Drug Coverage Policy

Effective Date 10/15/2025
Coverage Policy Number.....IP0066
Policy Title ..... Viltepso

Muscular Dystrophy – Viltepso

- Viltepso™ (viltolarsen intravenous infusion – Nippon Shinyaku)

INSTRUCTIONS FOR USE
The following Coverage Policy applies to health benefit plans administered by Cigna Companies. Certain Cigna Companies and/or lines of business only provide utilization review services to clients and do not make coverage determinations. References to standard benefit plan language and coverage determinations do not apply to those clients. Coverage Policies are intended to provide guidance in interpreting certain standard benefit plans administered by Cigna Companies. Please note, the terms of a customer's particular benefit plan document [Group Service Agreement, Evidence of Coverage, Certificate of Coverage, Summary Plan Description (SPD) or similar plan document] may differ significantly from the standard benefit plans upon which these Coverage Policies are based. For example, a customer's benefit plan document may contain a specific exclusion related to a topic addressed in a Coverage Policy. In the event of a conflict, a customer's benefit plan document always supersedes the information in the Coverage Policies. In the absence of a controlling federal or state coverage mandate, benefits are ultimately determined by the terms of the applicable benefit plan document. Coverage determinations in each specific instance require consideration of 1) the terms of the applicable benefit plan document in effect on the date of service; 2) any applicable laws/regulations; 3) any relevant collateral source materials including Coverage Policies and; 4) the specific facts of the particular situation. Each coverage request should be reviewed on its own merits. Medical directors are expected to exercise clinical judgment where appropriate and have discretion in making individual coverage determinations. Where coverage for care or services does not depend on specific circumstances, reimbursement will only be provided if a requested service(s) is submitted in accordance with the relevant criteria outlined in the applicable Coverage Policy, including covered diagnosis and/or procedure code(s). Reimbursement is not allowed for services when billed for conditions or diagnoses that are not covered under this Coverage Policy (see "Coding Information" below). When billing, providers must use the most appropriate codes as of the effective date of the submission. Claims submitted for services that are not accompanied by covered code(s) under the applicable Coverage Policy will be denied as not covered. Coverage Policies relate exclusively to the administration of health benefit plans. Coverage Policies are not recommendations for treatment and should never be used as treatment guidelines. In certain markets, delegated vendor guidelines may be used to support medical necessity and other coverage determinations.

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.

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.

Coverage Policy

Documentation: Documentation is required where noted in the criteria as **[documentation required]**. Documentation may include, but is not limited to, chart notes, laboratory tests, claims records, and/or other information.

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

FDA-Approved Indication

1. **Duchenne Muscular Dystrophy (DMD).** Approve for the duration noted if the patient meets ONE of the following (A or B):

A. Initial Therapy. Approve for 6 months if the patient meets the following (i, ii, iii, iv, and v):
   i. Diagnosis of Duchenne muscular dystrophy (DMD) **[Documentation Required]**; AND
   ii. Patient has a confirmed pathogenic or likely pathogenic variant of the DMD gene that is amenable to exon 53 skipping; AND
   iii. Patient is less than 10 years of age at start of therapy; AND
   iv. Patient is able to walk AND must submit baseline 6 minute walk test (6MWT) results; AND
   v. The medication is being prescribed by, or in consultation with, a neurologist, neuromuscular specialist, or by a Muscular Dystrophy Association (MDA) clinic

B. Patient is Continuing Therapy. Approve for 6 months if the patient meets the following (i, ii, iii, iv, v, and vi):
   i. Diagnosis of Duchenne muscular dystrophy (DMD) **[Documentation Required]**; AND

ii. Patient has a confirmed pathogenic or likely pathogenic variant of the DMD gene that is amenable to exon 53 skipping; AND
iii. Patient was less than 10 years of age at start of therapy; AND
iv. Patient is able to walk; AND
v. The medication is being prescribed by, or in consultation with, a neurologist, neuromuscular specialist, or by a Muscular Dystrophy Association (MDA) clinic

Conditions Not Covered

Viltepso for any other use is considered not medically necessary, including the following (this list may not be all inclusive; criteria will be updated as new published data are available):

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

Note: 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

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.
3. Bladen CL, Salgado D, Monges S, et al. The TREAT-NMD DMD Global Database: analysis of more than 7,000 Duchenne muscular dystrophy mutations. Hum Mutat. 2015;36(4):395-402.
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 Neromusc 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.

Revision Details

Type of Revision	Summary of Changes	Date
Selected Revision	**Updated** review date, disclaimer, refreshed background and references, addition of change history.	12/15/2024
Annual Revision	**Policy Title:** **Updated** from "Viltolarsen" to **"**Muscular Dystrophy – Viltepso." **Duchenne Muscular Dystrophy (DMD):** **Updated** criteria to split between "Initial Therapy" and "Patient is Continuing Therapy." **Updated** word "mutation" to "pathogenic or likely pathogenic variant." **Added** criteria for "Patient is Continuing Therapy." Approve for 6 months if the patient meets the following: 1. Diagnosis of Duchenne muscular dystrophy (DMD) **[Documentation Required].** 2. Patient has a confirmed pathogenic or likely pathogenic variant of the DMD gene that is amenable to exon 53 skipping. 3. Patient was less than 10 years of age at start of therapy. 4. Patient is able to walk. 5. The medication is being prescribed by, or in consultation with, a neurologist, neuromuscular specialist, or by a Muscular Dystrophy Association (MDA) clinic.	10/15/2025

The policy effective date is in force until updated or retired.