Subject: Vyondys 53 (golodirsen)_Not Medically Necessary	**Original Effective Date:** Q1 2020
Policy Number: MCP-359	**Revision Date(s):**
Review Dates:	
P&T Approval Date: Q1 2020; Q1 2021	

Contents

DISCLAIMER

This Molina Clinical Policy (MCP) is intended to facilitate the Utilization Management process. It expresses Molina's determination as to whether certain services or supplies are medically necessary, experimental, investigational, or cosmetic for purposes of determining appropriateness of payment. The conclusion that a particular service or supply is medically necessary does not constitute a representation or warranty that this service or supply is covered (i.e., will be paid for by Molina) for a particular member. The member's benefit plan determines coverage. Each benefit plan defines which services are covered, which are excluded, and which are subject to dollar caps or other limits. Members and their providers will need to consult the member's benefit plan to determine if there are any exclusion(s) or other benefit limitations applicable to this service or supply. If there is a discrepancy between this policy and a member's plan of benefits, the benefits plan will govern. In addition, coverage may be mandated by applicable legal requirements of a State, the Federal government or CMS for Medicare and Medicaid members. CMS's Coverage Database can be found on the CMS website. The coverage directive(s) and criteria from an existing National Coverage Determination (NCD) or Local Coverage Determination (LCD) will supersede the contents of this MCP document and provide the directive for all Medicare members.

RECOMMENDATIONS

This policy addresses the coverage of **Vyondys 53 (golodirsen)** for the treatment of Duchenne muscular dystrophy (DMD) patients who have a confirmed mutation of the dystrophin gene that is amenable to exon 53 skipping.

LIMITATIONS/EXCLUSIONS: Vyondys 53 (golodirsen) is considered not medically necessary for all indications, including DMD, due to insufficient evidence of therapeutic value since clinical benefit has not been established. Data from clinical studies of golodirsen in a small number of people with DMD have demonstrated a consistent safety and tolerability profile. However, the pivotal trials were not designed to evaluate long-term safety and a clinical benefit of Vyondys 53 has not been established.

Molina Healthcare will continue to evaluate and update this policy as relevant clinical evidence becomes available to determine whether Vyondys 53 (golodirsen) provides clear clinical benefit or slows progression of the disease.

Vyondys 53 (golodirsen) was granted †accelerated approval by the FDA four months after rejecting approval of the drug over safety concerns in the Complete Response Letter in August of 2019. The letter stated concerns of possible infection at the injection sites and renal toxicity that was seen in preclinical (animal) studies. The toxicity in those studies was observed at dosage levels ten-times what is being used in clinical trials. No toxicity was observed in the clinical trial used for the drug application. Sarepta Therapeutics filed an appeal and after meeting with the FDA, the FDA reversed its decision and gave Vyondys 53 accelerated approval in December of 2019.

†*While the accelerated approval pathway makes Vyondys 53 available to DMD patients based on initial data, the drug's clinical benefit must be established from the ongoing confirmatory clinical trial.*

Confirmatory Trial

The clinical benefit of treatment for DMD with Vyondys 53 (golodirsen), including improved motor function, has not been demonstrated. The manufacturer is required by the FDA to conduct ongoing clinical trials to establish the drug's clinical benefit. Continued approval of Vyondys 53 (golodirsen) may be contingent upon verification of a clinical benefit in these confirmatory trials. [Prescribing Information 2020]

Phase 3 placebo-controlled, post-marketing confirmatory trial to support the Vyondys 53 accelerated approval. **The study is ongoing and posted as 'recruiting'. The estimated primary completion date is May 2023.** [ESSENCE (4045-301); NCT02500381]

SUMMARY OF EVIDENCE/POSITION

Vyondys 53 (golodirsen)

- 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.

- The second approved exon-skipping RNA therapy for DMD (after Exondys 51); similar to Exondys 51, Vyondys 53 was granted FDA fast track designation, ‡priority review, and †orphan drug designation.

- An antisense oligonucleotide, administered via intravenous infusion, 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. Exon 53 skipping is intended to allow for production of an internally truncated dystrophin protein in patients with genetic mutations that are amenable to exon 53 skipping.

- Estimated 8% of patients with DMD have this mutation

Vyondys 53 (golodirsen) was granted accelerated approval based on a phase I/II trial (4053-101 study) 2-part clinical study (FDA news release 2019, Vyondys 53 prescribing information 2019).

Phase 1/2 Clinical Trial (4053-101 study)
This first-in-human study assessed the safety, tolerability, pharmacokinetics, and efficacy of weekly intravenous Vyondys 53 versus placebo in 25 boys with confirmed deletions of the DMD gene amenable to skipping exon 53. All patients were on a stable dose of corticosteroids for at least 6 months before entering the trials. (NCT02310906)

- Part 1: A randomized 12-week dose-escalation period to assess pharmacokinetics of 4 doses of golodirsen

  Part 1 primarily assessed safety and tolerability in a 12-week dose-escalation period. A double-blind, placebo-controlled, dose-titration study in 12 DMD patients age 6 to 15 years (n=12) (golodirsen n=8; placebo n=4). Vyondys 53-treated patients received 4 escalating dose levels, ranging from 4 mg/kg/week (less than the recommended dosage) to 30 mg/kg/week by intravenous infusion for 2 weeks at each dose level)

  Results: Part 1 of the trial demonstrated that golodirsen was safe, well tolerated, and increased exon 53 skipping in patients with DMD and confirmed genetic mutations eligible for exon 53 skipping. All 25 patients had increased exon 53 skipping and showed a ~16-fold increase over baseline in dystrophin protein expression at week 48, illustrating. It was also shown that golodirsen was also well tolerated in all patients.

- Part 2: A 168-week, open-label study assessing the efficacy and safety of golodirsen at a dose of 30 mg/kg/week in the 12 patients enrolled in Part 1, plus 13 additional treatment-naive patients with DMD amenable to exon 53 skipping, (n=24) (golodirsen)

  The second part included a 168-week open-label evaluation of weekly infusions of 30 mg/kg. In part two, the primary endpoints are change from baseline in 6MWT at 144 weeks and change in dystrophin protein levels at 48 weeks. Secondary endpoints include drug pharmacokinetics, change from baseline in FVC percent predicted, and change from baseline in dystrophin intensity at 144 weeks.

- **A clinical benefit of golodirsen has not been established. Continued approval for this indication may be contingent upon verification of a clinical benefit in confirmatory trials.** The FDA label includes the following statement, "A clinical benefit of Exondys 51 has not been established. Continued approval for this indication may be contingent upon verification of a clinical benefit in confirmatory trials."

  Similar to Exondys 51, Vyondys 53 was approved under the †accelerated approval pathway based only on dystrophin production "*that is reasonably likely to predict clinical benefit*" in DMD patients, according to the FDA—not on proven clinical improvements.

  Accelerated approval based on a †surrogate endpoint rather than measured clinical benefit. The surrogate endpoint is the improvement in production of the dystrophin protein in skeletal muscle; however, no correlation has been established between dystrophin levels and clinical outcomes in golodirsen-treated patients with DMD.

  ‡*A "surrogate marker" can be defined as "…a laboratory measurement or physical sign that is used in therapeutic trials as a substitute for a clinically meaningful endpoint that is a direct measure of how a patient feels, functions, or survives and is expected to predict the effect of the therapy."*
  †*Accelerated approval pathway provides for the approval of drugs that treat serious or life-threatening diseases and generally provide a meaningful advantage over existing treatments. Approval under this pathway can be based on adequate and well-controlled studies showing the drug has an effect on a surrogate endpoint that is reasonably likely to predict clinical benefit to patients. This pathway provides earlier patient access to promising new drugs while the company conducts clinical trials to verify the predicted clinical benefit. Under the accelerated approval provisions, the FDA is requiring Sarepta Therapeutics to conduct a clinical trial to confirm the drug's clinical benefit. The required ongoing study is designed to assess whether Vyondys 53 improves motor function of DMD patients with a confirmed mutation of the dystrophin gene amenable to exon 53 skipping. If the trial fails to verify clinical benefit, the FDA may initiate proceedings to withdraw approval of the drug.*

  As part of the accelerated approval process, the FDA is requiring the manufacturer to conduct a trial to determine whether golodirsen improves motor function of DMD patients with a confirmed mutation of the dystrophin gene amenable to exon 53 skipping. If the trial fails to verify clinical benefit, the FDA may initiate proceedings to withdraw approval of the drug. The FDA may withdraw approval of the drug if the trial fails to show clinical benefit.

- The FDA has concluded that the data submitted demonstrated an increase in dystrophin production that is **reasonably likely to predict clinical benefit in patients with DMD** who have a confirmed mutation of the dystrophin gene amenable to exon 53 skipping. **However, a clinical benefit of Vyondys 53, including improved motor function, has not been established.** In making this decision, the FDA considered the potential risks associated with the drug, the life-threatening and debilitating nature of the disease for these children and the lack of available therapy.

- **Confirmatory Study: ONGOING**

  Post-marketing Confirmatory Trial to Accelerated Approval

  The clinical benefit of treatment for DMD with Vyondys 53 (golodirsen), including improved motor function, has not been demonstrated. The manufacturer is required by the FDA to conduct ongoing clinical trials to establish the drug's clinical benefit. Continued approval of Vyondys 53 (golodirsen) may be contingent upon verification of a clinical benefit in these confirmatory trials. [Prescribing Information 2020]

  Phase 3 placebo-controlled, post-marketing confirmatory trial to support the Vyondys 53 accelerated approval:

  ESSENCE (4045-301): Study of SRP -4045 and SRP-4053 in DMD Patients (Phase III study) NCT02500381

  A Double-Blind, Placebo-Controlled, Multi-Center Study with an Open-Label Extension to Evaluate the Efficacy and Safety of SRP-4045 (Casimersen) and SRP-4053 (Vyondys 53) in Patients with DMD

  This 96-week double-blind, placebo-controlled, multi-center, Phase 3 study trial is currently ongoing and recruiting. The trial is evaluating the efficacy of SRP-4045 and SRP-4053 for up to 96 weeks and will be followed by an open label extension (OLE) period. In the OLE period, all patients will receive open-label active treatment for 48 weeks in patients with DMD amenable to skipping exon 45 and exon 53. Twice as many patients will receive active treatment as will receive placebo (2:1). Target estimated enrollment of 222 subjects, males aged 7-13 years. Clinical efficacy will be assessed via six-minute walk test. All patients will undergo a muscle biopsy at baseline and a second muscle biopsy either at Week 48 or Week 96. **The study is ongoing and posted as 'recruiting'. The estimated primary completion date is May 2023.**

- The safety and tolerability profile of golodirsen does not include significant adverse events. No serious hypersensitivity events were reported. Rash was the most frequently non-serious hypersensitivity event. All patients reported at least 1 adverse event after beginning treatment, however the majority of these events were non-serious, mild, and unrelated to study drug. No patients discontinued due to an adverse event.

- There is a lack of long-term data for exon-skipping therapies and thus the potential long-term benefits and harms of these drugs is unknown, particularly in comparison to supportive care and corticosteroids.

- Additional considerations
  - 100% of study participants were male, thus the safety and efficacy in female patients is unknown
  - The potential impact of race is not known because 92% of the patients in studies were Caucasians
  - Vyondys 53 has not been studied in patients with hepatic impairment
  - All patients in clinical trials were on a stable dose of corticosteroids for at least 6 months prior to initiating therapy with Vyondys 53; therefore, there is insufficient evidence to judge the net health benefit of adding golodirsen compared with using corticosteroids and supportive care alone.

- The **Institute for Clinical and Economic Review (ICER)**, published an **Evidence Report** assessing the comparative clinical benefit and value of the corticosteroid deflazacort (Emflaza), and two exon-skipping therapies eteplirsen (Exondys 51™) and golodirsen for the treatment DMD. ICER noted:
  - The exon-skipping therapies, eteplirsen and golodirsen, cannot be assessed for cost-effectiveness because "*no persuasive evidence yet exists to demonstrate the clinical effectiveness of either drug*."
  - Data for exon-skipping therapies consist primarily of surrogate outcomes (e.g., dystrophin levels) from very small trials that have no validated threshold that defines meaningful clinical improvement. The small increases in dystrophin levels seen in the RCTs are of uncertain clinical significance.
  - Both eteplirsen and golodirsen have been shown to increase production of dystrophin, which is deficient in DMD, although dystrophin levels remained very low. The best results were for golodirsen, according to the report; at 48 weeks, the mean level of dystrophin had increased to 1.019 percent of normal. There is no validated threshold in dystrophin levels associated with meaningful clinical improvement.
  - There is found no evidence demonstrating improvements in muscle strength, motor function, ambulation, or pulmonary function.
  - No functional outcome results have been reported for golodirsen.
  - There was insufficient evidence to judge the net health benefit of adding golodirsen compared with using corticosteroids and supportive care alone.

- **No published guidelines were identified that recommend the use of Vyondys 53 for the treatment of DMD**

ADDITIONAL STUDIES

Phase 3 Extension Study (NCT03532542)

A Phase 3 open-label interventional extension study to evaluate the safety and tolerability of long-term treatment with casimersen or golodirsen in patients with DMD who have been treated previously with these exon-skipping treatments in a clinical trial setting. Target estimated enrollment, by invitation, of 260 subjects (males between the ages of 7 to 23 years).

- Boys with mutations amenable to exon 53 skipping will be included in the Vyondys 53 treatment group, while those with mutations that can benefit from exon 45 skipping will be treated with Casimersen
- Patients will receive weekly intravenous infusions of treatment for up to 144 weeks, and the number of severe adverse events will be assessed.
- The estimated primary completion date is August 2026

FDA INDICATIONS

FDA-approved indication does not itself dictate coverage. Molina coverage Policy may not recommend coverage for all FDA-approved indications. Please review this Policy in its entirety for indications covered by Molina Healthcare. The covered FDA-approved indications are conditions that are considered medically necessary; however, it is not inclusive of all conditions which may be approved by the Medical Reviewer. At the discretion of the Medical Director and on a case-by-case basis, Molina Healthcare may consider authorization of the biologic therapy addressed in this Policy for members with exceptional circumstances and for members with severe disease who may fall outside of the defined criteria.

Duchenne muscular dystrophy (DMD): Vyondys 53 (golodirsen) 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.

- The accelerated approval of golodirsen is based on the surrogate endpoint of an increase in dystrophin production in the skeletal muscle observed in some participants treated with the drug. A clinical benefit of the drug, including improved motor function, has not been established.

Vyondys 53 (golodirsen) is the second drug approved to treat patients with DMD and was approved under the FDA's accelerated approval program. Vyondys 53 was granted FDA fast track designation, ‡priority review, and †orphan drug designation.

- †*Orphan drug designation provides incentives such as clinical trial tax credits, user fee waiver and eligibility for orphan drug exclusivity to assist and encourage the development of drugs for rare diseases.*
- ‡*The manufacturer received a rare pediatric disease priority review voucher, which comes from a program intended to encourage development of new drugs and biologics for the prevention and treatment of rare pediatric diseases. This is the seventh rare pediatric disease priority review voucher issued by the FDA since the program began.*

Available as: 100mg/2mL single dose vials for reconstitution and IV infusion

FDA Approved: Dec. 12, 2019

Administration & Dosage*: Consult FDA labeling for more detailed information on dosage and administration of this drug, cautions, precautions, contraindications, potential drug interactions, laboratory test interferences, and acute toxicity.*

- Dosage: 30 milligrams per kilogram of body weight once weekly
- Administer as an intravenous infusion over 35 to 60 minutes

Contraindications: No contraindications listed in the manufacturer's labeling

Black Box Warnings/REMS: None at the time of this writing

Most common adverse reactions (PI, 2019)

- No contraindications known at this time
- Most common AEs (incidence ≥ 20% and higher than placebo) were headache, pyrexia, fall, abdominal pain, nasopharyngitis, cough, vomiting, and nausea.
- Warnings/Precautions:
  - Hypersensitivity reactions, including rash, pyrexia, pruritus, urticaria, dermatitis, and skin exfoliation have occurred in patients receiving golodirsen. Appropriate medical treatment should be instituted and slowing of the infusion or interruption of golodirsen therapy should be considered.
  - Renal toxicity: Based on animal data, golodirsen may cause renal toxicity. Renal function should be monitored; creatinine may not be a reliable measure of renal function in DMD patients.

Special Populations (per FDA-approved labeling)

- Geriatric Use: DMD is largely a disease of children and young adults; therefore, there is no geriatric experience with Vyondys 53
- Lactation: There are no human or animal data to assess the effect of Vyondys 53 on milk production, the presence of Vyondys 53 in milk, or the effects of golodirsen on the breastfed infant. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for Vyondys 53 and any potential adverse effects on the breastfed infant from Vyondys 53 or from the underlying maternal condition.
- Pediatric Use: Vyondys 53 is indicated for the treatment of DMD in patients who have a confirmed mutation of the DMD gene that is amenable to exon 51 skipping, including pediatric patients.
- Pregnancy: There are no human or animal data available to assess the use of Vyondys 53 during pregnancy.
- Renal Impairment: Renal clearance of golodirsen is reduced in non-DMD adults with renal impairment, based on estimated glomerular filtration rate (GFR) calculated using the Modification of Diet and Renal Disease (MDRD) equation. However, because of the effect of reduced skeletal muscle mass on creatinine measurements in DMD patients, no specific dosage adjustment can be recommended for DMD patients with renal impairment based on estimated GFR. Patients with known renal function impairment should be closely monitored during treatment with Vyondys 53.

CLASSIFICATION: Antisense Oligonucleotide

COVERAGE EXCLUSIONS

Vyondys 53 (golodirsen) is considered <u>not</u> medically necessary for all indications, including DMD, due to insufficient evidence of therapeutic value since clinical benefit has not been established.

BACKGROUND/SUMMARY

Muscular dystrophy includes a group of genetic disorders that cause muscle weakness and progressive disability. Duchenne muscular dystrophy (DMD) is the most common and progresses most rapidly.

Duchenne muscular dystrophy (DMD)

- A rare genetic disorder characterized by progressive muscle deterioration and weakness
- An X-chromosome-linked disease recessive disorder caused by mutations (mainly deletions) in the dystrophin gene that lead to an absence or defect in the dystrophin protein, dystrophin is essential for maintenance of myocyte integrity and helps keep muscle cells intact
- As males have only one X chromosome, and therefore one single copy of the dystrophin gene, they have a much higher probability of developing DMD. A small number of females are also affected but remain asymptomatic and only rarely present with a mild form of the disease.
- The most common type of muscular dystrophy; DMD is caused by an absence of dystrophin, a protein that helps keep muscle cells intact
- Based on population studies, the prevalence of DMD in the US is estimated to be 0.4 per 10,000 males, resulting in approximately 6,000 affected people in the US (Romitti, 2015)
- Associated with complete inability to produce functional dystrophin protein
- Affected children with DMD typically develop symptoms in early childhood around 3-5 years old, experiencing progressive muscle weakness and deterioration. Patients with DMD progressively lose the ability to perform activities independently and usually become non-ambulatory by their early teenage years and require the use of a wheelchair.
- As the disease progresses, life-threatening heart and respiratory conditions can occur. Patients typically succumb to the disease in their 20s or 30s; however, disease severity and life expectancy vary.
- In absence of treatment, the patient experiences:
    - wheelchair dependence before age 13 years
    - death occurs by, or around, age 20 years

Prognosis of DMD

- Death occurs around age 20 in absence of treatment and is usually due to cardiac or respiratory failure
- Disease progression in patients with DMD
    - Scoliosis is frequent after loss of ambulation
    - Risk for cardiomyopathy increases with age in absence of ventilatory intervention

Treatment Overview: Pharmacologic Agents/Conventional Therapy

There is no curative therapy, but management of disease manifestations can prolong survival and improve quality of life. A multidisciplinary team is required for management of patient with DMD and treatment options for DMD predominantly focus on management of symptoms and secondary complications.

Goals of management for DMD

- Preserve strength, ambulation, and ventilatory and cardiac function
- Minimize of steroid complications where applicable
- Prevent and treat complications including contractures, scoliosis, ventilatory function impairment or failure, and cardiomyopathy
- Determine and arrange appropriate school environment and manage family stressors

Other pharmacologic therapies for DMD are primarily aimed at the management of comorbidities such as cardiomyopathy, osteoporosis, pain management, and respiratory failure. These treatment options include: angiotensin-converting-enzyme (ACE) inhibitors, beta-blockers, calcium and vitamin D supplements, muscle relaxants, and non-steroidal anti-inflammatory drugs.

- Corticosteroids
  - DMD Care Considerations Working Group consensus guidelines urge consideration of glucocorticoid therapy (prednisone or deflazacort) for all patients with DMD (optimal dose ranges not established)
    - Goal in the ambulatory child is to preserve ambulation and minimize later respiratory, cardiac, and orthopedic complications
    - Goal of continuing glucocorticoid therapy after loss of ambulation is to preserve upper limb strength, reduce scoliosis progression, and delay declines in respiratory and cardiac function
  - Generally used to preserve ambulation and minimize complications in patients with DMD
  - In ambulatory patients, recommended if motor skills have plateaued or begun to decline
  - In non-ambulatory patients, glucocorticoids often continued if already started while ambulatory, but limited evidence regarding starting glucocorticoids
  - Daily dosing preferred over alternative regimens (alternate day, high-dose weekend, or 10-day cycles)
  - Monitor and manage side effects associated with chronic steroid therapy
- Vitamin D and calcium supplementation suggested to manage bone health in patients with DMD
- Respiratory care including airway clearance techniques, nocturnal ventilatory support, daytime non-invasive ventilation, and tracheostomy may be indicated/desired as disease progresses
- For management of cardiac dysfunction, consider:
  - Diuretics, angiotensin-converting enzyme (ACE) inhibitors, and/or beta blockers to treat manifestations of cardiac dysfunction

Anticoagulation therapy in patients with severe cardiac dysfunction to prevent systemic thromboembolic events

DEFINITIONS

6-Minute Walk Test (6MWT): Developed as an integrated assessment of cardiac, respiratory, circulatory, and muscular capacity for use in clinical trials of various cardiac and pulmonary conditions. In recent years, the 6MWT has been adapted to evaluate functional capacity in neuromuscular diseases and has served as the basis for regulatory approval of a number of drugs for rare diseases, with mean changes in the 6MWT ranging from 28 to 44 meters.

Duchenne muscular dystrophy (DMD) gene: Human gene, which provides instructions for making dystrophin (a protein that that protects muscles from deterioration). Dystrophin is located primarily in skeletal and heart muscle.

Dystrophinopathy: spectrum of muscle disease caused by pathogenic variants of *DMD* gene that encodes dystrophin protein

- Mild forms include asymptomatic disease with elevated serum creatine phosphokinase or muscle cramps with myoglobinuria
- Severe forms are progressive and classified as DMD or Becker muscular dystrophy

North Star Ambulatory Assessment: a functional scale designed for ambulant boys affected by DMD

APPENDIX

Appendix 1: Guidelines

American Academy of Neurology guideline update on corticosteroid treatment of Duchenne dystrophy: Neurology 2016 Feb 2;86(5):465 or at National Guideline Clearinghouse 2016 Jun 6:50008

American Academy of Pediatrics (AAP) policy statement on cardiovascular health supervision for individuals affected by Duchenne or Becker muscular dystrophy: Pediatrics 2005 Dec;116(6):1569 full-text, reaffirmed 2008 Dec, commentary can be found in Pediatrics 2006 May;117(5):1864 full-text

United States expert consensus guideline on diagnosis and management of Duchenne muscular dystrophy

- Part 1: Diagnosis, pharmacological and psychosocial management can be found in Lancet Neurol 2010 Jan;9(1):77 PDF or at National Guideline Clearinghouse 2010 Aug 2:15644
- Part 2: Implementation of multidisciplinary care can be found in Lancet Neurol 2010 Feb;9(2):177 PDF or at National Guideline Clearinghouse 2010 Aug 2:15645

CODING INFORMATION: THE CODES LISTED IN THIS CLINICAL POLICY ARE FOR INFORMATIONAL PURPOSES ONLY. LISTING OF A SERVICE OR DEVICE CODE IN THIS POLICY DOES NOT IMPLY THAT THE SERVICE DESCRIBED BY THIS CODE IS A COVERED OR NON-COVERED. COVERAGE IS DETERMINED BY THE BENEFIT DOCUMENT. THIS LIST OF CODES MAY NOT BE ALL INCLUSIVE AND INCLUSION OR EXCLUSION OF ANY CODES DOES NOT GUARANTEE COVERAGE. PROVIDERS SHOULD REFERENCE THE MOST UP-TO-DATE SOURCES OF PROFESSIONAL CODING GUIDANCE PRIOR TO THE SUBMISSION OF CLAIMS FOR REIMBURSEMENT OF COVERED SERVICES.

CPT	Description

HCPCS	Description
C9399	Unclassified drugs or biologicals (hospital outpatient use)
J3490, J3590	Unclassified drugs or biologicals
Billing Units: When billing for **Vyondys** using the NOC (Not Otherwise Classified) codes **C9399** or **J3490**, the units billed should be represented as milliliters **(mL)**	

ICD-10	Description
G71.01	Duchenne or Becker muscular dystrophy

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Policy History	Approval
Policy Developed Peer Review: AMR Peer Review Network. 1/9/2020. Practicing Physician. Board certified in Neurology, Sleep Medicine.	P&T Q1 2020
Policy Reviewed* No coverage criteria changes with this annual review. Content update includes: FDA granted accelerated approval based on a phase I/II trial (4053-101 study)—updated policy with published results from Part 1 (Frank, DE et al. 2020)	P&T Q1 2021

**All content, clinical evidence, coverage criteria, practice guidelines, appendices and reference sections reviewed and revised with the most recent medical literature and available evidence for both 'Annual Reviews' and 'Policy Revisions.' Annual Reviews without notable changes to coverage criteria or position may not require Peer Review. Policy Revisions include notable content updates or revisions that which may have affected criteria or requires review by a practicing specialist, Peer Reviewer.*