Viltepso® (Viltolarsen) (for New Jersey Only)

Policy Number: CSNJ2025D0095M
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Related Policies

None

Application

This Medical Benefit Drug Policy only applies to the state of New Jersey.

Coverage Rationale

Viltepso (viltolarsen) may be covered for the treatment of Duchenne muscular dystrophy (DMD) in patients who meet all of the following criteria:

Initial Therapy

- Diagnosis of Duchenne muscular dystrophy by, or in consultation with, a neurologist with expertise in the diagnosis of DMD; **and**
- Submission of medical records (e.g., chart notes, laboratory values) confirming the mutation of the DMD gene is amenable to exon 53 skipping; **and**
- Submission of medical records (e.g., chart notes) that provides baseline status of the patient prior to starting therapy (e.g., confirming that the patient is walking without needing an assistive device such as a cane, walker, wheelchair, etc.); **and**
- **One** of the following:
  - Patient has not previously received gene therapy [e.g., Elevidys (delandistrogene moxparvovec-rokl)] for the treatment of DMD; **or**
  - **Both** of the following:
    - Patient has previously received gene therapy [e.g., Elevidys (delandistrogene moxparvovec-rokl)] for the treatment of DMD; **and**
    - Submission of medical records (e.g., chart notes, laboratory values) documenting a clinically meaningful functional decline resulting from loss of muscle strength/motor ability (e.g., loss of a motor milestone) since receiving gene replacement therapy [e.g., Elevidys (delandistrogene moxparvovec-rokl)]

  and
- Viltepso is not used concomitantly with other exon skipping therapies for DMD [e.g., Amondys (casimersen), Exondys 51 (eteplirsen), Vyondys 53 (golodirsen)]; **and**
- Prescribed by, or in consultation with, a neurologist with expertise in the treatment of DMD; **and**
- Dosing is in accordance with the United States Food and Drug Administration approved labeling; **and**
- Initial authorization will be for no more than 12 months

Continuation Therapy

- Submission of medical records (e.g., chart notes) confirming that the patient is receiving clinical benefit (e.g., walking without needing an assistive device such as a cane, walker, wheelchair, etc.); **and**
- Viltepso is not used concomitantly with other exon skipping therapies for DMD [e.g., Amondys (casimersen), Exondys 51 (eteplirsen), Vyondys 53 (golodirsen)]; **and**
- Prescribed by, or in consultation with, a neurologist with expertise in the treatment of DMD; **and**
- Dosing is in accordance with the U.S. Food and Drug Administration (FDA)-approved labeling; **and**
- Reauthorization will be for no more than 12 months

Unproven

Viltepso is unproven and not medically necessary for the treatment of other forms of muscular dystrophy (e.g., Becker muscular dystrophy).

Applicable Codes

The following list(s) of procedure and/or diagnosis codes is provided for reference purposes only and may not be all inclusive. Listing of a code in this policy does not imply that the service described by the code is a covered or non-covered health service. Benefit coverage for health services is determined by federal, state, or contractual requirements and applicable laws that may require coverage for a specific service. The inclusion of a code does not imply any right to reimbursement or guarantee claim payment. Other Policies and Guidelines may apply.

HCPCS Code	Description
J1427	Injection, viltolarsen, 10 mg

Diagnosis Code	Description
G71.01	Duchenne or Becker muscular dystrophy

Background

Duchenne muscular dystrophy (DMD) is an X-linked disorder affecting approximately 1 in 3500 to 5000 live male births. Progressive weakness and skeletal muscle degeneration are caused by an absence of functional dystrophin protein secondary to loss-of-function variants in the DMD gene. Patients with DMD typically exhibit dystrophin levels less than 3% of normal. Dystrophin deficiency in DMD leads to progressive disability and early death owing to respiratory failure and cardiac dysfunction.

Viltolarsen 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. Approximately 8% to 10% of DMD patients have out of frame deletion mutations amenable to exon 53 skipping. Exon skipping is intended to allow for production of an internally truncated dystrophin protein.

Clinical Evidence

Viltolarsen 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.

A phase II study evaluated two doses of viltolarsen in 16 ambulatory boys aged 4 to 9 years with a DMD diagnosis and DMD gene amenable to exon 53 skipping over 24 weeks. Ambulatory boys on a stable corticosteroid regimen for at least 3 months who could complete time to stand from supine, time to run/walk 10 m, and time to climb four stairs assessments were included. The study was a multicenter, two period dose-finding clinical trial. The first study period, which corresponded to the first 4 weeks of treatment following enrollment, was double-blinded and placebo-controlled. Participants in both dose cohorts were randomized 3:1 to receive viltolarsen or placebo. The second study period began at week 5 for each participant. During this period, all participants received viltolarsen according to their cohort dose for a 20-week open-label treatment. Primary study outcomes included safety, tolerability, and pharmacokinetics of low-dose (40 mg/kg per week) and high-dose (80 mg/kg per week) viltolarsen in ambulant boys with DMD. Efficacy was assessed based on change from baseline in dystrophin protein level (measured as % of the dystrophin level in healthy subjects, i.e., % of normal) at Week 25. Muscle dystrophin production was assessed as protein production by Western blot for the primary study efficacy outcome and as dystrophin mRNA splicing on RT-PCR, dystrophin protein production by MS, and

dystrophin localization by IF staining for secondary study efficacy outcomes. Additional secondary efficacy outcomes were gross motor skill assessments of timed function tests, including time to stand from supine, time to run/walk 10 m, time to climb four stairs, North Star Ambulatory Assessment, and 6-minute walk test as well as quantitative muscle testing. These outcomes were compared with a matched natural history control group from the Cooperative International Neuromuscular Research Group (CINRG) Duchenne Natural History Study (DNHS).

In patients who received viltolarsen 80 mg/kg once weekly, mean dystrophin levels increased from 0.6% of normal at baseline to 5.9% of normal by week 25, with a mean change in dystrophin of 5.3% of normal levels ($p = 0.01$) as assessed by validated Western blot; the median change from baseline was 3.8%. All patients demonstrated an increase in dystrophin levels over their baseline values. As assessed by mass spectrometry, mean dystrophin levels increased from 0.6% of normal at baseline to 4.2% of normal by week 25, with a mean change in dystrophin of 3.7% of normal levels; the median change from baseline was 1.9%.

Comparison of viltolarsen-treated participants with 65 age-matched and treatment matched natural history controls from CINRG DNHS suggested evidence of clinical benefit of viltolarsen treatment. Viltolarsen-treated participants showed improvement or stabilization of function over the 25-week period, whereas the CINRG DNHS external comparator group exhibited a decline in all timed function tests, except for time to climb four stairs. Velocity in the time to run/walk 10 m test significantly improved in viltolarsen-treated participants at weeks 13 and 25 compared with a decline in controls from CINRG DNHS (change at 25 weeks compared with baseline: viltolarsen, 0.23 m/s; control, −0.04 m/s). The 6-minute walk test showed significant improvement at week 25 in viltolarsen-treated participants, whereas results from CINRG DNHS controls declined over the same period (change at 25 weeks compared with baseline: viltolarsen, 28.9 m; control, −65.3 m). Significant improvements in time to stand from supine were observed (change at 25 weeks compared with baseline: viltolarsen, −0.19 s; control, 0.66 s). Velocity in the time to stand from supine test and time to climb four stairs test as well as North Star Ambulatory Assessment similarly displayed improvement or stabilization, but the differences between viltolarsen treatment and external comparator controls were not significant. Measures of muscle strength by isometric testing showed no differences between viltolarsen-treated participants and the CINRG DNHS external comparator control group.

In 2023, Clemens et all published the results of the phase 2, open-label, 192-week long-term extension (LTE) study which evaluated the long-term efficacy and safety of viltolarsen in patients aged 4 to < 10 years at baseline with DMD amenable to exon 53 skipping therapy. All 16 participants from the initial 24-week study enrolled into this LTE. Timed function tests were compared to the CINRG DNHS group. All participants received glucocorticoid treatment. The primary endpoint was time to stand (TTSTAND); secondary endpoints included time to run/walk (TTRW), time to climb (TTCLIMB), 6 meter walk test (6MWT), and North Star Ambulatory Assessment (NSAA). Safety was continuously assessed. Viltolarsen was administered as an intravenous infusion at a dosage of 40 mg/kg or 80 mg/kg once weekly. Efficacy assessments were conducted every 12 weeks and safety was assessed throughout the open-label extension study. The primary endpoint was time to stand (TTSTAND); secondary endpoints included time to run/walk (TTRW), time to climb (TTCLIMB), 6 meter walk test (6MWT), and North Star Ambulatory Assessment (NSAA).

Change from baseline improvements were statistically significant ($p < 0.05$) for TTSTAND (seconds) beginning at week 73 and remained significantly different through week 205, and for TTSTAND (velocity) beginning at week 37 and remained significantly ($p < 0.05$) different through week 205. The change from baseline for TTRW showed stabilization of motor function over the first two years and significant slowing of motor function loss over the following two years for viltolarsen-treated participants compared with the CINRG DNHS comparator group. The change from baseline (seconds) was significant for TTRW at the beginning of week 73 ($p = 0.01$) and remained significantly different through week 205 ($p \leq 0.0001$) and for TTRW (velocity) beginning at week 37 ($p = 0.01$) and remained significantly different through week 205 ($p \leq 0.0001$). TTCLIMB (seconds) did not show a significant difference between the viltolarsen and the CINRG DNHS comparator group, whereas TTCLIMB (velocity) was significant at week 73 ($p = 0.01$) and week 205 ($p = 0.007$). 6MWT and NSAA efficacy endpoints were added later in the clinical study to the CINRG DNHS protocol, and as a result the historical comparator control group did not have sufficient data on 6MWT and NSAA to adequately compare with the viltolarsen-treated participants. Viltolarsen was well tolerated, with most of the reported TEAEs being mild or moderate with no deaths or study discontinuations. No treatment-related SAEs and no new or unexpected safety findings with viltolarsen were observed.

RACER53 is an ongoing 48-week, phase 3 double-blind, placebo controlled, randomized clinical trial that is evaluating the efficacy of viltolarsen in ambulatory DMD patients with out-of-frame deletion mutations amenable to skipping exon 53. The study will enroll 74 boys from 4 to 8 years of age with genotypically confirmed DMD on a stable dose of corticosteroids who can walk independently without assistive devices with a time to stand of less than 10 seconds. The primary endpoint is the change from baseline to week 48 in the time to stand. Secondary outcomes include the change in time to run/walk

10 meters, change in 6MWT, change in the NSAA, change in time to climb four steps, and change in muscle force contraction measured by dyanometry.

Viltolarsen has not been studied in DMD that is not amenable to exon 53 skipping, nor in other forms of muscular dystrophy (e.g., Becker muscular dystrophy).

U.S. Food and Drug Administration (FDA)

This section is to be used for informational purposes only. FDA approval alone is not a basis for coverage.

Viltepso 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. This indication is approved under accelerated approval based on an increase in dystrophin in skeletal muscle observed in some patients treated with Viltepso. Continued approval for this indication may be contingent upon verification of a clinical benefit in confirmatory trials.

References

1. Viltepso [package insert]. Paramus, NJ; NS Pharma, Inc, January 2023.
2. 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. 2020; 26;77(8):1-10.
3. Clemens PR, Rao VK, Connolly AM, et al. Long-Term Functional Efficacy and Safety of Viltolarsen in Patients with Duchenne Muscular Dystrophy. *J Neuromuscul Dis*. 2022;9(4):493-501.
4. 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.
5. Study to Assess the Efficacy and Safety of Viltolarsen in Ambulant Boys With DMD (RACER53) https://clinicaltrials.gov/ct2/show/NCT04060199?term=viltolarsen&draw=2&rank=1. Accessed February 27, 2024.

Policy History/Revision Information

Date	Summary of Changes
07/01/2025	**Coverage Rationale** • Revised coverage criteria for initial therapy; added criterion requiring **one** of the following: o The patient has not previously received gene therapy [e.g., Elevidys (delandistrogene moxparvovec-rokl)] for the treatment of Duchenne muscular dystrophy (DMD) o **Both** of the following: § Patient has previously received gene therapy [e.g., Elevidys (delandistrogene moxparvovec-rokl)] for the treatment of DMD § Submission of medical records (e.g., chart notes, laboratory values) documenting a clinically meaningful functional decline resulting from loss of muscle strength/motor ability (e.g., loss of a motor milestone) since receiving gene replacement therapy [e.g., Elevidys (delandistrogene moxparvovec-rokl)] **Supporting Information** • Archived previous policy version CSNJ2025D0095L

Instructions for Use

This Medical Benefit Drug Policy provides assistance in interpreting UnitedHealthcare standard benefit plans. When deciding coverage, the federal, state, or contractual requirements for benefit plan coverage must be referenced as the terms of the federal, state, or contractual requirements for benefit plan coverage may differ from the standard benefit plan. In the event of a conflict, the federal, state, or contractual requirements for benefit plan coverage govern. Before using this policy, please check the federal, state, or contractual requirements for benefit plan coverage. UnitedHealthcare reserves the right to modify its Policies and Guidelines as necessary. This Medical Benefit Drug Policy is provided for informational purposes. It does not constitute medical advice.

UnitedHealthcare may also use tools developed by third parties, such as the InterQual® criteria, to assist us in administering health benefits. The UnitedHealthcare Medical Benefit Drug Policies are intended to be used in connection with the independent professional medical judgment of a qualified health care provider and do not constitute the practice of medicine or medical advice.