SmartPA Criteria Proposal

Drug/Drug Class:	Duchenne Muscular Dystrophy (DMD) Clinical Edit
First Implementation Date:	February 6, 2020
Proposed Date:	March 19, 2020
Prepared for:	MO HealthNet
Prepared by:	MO HealthNet/Conduent
Criteria Status:	☐Existing Criteria ☒Revision of Existing Criteria ☐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 mutations in the dystrophin gene; these mutations 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® (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® (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™ (golodirsen) was FDA approved in December 2019, 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). Both Exondys 51 and Vyondys 53 are manufactured by Sarepta Therapeutics, who also have an exon 45 skipping therapy currently in Phase III trials. Both Exondys 51 and Vyondys 53 are delivered by a once weekly IV infusion. Although patients receiving either Exondys 51 or Vyondys 53 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. Exondys 51 was to have post-marketing results finalized by 2021, but the manufacturer has revealed delays in initiation of the trial and now expects results to be finalized by 2024. The post-marketing confirmatory trial for Vyondys 53 is expected to be completed by 2024 as well.

Program-Specific Information:

Date Range FFS 1-1-2019 to 12-31-2019			
Drug	**Claims**	**Spend**	**Cost per unit**
Emflaza® 22.75mg/mL susp	0	-	$278.49 per ml MAC
Emflaza® 6mg tablet	0	-	$54.95 per tab MAC
Emflaza® 18mg tablet	0	-	$164.86 per tab MAC
Emflaza® 30mg tablet	32	$170,164.32	$274.79 per tab MAC
Emflaza® 36mg tablet	19	$159,681.33	$306.21 per tab MAC
Exondys 51® 100mg/2ml vial	102	$708,531.67	$808.00 per ml MAC
Exondys 51® 500mg/10ml vial	152	$9,351,819.15	$808.00 per ml MAC
Vyondys 53™ 100mg/2ml vial	0	-	$808.00 per ml MAC

Drug	Dose based on a 25kg participant	Cost per month
Emflaza® susp (dose = 22.5mg/day)	22.75mg daily (2 bottles of 13 ml)	$7,240.74 per 26 day supply
Emflaza® tablets (dose = 22.5mg/day)	18mg tab daily	$4,945.80 per 30 day supply
	24mg daily (18mg tab + 6mg tab)	$6,594.30 per 30 day supply
Exondys 51®	750mg once weekly (3 of 2ml vials + 10ml vial)	$51,712.00 per 28 day supply
Vyondys 53™	750mg once weekly (8 of 2ml vials)	$51,712.00 per 28 day supply

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:
  - 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 or stabilization 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 30mg/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 or stabilization 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:**
  - **Age ≥ 6 years and ≤ 15 years AND**
  - **Genetic testing to confirm pathogenic variant of DMD gene amenable to exon 53 skipping AND**
  - **Dosed at 30mg/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 or stabilization 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)**
    - **Documentation of monthly monitoring for proteinuria < 2+ AND**
    - **Documentation of monitoring for elevated serum cystatin C every three months**

Denial Criteria

- Therapy will be denied if no approval criteria are met

Required Documentation

Laboratory Results:	X	Progress Notes:	X
MedWatch Form:		Other:	X

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.
- 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.
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- 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.
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- 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.