Medica (formerly WellFirst Health)

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☒ Commercial (Small & Large Group) ☒ ASO ☒ Exchange/ACA
☐ Medicare Advantage (MAPD)

Vyondys 53 (golodirsen), Exondys 51 (eteplirsen), Viltepso (viltolarsen), Amondys (casimersen), Elevidys (delandistrogene moxeparvovec-rokl)

MB2118

Covered Service:	NO
Prior Authorization Required:	NO
Additional Information:	Prescribed by (or in consultation with) Neurologist specialists with prior authorization through The Plan Pharmacy Services.
Medicare Policy:	Prior authorization is not required for Medicare Cost products (Dean Care Gold) and Medicare Supplement (Select) when this drug is provided by participating providers. Prior authorization is required if a member has Medicare primary and the plan secondary coverage. This policy is not applicable to our Medicare Replacement products.
Wisconsin Medicaid Policy	Coverage of prescription drug benefits is administered by the Wisconsin Medicaid program. Coverage of medical drug benefits is administered by the Wisconsin Medicaid fee-for-service program. Medical drugs not paid on a fee-for-service basis by the Wisconsin Medicaid program are covered by the plan with no PA required.

1.0 FDA Indication

1.1 Eteplirsen

1.1.1 Eteplirsen (Exondys 51™; Sarepta Therapeutics) was approved by the U.S. Food and Drug Administration under the orphan drug designation for DMD patients who have a confirmed variant of the DMD gene that is amenable to exon 51 skipping. This indication was approved with a fast track designation

based on an increase in a surrogate endpoint marker, dystrophin, found in skeletal muscle and observed in some patients treated with eteplirsen.

1.2 Golodirsen

1.2.1 Golodirsen (Vyondys™; Sarepta Therapeutics) was approved by the U.S. Food and Drug Administration under a New Drug Application (NDA) seeking accelerated approval for DMD patients who have a confirmed variant of the DMD gene that is amenable to exon 53 skipping. This indication was approved with a fast track designation based on an increase in a surrogate endpoint marker, dystrophin, found in skeletal muscle and observed in some patients treated with golodirsen.

1.3 Viltolarsen (Viltepso)

1.3.1 Viltoarsen; (Viltepso™, NS Pharma) was approved under the accelerated approval by the U.S. Food and Drug Administration under accepted the New Drug Application (NDA) seeking accelerated approval for viltolarsen for DMD patients who have a confirmed variant of the DMD gene that is amenable to exon 53 skipping. This indication was approved with a fast track designation based on an increase in a surrogate endpoint marker, dystrophin, found in skeletal muscle and observed in some patients treated with Viltolarsen.

1.4 Casimersen (Amondys)

1.4.1 Casimersen; (Amondys™, NS pharma) was approved under the accelerated approval by the U.S. Food and Drug Administration under accepted the New Drug Application (NDA) seeking accelerated approval for casimersen for DMD patients who have a confirmed variant of the DMD gene that is amenable to exon 54 skipping. This indication was approved with a fast track designation based on an increase in a surrogate endpoint marker, dystrophin, found in skeletal muscle and observed in some patients treated with Viltolarsen

1.5 Delandistrogene moxeparvovec-rokl (Elevidys)

1.5.1 Elevidys: On June 22, 2023, the U.S. Food and Drug Administration (FDA) granted accelerated approval to Sarepta Therapeutics' Elevidys (delandistrogene moxeparvovec-rokl) for the treatment of ambulatory pediatric patients 4 through 5 years of age with Duchenne muscular dystrophy (DMD) with a confirmed mutation in the DMD gene. The accelerated approval was based on the expression of Elevidys micro-dystrophin observed in patients treated with Elevidys. Elevidys did not demonstrate a statistically significant treatment effect on functional outcomes; however, an exploratory subgroup analysis of the 16 participants (Elevidys: n = 8; placebo: n = 8) 4 through 5 years of age showed a numerical advantage for Elevidys compared to placebo in the change in North Star Ambulatory Assessment (NSAA) total score.

1.6 Institute for Clinical and Economic Review (ICER)[14]:

1.6.1 In August 2019, ICER released guidance on DMD treatment. In this review, the following clinical determinations were made regarding eteplirsen and golodirsen (viltolarsen was not FDA-approved at the time):

1.6.1.1 Eteplirsen, Viltoarsen, Casimersen, and Golodirsen treatment results in very small increases in dystrophin, but the clinical significance of these small increases is unknown

1.6.1.2 Functional outcomes cannot be compared for these drugs because golodirsen did not report functional outcomes.

1.6.1.3 Neither drug has demonstrated concerning safety issues, but this may be misleading due to the small populations involved in clinical trials and limited follow-up data.

1.6.1.4 Data for these drugs is insufficient.

1.7 Treatment Guidelines/Consensus statements:

1.7.1 The US Centers for Disease Control and Prevention: Diagnosis and management of DMD (updated in 2018)[12]

1.7.1.1 Start treatment as soon as possible:

1.7.1.2 Physical therapy and glucocorticoids are first-line and should be continued beyond loss of ambulation

1.7.1.3 Prednisone 0.75 mg/kg per day or deflazacort 0.9 mg/kg per day

1.7.2 The American Academy of Neurology guideline on corticosteroid treatment of DMD (reaffirmed in 2019)[13]

1.7.2.1 Prednisone to improve strength and pulmonary function (Level B) 0.75 mg/kg per day (Level B) or 10 mg/kg per weekend (Level B)

1.7.2.2 Deflazacort to improve strength, timed motor function, and delay loss of ambulation by 1.4 to 2.5 years (Level C)

2.0 Policy / Criteria:

2.1 Vyondys 53™ is considered not covered due to insufficient evidence to demonstrate clinical efficacy for treatment of DMD in patients who have a confirmed mutation of the DMD gene that is amenable to exon 53 skipping based on all of the following:

2.1.1 Vyondys 53™ was approved based on an observed increase in dystrophin in skeletal muscle,[1] but it is unknown if that increase is clinically significant. Currently there is no clear threshold for the amount of dystrophin increase required to produce clinical benefit. Previous research has suggested dystrophin levels of at least 20-29% of normal are needed to avoid muscular

dystrophy, and levels of at least 10% of normal can produce a more mild form of dystrophy. [2,3] At week 48 of Vyondys 53's pivotal study (Study 4053-US-101, NCT02310906, a 168-week two part (Part 1 randomized double-blind; Part 2 Open-label) trial; N=25), golodirsen treated patients had a mean percent dystrophin protein of 1.019% of normal per Western blot analysis. The mean change from baseline in dystrophin protein levels after 48 weeks of treatment was 0.924%. [1]

2.1.2 True clinical benefit has not been established based the following:

2.1.2.1 The evaluation of the co-primary endpoint evaluating the change from baseline in the total distance walked during 6MWT at Week 144 is not available. [1]

2.1.2.2 The design of the study had a small sample size, variability in the DMD disease course, an open-label trial design, and the known limitations with historical control groups for comparison.

2.2 Exondys 51™ is considered not covered due to insufficient evidence to demonstrate clinical efficacy for treatment for DMD in patients who have a confirmed mutation of the DMD gene that is amenable to exon 51 skipping based on the following (all of the following)

2.2.1 Exondys was approved based on an observed increase in dystrophin in skeletal muscle, but it is unknown if that increase is clinically significant. Currently there is no clear threshold for the amount of dystrophin increase required to produce clinical benefit. Previous research has suggested dystrophin levels of at least 20-29% of normal are needed to avoid muscular dystrophy, and levels of at least 10% of normal can produce a more mild form of dystrophy.[2,3] In Study 202 of Exondy's studies, mean change from baseline of dystrophin levels at 180 weeks was 0.93%(compared to external control) and in study 301, it was 0.28% (p=0.008). [6,7,8,9]

2.2.2 True clinical benefit has not been established based the following:

2.2.2.1 The evaluation of the co-primary endpoint in Study 201 when evaluating the change from baseline in the total distance walked during 6MWT at Week 24 (n=6) the mean change in placebo was –25.8±30.6, mean change in 30 mg/kg/wk group was –128.2±31.2 m (NS compared to placebo), and mean change in 50 mg/kg/wk group was –0.3±31.2 m (p≤0.016 compared to placebo). Two patients out of 6 had very large 6MWT decreases and were considered outliers by the investigators and were removed from results.[8,10]

2.2.2.2 The design of the study had a small sample size, variability in the DMD disease course, an open-label trial design, and no correlation between dystrophin levels was determined by Western blot and clinical outcome.

2.3 Viltolarsen™ is considered not covered due to insufficient evidence to demonstrate clinical efficacy for treatment for DMD in patients who have a confirmed mutation of the DMD gene that is amenable to exon 53 skipping based on the following (all of the following)

2.3.1 Viltolarsen was approved based on an observed increase in dystrophin in skeletal muscle, but it is unknown if that increase is clinically significant. Currently there is no clear threshold for the amount of dystrophin increase required to produce clinical benefit. Previous research has suggested dystrophin levels of at least 20-29% of normal are needed to avoid muscular dystrophy, and levels of at least 10% of normal can produce a more mild form of dystrophy.[2,3] In clinical Vitlepso study, n=32 showed a mean increased dystrophine 5.9% of normal versus 0.6% at baseline.[11]

2.3.2 True clinical benefit has not been established based the following:

2.3.2.1 The evaluation of the primary and key secondary endpoints in study when evaluating the change from baseline demonstrated statistically significant improvements in dystrophin levels, time to stand from supine, time to run/walk and 6 minute walk test. Although the motor function test results do not appear to be clinically significant, it is important to note that times were stable or improved for all viltarolsen groups while the CINRG DNHS comparator group continuously saw reduced motor function.[11]

2.3.2.2 The design of the study had a small sample size, variability in the DMD disease course, an open-label trial design, and no correlation between dystrophin levels was determined by Western blot and clinical outcome.

2.4 Casimersen™ is considered not covered due to insufficient evidence to demonstrate clinical efficacy for treatment for DMD in patients who have a confirmed mutation of the DMD gene that is amenable to exon 54 skipping based on the following (all of the following)

2.4.1 Casimersen was approved based casimersen was based on the interim results from 43 patients in ESSENCE, a randomized, double-blind, placebo-controlled, phase III trial.1 The study enrolled ambulatory patients, age 7 to 13 years, with mutations that were amenable to exon 45 skipping and who were stable on steroid therapy for at least six months. Additionally, patients were only included if they had stable pulmonary function, which was defined as a forced vital capacity (FVC) of greater than or equal to 50% predicted, and a 6-Minute Walk Time between 300 meters and 450 meters. Patients were randomized 2:1 to receive either casimersen 30mg/kg or placebo. Interim efficacy was assessed based on the change from baseline to week 48 in dystrophin protein level. Dystrophin protein levels were measured via muscle biopsy and were reported as a percent of the dystrophin level of health subjects (percent of normal levels). The patients who received

casimersen showed a statistically greater increase in dystrophin protein levels in skeletal muscle compared to patients in the placebo group. ESSENCE is ongoing (expected completion 2024) and further data is needed to establish a clinical benefit (i.e. improved motor function) for casimersen

2.4.2 True clinical benefit has not been established based the following:

2.4.2.1 The evaluation of study was assessed based on the change from baseline at 48 weeks demonstrated statistically significant improvements in dystrophin levels, but failed to establish a clinical benefit with member 6 minute walk test or stable FVC.

2.4.2.2 The design of the study had a small sample size, including only patients with stable ambulation and stable pulmonary functions tests and were stable on steroid therapy.

2.5 Elevidys is considered not covered due to insufficient evidence to demonstrate clinical efficacy for treatment for DMD in patients who have a confirmed mutation of the DMD gene based on the following (all of the following):

2.5.1 The clinical effectiveness of Elevidys is uncertain. Elevidys increased the expression of the micro-dystrophin protein observed in patients 4–7 years of age with DMD. Study 102 did not demonstrate a statistically significant treatment effect on NSAA total scores. However, an exploratory subgroup analysis of the 16 participants 4 through 5 years of age showed a numerical advantage for Elevidys compared to placebo in the change in NSAA total score. Conversely, subgroup analysis of the 24 participants 6 through 7 years of age showed a numerical disadvantage for Elevidys compared to placebo in the change in NSAA total score.

2.5.2 There are also significant safety concerns with the administration of the gene therapy, including acute serious liver injury, immune-mediated myositis, and myocarditis. Additionally, as an AAV vector-based gene therapy, treatment with Elevidys would prevent patients from later receiving another AAV-based therapy due to immunogenicity.

2.5.3 Clinical trials have not provided much insight into the long-term durability of gene therapy in DMD. Study 101, a Phase 1/2, open-label, safety and proof-of-concept study in four ambulatory boys 4–7 years of age, has provided functional data for up to 4 years. The LS mean change from baseline in NSAA total score over 4 years was 9.4 (P = 0.0125) in the Elevidys group compared to a propensity-score weighted external control. However, given the small number of participants and the heterogeneity of the disease, it is difficult to draw conclusions regarding durability based upon the data available at this time.

3.0 Policy Rationale

3.1 The clinical benefit of Vyondys, Exondys, Vitelpso, Amondys, or Elevidys for the treatment of DMD has not been established based on Practice and Consensus guidelines, ICER and each drug clinical studies. Today, it is not clear if there are clinically significant benefits to any of the DMD drugs**.**

3.2 Practice and Consensus Guidelines have not been updated to include any of the four FDA approved therapies was insufficient.

3.3 Surrogate Endpoint Definition - A surrogate endpoint is a marker, such as a laboratory measurement, radiographic image, physical sign or other measure that is thought to predict clinical benefit, but is not itself a measure of clinical benefit. Therefore, the accelerated FDA approval required a confirmatory trial to confirm or refute a clinical benefit.

Comment(s):

1.0 *Codes and descriptors listed in this document are provided for informational purposes only and may not be all inclusive or current. Listing of a code in this drug policy does not imply that the service described by the code is a covered or non-covered service. Benefit coverage for any service is determined by the member's policy of health coverage with the plan. Inclusion of a code in the table does not imply any right to reimbursement or guarantee claim payment. Other drug or medical policies may also apply.

1.1 NDC and HCPCS codes

Medication Name		How Supplied	National Drug Code (NDC)	HCPCS code
Brand	Generic			
Vyondys 53	golodirsen	100 MG/2ML	60923-0465-02	J1429
Exondys 51	eteplirsen	100 MG/2ML 500 MG/10ML	60923-0363-02 60923-0284-10	J1428
Viltepso	viltolarsen	250 MG/5ML	73292-0011-01	J1427
Amondys	Casimersen	100mg/2ml	60923-0227-02	J1426
Elevidys	delandistrogene moxeparvovec-rokl	10mL vials	various	J1413

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References:

1. Vyondys 53 Prescribing Information. Cambridge, MA: Sarepta Therapeutics, Inc.; December 2019. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2019/211970s000lbl.pdf. Accessed January 2, 2020.
2. Chamberlain JS. Dystrophin levels required for genetic correction of Duchenne muscular dystrophy. Basic Apply. Myol. 1997; 7(3&4): 251-255.
3. Neri M, Torelli S, Brown S, et al. Dystrophin levels as low as 30% are sufficient to avoid muscular dystrophy in the human. Neuromuscul Disord. 2007; doi:10.1016/j.nmd.2007.07.005.
4. Institute for Clinical and Economic Review. Deflazacort, eteplirsen, and golodirsen for Duchenne muscular dystrophy: Effectiveness and value. Published August 15, 2019.

Available at: https://icer-review.org/material/dmd-final-evidence-report/. Accessed October 7, 2019.
5. Muscular Dystrophy Association (MDA). Duchenne Muscular Dystrophy. https://www.mda.org/disease/duchenne-muscular-dystrophy/overview. Accessed July 2019.
6. Clinicaltrials.gov. NCT02310906. https://clinicaltrials.gov/ct2/show/NCT02310906?term=NCT02310906&rank=1. Accessed July 2019.
7. Exondys 51 (package insert). Cambridge, MA. Sarepta Pharmaceuticals; 2016
8. Ann Neurol. 2013 Nov;74(5):637-47. doi: 10.1002/ana.23982
9. Ann Neurol. 2016 Feb; 79(2): 257–271. doi: 10.1002/ana.24555
10. ClinicalTrials.gov NCT01396239, NCT01540409, NCT02255552
11. Viltepso [prescribing information]. Paramus, NJ: NS Pharma, Inc.; November 2020
12. Birnkrant DJ, Bushby K, Bann CM, et al. Diagnosis and management of Duchenne muscular dystrophy, part 1: diagnosis, and neuromuscular, rehabilitation, endocrine, and gastrointestinal and nutritional management. Lancet Neurol. 2018;17(3):251-267.
13. Gloss D, Moxley RT, Ashwal S, Oskoui M. Practice guideline update summary: corticosteroid treatment of Duchenne muscular dystrophy: report of the Guideline Development Subcommittee of the American Academy of Neurology. Neurology. 2016;86(5):465-472
14. Lin GA, Koola C, Agboola F, et al. Deflazacort, eteplirsen, and golodirsen for Duchenne muscular dystrophy: effectiveness and value. Institute for Clinical and Economic Review, August 15, 2019. Available at: https://icer.org/wp-content/uploads/2020/10/ICER_DMD-Final-Report_081519-2-1.pd
15. Amondys 45 [prescribing information]. Cambridge, MA: Sarepta Therapeutics Inc; February 2021