Pharmacy Management Drug Policy

SUBJECT: Duchenne Muscular Dystrophy (DMD): Agamree (Vamorolone), Amondys 45 (casimersen), Duvyzat (givinostat), Emflaza and generic deflazacort, Exondys 51 (eteplirsen), Viltepso (vilotarsen) and Vyondys 53 (golodirsen)
POLICY NUMBER: PHARMACY-85
EFFECTIVE DATE: 12/30/2019
LAST REVIEW DATE: 11/20/2025

If the member's subscriber contract excludes coverage for a specific service or prescription drug, it is not covered under that contract. In such cases, medical or drug policy criteria are not applied. This drug policy applies to the following line/s of business:

Policy Application

Category:	☒ Commercial Group (e.g., EPO, HMO, POS, PPO)	☒ Medicare Advantage
	☒ On Exchange Qualified Health Plans (QHP)	☐ Medicare Part D
	☒ Off Exchange Direct Pay	☒ Essential Plan (EP)
	☒ Medicaid & Health and Recovery Plans (MMC/HARP)	☒ Child Health Plus (CHP)
	☐ Federal Employee Program (FEP)	☐ Ancillary Services
	☒ Dual Eligible Special Needs Plan (D-SNP)	

DESCRIPTION:

Duchenne muscular dystrophy (DMD) is a rare genetic disease that affects approximately 20,000 boys and young men in the United States. A mutation in the gene for dystrophin causes progressive muscle wasting, leading to the need for wheelchairs and ventilators.[4] There are numerous mutations in the DMD gene that have been identified and the type of mutation and its effect on the production of dystrophin accounts for variable symptoms/progression rates in each affected patient.[3] Approximately 13% of patients with DMD contain genetic mutations that are amenable to exon 51 skipping, approximately 8% of patients with DMD contain genetic mutations that are amenable to exon 45 and 53 skipping, each. In general, death occurs around 19 years of age if no interventions are made.[5] Respiratory, cardiac, orthopedic, and rehabilitative interventions and the use of corticosteroids can lead to an extended life expectancy of up to 40 years.

Agamree is indicated for the treatment of Duchenne muscular dystrophy (DMD) in patients 2 years of age and older. It is a corticosteroid that acts through the glucocorticoid receptor to exert anti-inflammatory and immunosuppressive effects. The precise mechanism by which Agamree exerts its effect in patients with DMD is unknown.

Amondys 45 (casimersen) is indicated for the treatment of DMD in patients who have a confirmed mutation of the DMD gene that is amenable to exon 45 skipping. It is designed to bind to exon 45 of dystrophin pre-mRNA, allowing for production of an internally truncated dystrophin protein in these patients. The drug is approved under accelerated approval which allows a surrogate endpoint (dystrophin level) to be used for serious disease in which there is an unmet need for therapy.

The accelerated approval of Amondys 45 was based upon interim results form an ongoing global, randomized, double-blind, placebo-controlled Phase 3 trial (ESSENCE). 43 patients were randomized in a 2:1 manner to receive either Amondys 45 or placebo for 96 weeks (interim results were assessed at 48 weeks). All patients were ambulatory and were required to have been on stable doses of oral corticosteroids for at least 24 weeks prior to the start of treatment. The efficacy endpoint was based on change from baseline in the dystrophin protein level at week 48. Patients who received Amondys 45 showed a significantly greater increase in dystrophin protein levels (mean 0.81% of normal) compared to those who received placebo (0.22% of normal). It is not yet known whether this increase in dystrophin

contributes to clinical benefit in patients. No confirmatory trials have yet been conducted to demonstrate that Amondys 45 provides clinical benefit in DMD patients amenable to exon 45 skipping.

Duvyzat (givinostat) is indicated for patients 6 years and older with DMD. It is the first nonsteroidal drug approved to treat patients with all genetic variants of DMD. It is a histone deacetylase inhibitor (HDAC). The inhibition of DHAC may activate repair mechanisms that can prevent muscle degeneration and reduce inflammation. The precise mechanism by which Duvyzat exerts its effect in patients with DMD is unknown.

Emflaza (deflazacort) is indicated for patients 2 years of age and older with DMD. It is a corticosteroid for symptomatic therapy that works by decreasing inflammation and reducing the activity of the immune system. It is an oxazoline derivative of prednisone and has an estimated dosage equivalency of 1:1.3 compared to prednisone. It was approved by the FDA in 2017 but has been available outside the US for decades.

Exondys 51 (eteplirsen) 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. It is designed to skip exon 51, allowing for the synthesis of a truncated partial functioning form of dystrophin protein. The drug is approved under accelerated approval which allows a surrogate endpoint (dystrophin level) to be used for serious disease in which there is an unmet need for therapy.

The efficacy of Exondys 51 was evaluated in three open-label pivotal studies (designated as studies 1,2, and 3 in the package insert) in patients with DMD that is amenable to exon 51 skipping. Study 1 assessed the effect of Exondys on dystrophin levels and on improved distance walked in 12 patients, Study 2 was an extension study evaluating the same patients from study 1 as compared to a matched historical control population, and study 3 is an ongoing study that included 12 different patients with DMD and studied the effect of Exondys 51 on dystrophin levels. In all 3 clinical trials, patients were required to be on stable doses of corticosteroids for at least 6 months prior to trial enrollment. Additionally, patients in all 3 clinical trials were ambulatory with a baseline minimum 6-minute walk test of at least 200 meters in study 1/2. It has been proposed that the 6MWT is a reliable tool used to measure progression in DMD.

Study 1 and 2 reported that the use of Exondys contributed to an increase in dystrophin levels and 6MWT results, however the FDA has recommended retraction of this study due to concerns related to methodology and interpretation of its findings. The FDA approval of Exondys 51 was based on results from Study 3, which reported a statistically significant increase in dystrophin levels. The median increase after 48 weeks was 0.1%. It is not yet known whether this increase in dystrophin contributes to clinical benefit in patients. The FDA labeling for Exondys 51 specifically states that a clinical benefit has not yet been established and continued approval is contingent upon verification of a clinical benefit in ongoing confirmatory clinical trials.

Following FDA approval of Exondys 51, Kinane, et al published a 2018 analysis that evaluated the effect of eteplirsen on lung function in DMD patients that participated in the aforementioned Study 1 and 2. This analysis compared Forced Vital Capacity (FVC) to historical controls from the United Dystrophinopathy Project (UDP, N=34) and Maximum Expiratory Pressure (MEP)/ Maximum Inspiratory Pressure (MIP) were compared to published natural history. The data showed a decline in FVC of 2.3% predicted per year in eteplirsen-treated patients compared with a decline of 4.1% predicted per year in the natural history cohort. There was an annual decline in MEP% predicted of 2.6% compared to a decline of 2.7%-3.6% in historical published reports of DMD and an increase in MIP% predicted of 0.6% vs a decline of 3.8-3.8% in eteplirsen-treated patients vs historic published reports. However, this analysis only reported pulmonary function endpoints that were collected as exploratory assessments

from previously reported trials (Study 1 and 2) and there are no other published prospective trials that have compared these pulmonary endpoints to an active placebo control. Due to potential heterogeneity in the historical population that was used for comparison in this analysis, the benefit of Eteplirsen on pulmonary function cannot be fully assessed and the FDA labeling for Exondys 51 continues to state that a clinical benefit has not yet been established for Exondys 51.
Khan, et al published a 2019 analysis evaluating the effect of eteplirsen on lung function in DMD patients in studies 1/ 2 as well as two additional open-label, multicenter studies (204 and 301). Study 204 is an unpublished study that enrolled boys aged 7 to 21 who were primarily non-ambulatory or minimally ambulatory (6MWT < 300 meters). Study 301 is an ongoing phase 3 trial in boys aged 7 to 16 years old who are ambulatory (6MWT distance of at least 300 meters). The analysis of these 3 studies compared Percent Predicted Forced Vital Capacity (FVC% p) annual change to matched Cooperative International Neuromuscular Research Group Duchenne Natural History Study (CINRG DNHS) controls. Statistical analysis was presented for patients aged 10 to<18 years who were expected to be in a linear phase of FEV%p decline based on a 2015 study by Mayer, et al which demonstrated that DMD patients between the ages of 10 to 18 years will have a decline in FEV%p of 5% annually. The results of studies 204 and 301 demonstrated a FEV%p annual change of -3.66% in Study 204 participants and -3.79% in Study 301 participants compared to a range of 5.5-6% in the historical control group. Like the Kinane article, this analysis only reported FVC values collected as exploratory assessments from previously reported trials with no active placebo control. The FDA labeling for Exondys 51 continues to state that a clinical benefit has not yet been established for Exondys 51.

Viltepso (vilotarsen) is indicated for the treatment of DMD in patients who have a confirmed mutation of the DMD gene that is amenable to exon 53 skipping. It is designed to bind to exon 53, resulting in production of an internally truncated dystrophin protein in patients with genetic mutations that are amenable to exon 53 skipping. The drug is approved under accelerated approval which allows a surrogate endpoint (dystrophin level) to be used for serious disease in which there is an unmet need for therapy.

The accelerated approval of Viltepso was based on results from a multicenter, 2-period, dose-fining study in patients with a confirmed mutation of the DMD gene that is amenable to exon 53 skipping. During the initial period, patients were randomized to Viltepso or placebo and then all patients received 20 weeks of open-label Viltepso (40mg/kg once weekly or 80mg/kg once weekly) in the second period. Efficacy was assessed based on change from baseline in dystrophin protein level at Week 25. In patients who received Viltepso 80mg/kg once weekly, mean dystrophin levels increased from 0.6% of normal at baseline to 5.9% of normal by week 25, with a mean change of 5.3% of normal. All patient demonstrated an increase in dystrophin levels over their baseline values. It is not yet known whether this increase in dystrophin contributes to clinical benefit in patients. No confirmatory trials have yet been conducted to demonstrate that Viltepso provides clinical benefit in DMD patients amenable to exon 53 skipping.

Vyondys 53 (golodirsen) is indicated for the treatment of DMD in patients with a confirmed mutation of the DMD gene that is amenable to exon 53 skipping. It is designed to skip exon 53, allowing for the synthesis of a truncated partial functioning form of dystrophin protein. The drug is approved under accelerated approval which allows a surrogate endpoint (dystrophin level) to be used for serious disease in which there is an unmet need for therapy.

The accelerated approval of Vyondys 53 was based on results from a two-part Phase I/II clinical study in patients with DMD amenable to exon 53 skipping. Part I was a randomized, placebo-controlled study to assess the safety and pharmacokinetics of Vyondys 53 (SRP-4053) in 12 patients. Part II of this study was a 168-week, open-label evaluation of 25 patients including eligible patients from part 1 of the study as well as 13 additional patients with DMD amenable to exon 53 skipping. Primary endpoints for part 2

of this study were change from baseline in dystrophin protein levels at week 48 and change from baseline on a 6-minute walk test (6MWT) at week 144. All patients were required to be on a stable dose of corticosteroids for at least 6 months prior to initiation of therapy and demonstrate minimum performance on a 6MWT, North Star Ambulatory Assessment, and Gowers test. Results of this study showed an increase in mean dystrophin levels from 0.10% of normal at baseline to 1.02% at week 48 (mean change of 0.92%). It is not yet known whether this increase in dystrophin contributes to clinical benefit in patients. No confirmatory trials have yet been conducted to demonstrate that Vyondys 53 provides clinical benefit in DMD patients amenable to exon 53 skipping.

POLICY:

AGAMREE

Based upon our assessment and review of the peer-reviewed literature, Agamree has been medically proven to be effective and therefore, **medically appropriate** for the following:

1. Must be ≥ 2 years of age **AND**
2. Must be prescribed by or in consultation with a provider who specializes in the treatment of Duchenne Muscular dystrophy (DMD) and/or neuromuscular disorders **AND**
3. Must have a diagnosis of DMD with a confirmed mutation of the DMD gene **AND**
4. Must have had a trial of prednisone or deflazacort for ≥ 6 months (documentation required) and at least ONE of the following intolerable adverse effects:
    a. Decline in height percentile that involves crossing at least one of the major percentile curves (documentation required)
        i. Major percentile curves are defined as the 5th, 10th, 25th, 50th, 75th, 90th, and 95th percentile lines on CDC Clinical Growth Charts
            1. Patients with a baseline height under the 5th percentile will only require documentation of a significant decrease in height percentile **OR**
    b. Treatment emergent vertebral fractures (documentation required) **OR**
    c. Reduction in serum biomarkers of bone formation (osteocalcin, procollagen 1 intact N-terminal propeptide [PINP]) and bone turnover (type 1 collagen cross-linked C-telopeptide [CTX1]) (documentation required) **OR**
    d. Diabetes and/or hypertension that is unable to be managed **OR**
    e. Experienced unmanageable side effects that required hospitalization or significant clinical intervention at any point during prednisone therapy (a full 6-month trial is not required)
        i. Examples included steroid induced mania, sepsis, or severe behavioral changes which negatively impact school, home, etc.
5. Initial approval will be 12 months. Subsequent approvals for 12 months at a time will require documentation of a stabilization or slowing of decline in motor function, pulmonary function, or orthopedic outcomes as measured from pretreatment baseline status
6. The dose of Agamree must not exceed 6 mg/kg/day and must not exceed a total daily dosage of 300mg for patients weighing more than 50kg. Quantity will be limited to 100ml per 30 days
    a. Requests for additional quantity of Agamree liquid suspension will only be allowed for children aged whose weight warrants an increased quantity

AMONDYS 45

Based upon our assessment and review of the peer-reviewed literature, Amondys 45 has been medically proven to be effective and therefore, **medically appropriate** for the following:

1. Must have a diagnosis of DMD with a confirmed mutation of the DMD gene that is amenable to exon 45 skipping **AND**
2. Must be on a stable dose of corticosteroids for at least 6 months prior to therapy or a documented reason not to be on corticosteroids **AND**
3. Documentation must indicate kidney function testing prior to starting therapy **AND**
4. Patient must not concurrently be on another exon skipping therapy for DMD **AND**
5. Amondys 45 will not be approved for use in patients that have previously been treated with Elevidys **AND**
6. All the below criteria must be met (The below criteria are NOT applicable to **Medicaid Managed Care**)
    a. Prescribed by or in consultation with a provider who specializes in the treatment of Duchenne Muscular dystrophy (DMD) and/or neuromuscular disorders **AND**
    b. The patients must be ambulatory and must have a baseline unassisted 6-minute walk test (6MWT) of at least 300 meters **AND**
    c. Must have stable cardiac function with left ventricular ejection fraction (LVEF) of >40% **AND**
    d. Must have stable pulmonary function with forced vital capacity ≥ 50% of predicted and not require supplemental oxygen **AND**
    e. Dose must not exceed 30mg/kg infused over 35-60 minutes, once weekly **AND**
    f. Initial approval for new starts will be for 3 months. Continued approval in non-new starts for additional 6-month periods will require recent documentation that the patient continues to remain ambulatory with an unassisted 6MWT of at least 100 meters. In addition, the patient must meet the following criteria (Progress notes/test results must be dated after the most recent drug approval and within 3 months of the continuation period that is being requested):
        i. Must have stable cardiac function with left ventricular ejection fraction (LVEF) of >40% **AND**
        ii. Must have stable pulmonary function with forced vital capacity ≥ 50% of predicted and not require supplemental oxygen **AND**
        iii. Must have a < 5% annual decline in percent predicted FVC (FVC% p)

DUVYZAT

Based upon our assessment and review of the peer-reviewed literature, Duvyzat has been medically proven to be effective and therefore, **medically appropriate** for the following:

1. Must be ≥ 6 years of age **AND**
2. Must be prescribed by or in consultation with a provider who specializes in the treatment of Duchenne Muscular dystrophy (DMD) and/or neuromuscular disorders **AND**
3. Must have a diagnosis of DMD with a confirmed mutation of the DMD gene **AND**
4. Must be ambulatory upon initiation of therapy **AND**
5. Must be on baseline corticosteroids for 6 months with intention for ongoing concomitant use
6. Patients with any of the following will not be eligible for coverage (documentation, including laboratory results [taken within the past 3 months], is required):
    a. Platelet, white blood cell, or hemoglobin counts less than the lower limit of normal
    b. Triglycerides >300 mg/dL (3.42 mmol/L) in fasting condition
    c. Baseline-corrected QT interval, Fridericia's correction (QTcF) of >450 msec (mean of 3 consecutive readings 5 minutes apart) or a history of additional risk factors for torsades de pointes (e.g. heart failure, hypokalemia, or family history of long QT syndrome)
7. Duvyzat will not be covered in combination with exon-skipping therapies or prior use of Elevidys

8. Initial approval will be 12 months. Subsequent approvals for 12 months at a time will require documentation of a stabilization or slowing of decline in motor function and that patient remains ambulatory
9. The dose of Duvyzat must not exceed a total daily dosage of 106.4 mg for patients weighing more than 60kg. Quantity will be limited to 140 ml per 30 days.
10. Requests for additional quantity of Duvyzat will be approved for children whose weight warrants an increased quantity.

EMFLAZA, generic deflazacort, Jaythari, Kymbee, and Pyquvi

Based upon our assessment and review of the peer-reviewed literature, Emflaza and generic deflazacort has been medically proven to be effective and therefore, **medically appropriate** for the following:

1. Must be ≥ 2 years of age or older **AND**
2. Must be prescribed by or in consultation with a provider who specializes in the treatment of Duchenne Muscular dystrophy (DMD) and/or neuromuscular disorders **AND**
3. Must have a diagnosis of DMD with a confirmed mutation of the DMD gene **AND**
4. Must have had trial of prednisone for ≥ 6 months (documentation required) and at least ONE of the following intolerable adverse effects:
    a. Cushingoid appearance (documentation required) **OR**
    b. Central (truncal) obesity (documentation required) **OR**
    c. Undesirable weight gain defined as a ≥10% of body weight gain increase over a 6-month period (documentation required) **OR**
    d. Diabetes and/or hypertension that is unable to be managed **OR**
    e. Experienced unmanageable side effects that required hospitalization or significant clinical intervention at any point during prednisone therapy (a full 6-month trial is not required)
        i. Examples included steroid induced mania, sepsis, or severe behavioral changes which negatively impact school, home, etc.
5. Coverage of Jaythari, Kymbee, and Pyquvi may be considered only when the member has a documented, clinically significant hypersensitivity or serious adverse reaction attributable to an inactive ingredient in Emflaza or generic deflazacort that is absent from the requested product.
6. Initial approval will be 12 months. Subsequent approvals for 12 months at a time will require documentation of a stabilization or slowing of decline in motor function, pulmonary function, or orthopedic outcomes as measured from pretreatment baseline status
7. Quantity Limit
    a. Emflaza, deflazacort, Jaythari, and Kymbee: 30 tablets per 30 days
    b. Emflaza, deflazacort, and Pyquvi suspension: 30 mL per 30 days
    c. If tablets are used, dose should be rounded up to the nearest possible dose. If suspension is used, dose should be rounded up to the nearest tenth of a milliliter
    d. Requests for additional quantity of Emflaza liquid suspension will only be allowed for children aged 7 years and under whose weight warrants an increased quantity
        i. Children over 8 years of age will require documentation of an attempt and inability to swallow an oral pill (whole or crushed)

EXONDYS 51

Based upon our assessment and review of the peer-reviewed literature, Exondys 51 has been medically proven to be effective and therefore, **medically appropriate** for the following:

1. Must have a diagnosis of DMD with a confirmed mutation of the DMD gene that is amenable to exon 51 skipping **AND**
2. Must be on a stable dose of corticosteroids for at least 6 months prior to therapy or a documented reason not to be on corticosteroids **AND**
3. Patient must not concurrently be on another exon skipping therapy for DMD **AND**
4. Exondys 51 will not be approved for use in patients that have previously been treated with Elevidys **AND**
5. All the below criteria must be met (The below criteria is NOT applicable to **Medicaid Managed Care**)
    a. Prescribed by or in consultation with a provider who specializes in the treatment of Duchenne Muscular dystrophy (DMD) and/or neuromuscular disorders **AND**
    b. The patient must be ambulatory with a baseline unassisted 6-minutewalk test (6MWT) of at least 200 meters **AND**
    c. Must have stable cardiac function with left ventricular ejection fraction (LVEF) of >40% **AND**
    d. Must have stable pulmonary function with forced vital capacity ≥ 50% of predicted and not require supplemental oxygen **AND**
    e. Dose must not exceed 30mg/kg of body weight infused once weekly **AND**
    f. Initial approval for new starts will be for 3 months. Continued approval in non-new starts for additional 6-month periods will require documentation that the patient continues to remain ambulatory with an unassisted 6MWT of at least 100 meters. In addition, the patient must meet the following criteria (Progress notes/test results must be dated after the most recent drug approval and within 3 months of the continuation period that is being requested):
        i. Must have stable cardiac function with left ventricular ejection fraction (LVEF) of > 40% **AND**
        ii. Must have stable pulmonary function with forced vital capacity ≥ 50% of predicted and not require supplemental oxygen **AND**
        iii. Must have a < 5% annual decline in percent predicted FVC (FVC% p)

VILTEPSO

Based upon our assessment and review of the peer-reviewed literature, Viltepso has been medically proven to be effective and therefore, **medically appropriate** for the following:

1. Must have a diagnosis of DMD with a confirmed mutation of the DMD gene that is amenable to exon 53 skipping **AND**
2. Must be on a stable dose of corticosteroids for at least 3 months prior to therapy or a documented reason not to be on a corticosteroid **AND**
3. Documentation must indicate kidney function testing prior to starting therapy **AND**
4. Patient must not concurrently be on another exon skipping therapy for DMD **AND**
5. Viltepso will not be approved for use in patients that have previously been treated with Elevidys **AND**
6. All the below criteria must be met (The below criteria are NOT applicable to **Medicaid Managed Care**)
    a. Prescribed by or in consultation with a provider who specializes in the treatment of Duchenne Muscular dystrophy (DMD) and/or neuromuscular disorders **AND**
    b. The patients must be ambulatory and must have a baseline unassisted 6-minute walk test (6MWT) of at least 250 meters **AND**
    c. Must have stable cardiac function with left ventricular ejection fraction (LVEF) of >40% **AND**
    d. Must have stable pulmonary function with forced vital capacity ≥ 50% of predicted and not require supplemental oxygen **AND**
    e. Dose must not exceed 80mg/kg infused over 60 minutes, once weekly **AND**

f. Initial approval for new starts will be for 3 months Continued approval in non-new starts for additional 6-month periods will require recent documentation that the patients continue to be ambulatory with an unassisted 6MWT of at least 100 meters. In addition, the patient must meet the following criteria (Progress notes/test results must be dated after the most recent drug approval and within 3 months of the continuation period that is being requested):
   i. Must have stable cardiac function with left ventricular ejection fraction (LVEF) of >40% **AND**
   ii. Must have stable pulmonary function with forced vital capacity ≥ 50% of predicted and not require supplemental oxygen **AND**
   iii. Must have a < 5% annual decline in percent predicted FVC (FVC% p)

VYONDYS 53

Based upon our assessment and review of the peer-reviewed literature, Vyondys 53 has been medically proven to be effective and therefore, **medically appropriate** for the following:

1. Must have a diagnosis of DMD with a confirmed mutation of the DMD gene that is amenable to exon 53 skipping **AND**
2. Must be on a stable dose of corticosteroids for at least 6 months prior to therapy or a documented reason not to be on corticosteroids **AND**
3. Documentation must indicate kidney function testing prior to starting therapy **AND**
4. Patient must not concurrently be on another exon skipping therapy for DMD **AND**
5. Vyondys 53 will not be approved for use in patients that have previously been treated with Elevidys **AND**
6. All the below criteria must be met (The <u>below</u> criteria are NOT applicable to **Medicaid Managed Care**)
   a. Prescribed by or in consultation with a provider who specializes in the treatment of Duchenne Muscular dystrophy (DMD) and/or neuromuscular disorders **AND**
   b. The patient must be ambulatory must have a baseline unassisted 6-minutewalk test (6MWT) of at least 250 meters **AND**
   c. Must have stable cardiac function with left ventricular ejection fraction (LVEF) of >50% **AND**
   d. Must have stable pulmonary function with forced vital capacity ≥ 50% of predicted and not require supplemental oxygen **AND**
   e. Dose must not exceed 30 mg/kg infused IV over 35 to 60 minutes, once weekly
   f. Initial approval for new starts will be for 3 months. Continued approval in non-new starts for additional 6-month periods will require documentation that the patient continues to be ambulatory with an unassisted 6MWT of at least 100 meters. In addition, the patient must meet the following criteria (Progress notes/test results must be dated after the most recent drug approval and within 3 months of the continuation period that is being requested):
      i. Must have stable cardiac function with left ventricular ejection fraction (LVEF) of >50% **AND**
      ii. Must have stable pulmonary function with forced vital capacity ≥ 50% of predicted and not require supplemental oxygen **AND**
      iii. Must have a < 5% annual decline in percent predicted FVC (FVC% p)

<u>POLICY GUIDELINES</u>:

1. Amondys 45, Exondys 51, Vyondys 53, and Viltepso are administered as an IV infusion and will be covered under the medical benefit. Duvyzat, Emflaza, generic deflazacort and Agamree are self-administered oral medications and will be covered under the pharmacy benefit.
2. Amondys 45, Exondys 51, Vyondys 53 and Viltepso will not be approved for patients who have lost ambulation or who have LVEF or FVC% predicted test results that indicate severe decompensation. These medications have only been evaluated in ambulatory patients, and it is unknown if patients with more advanced disease and greater muscle deterioration would receive any benefit with

treatment. Pivotal studies do not provide adequate support to determine if the drug provides clinical benefit related to cardiac and respiratory complications, which can lead to morbidity and mortality in DMD. (Not applicable to **Medicaid Managed Care**)

3. Continued approval at time of recertification will require documentation via current progress notes (dated after the most recent drug approval and within 3 months of the continuation period that is being requested) that the drug is providing ongoing benefit to the patient in terms of improvement or stability in disease state or condition and meets all other criteria under the policy. Such documentation may include progress notes, imaging or laboratory findings, and other objective or subjective measures of benefit which support that continued use of the requested product is medically necessary. Also, ongoing use of the requested product must continue to reflect the current policy's preferred formulary. Recertification reviews may result in the requirement to try more cost-effective treatment alternatives as they become available (i.e., generics, biosimilars, or other guideline-supported treatment options). Requested dosing must continue to be consistent with FDA-approved or off-label/guideline-supported dosing recommendations.
4. This policy does not apply to Medicare Part D and D-SNP pharmacy benefits. The drugs in this policy may apply to all other lines of business including Medicare Advantage.
5. For members with Medicare Advantage, medications with a National Coverage Determination (NCD) and/or Local Coverage Determination (LCD) will be covered pursuant to the criteria outlined by the NCD and/or LCD. NCDs/LCDs for applicable medications can be found on the CMS website at https://www.cms.gov/medicare-coverage-database/search.aspx. Indications that have not been addressed by the applicable medication's LCD/NCD will be covered in accordance with criteria determined by the Health Plan (which may include review per the Health Plan's Off-Label Use of FDA Approved Drugs policy). Step therapy requirements may be imposed in addition to LCD/NCD requirements.
6. All requests will be reviewed to ensure they are being used for an appropriate indication and may be subject to an off-label review in accordance with our Off-Label Use of FDA Approved Drugs Policy (Pharmacy-32).
7. All utilization management requirements outlined in this policy are compliant with applicable New York State insurance laws and regulations. Policies will be reviewed and updated as necessary to ensure ongoing compliance with all state and federally mandated coverage requirements.
8. Manufacturers may either discontinue participation in, or may not participate in, the Medicaid Drug Rebate Program (MDRP). Under New York State Medicaid requirements, physician-administered drugs must be produced by manufacturers that participate in the MDRP. Products made by manufacturers that do not participate in the MDRP will not be covered under Medicaid Managed Care/HARP lines of business. Drug coverage will not be available for any product from a non-participating manufacturer. For a complete list of New/Reinstated & Terminated Labelers please visit: https://www.medicaid.gov/medicaid/prescriptiondrugs/medicaid-drug-rebate-program/newreinstated-terminated-labeler-information/index.html

CODES:

Eligibility for reimbursement is based upon the benefits set forth in the member's subscriber contract.

CODES MAY NOT BE COVERED UNDER ALL CIRCUMSTANCES. PLEASE READ THE POLICY AND GUIDELINES STATEMENTS CAREFULLY.

Codes may not be all inclusive as the AMA and CMS code updates may occur more frequently than policy updates.

HCPCS:

J1426 Amondys 45
J1428 Exondys 51
J1427 Viltepso
J1429 Vyondys 53

UPDATES:

Date	Revision
11/20/2025	Revised
11/19/2025	Revised
11/13/2025	P&T Committee Review & Approval
03/06/2025	Revised
11/21/2024	P&T Committee Review & Approval
08/27/2024	Revised
07/02/2024	Revised
06/20/2024	Revised
05/28/2024	Revised
04/01/2024	Revised
03/14/2024	Revised
01/02/2024	Revised
11/30/2023	P&T Committee Review & Approval
9/22/2022	P&T Committee Review & Approval
3/31/2022	Revised
12/3/2021	Revised
9/16/2021	P&T Committee Review & Approval
6/15/2021	Revised
5/6/2021	P&T Committee Review & Approval
4/15/2021	Revised
1/29/2021	Revised
9/16/2020	P&T Committee Review & Approval
9/3/2020	Revised
7/1/2020	Revised
2/20/2020	Revised
12/30/2019	Created

REFERENCES:

1. Sarepta Therapuetics, Inc. Exondys 51 Package Insert; September 2016
2. Mendell J, Goemans Nathalie, Lowes Linda, et al. Longitudinal Effect of Etiplirsen versus Historical Control on Ambulation in Duchenne Muscular Dystrophy. *Ann Neurol.* 2016;79:257-271
3. Annexstad EJ, Lund-Petersen I, Rasmussen M. Duchenne muscular dystrophy. *Tidsskr Nor Laegeforen.* 2014;134(14)1361-1364
4. Wood MJA. To skip or not to skip: that is the question for Duchenne muscular dystrophy. *Mol Ther*. 2013; 21(12)2131-2132
5. Bushby K, Finkel R, Birnkrant DJ, et al. Diagnosis and management of Duchenne muscular dystrophy, part 1: diagnosis, and pharmacological and psychosocial management. *Lancet Neurol.* 2010;9(1):77-93

6. Sarepta Therapuetics, Inc. Vyondys 53 Package Insert; December 2019
7. FDA Grants Accelerated Approval to First Targeted Treatment for Rare Duchenne Muscular Dystrophy Mutation. Pharmacy Times. https://www.pharmacytimes.com/news/fda-grants-accelerated-approval-to-first-targeted-treatment-for-rare-duchenne-muscular-dystrophy-mutation. Published 2019. Accessed December 19, 2019.
8. Phase I/II Study of SRP-4053 in DMD Patients (2019). Retrieved from https://clinicaltrials.gov/ct2/show/study/NCT02310906 (Identification No. NCT02310906)
9. Product Information: VYONDYS 53(TM) intravenous injection, golodirsen intravenous injection. Sarepta Therapeutics Inc (per FDA), Cambridge, MA, 2019.
10. Kinane T, Mayer O, Duda P, et al. Long-Term Pulmonary Function in Duchenne Muscular Dystrophy: Comparison of Eteplirsen-Treated Patients to Natural History. *Journal of Neuromuscular Diseases.* 2018; 5: 47-58
11. Khan N, Eliopoulos H, Han L, et al. Eteplirsen treatment attenuates respiratory decline in ambulatory and non-ambulatory patients with duchenne muscular dystrophy. *J Neuromuscul Dis.* 2019;6(2):213-225.
12. Mayer OH, Finkel RS, Rummey C, Benton MJ, Glanzman AM, Flickinger J, Lindstrom BM, Meier T. Characterization of pulmonary function in Duchenne muscular dystrophy. *Pediatr Pulmonol.* 2015;50(5):487–94
13. NS Pharmaa, Inc. Viltepso Package Insert; August 2020
14. Sarepta Therapuetics, Inc. Amondys 45 Package Insert; Februrary 2021
15. Study of SRP-4045 and SRP-4053 in DMD Patients (ESSENCE). Retrieved from https://clinicaltrials.gov/ct2/show/NCT02500381 (Identification No. NCT02500381)
16. PTC Therapuetics, Inc. Emflaza Package Insert; July 2020
17. Gloss D, Moxley R, Ashwal S, et al. Practice guideline update summary: Corticosteroid treatment of Duchenne muscular dystrophy. *Neurology* 2016; 86 :465-472
18. McDonald C, Henricson E, Abresch R, et al. Long-term effects of glucocorticoids on function, quality of life, and survival in patients with Duchenne muscular dystrophy: a prospective cohort study. Lancet 2018: 391 (10119):451-461
19. Catalyst Pharmaceueticals, Inc. Agamree Package Insert; March 2024
20. ITF Therapeutics, LLC Duvyzat Package Insert; March 2024