Policy Number	**RX501.178**
Policy Effective Date	**TBD**

Eladocagene exuparvovec-tneq

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Related Policies (if applicable)
None

Disclaimer

Medical policies are a set of written guidelines that support current standards of practice. They are based on current peer-reviewed scientific literature. A requested therapy must be proven effective for the relevant diagnosis or procedure. For drug therapy, the proposed dose, frequency and duration of therapy must be consistent with recommendations in at least one authoritative source. This medical policy is supported by FDA-approved labeling and/or nationally recognized authoritative references to major drug compendia, peer reviewed scientific literature and acceptable standards of medical practice. These references include, but are not limited to: MCG care guidelines, DrugDex (IIa level of evidence or higher), NCCN Guidelines (IIb level of evidence or higher), NCCN Compendia (IIb level of evidence or higher), professional society guidelines, and CMS coverage policy.

Carefully check state regulations and/or the member contract.

Each benefit plan, summary plan description or contract defines which services are covered, which services are excluded, and which services are subject to dollar caps or other limitations, conditions or exclusions. Members and their providers have the responsibility for consulting the member's benefit plan, summary plan description or contract to determine if there are any exclusions or other benefit limitations applicable to this service or supply. **If there is a discrepancy between a Medical Policy and a member's benefit plan, summary plan description or contract, the benefit plan, summary plan description or contract will govern.**

Legislative Mandates

EXCEPTION: For Illinois only: Illinois Public Act 103-0458 [Insurance Code 215 ILCS 5/356z.61] (HB3809 Impaired Children) states all group or individual fully insured PPO, HMO, POS plans amended, delivered, issued, or renewed on or after January 1, 2025 shall provide coverage for therapy, diagnostic testing, and equipment necessary to increase quality of life for children who have been clinically or genetically diagnosed with any disease, syndrome, or disorder that includes low tone neuromuscular impairment, neurological impairment, or cognitive impairment.

Coverage

Eladocagene exuparvovec-tneq (Kebilidi) for the treatment of adult and pediatric patients with aromatic L-amino acid decarboxylase (AADC) deficiency **is considered not medically necessary** as a clinical benefit has not been established.

Eladocagene exuparvovec-tneq (Kebilidi) for the treatment of all other indications **is considered experimental, investigational and/or unproven**.

Policy Guidelines

Eladocagene exuparvovec-tneq (Kebilidi) should be administered in a medical center which specializes in stereotactic neurosurgery.

Description

Aromatic L-amino acid decarboxylase (AADC) deficiency is a very rare inherited genetic disorder that affects the way nerve cells transmit information to other cells. It may also be known as AACD deficiency; AADCD; DDC deficiency; or Dopa decarboxylase deficiency. Signs and symptoms typically appear in the first 6 months of life, including feeding problems, weak muscle tone (hypotonia), involuntary upward-rolling movements of the eyes (oculogyric crises), movement disorders (dystonia), autonomic dysfunction (excessive sweating, temperature instability, ptosis [drooping eyelids]), hypoglycemic episodes, and sleep disturbances. (1-3)

AADC deficiency is a rare disorder, affecting approximately 350 individuals. It is more prevalent in certain Asian populations, particularly among people from Taiwan, Japan, and China. (1-3) Males and females seem to be equally affected. The estimated prevalence in the United States based on cerebrospinal fluid analysis and genetic testing is roughly 1-2:1,000,000 live newborns. (1)

Medications may manage symptoms; however, the optimal medication regimen varies among affected individuals. There is limited evidence for the efficacy of most treatments due to the rarity of the disease. This may include the use of dopamine agonists to increase the concentration of dopamine in the nervous system or monoamine oxidase B (MAO-B) inhibitors to decrease it's degradation. Melatonin might be tried for sleep disturbances, and benzodiazepines or anticholinergics might help individuals with oculogyric crises or other motor symptoms. (1)

Eladocagene exuparvovec-tneq (Kebilidi)
Eladocagene exuparvovec-tneq (Kebilidi, PTC Therapeutics, Inc. Warren, NJ) is an adeno-associated virus (AAV) vector-based gene therapy that expresses the human aromatic L-amino acid decarboxylase enzyme (hAACD). It is designed to deliver a copy of the DDC gene which encodes the AADC enzyme. Intraputaminal infusion of Kebilidi results in AADC enzyme expression and subsequent production of dopamine in the putamen. (4) The putamen is a structure in the forebrain, and along with the caudate nucleus, it forms the dorsal striatum. It is

the outermost portion of the basal ganglia. The putamen is interconnected with many other structures and works in conjunction with them to influence many motor behaviors such as motor planning, learning and execution, and movement sequences.

Regulatory Status
In 2024, the U.S. Food and Drug Administration (FDA) approved eladocagene exuparvovec-tneq (Kebilidi) for the treatment of adult and pediatric individuals with aromatic L-amino acid decarboxylase (AADC) deficiency. This indication was approved under accelerated approval based on change from baseline in gross motor milestone achievement at 48 weeks post-treatment. Continue approval for this indication may be contingent upon verification and description of benefit in a confirmatory clinical trial. (4)

Rationale

Eladocagene exuparvovec-tneq (Kebilidi) (4)
The efficacy of Kebilidi was evaluated in one open-label, single arm study (Study 1; NCT04903288). The study enrolled pediatric patients with genetically confirmed, severe aromatic L-amino acid decarboxylase (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 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 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 White, 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 Study 1 (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).

Ongoing and Unpublished Clinical Trials

Some currently ongoing and unpublished trials that might influence this medical policy are listed in Table 1.

Table 1. Summary of Key Trials

NCT. No.	Trial Name	Planned Enrollment	Completion Date
NCT04903288[a]	An Open-Label Trial to Address the Safety of the SmartFlow MR-Compatible Ventricular Cannula for Administering Eladocagene Exuparvovec to Pediatric Subjects	13	Apr 2028

[a] Industry sponsored.
NCT: national clinical trial.

Coding

Procedure codes on Medical Policy documents are included **only** as a general reference tool for each policy. **They may not be all-inclusive.**

The presence or absence of procedure, service, supply, or device codes in a Medical Policy document has no relevance for determination of benefit coverage for members or reimbursement for providers. **Only the written coverage position in a Medical Policy should be used for such determinations.**

Benefit coverage determinations based on written Medical Policy coverage positions must include review of the member's benefit contract or Summary Plan Description (SPD) for defined coverage vs. non-coverage, benefit exclusions, and benefit limitations such as dollar or duration caps.

CPT Codes	None
HCPCS Codes	C9399, J3490, J3590

*Current Procedural Terminology (CPT®) ©2023 American Medical Association: Chicago, IL.

References

1. NORD. Aromatic L-Amino Acid Decarboxylase Deficiency. Last updated Nov 14 2024. Available at <https://www.rarediseases.org> (accessed November 18, 2024).
2. MedlinePlus. Aromatic l-amino acid decarboxylase deficiency. Last updated May 13 2024. Available at <https://www.medlineplus.gov> (accessed November 18, 2024).
3. Blau N, Pearson TS, Jurian MA, et al. Aromatic L-Amino Acid Decarboxylase Deficiency. Oct 12 2023. Available at <https://www.ncbi.nlm.nih.gov> (accessed November 18, 2024).
4. FDA. Highlights of Prescribing Information Kebilidi (elcadogene exuparvovec-tneq). Revised Nov 2024. Available at <https://www.fda.gov> (accessed November 18, 2024).

Centers for Medicare and Medicaid Services (CMS)

The information contained in this section is for informational purposes only. HCSC makes no representation as to the accuracy of this information. It is not to be used for claims adjudication for HCSC Plans.

The Centers for Medicare and Medicaid Services (CMS) does not have a national Medicare coverage position. Coverage may be subject to local carrier discretion.

A national coverage position for Medicare may have been developed since this medical policy document was written. See Medicare's National Coverage at <https://www.cms.hhs.gov>.

Policy History/Revision	
Date	**Description of Change**
TBD	New medical document. Eladocagene exuparvovec-tneq (Kebilidi) for the treatment of adult and pediatric patients with aromatic L-amino acid decarboxylase (AADC) deficiency is considered not medically necessary as a clinical benefit has not been established. Eladocagene exuparvovec-tneq (Kebilidi) for the treatment of all other indications is considered experimental, investigational and/or unproven.