Kebilidi (eladocagene exuparvovec-tneq) – New orphan drug approval

- On November 14, 2024, the FDA announced the approval of PTC Therapeutics' Kebilidi (eladocagene exuparvovec-tneq), for the treatment of adult and pediatric patients with aromatic L-amino acid decarboxylase (AADC) deficiency.
    - This indication is approved under accelerated approval based on the 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.
- AADC deficiency is a rare genetic disorder that affects the production of some neurotransmitters. Affected individuals may experience symptoms such as delays in gross motor function, weak muscle tone, and developmental and cognitive delays.
    - Physical, occupational and speech therapy, and interventions, including surgery, are also often required to manage potentially life-threatening complications, such as infections and severe feeding and breathing problems.
- Kebilidi, a gene therapy, is the first therapy approved for AADC deficiency.
    - Kebilidi is administered via four infusions in one surgical session into a large structure in the brain involved in motor control. Kebilidi should be administered in a medical center that specializes in pediatric stereotactic neurosurgery – a technique that uses imaging and special equipment to deliver therapies to specific areas in the brain.
    - After infusion of Kebilidi, treatment results in the expression of AADC and subsequent increase in the production of dopamine, a critical neurotransmitter in the brain associated with movement, attention, learning and memory.
- The efficacy of Kebilidi was established in an open-label, single arm study in patients with severe AADC deficiency who had achieved skull maturity assessed with neuroimaging. The main 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.
    - 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).
- Kebilidi is contraindicated in patients who have not achieved skull maturity assessed by neuroimaging.
- Warnings and precautions for Kebilidi include procedural complications and dyskinesia.

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- The most common adverse reactions (≥ 15%) with Kebilidi use were dyskinesia, pyrexia, hypotension, anemia, salivary hypersecretion, hypokalemia, hypophosphatemia, insomnia, hypomagnesemia, and procedural complications.

- PTC Therapeutics' launch plans for Kebilidi are pending.

Optum