Clinical Criteria

Subject:	**Viltepso (viltolarsen)**		
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Table of contents

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 incorporated ambulation status – patients were required to be ambulatory – and 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). 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) is currently ongoing in boys 4-10 years with primary outcomes of change in TTSTAND as well as adverse events. This study is expected to be completed in December 2020.

Finally, recruiting is ongoing for the Viltepso phase 3 study (NCT04060199; RACER53 trial). The phase 3 study is intended to assess efficacy and safety. Inclusion criteria are: male, 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. This study's estimated completion date is December 2024.

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. 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. Individual is ambulatory and 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; AND
VI. Individual will not use with any other exon skipping agents for DMD (including but not limited to Vyondys 53).

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. Individual remains ambulatory (with or without needing an assistive device, such as a cane or walker).

Approval Duration: 6 months

Requests for Viltepso (viltolarsen) may not be approved when the criteria above are not met and for all other indications.

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

J3490	Unclassified drugs (when specified as [Viltepso] viltolarsen)
J3590	Unclassified biologics (when specified as [Viltepso] viltolarsen)
C9399	Unclassified drugs or biologicals (when specified as [Viltepso] viltolarsen)

ICD-10 Diagnosis

All Diagnosis

Document history

New: 8/21/2020
Document History:

- **8/21/2020 – 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**
- **02/21/2020 – Select Review – Preliminary Review (pre-FDA approval) of viltolarsen**

References

1. **Kole R, Krieg AM. Exon skipping therapy for Duchenne muscular dystrophy. *Ad Drug Del Rev*. 2015; 87:140-107.**
2. **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.**
3. **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. *JAMA Neurol*. May 2020. doi:10.1001/jamaneurol.2020.1264.**
4. **Viltepso [package insert]. Paramus, NJ; NS Pharma, Inc; 2020.**