Clinical Policy: Golodirsen (Vyondys 53)

Description
Golodirsen (Vyondys 53™) is an antisense oligonucleotide.

FDA Approved Indication(s)
Vyondys 53 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 Vyondys 53. Continued approval for this indication may be contingent upon verification of a clinical benefit in confirmatory trials.

Policy/Criteria
I. Vyondys 53 is not medically necessary for DMD in patients who have a confirmed mutation of the DMD gene that is amenable to exon 53 skipping based on the following (all of the following):
   A. Golodirsen does not have proven efficacy in the treatment of DMD.
      1. Vyondys 53 was approved based on an observed increase in dystrophin in skeletal muscle, but it is unknown if that increase is clinically significant. Currently there is no clear threshold for the amount of dystrophin increase required to produce clinical benefit. Previous research has suggested dystrophin levels of at least 20-29% of normal are needed to avoid muscular dystrophy, and levels of at least 10% of normal can produce a more mild form of dystrophy. At week 48 of Vyondys 53’s pivotal study (Study 4053-US-101, NCT02310906, a 168-week two part (Part 1 randomized double-blind; Part 2 Open-label) trial; N=25), golodirsen treated patients had a mean percent dystrophin protein of 1.019% of normal per Western blot analysis. The mean change from baseline in dystrophin protein levels after 48 weeks of treatment was 0.924%.
      2. True clinical benefit has not been established. Results of the co-primary endpoint evaluating the change from baseline in the total distance walked during 6MWT at Week 144 is not available. There is insufficient evidence to support clinical benefit of golodirsen given the small sample size, variability in the DMD disease course, and open-label trial design and resulting known limitations with using historical control groups for comparison.
   B. There is an alternative treatment option (corticosteroids; see Appendix B) with well-established efficacy in slowing decline of muscle strength and function (including motor, respiratory, and cardiac).
II. 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

Appendix B: Therapeutic Alternatives

This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may not be a formulary agent for all relevant lines of business and may require prior authorization.

<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</td>
<td>Based on weight</td>
</tr>
<tr>
<td>Emflaza™ (deflazacort)</td>
<td>0.9 mg/kg/day orally once daily</td>
<td>Based on weight</td>
</tr>
</tbody>
</table>

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

- 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 Vyondys 53 has 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.

III. Dosage and Administration

<table>
<thead>
<tr>
<th>Indication</th>
<th>Dosing Regimen</th>
<th>Maximum Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>DMD</td>
<td>30 mg/kg IV once weekly</td>
<td>30 mg/kg</td>
</tr>
</tbody>
</table>
IV. Product Availability
   Single-dose vial for injection: 100 mg/2 mL (50 mg/mL)

V. References

<table>
<thead>
<tr>
<th>Reviews, Revisions, and Approvals</th>
<th>Date</th>
<th>P&amp;T Approval Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>Policy created</td>
<td>01.05.20</td>
<td>02.20</td>
</tr>
</tbody>
</table>

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. The Health Plan makes no representations and
accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. “Health Plan” means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan’s affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment or medical care. It is not intended to dictate to providers how to practice medicine. 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. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

This clinical policy is the property of the Health Plan. Unauthorized copying, use, and distribution of this clinical policy or any information contained herein are strictly prohibited. Providers, members and their representatives are bound to the terms and conditions expressed herein through the terms of their contracts. Where no such contract exists, providers, members and their representatives agree to be bound by such terms and conditions by providing services to members and/or submitting claims for payment for such services.

Note:
For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.