Exondys 51™ (eteplirsen) – New Orphan Drug Approval

- On September 19, 2016, the FDA announced the approval of Sarepta Therapeutics' Exondys 51 (eteplirsen) for the treatment of Duchenne muscular dystrophy (DMD) in patients who have a confirmed mutation of the DMD gene that is amenable to exon 51 skipping.
    - This indication was approved under accelerated approval based on an increase in dystrophin in skeletal muscle observed in some patients treated with Exondys 51.
    - A clinical benefit of Exondys 51 has not been established. Continued approval for this indication may be contingent upon verification of a clinical benefit in confirmatory trials.
- DMD is a rare genetic disorder characterized by progressive muscle deterioration and weakness. It is the most common form of muscular dystrophy and is caused by an absence of dystrophin, a protein that helps keep muscle cells intact.
    - DMD occurs in about one out of every 3,600 male infants worldwide. It primarily affects boys, but in rare cases it can affect girls.
    - The first symptoms are usually seen between 3 and 5 years of age, and worsen over time. People with DMD progressively lose the ability to perform activities independently and often require use of a wheelchair by their early teens. As the disease progresses, life-threatening heart and respiratory conditions can occur. Patients typically succumb to the disease in their 20s or 30s; however, disease severity and life expectancy vary.
- Exondys 51 contains eteplirsen and is the first FDA approved drug for DMD. Eteplirsen is designed to bind to exon 51 of dystrophin pre-messenger RNA (mRNA), resulting in exclusion of this exon during mRNA processing, which allows for the production of an internally truncated dystrophin protein.
    - Mutation of the dystrophin gene amenable to exon 51 skipping affects an estimated 13% of the DMD population.
- The approval of Exondys 51 is based on the surrogate endpoint of dystrophin increase in skeletal muscle observed in some Exondys 51-treated patients.
    - The FDA has concluded that the demonstrated increase in dystrophin production was reasonably likely to predict clinical benefit in some patients with DMD who have a confirmed mutation of the dystrophin gene amenable to exon 51 skipping.
    - However, a clinical benefit of Exondys 51, including improved motor function, has not been established.
- In making this decision, the FDA considered the potential risks associated with the drug, the life-threatening and debilitating nature of the disease for these children, and the lack of available therapy.
    - Under the accelerated approval provisions, the FDA is requiring Sarepta to conduct a clinical trial to confirm the drug's clinical benefit.
- The most common adverse reactions (incidence ≥ 35% and higher than placebo) with Exondys 51 use were balance disorder and vomiting.

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- The recommended dose of Exondys 51 is 30 mg/kg by intravenous infusion once weekly.
    - Application of a topical anesthetic cream to the infusion site may be considered prior to administration of Exondys 51.
- Sarepta plans to launch Exondys 51 immediately. Exondys 51 will be available as 100 mg/2 mL and 500 mg/10 mL single-dose vials.
- During a hosted conference call, Sarepta announced that the estimated average cost for Exondys 51 will be $300,000 per year. The specific cost of the drug will vary by patient as Exondys 51 is dosed based on individual body weight.
    - Exondys 51 will cost $1,600 and $8,000 for each 100 mg/2 mL and 500 mg/10 mL vial, respectively.