Clinical Policy: Viltolarsen (Viltepso)
Reference Number: ERX.SPA.390
Effective Date: 08.12.20
Last Review Date: 11.20
Line of Business: Commercial, Medicaid

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, 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., Exondys 51™, Vyondys 53™);
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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., 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
<table>
<thead>
<tr>
<th>Drug Name</th>
<th>Dosing Regimen</th>
<th>Dose Limit/Maximum Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>prednisone*</td>
<td>0.3-0.75 mg/kg/day or 10 mg/kg/weekend PO</td>
<td>Based on weight</td>
</tr>
<tr>
<td>Emflaza™ (deflazacort)</td>
<td>0.9 mg/kg PO QD</td>
<td>Based on weight</td>
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   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,
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

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<tr>
<th>Indication</th>
<th>Dosing Regimen</th>
<th>Maximum Dose</th>
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<tbody>
<tr>
<td>DMD</td>
<td>80 mg/kg IV once weekly</td>
<td>80 mg/kg/week</td>
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VI. Product Availability

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

VII. References


<table>
<thead>
<tr>
<th>Reviews, Revisions, and Approvals</th>
<th>Date</th>
<th>P&amp;T Approval Date</th>
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<tbody>
<tr>
<td>Policy created pre-emptively</td>
<td></td>
<td>03.31.20</td>
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<tr>
<td>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</td>
<td>08.25.20</td>
<td>11.20</td>
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<td>Reviews, Revisions, and Approvals</td>
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<td>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.</td>
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**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.

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