VENTURA COUNTY
HEALTH CARE PLAN

UTILIZATION MANAGEMENT MEDICAL POLICY

POLICY: Muscular Dystrophy – Viltepso Utilization Management Medical Policy
- Viltepso™ (viltolarsen intravenous infusion – Nippon Shinyaku)

REVIEW DATE: 08/13/2025

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 glucocorticoids 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.

POLICY STATEMENT

The prescribing information for Viltepso states that approval is based on dystrophin production in a limited number of patients (n = 8 treated with the approved dose) with DMD, but continued approval may be contingent upon a confirmatory trial. Due to inadequate clinical efficacy data, **approval is not recommended** for Viltepso.

Automation: None.

RECOMMENDED AUTHORIZATION CRITERIA

None.

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Coverage of Viltepso is not recommended in the following situations:

1. **Duchenne Muscular Dystrophy (DMD).** Approval is not recommended due to the unclear benefit of Viltepso and lack of clinical efficacy data. Shortcomings of the clinical data with Viltepso are numerous. Although the pivotal study demonstrated a measurable increase in dystrophin levels, the significance of this small change has not yet been correlated with a clinical benefit. Data from the pivotal study did not provide any information to determine if Viltepso provides a benefit in regard to cardiac and respiratory complications, which contribute greatly to morbidity and mortality in DMD. The pivotal data are also lacking robust functional outcomes related to motor function. Viltepso has not been proven to alter or delay the disease progress in patients with DMD amenable to exon 53 skipping. A systematic review and meta-analysis of other exon skipping therapies (i.e., Exondys 51, drisapersen) does not show benefit of these therapies for DMD.[5] The prescribing information notes that continued approval for this indication may be contingent upon verification of clinical benefit in a confirmatory trial.[1] FDA has required a post-marketing trial to verify clinical efficacy of Viltepso. Thus, patients are being recruited for the Phase III RACER53 study, to further evaluate safety and efficacy of Viltepso in 74 ambulatory patients with DMD.[9] The estimated primary completion date for this study is October 2025.

   Viltepso is under evaluation in one ongoing Phase II pivotal study in patients with DMD amenable to exon 53 skipping.[6] The primary endpoint is the effect of Viltepso on dystrophin as a surrogate outcome marker. Functional outcomes were among the secondary endpoints and were compared with a natural history cohort controlled for age, functional status, geographic location, and glucocorticoid treatment status. In this pivotal study (n = 16), the proportion of normal dystrophin protein level was higher at Week 25 (0.6% of normal at baseline vs. 5.9% of normal at Week 24 biopsy). Some functional outcomes were significantly improved from baseline with Viltepso vs. the natural history cohort (time to run/walk 10 meters [0.23 meters/second vs. -0.04 meters/second], time to stand from supine [-0.19 seconds vs. 0.66 seconds], and distance on the 6-minute walk test [28.9 meters vs. -65.3 meters]). However, velocity in the time to stand from supine test, time to climb 4 stairs test, North Star Ambulatory Assessment (NSAA) test, and measures of muscle strength by isometric testing were <u>not</u> significantly different from the control group. Data from the long-term extension (out to 109 weeks) of the pivotal trial have been published.[7] All 16 patients who completed the Phase II trial continued into the long-term extension. Functional outcomes (time to stand and time to run/walk 10 meters) were maintained in the Viltepso group over 109 weeks while they were worsened in the natural history cohort. The time to climb 4 stairs was not significantly different from the natural history cohort over the 109 weeks. Final results from the 192-week long-term extension study (4 years post-treatment) showed stabilization of motor function over the first 2 years for the primary endpoint of time to stand and significant slowing of motor function loss (compared to historical control groups) over the following 2 years.[8] Similar results were observed with time to run/walk. Time to climb results were not significantly different between Viltepso and control groups.

   A Phase II study (Galactic53) evaluated the pulmonary and motor function of Viltepso in ambulatory and nonambulatory males aged ≥ 8 years of age, with DMD amenable to exon 53 skipping.[10] A total of 20 participants were enrolled to receive once weekly Viltepso for 48 weeks. Patients were well-matched between the Viltepso and the control group from the Cooperative International Neuromuscular Research Group (CINRG) Duchenne Natural History Study (DNHS). All ambulatory patients received

Viltepso and the CINRG DNHS control cohort were on a stable dose of glucocorticoids. At baseline, the forced vital capacity (FVC)% was 83.5% for Viltepso group and 85.3% for the control group in ambulatory patients and it was 58.8% and 59.7%, respectively, in non-ambulatory patients. The least square (LS) mean change from baseline in ambulatory patients treated with Viltepso was significant at Week 49 (n = 10; 8.3%; p = 0.02). The LS mean change for FVC% was 1.2% in the control group. The peak cough flow (PCF) was also numerically higher (22.6 L/min) with Viltepso vs. control (1.8 L/min). For non-ambulatory patients, the LS mean change from baseline for FVC% increased for patients with Viltepso (1.6%) and decreased for the control cohort (-3.2%). The LS mean change from baseline in PCF for non-ambulatory patients receiving Viltepso vs. control was 56.7 L/min vs. 15.1 L/min, respectively. The NSAA score at Week 49 for ambulatory patients was 2.2 points for the Viltepso group vs. -2.5 points for the control group; however, only 3 participants had NSAA data in the control group to compare with Viltepso group.

2. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

REFERENCES

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HISTORY

Type of Revision	Summary of Changes	Review Date
Annual Revision	No criteria changes	08/30/2023
Annual Revision	No criteria changes	08/21/2024
Annual Revision	No criteria changes.	08/13/2025