

# SmartPA Criteria Proposal

<b>Drug/Drug Class:</b>	Duchenne Muscular Dystrophy (DMD) Clinical Edit
<b>First Implementation Date:</b>	February 6, 2020
<b>Proposed Date:</b>	December 17, 2020
<b>Prepared for:</b>	MO HealthNet
<b>Prepared by:</b>	MO HealthNet/Conduent
<b>Criteria Status:</b>	<input type="checkbox"/> Existing Criteria <input checked="" type="checkbox"/> Revision of Existing Criteria <input type="checkbox"/> New Criteria

## Executive Summary

**Purpose:** Ensure appropriate utilization and control of agents for Duchenne Muscular Dystrophy (DMD)

**Why Issue Selected:** Duchenne muscular dystrophy (DMD) is a fatal, X-linked recessive neuromuscular disorder caused by pathogenic variants in the dystrophin gene; these variants lead to absent or insufficient functional dystrophin, a cytoskeletal protein which enables the strength, stability, and functionality of myofibers. The absence or lack of dystrophin results in muscle degradation and scarring, leading to muscle weakness, associated motor delays, loss of ambulation, respiratory impairment, and cardiomyopathy. DMD is the most common pediatric muscular dystrophy, with a prevalence of 1 in 3,500 to 5,000 live male births (about 400-600 boys per year in the US); rarely females who are carriers may be symptomatic. Although the clinical course may vary, death usually occurs as a result of cardiac or respiratory compromise.

Emflaza<sup>®</sup> (deflazacort), an oxazoline derivative of prednisone, was FDA approved in February 2017, and is currently indicated to treat DMD in patients 2 years of age and older. Emflaza is a corticosteroid that works by decreasing inflammation and reducing the activity of the immune system. Prednisone, although it is not FDA approved for the indication, is also frequently prescribed for DMD. Long term steroid therapy has shown benefits in treating DMD, including loss of ambulation at a later age, preserved upper limb and respiratory function, and avoidance of scoliosis surgery. The benefit-to-risk ratio of Emflaza compared to prednisone is being further studied at this time. The Duchenne Muscular Dystrophy Care Considerations committee noted in 2018 that compared to prednisone, Emflaza may increase the risk of growth delay and cataracts and lower the risk for weight gain and behavioral problems.

Exondys 51<sup>®</sup> (eteplirsen) was FDA approved in September 2016, via an accelerated pathway, for the treatment of DMD in patients who have a confirmed mutation of the DMD gene that is amenable to exon 51 skipping (approximately 13% of the DMD population). Vyondys 53<sup>®</sup> (golodirsen), FDA approved in December 2019, and Viltepso<sup>®</sup> (viltolarsen), FDA approved in August 2020, are both indicated for the treatment of DMD in patients who have a confirmed mutation of the DMD gene that is amenable to exon 53 skipping (approximately 8% of the DMD population). In clinical trials, it appears that Viltepso helps patients produce more dystrophin than Vyondys 53. All 3 agents are antisense oligonucleotides delivered by a once weekly IV infusion. Although patients receiving either Exondys 51, Vyondys 53, or Viltepso had an increase in dystrophin in

skeletal muscle, a clinical benefit of this increase has not been established; continued FDA approval may be contingent upon verification of a clinical benefit in a confirmatory trial.

Program-Specific Information:	Date Range FFS 10-01-2019 to 9-30-2020			
	Drug	Claims	Spend	Cost per unit (MAC)
	EMFLAZA 22.75 MG/ML SUSP	0	-	\$303.83 per ml
	EMFLAZA 6 MG TABLET	0	-	\$59.95 per tab
	EMFLAZA 18 MG TABLET	6	\$29,733.66	\$179.87 per tab
	EMFLAZA 30 MG TABLET	41	\$211,904.13	\$299.80 per tab
	EMFLAZA 36 MG TABLET	18	\$164,146.39	\$334.08 per tab
	EXONDYS 51 100 MG/2 ML VIAL	169	\$992,702.02	\$800.00 per ml
	EXONDYS 51 500 MG/10 ML VIAL	219	\$11,108,702.07	\$800.00 per ml
	VILTEPSO 250 MG/5 ML	0	-	\$282.00 per ml
	VYONDYS 53 100 MG/2 ML VIAL	0	-	\$800.00 per ml

Drug	Dose based on a 25kg participant	Cost per month (MAC)
EMFLAZA SUSP (dose = 22.5 mg/day)	22.75 mg daily (2 bottles of 13 ml)	\$7,899.69 per 26 days
EMFLAZA TABLETS (dose = 22.5 mg/day)	18 mg tab daily	\$5,396.15 per 30 days
	24 mg daily (18 mg tab + 6 mg tab)	\$7,194.82 per 30 days
EXONDYS 51	750 mg once weekly (3 of 2 ml vials + 10 ml vial)	\$51,200.00 per 28 days
VILTEPSO	2,000 mg once weekly (8 of 5 ml vials)	\$45,120.00 per 28 days
VYONDYS 53	750 mg once weekly (8 of 2 ml vials)	\$51,200.00 per 28 days

- Type of Criteria:  Increased risk of ADE  Preferred Drug List  
 Appropriate Indications  Clinical Edit
- Data Sources:  Only Administrative Databases  Databases + Prescriber-Supplied

## Setting & Population

- Drug class for review: Agents for the treatment of Duchenne Muscular Dystrophy (DMD)
- Age range: All appropriate MO HealthNet participants aged 2 years and older

## Approval Criteria

- Documented diagnosis of Duchenne Muscular Dystrophy (DMD) confirmed by:
  - genetic testing for dystrophin gene deletion or duplication **OR**
  - genetic sequencing screening for mutations attributed to DMD **OR**
  - positive muscle biopsy showing absence of dystrophin protein **AND**
- Prescribed by or in consultation with a neurologist or other appropriate specialist **AND**
- Documentation of baseline clinical criteria (ex: BMI, weight, ambulatory status, 6-minute walk test (6MWT), North Star Ambulatory Assessment (NSAA), Brooke Upper Extremity Function Scale, Forced Vital Capacity (FVC), GFR, ejection fraction) **AND**
- For Emflaza:

### SmartPA Clinical Proposal Form

© 2020 Conduent Business Services, LLC. All rights reserved. Conduent™ and Conduent Design™ are trademarks of Conduent Business Services, LLC in the United States and/or other countries.

Other company trademarks are also acknowledged.

- Age ≥ 2 years or older **AND**
- Dosed at 0.9mg/kg/day, rounding up to the nearest possible dose **AND**
- Documentation of adequate trial and therapy failure, intolerance, or significant weight gain while on prednisone at a therapeutic dose (at least 0.75mg/kg/day or 10mg/kg/weekend)
  - Adequate trial defined as ≥ 6 months of prednisone therapy
  - Intolerance defined as Cushingoid appearance, central (truncal) obesity, diabetes and/or hypertension that is difficult to manage, or behavioral adverse effect
  - Significant weight gain defined as 1 standard deviation above baseline percentile rank weight for height OR ≥ 10% body weight gain over a 6 month period
- Approval for 6 months, renewal requests must provide documentation of clinical benefit
  - Improvement, stabilization, **or less than expected decline in disease progression** of motor, pulmonary, or cardiac function from baseline (ex: 6MWT, NSAA, Brooke Upper Extremity Scale, FVC, ejection fraction) **AND**
  - Documentation that adverse events associated with prednisone therapy were resolved through treatment with Emflaza
- For Exondys 51:
  - Age ≥ 4 years and ≤ 19 years **AND**
  - Genetic testing to confirm pathogenic variant of DMD gene amenable to exon 51 skipping **AND**
  - Dosed at 30 mg/kg once weekly **AND**
  - Documentation of concurrent prednisone or deflazacort therapy, defined as 6 months in the past 9 months
  - Approval for 6 months, renewal requests must provide documentation of clinical benefit
    - Improvement, stabilization, **or less than expected decline in disease progression** of motor, pulmonary, or cardiac function from baseline (ex: 6MWT, NSAA, Brooke Upper Extremity Scale, FVC, ejection fraction) **AND**
    - Participant retains meaningful voluntary motor function (ex: participant is able to speak, manipulate objects using upper extremities, ambulate)
- For Vyondys 53 **and Viltepso**:
  - **Age ≥ 4 years and ≤ 19 years AND**
  - **For Viltepso: Dosed at 80 mg/kg once weekly**
  - For Vyondys 53:
    - Dosed at 30 mg/kg once weekly **AND**
    - **Documentation of clinical reason why participant cannot take Viltepso**
  - Genetic testing to confirm pathogenic variant of DMD gene amenable to exon 53 skipping **AND**
  - Documentation of concurrent prednisone or deflazacort therapy, defined as 6 months in the past 9 months
  - Approval for 6 months, renewal requests must provide documentation of clinical benefit
    - Improvement, stabilization, **or less than expected decline in disease progression** of motor, pulmonary, or cardiac function from baseline (ex: 6MWT, NSAA, Brooke Upper Extremity Scale, FVC, ejection fraction) **AND**
    - Participant retains meaningful voluntary motor function (ex: participant is able to speak, manipulate objects using upper extremities, ambulate) **AND**
    - Documentation of monthly monitoring for proteinuria < 2+ **AND**
    - Documentation of **appropriate monitoring for renal function** every three months

## Denial Criteria

- Therapy will be denied if all approval criteria are not met

## Required Documentation

Laboratory Results:  
MedWatch Form:

X

Progress Notes:  
Other:

X
X

SmartPA Clinical Proposal Form

© 2020 Conduent Business Services, LLC. All rights reserved. Conduent™ and Conduent Design™ are trademarks of Conduent Business Services, LLC in the United States and/or other countries.

Other company trademarks are also acknowledged.

## Disposition of Edit

Denial: Exception code “0682” (Clinical Edit)  
Rule Type: CE

## Default Approval Period

6 months

## References

- Exondys 51 (eteplirsen) [package insert]. Cambridge, MA: Sarepta Therapeutics, Inc.; October 2018.
- Emflaza (deflazacort) [package insert]. South Plainfield, NJ: PTC Therapeutics, Inc.; June 2019.
- Vyondys 53 (golodirsen) [package insert]. Cambridge, MA: Sarepta Therapeutics, Inc.; December 2019.
- Viltepso (viltolarsen) [package insert]. Paramus, NJ: NS Pharma, Inc.; August 2020.
- IPD Analytics. New Drug Review: Viltepso (viltolarsen). August 2020.
- IPD Analytics. New Drug Review: Vyondys 53 (golodirsen). December 2019.
- IPD Analytics. CNS: Duchenne Muscular Dystrophy. Accessed June 25, 2019.
- IPD Analytics. Emflaza (deflazacort)/Marathon: Summary of issues and management in patients with DMD. February 2017.
- Institute for Clinical and Economic Review (ICER). Deflazacort, Eteplirsen, and Golodirsen for Duchenne Muscular Dystrophy: Effectiveness and Value, Draft Background and Scope; January 11, 2019.
- Institute for Clinical and Economic Review (ICER). Deflazacort, Eteplirsen, and Golodirsen for Duchenne Muscular Dystrophy: Effectiveness and Value, Draft Evidence Report; May 22, 2019.
- NIH: U.S. National Library of Medicine. “Safety and Dose Finding Study of NS-065/NCNP-01 in Boys with Duchenne Muscular Dystrophy (DMD). <https://clinicaltrials.gov/ct2/show/NCT02740972?term=NCT02740972&draw=2&rank=1>. Accessed 25 August 2020.
- 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 Mar;17(3):251-267. doi: 10.1016/S1474-4422(18)30024-3. Epub 2018 Feb 3.
- Birnkrant DJ, Bushby K, Bann CM, et al. Diagnosis and management of Duchenne muscular dystrophy, part 2: respiratory, cardiac, bone health, and orthopaedic management. *Lancet Neurol*. 2018 Apr;17(4):347-361. doi: 10.1016/S1474-4422(18)30025-5. Epub 2018 Feb 3.
- Birnkrant DJ, Bushby K, Bann CM, et al. Diagnosis and management of Duchenne muscular dystrophy, part 3: primary care, emergency management, psychosocial care, and transitions of care across the lifespan. *Lancet Neurol*. 2018 May;17(5):445-455. doi: 10.1016/S1474-4422(18)30026-7. Epub 2018 Feb 2.
- Guglieri M, Bushby K, McDermott M, et al. Developing Standardized Corticosteroid Treatment for Duchenne Muscular Dystrophy. *Contemp Clin Trials*. 2017 July;58: 34–39. doi:10.1016/j.cct.2017.04.008.

### SmartPA Clinical Proposal Form

© 2020 Conduent Business Services, LLC. All rights reserved. Conduent™ and Conduent Design™ are trademarks of Conduent Business Services, LLC in the United States and/or other countries.

Other company trademarks are also acknowledged.