Elevidys® (delandistrogene moxeparvovec-rokl) – Accelerated approval converted to traditional approval, expanded indication

- On June 20, 2024, the FDA announced the traditional approval of Sarepta's Elevidys (delandistrogene moxeparvovec-rokl), for the treatment of Duchenne muscular dystrophy (DMD) in individuals at least 4 years of age who are ambulatory and have a confirmed mutation in the *DMD* gene.
    - Elevidys was previously approved via accelerated approval for ambulatory pediatric patients aged 4 through 5 years with DMD.
- In addition, the FDA granted an accelerated approval for Elevidys for treatment of DMD in individuals at least 4 years of age who are non-ambulatory and have a confirmed mutation in the *DMD* gene.
    - The DMD indication in non-ambulatory patients is approved based on expression of Elevidys micro-dystrophin (micro-dystrophin) in skeletal muscle. Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial(s).
- The data supporting traditional approval of Elevidys in ambulatory patients was based on two double-blind, placebo-controlled studies and two open-label studies, which enrolled a total of 218 male patients with a confirmed disease-causing mutation in the *DMD* gene. In one of the studies, the outcome measures were to evaluate expression of micro-dystrophin in skeletal muscle, and to evaluate the effect of Elevidys on the total score of patients on the North Star Ambulatory Assessment (NSAA) – a scale used to rate the motor function in ambulatory patients. In another study, the primary outcome measure was to evaluate the effect of Elevidys on physical function as assessed by the NSAA total score. Key secondary outcome measures were to evaluate expression of micro-dystrophin in skeletal muscle, time to rise from floor and time of 10-meter walk/run. Additional efficacy measures included time of 100-meter walk/run and time to ascend four steps.
    - While the large, randomized study of Elevidys failed to meet its statistical primary endpoint of improvement vs. placebo in the NSAA, the FDA found the observations regarding the secondary endpoints and exploratory endpoints to be compelling and to indicate clinical benefit compared to placebo. These endpoints include improvements in time to rise from the floor, 10-meter walk/run, time to ascend four steps and creatine kinase levels.
    - Based on the totality of the evidence, the FDA determined the available evidence verifies the product's clinical benefit for its original indication, and provides substantial evidence of effectiveness to support traditional approval of Elevidys in ambulatory individuals 4 years of age and older with a confirmed mutation in the *DMD* gene except in those with any deletion in exon 8 and/or exon 9 in the *DMD* gene, in whom its use is contraindicated.
- Additionally, the accelerated approval of Elevidys in non-ambulatory individuals aged 4 and older was based on the FDA's review of the totality of the evidence, including clinical data in ambulatory individuals from a study in 4- to 7-year-olds, as well as from a study in 4- to 5-year-olds indicating a correlation of Elevidys micro-dystrophin levels with clinical outcome measures.
    - Based on the evidence and given that the mechanism of action of Elevidys is similar for ambulatory and non-ambulatory populations, the FDA determined that increased levels in micro-dystrophin is reasonably likely to predict clinical benefit in the non-ambulatory population. This conclusion, along with the evidence that Elevidys elevates micro-dystrophin

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levels, provides substantial evidence of effectiveness to support accelerated approval in non-ambulatory individuals at least 4 years of age with DMD considering the serious nature of the disease and the extent of unmet medical need in this group of individuals.
    - A confirmatory randomized, controlled clinical trial in the non-ambulatory population is currently underway.

- The recommended intravenous single-dose of Elevidys is 1.33×10^{14} vector genomes per kilogram (vg/kg) of body weight (or 10 mL/kg body weight) for patients weighing less than 70 kg or 9.31×10^{15} vg total fixed dose for patients weighing 70 kg or greater.
    - There is limited safety data available in non-ambulatory patients weighing 70 kg or greater, who received the maximum dose of Elevidys, 9.31×10^{15} vg, in clinical trials.