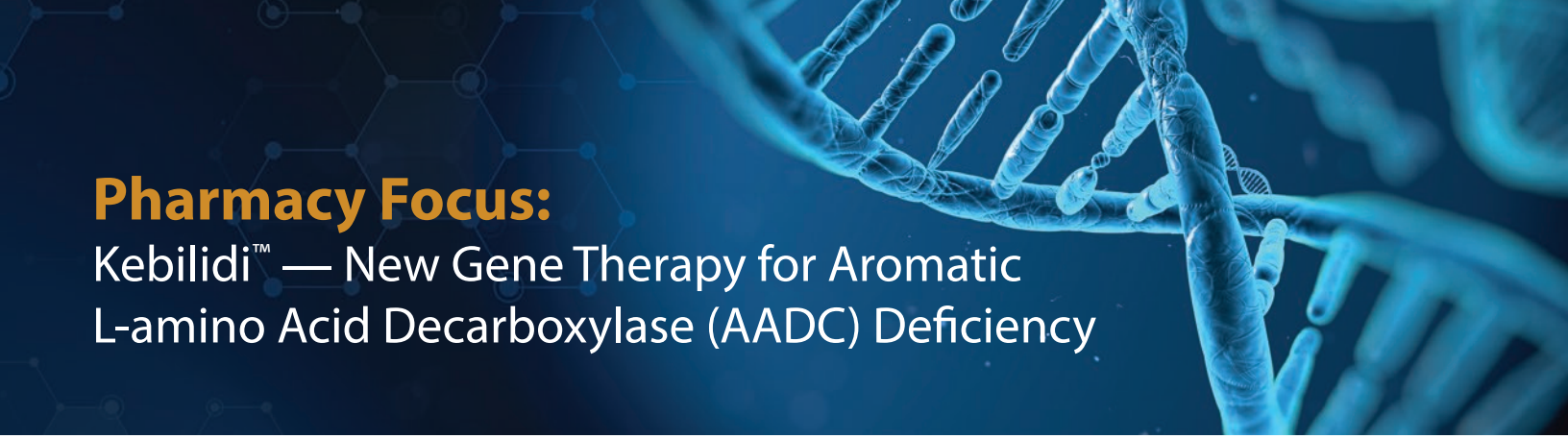

Pharmacy Focus:

Kebilidi™ — New Gene Therapy for Aromatic L-amino Acid Decarboxylase (AADC) Deficiency

Key Takeaways

- Using the Accelerated Approval pathway, Kebilidi (eladocagene exuparvovec-tneq) was approved by the FDA November 13, 2024, as the first treatment option for AADC deficiency, an ultra-rare genetic disorder.
- The treatment was approved for use with children ages 18 months and older and adults.
- Kebilidi is the first-ever gene therapy directly administered to the brain.
- The projected cost of Kebilidi is between $3 million and $4 million plus hospitalization costs.

AADC Deficiency Overview[1–3]

AADC deficiency is an ultra-rare, genetic, nervous system disorder where there is a deficiency of the AADC enzyme. Without enough of this enzyme, production of the vital neurotransmitters dopamine and serotonin is greatly reduced, resulting in widespread physical, mental, and behavioral manifestations. Symptoms generally start within the first year of life and can include delays in neurological development that result in missed milestones, such as sitting up or walking; autonomic dysfunction, such as the improper regulation of body temperature or heart rate; and movement disorders.

The exact prevalence of this disease is unknown, with less than 125 known reported cases worldwide (less than 50 of which are in the United States), but it may be more prevalent in certain Asian populations, with males and females being affected equally. The greatly shortened life expectancy of those with AADC deficiency is estimated to be between five and seven years of age.

Treatment Options[1–3]

Historically, there has been no cure or approved treatment for AADC. Supportive care with symptom management has been the general standard of care for AADC with options including vitamin supplements or other drugs, i.e., monoamine oxidase inhibitors (MAOIs) and dopamine receptor agents, and non-drug treatments like physiotherapy, occupational therapy, or speech therapy. A multidisciplinary approach is essential in helping to manage potentially life-threatening complications, including feeding and breathing problems.

Kebilidi Overview[3–5]

Kebilidi (eladocagene exuparvovec-tneq) was approved November 13, 2024, as the first FDA-approved gene therapy treatment for AADC deficiency in children (at least 18 months of age) and adults, regardless of disease severity. Prior to approval in the United States, Kebilidi was approved by the European Commission in 2022 with the name of Upstaza™. Continued approval for the gene therapy may be contingent upon verification of clinical benefit through a confirmation clinical trial that is currently ongoing.

Kebilidi is a modified adeno-associated virus serotype 2 (AAV2) vector-based gene therapy. It is administered by a neurosurgeon directly into the brain's putamen area, which is the part of the brain involved in learning and motor control. The procedure, which is considered stereotactic neurosurgery and, therefore, minimally invasive, includes four infusions during one surgical session. Infusion of the gene therapy requires use of the SmartFlow® Neuro Cannula, which is the only FDA-authorized device for the administration of Kebilidi. Following administration, the patient undergoes inpatient hospitalization monitoring for at least 14 days.

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Approval for Kebilidi was based on the safety and efficacy data from an open-label, single-arm clinical study where 13 pediatric patients with severe presentation of AADC deficiency with no baseline gross motor function were treated with the gene therapy. At week 48 following administration of Kebilidi, gross motor function improved in eight of 12 treated patients. Common adverse reactions associated with Kebilidi include involuntary muscle movements, fever, low blood pressure, anemia, low potassium, low magnesium, and low phosphate, as well as insomnia and procedural complications. Contraindications to the gene therapy include patients who have not reached skull maturity.

Although currently unknown, the cost of Kebilidi is projected to be between $3 million and $4 million in the United States for the cost of the drug alone. Due to the inpatient hospitalization required to receive this treatment, ancillary costs also are likely to be involved and associated with acute care under the medical benefits, along with the continuation of therapy and outpatient care following administration.

Cost Containment Considerations

As part of its HMConnects™ cost containment program, HM Insurance Group (HM) works to support cost management opportunities around the use of gene and cell therapies and other high-cost pharmaceutical treatment options that can impact our clients' bottom line. The Pharmacy Operations (RxOps) team watches the market — and our book of business — to anticipate how current and future advancements will impact financial risk levels for HM's client base. Standard practices include reviewing, auditing, and collaborating on the content of current policies, monitoring trends, and implementing appropriate cost savings techniques. Additional practices include the prevention of stockpiling, working to ensure prescriptions are filled via in network pharmacies and assessing to determine if patients are properly dosed based on weight and lab values when appropriate. All these services are provided to HM's clients at no additional cost to them.

Pharmacy Focus provides valuable information about pharmaceutical industry developments and their associated costs that can impact the growing claims trend in the self-funded insurance market. Be aware of influences and gain insight into approaches that may help to contain costs. Please share topic suggestions or feedback with **HMPharmacyServices@hmig.com**.

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Resources: [1] 'Aromatic L-Amino Acid Decarboxylase Deficiency,' National Organization for Rare Disorders, rarediseases.org/rare-diseases/aromatic-l-amino-acid-decarboxylase-deficiency/, accessed November 18, 2024;[2]Aromatic L-Amino Acid Decarboxylase Deficiency Clinical Compendium: Clinical Features, Diagnosis, Treatment, and Care Management,' Emerging Therapy Solutions, 2023; [3]'Upstaza (eladocagene exuparvovec),' IPD Analytics, July 2024; [4]"PTC Therapeutics Announces FDA Approval of AADC Deficiency Gene Therapy," PTC Therapeutics, PTC Therapeutics Investor Relations, https://ir.ptcbio.com/node/17026/pdf, accessed November 18, 2024; [5]"FDA Approves First Gene Therapy Treatment for Aromatic L-Amino Acid Decarboxylase Deficiency." U.S. Food and Drug Administration, November 14, 2024, www.fda.gov/news-events/press-announcements/fda-approves-first-gene-therapy-treatment-aromatic-l-amino-acid-decarboxylase-deficiency, accessed November 14, 2024.

MX4391050 (12/24)