Medical Policy

BlueCross BlueShield of Kansas
An independent licensee of the Blue Cross Blue Shield Association

Title: Translarna (ataluren)

Professional
Original Effective Date: October 6, 2017
Revision Date(s): October 6, 2017
Current Effective Date: October 6, 2017

Institutional
Original Effective Date: October 6, 2017
Revision Date(s): October 6, 2017
Current Effective Date: October 6, 2017

POLICY

Ataluren (Translarna) is considered **experimental / investigational** for all indications, including but not limited to nonsense mutation Duchenne muscular dystrophy (nmDMD), as clinical benefit has not been established.

RATIONALE [7-8]

Duchenne muscular dystrophy (DMD) is one of nine primary types (>30 forms known) of muscular dystrophy. Prevalence in the United States is not exactly known, but is estimated to be approximately 1.0-1.8 per 10,000 males age 5-24 years old. It is an X-linked recessive inherited genetic disorder. Specifically, the dystrophin gene is affected. Dystrophin is located on the cytoplasmic face of the plasma membrane of muscle fibers and provides mechanical reinforcement to the sarcolemma and stabilizes the glycoprotein complex. This helps stave off degradation and digestion of the glycoprotein complex by

proteases. A nonsense mutation in DNA results in a premature stop codon within an mRNA. McDonald, et al indicates that approximately 10-15% of DMD patients have a nonsense mutation, which introduces a premature stop codon into the dystrophin mRNA. This premature stop codon in the mRNA causes disease by terminating translation before a full-length protein is generated. Mutations in the dystrophin gene, and subsequent lack of dystrophin in the glycoprotein complex, result in a rapidly progressing disease involving muscle degeneration and weakness. Symptom onset is in early childhood and many are using a wheelchair in some capacity by 7-12 years of age. Beyond muscle weakness, some common symptoms are pseudohypertrophy of the calf muscles, cardiomyopathy, and poor respiratory function. Currently, there is no cure for DMD and therapies are supportive in nature. Physical therapy, occupational therapy, respiratory care, speech therapy, braces/wheelchairs/contractures and glucocorticoid therapy are among the many common therapies. Historically, glucocorticoids were the only pharmacologic treatment for DMD utilized to slow the progression of weakness.

CLINICAL TRIAL[7-8]

A multicentre, randomized, double-blind, placebo-controlled phase 3 trial was completed (NCT01826487). All patients were boys aged 7-16 years with nonsense mutation DMD. Additionally, all patients had a baseline 6MWD of 150 meters or more and 80% or less of the predicted normal value for age and height. The intention-to-treat population (n=228) were randomized (1:1) to either ataluren orally three times daily (40 mg/kg per day) or matching placebo. The trial had a 48 week treatment period with a primary endpoint of change in 6-minute walk distance (6MWD). The least-squares mean change in 6MWD from baseline to week 48 was –47.7 m (SE 9.3) for ataluren-treated patients and –60.7 m (9.3) for placebo-treated patients (difference 13.0 m [SE 10.4], 95% CI –7.4 to 33.4; p=0.213). This is numerically in favor of ataluren, but did not reach statistical significance. The least-squares mean change for ataluren versus placebo in the prespecified subgroups was –7.7 m (SE 24.1, 95% CI –54.9 to 39.5; p=0.749) in the group with a 6MWD of less than 300 m, 42.9 m (15.9, 11.8–74.0; p=0.007) in the group with a 6MWD of 300 m or more to less than 400 m, and −9.5 m (17.2, −43.2 to 24.2; p=0.580) in the group with a 6MWD of 400 m or more.

The study states the following for its interpretation of the information, “change in 6MWD did not differ significantly between patients in the ataluren group and those in the placebo group, neither in the intention-to-treat population nor in the prespecified subgroups with a baseline 6MWD of less than 300 m or 400 m or more. However, we recorded a significant effect of ataluren in the prespecified subgroup of patients with a baseline 6MWD of 300 m or more to less than 400 m.” At the time of review, UpToDate notes that “there was no significant benefit of ataluren for the primary endpoint (in the phase 3 trial), change from baseline in the six-minute walk test, though there was benefit for some secondary endpoints.”

REVISIONS

10-06-2017	Policy added to the bcbsks.com web site.

REFERENCES

1. UpToDate. Duchenne muscular dystrophy. Accessed 08/14/17.
2. Muscular Dystrophy Association (MDA). Duchenne Muscular Dystrophy. https://www.mda.org/disease/duchenne-muscular-dystrophy/overview. Accessed 08/15/17.
3. National Institutes of Health. U.S. National Library of Medicine. Medline Plus. Duchenne muscular dystrophy. https://www.nlm.nih.gov/medlineplus/ency/article/000705.htm. Accessed 08/15/17.
4. Centers for Disease Control and Prevention (CDC). Muscular Dystrophy. http://www.cdc.gov/ncbddd/musculardystrophy/data.html; http://www.cdc.gov/ncbddd/musculardystrophy/features/key-findings-population-duchenne.html. Accessed 08/15/17.
5. National Institutes of Health (NIH). "What are the types of muscular dystrophy?" https://www.nichd.nih.gov/health/topics/musculardys/conditioninfo/pages/types.aspx. Accessed 08/15/17.
6. Romitti et al. Prevalence of Duchenne and Becker Muscular Dystrophies in the United States. Pediatrics. 2015;135(3):513-521. http://pediatrics.aappublications.org/content/135/3/513. Accessed 08/15/2017.
7. McDonald CM, Campbell C, et al. Ataluren in patients with nonsense mutation Duchenne muscular dystrophy (ACT DMD): a multicentre, randomized, double-blind, placebo-controlled, phase 3 trial. Published online July 17, 2017. http://dx.doi.org/10.1016/S0140-6736(17)31611-2
8. Darras MD, Basil. UpToDate. Treatment of Duchenne and Becker muscular dystrophy. Literature review current through July 2017. Topic last updated July 18, 2017.