BlueCross BlueShield
Federal Employee Program

VYONDYS 53
(golodirsen)

RATIONALE FOR INCLUSION IN PA PROGRAM

Background

Vyondys 53 (golodirsen) is an antisense oligonucleotide indicated for the treatment of Duchenne muscular dystrophy (DMD) designed to bind to exon 53 of dystrophin pre-mRNA resulting in exclusion of this exon during mRNA processing in patients with genetic mutations that are amenable to exon 53 skipping. Exon 53 skipping is intended to allow for production of an internally truncated dystrophin protein in patients with genetic mutations that are amenable to exon 53 skipping (1).

Regulatory Status

FDA-approved indication: Vyondys 53 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 53 skipping (1).

Hypersensitivity reactions during and after administration of Vyondys 53 have occurred. Clinical manifestations may include generalized rash, rash, pyrexia, pruritus, urticaria, dermatitis, and skin exfoliation. If a hypersensitivity reaction occurs, institute appropriate medical treatment and consider slowing the infusion or interrupting the Vyondys 53 therapy (1).

Renal toxicity, including potentially fatal glomerulonephritis, has been observed after administration of some antisense oligonucleotides. Measurement of glomerular filtration rate prior to initiation of Vyondys 53 and monitoring for renal toxicity during treatment is recommended. No specific dosage adjustments can be recommended for DMD patients with renal impairment based on estimated glomerular filtration rate, due to the effect of reduced skeletal muscle mass on creatinine measurements in DMD patients. Patients with known renal function impairment should be closely monitored during treatment (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).

Vyondys 53 is indicated for patients who have a confirmed mutation of the *DMD* gene that is amenable to exon 53 skipping, including pediatric patients. There is no experience with the use of Vyondys 53 in DMD patients 65 years of age or older (1).

Summary

Vyondys 53 (golodirsen) 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 53 skipping. Hypersensitivity reactions during and after administration of Vyondys 53 have occurred. Renal toxicity, including potentially fatal glomerulonephritis, has been observed after administration of some antisense oligonucleotides. There is no experience with the use of Vyondys 53 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 Vyondys 53 while maintaining optimal therapeutic outcomes.

References

1. Vyondys 53 [package insert]. Cambridge, MA: Sarepta Therapeutics, Inc; June 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.