Medical Drug Clinical Criteria

Subject:	Viltepso (viltolarsen)		
Document #:	CC-0172	**Publish Date**:	09/23/2024
Status:	Reviewed	**Last Review Date**:	08/16/2024

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Overview

This document addresses the use of Viltepso (viltolarsen) (NS-065/NCNP-01), a phosphorodiamidate morpholino oligomer antisense oligonucleotide, in the treatment of Duchenne muscular dystrophy (DMD) with a mutation amenable to exon 53 skipping. Viltepso was approved under accelerated approval based on an increase in dystrophin production in skeletal muscle. Continued approval for DMD may be contingent upon verification and description of clinical benefit in a confirmatory trial (Viltepso label).

DMD is a genetic disorder characterized by decrease in muscle mass over time, including progressive damage and weakness of facial, limb, respiratory and heart muscles. In DMD patients, dystrophin, a protein that is present in skeletal and heart muscles allowing the muscles to function properly, is either absent or found in very small amounts. In theory, exon 53 skipping allows for the creation of a shorter-than-normal, but partially functional, dystrophin protein in patients with a specific type of DMD mutation. Exon 53 skipping is applicable in those with deletions in exons 45-52, 47-52, 48-52, 49-52, 50-52 and 52.

Viltepso (viltolarsen) was studied in a phase II, multi center, 2-period, randomized, placebo-controlled, dose finding study in ambulant boys ages 4-9 years of age with DMD (NCT02740972). Inclusion criteria required patients to be ambulatory and have the ability to complete the following assessments: time to stand from supine, time to run/walk 10 m, and time to climb 4 stairs. While primary outcome measures were centered around adverse events, dystrophin protein in muscle and drug concentration in plasma, secondary outcomes included 6-minute walk test (6MWT), change in time to climb 4 stairs (TTCLIMB), change in time to run/walk 10 meters (TTRW), change in time to stand (TTSTAND) and North Star Ambulatory Assessment results (NSAA) were also accounted for. The secondary outcomes were measured against matched controls in an external comparator group provided by the Cooperative International Neuromuscular Research Group (CINRG) Duchenne Natural History Study (DNHS) (Clemens 2020).

An extension trial of NCT02740972 (NCT03167255) was completed in boys ≥ 4 years and <10 years of age with primary outcomes of change in TTSTAND as well as adverse events. To confirm the clinical findings from this limited study, NCT04060199 (RACER53), a phase 3 randomized, double-blind, placebo-controlled study was initiated and completed. Inclusion criteria included males, age 4-7 (between ≥4 years and < 8 years); confirmed DMD amenable to exon 53 skipping; able to walk independently without assistive devices; TTSTAND < 10 seconds; stable dose of glucocorticoid for at least 3 months prior to study inclusion; other inclusion criteria may apply. Primary endpoint is the change in TTSTAND at 48 weeks of treatment. Secondary outcome measures include change in TTRW, 6MWT, NSAA, TTCLIMB and hand-held dynamometer. Study results have not been published yet.

Viltepso (viltolarsen) is administered at a dose of 80 mg/kg via a weekly intravenous infusion. Although kidney toxicity was not observed in clinical studies with Viltepso, it was observed in animals who had received viltolarsen. Therefore, kidney function should be monitored in patients taking Viltepso. Because serum creatinine may not be a reliable measure of kidney function in DMD patients, other measures should be monitored. Serum cystatin C, urine dipstick, and urine protein-to-creatinine ratio should be measured before starting Viltepso. Urine dipstick should be monitored every month; serum cystatin C and urine protein-to-creatinine ratio should be monitored every 3 months. In the event of persistent elevation in serum cystatin C or proteinuria, the patient should be referred to a pediatric nephrologist for further evaluation.

Clinical criteria

When a drug is being reviewed for coverage under a member's medical benefit plan or is otherwise subject to clinical review (including prior authorization), the following criteria will be used to determine whether the drug meets any applicable medical necessity requirements for the intended/prescribed purpose.

Viltepso (viltolarsen)

Initial requests for Viltepso (viltolarsen) may be approved if the following criteria are met:

I. Individual has a confirmed diagnosis of Duchenne muscular dystrophy (DMD); **AND**
II. Documentation is provided that individual has a genetic mutation that is amenable to exon 53 skipping; **AND**
III. Individual is age 4-9 years (NCT02740972) (Clemens 2020); **AND**
IV. Individual is using a corticosteroid; **AND**
V. Documentation is provided that individual is ambulatory; **AND**
VI. Individual is able to complete the following assessments: (NCT02740972, NCT04060199; Clemens 2020)
    A. Time to stand from supine; **AND**
    B. Time to run/walk 10 meters; **AND**
    C. Time to climb 4 stairs.

Continuation of therapy with Viltepso (viltolarsen) may be approved if the following criterion are met:

I. Criteria above were met at initiation of therapy; **AND**
II. Documentation is provided that individual remains ambulatory (with or without needing an assistive device, including but not limited to a cane or walker).

Viltepso (viltolarsen) may not be approved for the following:

I. Individual is using another exon skipping agent for DMD (including but not limited to Exondys 51, Vyondys 53); **OR**,
II. When the above criteria are not met and for all other indications.

Approval Duration: 6 months

Quantity Limits

Viltepso (viltolarsen) Quantity Limits

Drug	Limit
Viltepso (viltolarsen)	80 mg/kg once weekly

Coding

The following codes for treatments and procedures applicable to this document are included below for informational purposes. Inclusion or exclusion of a procedure, diagnosis or device code(s) does not constitute or imply member coverage or provider reimbursement policy. Please refer to the member's contract benefits in effect at the time of service to determine coverage or non-coverage of these services as it applies to an individual member.

HCPCS

J1427	Injection, viltolarsen, 10 mg

ICD-10 Diagnosis

G71.01	Duchenne or Becker muscular dystrophy

Document history

Reviewed: 08/16/2024
Document History:

- 08/16/2024 – Annual Review: No changes. Coding Reviewed: No changes.
- 08/18/2023 – Annual Review: Wording and formatting changes. Coding Reviewed: No changes.
- 08/20/2021 – Annual Review: No changes. Coding reviewed: No changes.
- 08/01/2021 – Administrative update to add documentation.
- 08/21/2020 – Annual Review: First review of Viltepso (viltolarsen); New clinical criteria for Viltepso; new quantity limit for Viltepso. Coding reviewed: Added HCPCS J3490, J3590, C9399, All diagnosis pend. Effective 1/1/21 Added HCPCS C9071, Removed C9399. Added ICD-10-CM G71.01. Effective 4/1/2021- Added HCPCS J1427. Removed J3490, J3590, C9071. Removed All diagnosis pend.
- 02/21/2020 – Select Review – Preliminary Review (pre-FDA approval) of viltolarsen

References

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2. DrugPoints® System [electronic version]. Truven Health Analytics, Greenwood Village, CO. Updated periodically.
3. Lexi-Comp ONLINE™ with AHFS™, Hudson, Ohio: Lexi-Comp, Inc. Updated periodically.
4. 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: A Phase 2 Randomized Clinical Trial [published correction appears in JAMA Neurol. 2020 Aug 1;77(8):1040. doi: 10.1001/jamaneurol.2020.2025]. *JAMA Neurol*. 2020;77(8):982-991. doi:10.1001/jamaneurol.2020.1264.
5. 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 Neuromuscul Dis*. 2023;10(3):439-447. doi:10.3233/JND-221656.
6. Kole R, Krieg AM. Exon skipping therapy for Duchenne muscular dystrophy. *Ad Drug Del Rev*. 2015; 87:140-107.
7. Watanabe N, Nagata T, Satou Y, et.al. NS-065/NCNP-01: An antisense oligonucleotide for potential treatment of exon 53 skipping in Duchenne Muscular Dystrophy. *Molecular Therapy: Nucleic Acids*. 2018; 13:442-449.
8. Viltepso [package insert]. Paramus, NJ; NS Pharma, Inc; 2020.

Federal and state laws or requirements, contract language, and Plan utilization management programs or polices may take precedence over the application of this clinical criteria.