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Advance Release Article

IN THIS ISSUE

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IN BRIEF

Expanded Indication for *Elevidys*

The adeno-associated virus (AAV) vector-based gene therapy delandistrogene moxeparvovec-rokl (*Elevidys* – Sarepta) received accelerated approval from the FDA in 2023 for treatment of ambulatory children 4-5 years old with Duchenne muscular dystrophy (DMD) who have a confirmed mutation in the DMD gene.[1] It has now received full approval for use in ambulatory patients ≥4 years old and accelerated approval for use in nonambulatory patients with DMD.

MECHANISM OF ACTION — Delandistrogene moxeparvovec is a nonreplicating, recombinant AAV vector-based therapy that delivers a transgene encoding microdystrophin protein, a shortened protein that contains selected domains of the dystrophin protein expressed in normal muscle cells.

CLINICAL STUDIES — FDA approval of the expanded indications were based on the results of earlier trials in ambulatory patients 4-7 years old and an open-label trial in patients ≥3 years old with DMD. Patients who received a single IV infusion of delandistrogene moxeparvovec demonstrated increased expression of microdystrophin protein in skeletal muscle cells, a surrogate endpoint that is considered likely to predict clinical benefit in both ambulatory and nonambulatory patients. In one of the trials, changes were also observed in three secondary efficacy endpoints: time to rise from the floor, 10- meter walk/run, and time to ascend 4 steps. A double-blind, placebo-controlled trial (ENVISION) in nonambulatory patients with no age restrictions and older ambulatory patients (8-17 years old) is underway.[2]

ADVERSE EFFECTS — Acute serious liver injury has been reported with delandistrogene moxeparvovec. Immune-mediated myositis can occur, particularly in patients with deletions in exons 1-17 and/or exons 59-71 in the DMD gene. Nausea, vomiting, fever, thrombocytopenia, and myocarditis have also been reported.

DOSAGE AND COST — Delandistrogene moxeparvovec is contraindicated for use in patients with any deletion in exon 8 and/or exon 9 in the DMD gene. The recommended dosage is 1.33×10^{14} vector genomes/kg administered as a one-time IV infusion over 1-2 hours. The wholesale acquisition cost of one dose of *Elevidys* is $3.2 million.[3]

CONCLUSION — The adeno-associated virus (AAV) vector-based gene therapy delandistrogene moxeparvovec *(Elevidys)* has received approval for treatment of Duchenne muscular dystrophy (DMD) in ambulatory and nonambulatory patients ≥4 years old who have a confirmed mutation in the DMD gene. Continued approval of *Elevidys* for use in nonambulatory patients is contingent on the results of an ongoing trial. The expanded approval now makes the very expensive gene therapy available to children and young men with DMD. ■

1. Delandistrogene moxeparvovec (Elevidys) for Duchenne muscular dystrophy. Med Lett Drugs Ther 2023; 65:159.
2. F Muntoni et al. ENVISION, a phase 3, randomized trial evaluating the safety and efficacy of delandistrogene moxeparvovec in Duchenne muscular dystrophy: study design. 28th International Annual Congress of the World Muscle Society (WMS); Charleston, USA; October 3-7, 2023.
3. Approximate WAC. WAC = wholesaler acquisition cost or manufacturer's published price to wholesalers; WAC represents a published catalogue or list price and may not represent an actual transactional price. Source: AnalySource® Monthly. July 5, 2024. Reprinted with permission by First Databank, Inc. All rights reserved. ©2024. www.fdbhealth.com/policies/drug-pricing-policy.

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