healthfirst
Health Insurance for New Yorkers

Provider Alert

CLINICAL POLICY – MP-035v6

Medical Benefit

AMONDYS 45™ (casimersen), EXONDYS 51™ (eteplirsen), VYONDYS 53™ (golodirsen), VILTEPSO™ (viltolarsen)

Date of Initial Issue: October 2020 **Date Last Reviewed: May 2022**

Classification

- ☑ Managed Long Term Care (MLTC)
- ☑ Commercial
- ☐ Corporate
- ☑ Medicaid Advantage Plus (MAP)
- ☑ Qualified Health Plan (QHP)
- ☑ Medicare
  - ☑ Non-D-SNP
  - ☑ LIP D-SNP
- ☑ Medicaid Managed Care
  - ☑ CNX-MMC
- ☑ Essential Plan (EP)
- ☑ CNX-Medicare
- ☑ Personal Wellness Plan (PWP/HARP)
  - ☑ CNX-HARP
- ☑ Child Health Plus (CHP)

MEDICAL POLICY DISCLAIMER:

Healthfirst medical policies are intended to provide guidance in the administration of Healthfirst benefit plans and are used by medical directors and other clinical professionals in making medical necessity and other coverage determinations.

Healthfirst establishes medical policy based upon a review of evidence-based guidelines, peer reviewed published medical literature, CMS guidelines, NYS DOH Regulations and Food and Drug Administration recommendations. However, medical policies are not recommendations for treatment and should never be used as treatment guidelines. Treating health care professionals are solely responsible for diagnosis, treatment, and the provision of medical advice to Healthfirst members.

A medical policy does not constitute a plan authorization; nor does apparent satisfaction of the criteria contained in a medical policy necessarily mean that a plan authorization will be issued. Coverage decisions are subject to all terms and conditions of the applicable benefit plan, including specific exclusions and limitations, and to applicable state and/or federal law. Benefit plans vary in coverage and some plans may not provide coverage for certain services discussed in the medical policies.

I. Policy Overview

This policy is to provide guidance on the coverage guidelines utilized to review the request for prior authorization for Vyondys 53™ (golodirsen), Exondys 51™ (eteplirsen), Amondys 45™ (casimersen) and Viltepso™ (viltolarsen). These coverage guidelines will be used to determine medical necessity.

Coverage is based on the NYDOH guidance, patient's condition, the appropriateness of the dose and route of administration, based on the clinical condition and the standard of medical practice regarding the effectiveness of the drug for the diagnosis and condition. The drug must be used according to the indication and protocol listed in the accepted compendia listed below:

- FDA Labeled Indication
- National Comprehensive Cancer Network (NCCN) Drugs and Biologies Compendium
- American Hospital Formulary Service-Drug Information (AHFS-DI)
- Thomson Micromedex DrugDex
- Clinical Pharmacology
- Wolters Kluwer Lexi-Drugs

II. Responsible Parties and Related Departments

- Appeals and Grievances (Related)
- Legal (Related)
- Regulatory (Related)
- Reimbursement (Related)
- Pharmacy (Responsible)
- Utilization Management (Related)

III. Definitions

6-Minute Walk Test (6MWT) – A measure of how far a patient can walk in six minutes on a hard, flat surface. It is considered predictive of disease progression in muscular dystrophy patients over the age of one, and in DMD, the ability to walk distances greater than 325 meters during the test has been linked to slower disease progression.[3]

Dystrophin – is a protein found in muscle cells. It helps strengthen muscle fibers and protect them from breaking down as they contract and relax. Deficiency in dystrophin leads to muscle breakdown and loss of function and is the main defect in DMD.

Exon – The region of a gene that contains the code for producing protein. Each exon codes for a specific portion of the complete protein.

FVC – This is a measurement of lung size (in liters) and represents the volume of air in the lungs that can be exhaled following a deep inhalation.

Gowers' sign – is a medical sign that indicates weakness of the proximal muscles, namely those of the lower limb. The sign describes a patient that must use their hands and arms to "walk" up their own body from a squatting position due to lack of hip and thigh muscle strength.[9]

LVEF – is the measurement of how much blood is being pumped out of the left ventricle of the heart (the main pumping chamber) with each contraction. A normal heart's ejection fraction may be between 50 and 70 percent.[4]

North Star Ambulatory Assessment (NSAA) – a 17-item rating scale that is used to measure functional motor abilities in ambulant children with Duchenne Muscular Dystrophy (DMD). It is usually used to monitor the progression of the disease and treatment effects. (See Appendix A.)[8]

IV. Background information

Duchenne muscular dystrophy (DMD) is the most common of the more than 30 types of muscular dystrophy. It is a genetic disease that leads to progressive deterioration of muscle fibers. The condition usually affects boys only, but girls can also carry the mutated gene and experience some symptoms. Females have a 50 percent risk of passing the mutated gene on to their sons, who will be affected by the disease[7].

DMD is an X-linked recessive disease affecting 1 in 3,500 to 5,000 newborn male infants. The disease is attributed to large frame-shift deletions in the DMD gene (chromosome Xp21) which leads to loss of a structural protein of muscle cells (dystrophin). Over 4,700 mutations on the DMD gene have been identified which led to a deficiency in production of dystrophin. Therefore, the type of mutation and its effect on the production of dystrophin accounts for the variable phenotypic expression. Female's carriers are usually asymptomatic, but some may show mild symptoms. There are wide variances in how quickly DMD progresses, but without intervention death is at approximately 19 years of age. With respiratory, cardiac, orthopedic, and rehabilitative interventions and use of corticosteroids, children born today can have a life expectancy of up to 40 years.[10]

Treatment

Exondys 51 (eteplirsen) was approved in September 2016 (developed by Sarepta Therapeutics), and was the first treatment approved by the U.S. Food and Drug Administration (FDA) to treat patients with DMD amenable to exon 51 skipping. Exondys 51 binds to exon 51 of dystrophin pre- mRNA, resulting in exclusion of this exon during mRNA processing in patients with genetic mutations that are amenable to exon 51 skipping. The intention is to restore the reading frame of the resulting mRNA and production of a shortened, but partially functional dystrophin protein. These patients represent ~13% of all patients with DMD. (See Appendix B for Examples of DMD gene mutations (exon deletions) amenable to exon 51 skipping).

Vyondys 53 (golodirsen) was approved in the U.S. in December 2019 (developed by Sarepta Therapeutics), to treat patients with DMD amenable to exon 53 skipping. binds 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. The intention is to restore the reading frame of the resulting mRNA and production of a shortened, but partially functional dystrophin

protein. These patients represent up to 10% of all patients with DMD. (See Appendix C for Examples of DMD gene mutations (exon deletions) amenable to exon 53 skipping.)

Amondys 45 (casimersen) was approved on February 25, 2021, under accelerated review based on an increase in dystrophin production in skeletal muscle of patients amenable to exon 45 skipping. Approximately 8% of patients with DMD have an exon 45–skipping mutation. Continued approval may be contingent upon verification of a clinical benefit in confirmatory trials (ESSENCE trial: expected to conclude in 2024).

VILTEPSO™ (viltolarsen) 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. An estimated 10% of patients with DMD would be amenable to treatment with an exon 53 skipping therapy. VILTEPSO 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. Serum cystatin C, urine dipstick, and urine protein-to-creatinine ratio should be measured before starting VILTEPSO. Consider measurement of glomerular filtration rate prior to initiation of VILTEPSO. Monitoring for kidney toxicity during treatment is recommended[16].

Warnings and Precautions[11,12]

Exondys, Vyondys, Amondys and Viltepso may cause:

- Hypersensitivity reactions: rash, pyrexia, pruritus, urticaria, dermatitis and skin exfoliation, hypotension, bronchospasm, cough, dyspnea
- Renal toxicity (Vyondys 53, Amondys 45 and Viltepso™ only): renal toxicity, including potentially fatal glomerulonephritis

V. FDA Labeled Indications

A. **EXONDYS 51 (eteplirsen)** is an antisense oligonucleotide 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 51 skipping.

B. **VYONDYS 53 (golodirsen)** is an antisense oligonucleotide 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.

C. **AMONDYS 45 (casimersen)** is an antisense oligonucleotide 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 45 skipping.

D. **VILTEPSO™ (viltolarsen)** is an antisense oligonucleotide 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.

VI. Policy

Prior authorization requests for the Medicare lines of business are subject to applicable National and Local Coverage Guidelines (NCD/LCD). In the absence of applicable NCD/LCD guidelines, Healthfirst clinical criteria will be followed.

A. Due to the expense of these medications, they require a peer review

B. Coverage Guidelines:

EXONDYS 51™ (eteplirsen), VYONDYS 53™ (golodirsen), AMONDYS 45™ (casimersen), and VILTEPSO™ (viltolarsen) are considered medically necessary when ALL of the following criteria are met:

— patient must have a diagnosis of DMD; **AND**

— documentation of genetic testing must confirm the DMD gene mutation of the patient is amenable to exon 45, 51, or 53 skipping; **AND**

— documentation must confirm a stable dose of corticosteroids prior to starting therapy or a documented reason not to be on corticosteroids; **AND**

— documentation indicates kidney function testing prior to starting therapy (except for eteplirsen); **AND**

— patient is not concurrently being treated with another exon skipping therapy for DMD.

C. Investigational and Not Medically Necessary:

1. Eteplirsen, golodirsen, casimersen and viltolarsen is considered investigational and not medically necessary when the criteria above are not met, and for all other indications.

D. Duration of Approval

Up to 6 months

E. Access

Limited distribution

F. Dosing/Administration

— **Eteplirsen (Exondys 51)**: available as 100 mg/2 mL (50 mg/mL) single-dose vial and 500 mg/10 mL (50 mg/mL) single-dose vial, in a recommended dose of 30 mg/kg administered once weekly via intravenous infusion over 35 to 60 minutes. If a dose is missed, it may be administered as soon as possible after the scheduled time.

— **Golodirsen (Vyondys 53)**: available as 100 mg/2 mL (50 mg/mL) single-dose vial, in a recommended dose of 30 mg/kg administered once weekly via intravenous infusion over 35 to 60 minutes.

— **Casimersen (Amondys 45)**: available as 100 mg/2 mL (50 mg/mL) single-dose vial, in a recommended dose of 30mg/kg administered once weekly via intravenous infusion over 35 to 60 minutes.

— **Viltolarsen™ (Viltepso)**: available as 250 mg/5 mL (50 mg/mL) in a single-dose vial, in a recommended dose of 80 mg/kg administered once weekly via intravenous infusion over 60 minutes.

G. Limitations/Exclusions

1. Dose exceeding FDA-approved labeling specified in dosing section of this policy
2. Use of pharmacologic treatment or other experimental treatments within 12 weeks of week 1 (initiation of DMD therapy), other than corticosteroids that affects muscle strength or function
3. Presence of clinically significant comorbidities
4. In Vyondys 53, Exondys 51, Amondys 45 and Viltepso ™ clinical trials 100% of study participants were male, thus the safety and efficacy of these agents in females is unknown.
5. Geriatric population – DMD is largely a disease of children and young adults; therefore, there is no geriatric experience.

H. Applicable Billing Codes/Coding and Billing

HCPCS Code	Description	1 Billable Unit
J1428	Exondys 51 (eteplirsen)	10 mg
J1426	Amondys 45 (casimersen)	10 mg
J1429	Vyondys 53 (golodirsen)	10 mg
J1427	Viltepso™ (viltolarsen)	10 mg

Applicable NDCs	
60923-0363-02	Exondys 51 100mg/2ml Solution J1428 Injection, eteplirsen, 10 mg
60923-0284-10	Exondys 51 500mg/10ml Solution J1428 Injection, eteplirsen, 10 mg
60923-0465-02	Vyondys 53, single use vial; 50 mg/mL powder for injection
60923-0227-02	Amondys 45 Injection, 100 mg/2 mL (50 mg/ mL) solution in a single-dose vial
73292-0011-01	Viltepso single-dose vials containing 250 mg/5 mL (50 mg/mL)

Related Procedural Terminology (CPT) Codes	Description	Site of service
96365	Intravenous infusion, for therapy, prophylaxis, or diagnosis (specify substance or drug); initial, up to 1 hour	Physician office and hospital outpatient
96366	Intravenous infusion, for therapy, prophylaxis, or diagnosis (specify substance or drug); each additional hour	Physician office and hospital outpatient
96601	Home infusion/specialty drug administration, per visit (up to 2 hours)	Home health
S9379	Home infusion therapy, infusion therapy, not otherwise classified, administrative services, professional pharmacy services, care coordination, and all necessary supplies and equipment (drugs and nursing visits coded separately), per diem	Home health

Revenue codes

The following revenue codes may be appropriate when billing DMD drug and its administration in the hospital outpatient setting:

Code	Description	Appropriate use
0260	IV therapy, general	May be used by commercial private payers or Medicaid plans
0636	Drugs requiring detailed coding	Required by Medicare
0510	Clinic	May be used by any payer for the IV infusion service

Diagnosis coding:

The ICD-10-CM diagnosis code that describes the FDA-approved indication for DMD drugs is:

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

Billing Units

Claim forms require a provider to state the number of J-Code "billing units" used. This refers to the number of units used based on mg of DMD drug administered. For DMD drugs, 1 billing unit corresponds to 10 mg of drug. The following table lists the appropriate number of units per vial based on size of vial.

Description	Vial Quantity (mg)	J-code Billing Units
Exondys 51, 2ml vial	100 mg	10 units
Exondys 51, 10 ml vial	500 mg	50 units
Vyondys 53, 2 ml vial	100 mg	10 units
Amondys 45, 2 ml vial	100 mg	10 units
Viltepso, 5 ml vial	250 mg	25 units

VII. Sanctions

Violation of this policy will be considered in accordance with the Disciplinary Action policy.

VIII. Procedures/Job Aids/Documents/Forms

Appendix A:8 North Star Ambulatory Assessment (NSAA)

	ACTIVITY	2	1	0
1	**Stand**	Stands upright, still and symmetrically, without compensation (with heels flat and legs in neutral) for minimum count of 3 secs	Stands still but with some degree of compensation (e.g. on toes or with legs abducted or with bottom stuck out) for minimum count of 3 secs	Cannot stand still or independently, needs support (even minimal)
2	**Walk**	Walks with heel-toe or flat-footed gait pattern	Persistent or habitual toe walker, unable to heel-toe consistently	Loss of independent ambulation—may use KAFOs or walk short distances with assistance
3	**Stand up from chair**	Keeping arms folded. Starting position 90o hips and knees, feet on floor/supported on a box step.	With help from thighs or push on chair or prone turn	Unable
6	**Climb box step-Right**	Faces step—no support needed	Goes up sideways or needs support	Unable
7	**Climb box step- Left**	Faces step—no support needed	Goes up sideways or needs support	Unable
10	**Gets to sitting**	Starts in supine—may use one hand to assist	Self assistance e.g.–pulls on legs or uses head-on- hands or head flexed to floor	Unable
14	**Jump**	Both feet at the same time, clear the ground simultaneously	One foot after the other (skip)	Unable
17	**Run**	Both feet off the ground (no double stance phase during running)	'Duchenne jog'	Unable
			TOTAL 3 years (max score 16)	
4	**Stand on one leg—Right**	Able to stand in a relaxed manner (no fixation) for count of 3 seconds	Stands but either momentarily or needs a lot of fixation e.g. by knees tightly adducted or other trick	Unable
5	**Stand on one leg—Left**	Able to stand in a relaxed manner (no fixation) for count of 3 seconds	Stands but either momentarily or needs a lot of fixation e.g. by knees tightly adducted or other trick	Unable
8	**Descend box —Right**	Faces forward, climbs down controlling weight bearing leg. No support needed	Sideways, skips down or needs support	Unable
9	**Descend box —Left**	Faces forward, climbs down controlling weight bearing leg. No support needed	Sideways, skips down or needs support	Unable
13	**Stands on heels**	Both feet at the same time, clearly standing on heels only (acceptable to move a few steps to keep balance) for count of 3	Flexes hip and only raises forefoot	Unable
			TOTAL 3.5years (max score 26)	
11	**Rise from floor**	From supine—no evidence of Gowers' manoeuvre*	Gowers' evident	(a) NEEDS to use external support object e.g. chair OR (b) Unable
12	**Lifts head**	In supine, head must be lifted in mid-line. Chin moves towards chest	Head is lifted but through side flexion or with no neck flexion	
15	**Hop—Right**	Clears forefoot and heel off floor	Clears forefoot and heel off floor	Unable
16	**Hop—Left**	Clears forefoot and heel off floor	Clears forefoot and heel off floor	Unable
			TOTAL 4 years and above (max score 34)	

Appendix B: Examples of DMD gene mutations (exon deletions) amenable to exon 51 skipping

- Deletion of exon 50
- Deletion of exon 52
- Deletion of exons 45-50
- Deletion of exons 47-50
- Deletion of exons 48-50
- Deletion of exons 49-50

Appendix C: Examples of DMD gene mutations (exon deletions) amenable to exon 53 skipping

- Deletion of exon 52
- Deletion of exon 45-52
- Deletion of exon 47-52
- Deletion of exon 48-52
- Deletion of exon 49-52
- Deletion of exon 50-52

Appendix D: Examples of DMD gene mutations (exon deletions) amenable to exon 45 skipping

- Deletion of exon 44
- Deletion of exon 12-44
- Deletion of exon 46-48
- Deletion of exon 46-49
- Deletion of exon 18-44
- Deletion of exon 46-47
- Deletion of exon 46-53
- Deletion of exon 46-55

IX. References

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