Clinical Policy: Viltolarsen (Viltepso)

Reference Number: ERX.SPA.390
Effective Date: 08.12.20
Last Review Date: 02.22
Line of Business: Commercial, Medicaid

Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

Description
Viltolarsen (Viltepso®) is an antisense oligonucleotide.

FDA Approved Indication(s)
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.

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

Policy/Criteria
Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

Health plan approved formularies should be reviewed for all coverage determinations. Requirements to use preferred alternative agents apply only when such requirements align with the health plan approved formulary.

It is the policy of health plans affiliated with Envolve Pharmacy Solutions™ that Viltepso may be **medically necessary*** when the following criteria are met:

**** Viltepso was FDA-approved based on an observed increase in dystrophin in skeletal muscle, but it is unknown if that increase is clinically significant. Continued FDA-approval for this indication may be contingent upon verification of a clinical benefit in confirmatory trials.***

I. Initial Approval Criteria

A. Duchenne Muscular Dystrophy (must meet all)**:**

1. Diagnosis of DMD with mutation amenable to exon 53 skipping (see *Appendix D*) confirmed by genetic testing;
2. Prescribed by or in consultation with a neurologist;
3. Age ≤ 9 years at therapy initiation;
4. Member has all of the following assessed within the last 30 days (a, b, and c):
   a. Member has ambulatory function (e.g., ability to walk with or without assistive devices, not wheelchair dependent) with one of the following (i or ii):
      i. 6-minute walk test (6MWT) distance ≥ 201 m;
      ii. Time-to-stand (TTSTAND) < 10 seconds;
   b. Stable cardiac function with left ventricular ejection fraction (LVEF) ≥ 40%;
   c. Stable pulmonary function with predicted forced vital capacity (FVC) ≥ 50%;
5. Inadequate response (as evidenced by a significant decline in 6MWT, TTSTAND, LVEF, or FVC) despite adherent use of an oral corticosteroid (e.g., prednisone, Emflaza®) for ≥ 6 months, unless contraindicated or clinically significant adverse effects are experienced;
   **Prior authorization is required for Emflaza*
6. Viltepso is prescribed concurrently with an oral corticosteroid, unless contraindicated or clinically significant adverse effects are experienced;
7. Viltepso is not prescribed concurrently with other exon-skipping therapies (e.g., Amondys 45™, Exondys 51®, Vyondys 53™);

8. Dose does not exceed 80 mg/kg per week.

Approval duration: 6 months

II. Continued Therapy

A. Duchenne Muscular Dystrophy (must meet all)**:**

1. Currently receiving medication for DMD with mutation amenable to exon 53 skipping or member has previously met initial approval criteria;
2. Member is responding positively to therapy as evidenced by one of the following (a or b):
   a. All of the following assessed within the last 6 months (i, ii, and iii):
      i. Member has ambulatory function (e.g., ability to walk with or without assistive devices, not wheelchair dependent) with one of the following assessed (1 or 2):
         1) 6MWT distance ≥ 201 m;
         2) TTSTAND < 10 seconds;
      ii. Stable cardiac function with LVEF ≥ 40%;
      iii. Stable pulmonary function with predicted FVC ≥ 50%;
   b. Member has received this medication via a healthcare insurer without meeting the requirements above (see criterion 2a), and medical record shows improved or stable LVEF and FVC, assessed within the last 6 months;
3. Member has been assessed by a neurologist within the last 6 months;
4. Viltepso is prescribed concurrently with an oral corticosteroid, unless contraindicated or clinically significant adverse effects are experienced;
5. Viltepso is not prescribed concurrently with other exon-skipping therapies (e.g., Amondys 45, Exondys 51, Vyondys 53);
6. If request is for a dose increase, new dose does not exceed 80 mg/kg per week.

Approval duration: 6 months

III. Diagnoses/Indications for which coverage is NOT authorized:

A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off-label use policy – ERX.PA.01 or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

6MWT: 6-minute walk test
DMD: Duchenne muscular dystrophy
FDA: Food and Drug Administration
FVC: forced vital capacity
ICER: Institute for Clinical and Economic Review
LVEF: left ventricular ejection fraction
TTSTAND: time to stand

Appendix B: Therapeutic Alternatives

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
prednisone*	0.3-0.75 mg/kg/day or 10 mg/kg/weekend PO	Based on weight
Emflaza® (deflazacort)	0.9 mg/kg PO QD	Based on weight

Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) when the drug is available by both brand and generic.
**Off-label*

Appendix C: Contraindications/Boxed Warnings

None reported

Appendix D: General Information

- Common mutations amenable to exon 53 skipping include: 3-52, 4-52, 5-52, 6-52, 9-52, 10-52, 11-52, 13-52, 14-52, 15-52, 16-52, 17-52, 19-52, 21-52, 23-52, 24-52, 25-52, 26-52, 27-52, 28-52, 29-52, 30-52, 31-52, 32-52, 33-52, 34-52, 35-52, 36-52, 37-52, 38-52, 39-52, 40-52, 41-52, 42-52, 43-52, 45-52, 47-52, 48-52, 49-52, 50-52, 52, 54-58, 54-61, 54-64, 54-66, 54-76, 54-77.

- Corticosteroids are routinely used in DMD management with established efficacy in slowing decline of muscle strength and function (including motor, respiratory, and cardiac). They are recommended for all DMD patients per the American Academy of Neurology (AAN) and DMD Care Considerations Working Group; in addition, the AAN guidelines have been endorsed by the American Academy of Pediatrics, the American Association of Neuromuscular & Electrodiagnostic Medicine, and the Child Neurology Society.
  - The DMD Care Considerations Working Group guidelines, which were updated in 2018, continue to recommend corticosteroids as the mainstay of therapy.
  - In an evidence report published August 2019, the Institute for Clinical and Economic Review (ICER) states that current evidence is insufficient to conclude that other exon-skipping therapies (Exondys 51, Vyondys 53) have net clinical benefit when added to corticosteroids and supportive care versus corticosteroids and supportive care alone.
- Prednisone is the corticosteroid with the most available evidence. A second corticosteroid commonly used is deflazacort, which was FDA approved for DMD in February 2017.
- The phase 2 dose-finding, safety study for viltolarsen (NCT02740972) enrolled male patients age 4-9 years with the lowest 6MWT distance at baseline being 201 m. In addition, inclusion criteria for the ongoing phase 3 efficacy study for viltolarsen (RACER 53; NCT04060199) enrolled male patients age 4-7 years old with a TTSTAND < 10 seconds.
- Having an LVEF below 40% may indicate presence of cardiomyopathy or heart failure, while a predicted FVC below 50% may indicate presence of severe pulmonary disease.

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
DMD	80 mg/kg IV once weekly	80 mg/kg/week

VI. Product Availability

Solution for injection in a single-dose vial: 250 mg/5 mL (50 mg/mL)

VII. References

1. Viltepso Prescribing Information. Paramus, NJ: NS Pharma, Inc.; March 2021. Available at: www.viltepso.com. Accessed September 14, 2021.
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; 77(8) 982-991.
3. ClinicalTrials.gov. Study to assess the efficacy and safety of viltolarsen in ambulant boys with DMD (RACER53). Available at: https://clinicaltrials.gov/ct2/show/NCT04060199. Accessed September 14, 2021.
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: 251-267.
5. Gloss D, Moxley RT, Ashwal S, Oskoui M. Practice guideline update summary: corticosteroid treatment of Duchenne muscular dystrophy. Neurology. 2016; 86: 465-472. Reaffirmed on January 26, 2019.
6. Institute for Clinical and Economic Review. Deflazacort, eteplirsen, and golodirsen for Duchenne muscular dystrophy: Effectiveness and value. Published August 15, 2019. Available at: https://icer-review.org/material/dmd-final-evidence-report. Accessed September 14, 2021.
7. NS Pharma. Viltepso (viltolarsen) injection: Long-term efficacy and safety data presented at the PPMD 2021 Virtual Annual Conference. Published July 1, 2021. Press release available at: https://www.nspharma.com/pdfs/NSPharma_Long-term_Data_PPMD_New.pdf. Accessed September 14, 2021.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy created pre-emptively	03.31.20	05.20

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Drug is now FDA approved - criteria updated per FDA labeling; modified from requiring both 6MWT and TTSTAND to either 6MWT or TTSTAND; added requirement for stable cardiac and pulmonary function; added decline in 6MWT as an example of inadequate response to a corticosteroid; added option for continuation of therapy for patients who have been receiving the medication through another healthcare insurer and/or has been responding positively to therapy with stable disease; modified time frame for positive response parameters from within the last 30 days to within the last 6 months; added requirement for neurologist assessment within the last 6 months; references reviewed and updated.	08.25.20	11.20
1Q 2021 annual review: no significant changes; references reviewed and updated.	10.09.20	02.21
1Q 2022 annual review: no significant changes; references reviewed and updated.	09.14.21	02.22

Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information.

This Clinical Policy is not intended to dictate to providers how to practice medicine, nor does it constitute a contract or guarantee regarding payment or results. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members.