OPTUMRx®

Emflaza™ (deflazacort) – New Orphan Drug Approval

- On February 9, 2017, the FDA announced the approval of Marathon's Emflaza (deflazacort), for the treatment of Duchenne muscular dystrophy (DMD) in patients 5 years of age and older.
    - Emflaza is the first FDA-approved corticosteroid to treat DMD.
- DMD is a rare genetic disorder characterized by progressive muscle deterioration and weakness. DMD is caused by the absence of dystrophin, a protein that helps keep muscle cells intact.
    - The condition affects 1 in 3,600 male infants worldwide. In rare cases, DMD can occur in girls.
    - The first symptoms are often seen between 3 – 5 years of age and worsen over time.
    - People with DMD progressively lose the ability to perform independent activities and often require use of a wheelchair by their early teens. Life-threatening heart and respiratory conditions can occur as the disease progresses. Patients typically die in their 20s or 30s; however, disease severity and life expectancy may vary.
- Emflaza contains deflazacort, a corticosteroid. Corticosteroids (eg, prednisone) are commonly used off-label to treat DMD, and are thought to work by decreasing inflammation and reducing the activity of the immune system.
- The safety and efficacy of Emflaza were shown in a clinical trial involving 196 male patients with documented mutation of the dystrophin gene and onset of weakness before age 5. The primary endpoint was the change in the average strength of 18 muscle groups from baseline to week 12.
    - At week 12, patients in the deflazacort arm showed improvements in muscle strength compared to the placebo arm ($p = 0.017$).
    - In addition, although not a pre-specified statistical analysis, the deflazacort group demonstrated a persistence in the treatment effect at week 52.
- In another trial involving 29 male subjects for 104 weeks, deflazacort demonstrated a numerical advantage vs. placebo on an assessment of average muscle strength. However, the average muscle strength scores at 2 years were not statistically significant. Although not statistically controlled for multiple comparisons, patients on deflazacort appeared to lose the ability to walk later than those on placebo.
- Warnings and precautions of Emflaza include alterations in endocrine function, immunosuppression and increased risk of infection, alterations in cardiovascular/renal function, gastrointestinal perforation, behavioral and mood disturbances, effects on bones, ophthalmic effects, vaccination, serious skin rashes, effects on growth and development, myopathy, Kaposi's sarcoma, risk of serious adverse reactions in infants because of benzoyl alcohol preservative, thromboembolic events, and anaphylaxis.
- The most common adverse reactions(≥ 10% and greater than placebo) with Emflaza use were Cushingoid appearance, increased weight, increased appetite, upper respiratory tract infection, cough, pollakiuria, hirsutism, central obesity, and nasopharyngitis.
- The recommended dose of Emflaza is 0.9 mg/kg per day administered orally.
    - If the tablets are used, the dose should be rounded up to the nearest possible dose.

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    - If the oral suspension is used, the dose should be rounded up to the nearest tenth of a milliliter.
    - When discontinuing therapy, the dosage of Emflaza must be decreased gradually if the drug has been administered for more than a few days.

- Emflaza is expected to launch in the upcoming weeks. Emflaza will be available as tablets (6 mg, 18 mg, 30 mg, and 36 mg) and a 22.75 mg/mL oral suspension.