. Member has **NOT** previously received gene therapy (including eladocagene exuparvovec-tneq)
11. Eladocagene exuparvovec-tneq will be administered at a Kebilidi Qualified Treatment Center (QTC) which specializes in stereotactic neurosurgery
12. The administration of eladocagene exuparvovec-tneq (Kebilidi) will not exceed single dose of 1.8 × $10^{11}$ vector genomes given as 4 intraputaminal infusions in a single stereotactic neurosurgical procedure

**Approval duration**: 3 months to allow for a one-time therapy

Eladocagene exuparvovec-tneq (Kebilidi) is considered **experimental or investigational** for any other indications due to insufficient evidence in the peer-reviewed medical literature to support safety, efficacy, and net health outcome.

## DOSAGE/ADMINISTRATION:

**THIS INFORMATION IS PROVIDED FOR INFORMATIONAL PURPOSES ONLY AND SHOULD NOT BE USED AS A SOURCE FOR MAKING PRESCRIBING OR OTHER MEDICAL DETERMINATIONS. PROVIDERS SHOULD REFER TO THE MANUFACTURER'S FULL PRESCRIBING INFORMATION FOR DOSAGE GUIDELINES AND OTHER INFORMATION RELATED TO THIS MEDICATION BEFORE MAKING ANY CLINICAL DECISIONS REGARDING ITS USAGE.**

### FDA-approved

- Eladocagene exuparvovec-tneq (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 (i.e., biallelic mutations in the DDC gene). This indication is approved under accelerated approval based on change from baseline in gross motor milestone achievement at 48 weeks post-treatment. Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory clinical trial.
- The recommended dose of eladocagene exuparvovec-tneq (Kebilidi) is 1.8×$10^{11}$ vector genomes (vg) (0.32 mL total volume) delivered as four 0.08 mL infusions (2 sites in the anterior putamen and 2 sites in the posterior putamen) at a rate of 0.003 mL/minute (0.18 mL/hour) for a total of 27 minutes per site, administered in a single stereotactic surgery using a cannula that is FDA-

authorized for intraparenchymal infusion (i.e., ClearPoint SmartFlow Neuro Cannula Part Number NGS-NC-01-EE or 122 NGS-NC-02-EE).

- Eladocagene exuparvovec-tneq (Kebilidi) is stored and transported frozen at ≤ -65°C (-85°F). Thaw the eladocagene exuparvovec-tneq (Kebilidi) vial upright at room temperature before use. The contents of the vial will thaw in approximately 15 minutes at room temperature. Do not thaw or warm the vial any other way and do not refreeze thawed product. Gently invert the vial 3 times but do not shake the vial. Eladocagene exuparvovec-tneq (Kebilidi) should be used within 6 hours of starting product thaw, and the infusion takes 4 hours; therefore, the maximum time from thaw to completion of infusion should be no more than 10 hours.
- Strictly observe aseptic technique during preparation and administration of eladocagene exuparvovec-tneq (Kebilidi). Eladocagene exuparvovec-tneq (Kebilidi) should be inspected visually for particulate matter, and discoloration prior to administration; the color of should be a colorless to faint white suspension. Do not use if particulates, or discoloration are visible in the suspension. Eladocagene exuparvovec-tneq (Kebilidi) should be administered in a medical center which specializes in stereotactic neurosurgery. Dispose any remaining product or disposable material in compliance with institutional policy.

**Dose Adjustments**

- None

**Drug Availability**

- Eladocagene exuparvovec-tneq (Kebilidi) is supplied in a single-dose vial that contains $2.8\times10^{11}$ vg of eladocagene exuparvovec-tneq in an extractable volume of 0.5 mL of suspension. Each mL of suspension contains $5.6\times10^{11}$ vg of eladocagene exuparvovec-tneq.
  - Package (carton): NDC Number 52856-601-01
  - Container (vial): NDC Number 52856-601-11

## PRECAUTIONS:

**Boxed Warning**

- None

**Contraindications**

- Eladocagene exuparvovec-tneq (Kebilidi) is contraindicated in patients who have not achieved skull maturity assessed by neuroimaging.

**Precautions/Warnings**

- Procedural Complications: Procedural complications have been reported after neurosurgery required for eladocagene exuparvovec-tneq (Kebilidi) administration. These events included respiratory and cardiac arrest which occurred within 24 hours of the neurosurgical procedure and during post-surgical care. Eladocagene exuparvovec-tneq (Kebilidi) administration has the potential risk for additional procedure related adverse events including cerebrospinal fluid (CSF)

leak, intracranial bleeding, neuroinflammation, acute infarction, and infection. Monitor patients for procedure related adverse events with eladocagene exuparvovec-tneq (Kebilidi) administration, including continuous cardiorespiratory monitoring during hospitalization.

- Dyskinesia: Dyskinesia was reported after administration of eladocagene exuparvovec-tneq (Kebilidi). All events were reported within 3 months of administration and 2 events required hospitalization. Monitor patients for signs and symptoms of dyskinesia after treatment which may include involuntary movements of face, arm, leg, or entire body. These may present as fidgeting, writhing, wriggling, head bobbing or body swaying. The use of dopamine antagonists may be considered to control dyskinesia symptoms.

## BILLING/CODING INFORMATION:

The following codes may be used to describe:

### HCPCS Coding

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|---|---|
| J3590 | Unclassified biologics |

### ICD-10 Diagnosis Codes That Support Medical Necessity

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|---|---|
| E70.81 | Aromatic L-amino acid decarboxylase deficiency |

## REIMBURSEMENT INFORMATION:

Refer to section entitled **POSITION STATEMENT**.

## PROGRAM EXCEPTIONS:

**Federal Employee Program (FEP):** Follow FEP guidelines.

**State Account Organization (SAO):** Follow SAO guidelines.

**Medicare Part D:** Florida Blue has delegated to Prime Therapeutics authority to make coverage determinations for the Medicare Part D services referenced in this guideline.

**Medicare Advantage:** No National Coverage Determination (NCD) and/or Local Coverage Determination (LCD) were found at the time of the last guideline review date.

If this Medical Coverage Guideline contains a step therapy requirement, in compliance with Florida law 627.42393, members or providers may request a step therapy protocol exemption to this requirement if based on medical necessity. The process for requesting a protocol exemption can be found at Coverage Protocol Exemption Request

## DEFINITIONS:

**Gene therapy** - Gene therapies treat diseases by modifying or manipulating the expression of a gene or altering the properties of living cells for therapeutic use including: (1) replacing a disease-causing gene with a healthy copy of the gene, (2) inactivating a disease-causing gene that is not functioning properly, or (3) introducing a new or modified gene into the body to help treat a disease.

## RELATED GUIDELINES:

None

## OTHER:

None

## REFERENCES:


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6. Wassenberg T, Molero-Luis M, Jeltsch K, et al. Consensus guideline for the diagnosis and treatment of aromatic l-amino acid decarboxylase (AADC) deficiency. *Orphanet J Rare Dis*. 2017;12(1):12.


## COMMITTEE APPROVAL:

This Medical Coverage Guideline (MCG) was approved by the Florida Blue Pharmacy Policy Committee on 12/10/25.

## GUIDELINE UPDATE INFORMATION:

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| 01/15/25 | New Medical Coverage Guideline – Eladocagene exuparvovec-tneq (Kebilidi), an adeno-associated virus (AAV) vector-based gene therapy, for the treatment of adult and pediatric patients with genetically confirmed aromatic L-amino acid decarboxylase (AADC) deficiency. |
| 01/15/26 | Review and revision to guideline consisting of updating references. |