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Viltolarsen

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Overview

This policy supports medical necessity review for viltolarsen intravenous infusion (**Viltepso**™).

Receipt of sample product does not satisfy any criteria requirements for coverage.

Medical Necessity Criteria

Viltolarsen (Viltepso) is considered medically necessary when the following are met:

1. **Duchenne Muscular Dystrophy (DMD).** Individual meets **ALL** of the following criteria:
   A. Documented diagnosis of Duchenne muscular dystrophy (DMD)
   B. Confirmed mutation of the DMD gene that is amenable to exon 53 skipping
   C. Less than 10 years of age at start of therapy
   D. Able to walk AND must submit baseline 6 minute walk test (6MWT) results

E. Medication is being prescribed by, or in consultation with, a neurologist, neuromuscular specialist, or by a Muscular Dystrophy Association (MDA) clinic

When coverage is available and medically necessary, the dosage, frequency, duration of therapy, and site of care should be reasonable, clinically appropriate, and supported by evidence-based literature and adjusted based upon severity, alternative available treatments, and previous response to therapy.

Reauthorization Criteria

Continuation of viltolarsen (Viltepso) is considered medically necessary for Duchenne muscular dystrophy (DMD) when the above medical necessity criteria are met AND there is documentation of beneficial response, including the continued ability to walk.

Authorization Duration

Initial approval duration: up to 6 months.
Reauthorization approval duration: up to 6 months.

Conditions Not Covered

Any other use is considered experimental, investigational or unproven including the following (this list may not be all inclusive):

1. **Concurrent with use with other exon-skipping DMD agents** (for example, Amondys 45, Exondys 51, or Vyondys 53). Currently, there is no clinical evidence to support concurrent use of exon-skipping agents for the treatment of DMD.

Coding Information

1) This list of codes may not be all-inclusive.
2) Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement.

Considered Medically Necessary when criteria in the applicable policy statements listed above are met:

HCPCS Codes	Description
J1427	Injection, viltolarsen, 10 mg

Background

OVERVIEW
Viltepso, an antisense oligonucleotide, is 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] This indication was granted accelerated approval based on an increase in dystrophin in skeletal muscle observed in patients treated with Viltepso. The prescribing information notes that continued FDA approval for this indication may be contingent upon verification of clinical benefit in a confirmatory trial.

Viltepso is an antisense oligonucleotide 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.[1] These patients represent up to 10% of all patients with DMD.[2] This genetic manipulation intends to restore the reading frame of the resulting mRNA. The result would be production of a shortened, but partially functional dystrophin protein as seen in less severe forms of muscular dystrophy (e.g., Becker muscular dystrophy). Of note, the reading frame of certain deletions (e.g., exon 52 deletions) can be restored by skipping either exon 51 or exon

53.[3] Approximately 8% of mutations are amenable to skipping exon 53 with Viltepso but are not amenable to skipping of exon 51.

FDA Recommended Dosing
The recommended dosage of Viltepso is 80 mg/kg administered once weekly as a 60-minute intravenous infusion.[1]

Genetic mutations
Only five (45-52, 47-52, 48-52, 49-52, 50-52) were enrolled in the clinical studies with viltolarsen. It is reasonable to conclude that the restoration of the reading frame by viltolarsen should be beneficial for all DMD mutations amenable to exon 53 skipping.[7] Illustrated below are deletions that would be amenable to exon-53 skipping, this list may not be all inclusive.[8]

3-52	4-52	5-52	6-52	9-52					
10-52	11-52	13-52	14-52	15-52	16-52	17-52	19-52		
21-52	23-52	24-52	25-52	26-52	27-52	28-52	29-52		
30-52	31-52	32-52	33-52	34-52	35-52	36-52	37-52	38-52	39-52
40-52	41-52	42-52	43-52	45-52	47-52	48-52	49-52		
50-52	52	54-58	54-61	54-63	54-64	54-66	54-76	54-77	

Guidelines
Viltepso and other exon 53 skipping therapies are not addressed in guidelines for DMD. There are guidelines for the diagnosis and management of DMD available from the DMD Care Considerations Working Group (2018).[4] Genetic testing for a DMD mutation in a blood sample is always required. By fully characterizing the mutation, the predicted effect on the reading frame can be identified, which is the major determinant of phenotype and will determine eligibility for mutation-specific clinical trials. In patients with no mutation identified but with signs/symptoms of DMD, a muscle biopsy is clinically indicated. Glucocorticoids slow decline in muscle strength and function in DMD. Use of corticosteroids reduces the risk of scoliosis and stabilizes pulmonary function. Continued treatment after the patient loses ambulation provides a reduction in the risk of progressive scoliosis and stabilization of pulmonary function tests. Therefore, glucocorticoids should be considered for all patients with DMD. Exondys® 51 (eteplirsen intravenous infusion) is mentioned as an emerging product, approved by an accelerated pathway for those with a mutation in the dystrophin gene amenable to exon 51 skipping.

References

1. Viltepso™ intravenous infusion [prescribing information]. Paramus, NJ: Nippon Shinyaku; March 2021.
2. van Deutekom JC, Bremmer-Bout M, Janson AA, et al. Antisense-induced exon skipping restores dystrophin expression in DMD patient derived muscle cells. *Hum Mol Genet*. 2001;10(15):1547-1554.
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4. Birnkrant DJ, Bushby K, Bann CM, et al. Diagnosis and management of Duchenne muscular dystrophy, part 1: diagnosis, and neuromuscular, rehabilitation, endocrine, and gastrointestinal and nutritional management. *Lancet Neurol*. 2018;17(3):251-267.
5. Shimizu-Motohashi Y, Murakami T, Kimura E, et al. Exon skipping for Duchenne muscular dystrophy: a systematic review and meta-analysis. *Orphanet J Rare Dis*. 2018;13(1):93.
6. Clemens PR, Rao VK, Connolly AM, et al. Safety, tolerability, and efficacy of viltolarsen in boys with Duchenne muscular dystrophy amenable to exon 53 skipping. *JAMA Neurology*. 2020;77(8):982-991.
7. Clemens PR, Rao VK, Connolly AM, et al. Long-term functional efficacy and safety of vitolarsen in patients with Duchenne muscular dystrophy. *J Neuromusc Dis*. 2022;9:490-501.
8. Clemens PR, Rao VK, Connolly AM, et al. Efficacy and safety of viltolarsen in boys with Duchenne muscular dystrophy: results from the phase 2, open-label, 4-year extension study. *J Neuromusc Dis*. 2023;439-447.