POLICY: Muscular Dystrophy – Vyondys 53 Utilization Management Medical Policy
- Vyondys 53™ (golodirsen intravenous infusion – Sarepta)

EFFECTIVE DATE: 04/01/2020
LAST REVISION DATE: 01/15/2026

COVERAGE CRITERIA FOR: All UCare Plans

OVERVIEW

Vyondys 53, 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] Vyondys 53 was approved for this indication under accelerated approval based on an increase in dystrophin observed in the skeletal muscle of patients who received the drug. The Prescribing Information notes that continued FDA-approval for this indication may be contingent upon verification of clinical benefit in confirmatory trials.

Disease Overview

DMD is an X-linked recessive disease affecting 1 in 3,600 to 6,000 newborn male infants.[2] The disease is attributed to large frame-shift deletions in the DMD gene (chromosome Xp21) which lead to loss of a structural protein of muscle cells (dystrophin).[3] Over 4,700 mutations on the DMD gene have been identified which lead to a deficiency in production of dystrophin.[2] Therefore, the type of mutation and its effect on the production of dystrophin accounts for the variable phenotypic expression.[4] Female carriers are usually asymptomatic but some may show mild symptoms.[2] There are wide variances in how quickly DMD progresses, but without intervention death is at approximately 19 years of age.[2-4] With respiratory, cardiac, orthopedic and rehabilitative interventions, and use of corticosteroids, children born today can have a life expectancy of up to 40 years.

Vyondys 53 is 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.[5] 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.[6] Approximately 8% of mutations are amenable to skipping exon 53 with Vyondys 53 but are not amenable to skipping of exon 51.

Guidelines

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 corticosteroids 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. However, these guidelines do not specifically address exon 53 skipping or mention Vyondys 53.

POLICY STATEMENT

Prior authorization is recommended for medical benefit coverage of Vyondys 53. Approval is recommended for those who meet the Criteria and Dosing for the listed indication(s). Extended approvals are allowed if the patient continues to meet the Criteria and Dosing. Requests for doses outside of the established dosing documented in this policy will be considered on a case-by-case basis by an Express Scripts clinician (i.e., Medical Director or Pharmacist). Because of the specialized skills required for evaluation and diagnosis of patients treated with Vyondys 53, as well as the monitoring required for adverse events and long-term efficacy, initial approval requires Vyondys 53 to be prescribed by or in consultation with a physician who specializes in the condition being treated. All approvals are provided for the durations noted below. In cases where the approval is authorized in months, 1 month is equal to 30 days.

RECOMMENDED AUTHORIZATION CRITERIA

FDA-Approved Indications

1. **Duchenne Muscular Dystrophy (DMD).** Approve Vyondys 53 if the patients meets the following criteria. (A or B).
   - **A)** Initial Therapy. Approve Vyondys 53 for 6 months if the patient meets the following criteria (i, ii, iii, iv, v, vi, and vii).
     - **i.** Patient must have a diagnosis of Duchene muscular dystrophy (DMD); AND
     - **ii.** Patient must have a confirmed mutation of the DMD gene that is amenable to exon 53 skipping and provide documentation [documentation required]; AND
     - **iii.** Patient has been on a stable dose of corticosteroids, unless contraindicated or intolerance, for ≥ 6 months; AND
     - **iv.** Patient retains meaningful voluntary motor function (patient is able to speak, manipulate objects using upper extremities, ambulate, etc.); AND
     - **v.** Patient has documented ongoing physical therapy and/or occupational therapy; AND
     - **vi.** Baseline documentation of ≥ 1 of the following (a, b, c, d, or e):
       - **a.** Dystrophin level; OR
       - **b.** 6-minute walk test (6WMT) or other timed function tests; OR
       - **c.** Upper limb function (ULM) test; OR
       - **d.** North Star Ambulatory Assessment (NSAA); OR
       - **e.** Forced Vital Capacity (FVC) % predicted; AND
     - **vii.** Baseline glomerular filtration rate (GFR) by 24-hour urine collection and renal function monitoring plan must be submitted at time of request; AND

   - **B)** Patients Continuing Vyondys 53 Therapy. Approve Vyondys 53 for 6 months if the patient meets the following criteria (i, ii, and iii).

     - **i.** Patient has demonstrated a response to therapy compared to pretreatment baseline in ≥ 1 of the following (a, b, c, d, e, or f):
       - **a.** Increase in dystrophin level; OR

b. Stability, improvement, or slowed rate of decline in 6MWT or other timed function tests; OR
c. Stability, improvement, or slowed rate of decline in ULM test; OR
d. Stability, improvement, or slowed rate of decline in NSAA; OR
e. Stability, improvement, or slowed rate of decline in FVC% predicted; OR
f. Improvement in quality of life; AND

ii. There is documentation of monthly renal function monitoring is submitted at time of request; AND
iii. The patient has not experienced any treatment-restricting adverse effects (severe hypersensitivity reactions, renal toxicity/proteinuria, etc.)

Dosing in DMD. *Dosing must meet the following weight-based dosing*: 30 mg/kg once weekly - Patient's most current weight (rounded to the nearest kg) must be provided at time of request.

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Vyondys 53 has not been shown to be effective, or there are limited or preliminary data or potential safety concerns that are not supportive of general approval for the following conditions. (Note: This is not an exhaustive list of Conditions Not Recommended for Approval).

1. Patient is currently enrolled in clinical trials for Vyondys 53.
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.	12/16/2020
Annual Revision	No criteria changes.	12/15/2021
Annual Revision	No criteria changes per MN DHS PA criteria. No Care Continuum Updates.	01/25/2024
Annual Revision	Criteria update to align with MN DHS PA Criteria for Vyondys 53	04/30/2024
UCare P&T Review	Policy reviewed and approved by UCare P&T committee. Annual review process	09/16/2024
UCare P&T Review	Policy reviewed and approved by UCare P&T committee. Annual review process	09/15/2025
Annual Revision	No criteria changes per MN DHS PA criteria. No Care Continuum Updates.	01/15/2026