BlueCross BlueShield Federal Employee Program

AMONDYS 45 (casimersen)

RATIONALE FOR INCLUSION IN PA PROGRAM

Background

Amondys 45 (casimersen) is an antisense oligonucleotide indicated for the treatment of Duchenne muscular dystrophy (DMD) designed to bind to exon 45 of dystrophin pre-mRNA resulting in exclusion of this exon during mRNA processing in patients with genetic mutations that are amenable to exon 45 skipping. Exon 45 skipping is intended to allow for production of an internally truncated dystrophin protein in patients with genetic mutations that are amenable to exon 45 skipping (1).

Regulatory Status

FDA-approved indication: Amondys 45 is an antisense oligonucleotide indicated for the treatment of Duchenne muscular dystrophy (DMD) in patients who have a confirmed mutation of the *DMD* gene that is amenable to exon 45 skipping (1).

Kidney toxicity may occur in patients treated with Amondys 45. Kidney toxicity, including potentially fatal glomerulonephritis, has been observed after administration of some antisense oligonucleotides. Kidney function should be monitored in patients taking Amondys 45. Because of the effect of reduced skeletal muscle mass on creatinine measurements, creatinine may not be a reliable measure of kidney function in DMD patients. Serum cystatin C, urine dipstick, and urine protein-to-creatinine ratio should be measured before starting Amondys 45. During treatment, urine dipstick should be monitored every month, and serum cystatin C and urine protein-to-creatinine ratio every 3 months. Only urine expected to be free of excreted Amondys 45 should be used for monitoring of urine protein. Urine obtained on the day of Amondys 45 infusion prior to the infusion, or urine obtained at least 48 hours after the most recent infusion, may be used (1).

Monitoring motor changes in patients with DMD requires functional evaluation along with measurement of muscle strength. The need for a reliable outcome measure in diseases of rapid deterioration such as DMD has led to the use of motor functional tests. In a large, multicenter, international clinical trial, the six minute walk test (6MWT) proved to be feasible and highly reliable. Also used are the Motor Function Measure (MFM) and North Star Ambulatory Assessment (NSAA) to help predict loss of ambulation 1 year before its occurrence in order to allow time to adapt rehabilitation, change the patient's environment, and consider acquisition of assistive aids or the

use of medications (2-4).

Amondys 45 is indicated for patients who have a confirmed mutation of the *DMD* gene that is amenable to exon 45 skipping, including pediatric patients. There is no experience with the use of Amondys 45 in DMD patients 65 years of age or older (1).

Summary

Amondys 45 (casimersen) is an antisense oligonucleotide indicated for the treatment of Duchenne muscular dystrophy (DMD) in patients who have a confirmed mutation of the *DMD* gene that is amenable to exon 45 skipping. Kidney toxicity may occur in patients treated with Amondys 45. There is no experience with the use of Amondys 45 in DMD patients 65 years of age or older (1).

Prior approval is required to ensure the safe, clinically appropriate, and cost-effective use of Amondys 45 while maintaining optimal therapeutic outcomes.

References

1. Amondys 45 [package insert]. Cambridge, MA: Sarepta Therapeutics, Inc; July 2024.
2. Mcdonald C, Henricson E, et al. The 6-Minute Walk test and Other Clinical Endpoints in Duchenne Muscular Dystrophy: Reliability, Concurrent Validity, and Minimal Clinically Important Differences from a Multicenter Study. Muscle Nerve. 2013 Sep; 48(3): 357–368.
3. Mcdonald C, Henricson E, et al. The 6-Minute Walk test and Other Endpoints in Duchenne Muscular Dystrophy: Longitudinal Natural History Observations Over 48 weeks from a Multicenter Study. Muscle Nerve. 2013 Sep; 48(3): 343–356.
4. Vuillerot C, Girardot F, et al. Monitoring changes and predicting loss of ambulation in Duchenne muscular dystrophy with the Motor Function Measure. *Developmental Medicine & Child Neurology* 2010, 52: 60–65.