Abbreviated Drug Review

Exondys 51 (eteplirsen)		
Estimated prevalence of patients with Duchenne muscular dystrophy (DMD) and an exon 51 mutation is approximately 1 in 27,000 people	Claims: 0	Wholesale Acquisition Cost: $57,600/month for a 30 kg patient

Indications

- DMD in patients who have a confirmed mutation of the DMD gene that is amenable to exon 51 skipping

Dosage

- 30 mg/kg once weekly intravenous infusion given over 35 to 60 minutes
- Available as 100 mg/2 mL and 500 mg/10 mL single dose vials

Background

- DMD is a rare genetic disorder caused by the absence of a functional dystrophin protein. In approximately 13% of patients with DMD, the cause is a mutation in exon 51 of the pre-mRNA. Eteplirsen binds to exon 51 of dystrophin pre-mRNA leading to exclusion of this exon and formation of a partially functional, truncated dystrophin protein.
- DMD is characterized by progressive muscle deterioration leading to pulmonary problems, dilated cardiomyopathy, arrhythmias, and increased risk for thrombotic events. In many patients, these complications lead to wheelchair dependence and death before the age of 20. There is currently no curative treatment.

Efficacy

- Eteplirsen was evaluated in 3 studies. The primary outcome was dystrophin protein level in muscle tissue, measured as a percentage of normal levels in healthy patients without DMD. Clinical outcomes included change in 6-minute walking distance. All patients in these trials were ambulatory and on a stable dose of corticosteroids for at least 6 months.
- Study 1 was a double-blind, randomized, dose-response, placebo-controlled study for 24 weeks. It included 12 white, male, pediatric patients (age range 7-13, mean 9.4 years) with a mean 6-minute walking distance at baseline of 363 meters. Dystrophin levels at baseline were unknown. Patients were randomized (1:1:1) to eteplirsen 50 mg/kg weekly, eteplirsen 30 mg/kg weekly, or placebo. After 24 weeks, patients were enrolled in a long-term extension study at 30 or 50 mg/kg/week for up to 4 years (Study 2).
    - Study 1: No difference was observed in the 6-minute walk distance at 24 weeks compared to placebo. Change in dystrophin level from baseline could not be assessed.
    - Study 2: At 180 weeks (3.5 years), patients treated with eteplirsen had an average dystrophin level that was 0.93% of the normal protein level in health patients.
- Study 3 was an open-label study including 13 male patients treated with eteplirsen 30 mg/kg weekly for 48 weeks (mean age of 8.9 years).
    - Study 3: Mean change in dystrophin level from baseline to 48 weeks was 0.28% of normal (0.16% at baseline vs. 0.44% at 48 weeks; p=0.008).

Safety

Adverse events reported in patients receiving eteplirsen with greater than 10% frequency included vomiting, confusion, excoriation, contact dermatitis, arthralgia, rash, upper respiratory tract infection, balance disorders, and catheter site pain. Because few patients were enrolled in these trial, the exact frequency of these events is unclear.

Evidence Gaps/Limitations

- There is no evidence supporting improvement in clinical or functional outcomes with treatment of eteplirsen. The minimally significant difference in dystrophin level which correlates to clinical outcomes has not been established. It is unclear whether changes less than 1% of normal would result in clinically significant outcomes.
- There is no data available to assess efficacy or safety in specific populations including females, ethnic minorities, or in other types of DMD.
- Continued approval for this indication is dependent on further confirmatory trials which demonstrate clinical benefit.

Recommendation

Refer claims to DMAP Medical Director through Prior Authorization

References

- Duchenne and Becker muscular dystrophies. In: DynaMed [internet database]. Ipswich, MA: EBSCO Publishing. Updated December 30, 2016. Accessed February 7, 2017.
- Exondys 51 (eteplirsen injection) [prescribing information]. Cambridge, MA: Sarepta Therapeutics, Inc; 2016.
- Food and Drug Administration Center for Drug Evaluation and Research. Exondys 51 Summary Review. http://www.accessdata.fda.gov/scripts/cder/drugsatfda. Accessed February 3, 2017.

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