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). Exondys 51 is delivered by a once weekly IV infusion. Although patients receiving Exondys 51 had an increase in dystrophin in skeletal muscle, a clinical benefit of Exondys 51 has not been established; continued FDA approval may be contingent upon verification of a clinical benefit in a confirmatory trial slated to complete in November 2020 with final data due to the FDA in May 2021.
Program-Specific Information:

<table>
<thead>
<tr>
<th>Drug</th>
<th>Date Range FFS 1-1-2019 to 6-19-2019</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>Claims</td>
</tr>
<tr>
<td>Exondys 51® 50mg/mL IV Soln</td>
<td>46</td>
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<tr>
<td>Emflaza® 22.75mg/mL Susp</td>
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</tr>
<tr>
<td>Emflaza® 6mg tablet</td>
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<tr>
<td>Emflaza® 18mg tablet</td>
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<td>Emflaza® 30mg tablet</td>
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<tr>
<td>Emflaza® 36mg tablet</td>
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<table>
<thead>
<tr>
<th>Drug</th>
<th>Dose based on a 25kg participant</th>
<th>MAC per month</th>
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<tbody>
<tr>
<td>Exondys 51®</td>
<td>750mg once weekly (3 of 2ml vials + 10ml vial)</td>
<td>$51,712.00 per 28 day supply</td>
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<tr>
<td>Emflaza® tablets (dose = 22.5mg/day)</td>
<td>18mg tab daily</td>
<td>$4,533.30 per 30 day supply</td>
</tr>
<tr>
<td>Emflaza® susp (dose = 22.5mg/day)</td>
<td>22.75mg daily (2 bottles of 13 ml)</td>
<td>$6,636.76 per 26 day supply</td>
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<tr>
<td>Prednisone tablets (dose = 18.75mg/day)</td>
<td>15mg daily (3 of 5mg tabs)</td>
<td>$6.30 per 30 day supply</td>
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</tbody>
</table>

Type of Criteria: □ Increased risk of ADE ☒ Preferred Drug List □ 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)) 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

SmartPA Clinical Proposal Form
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Approval for 6 months, renewal requests must provide documentation of clinical benefit

- Improvement or stabilization of motor or pulmonary function from baseline (ex: 6MWT, NSAA, Brooke Upper Extremity Scale, FVC) 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 mutation 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 or pulmonary function from baseline (ex: 6MWT, NSAA, Brooke Upper Extremity Scale, FVC) AND
- Participant retains meaningful voluntary motor function (ex: participant is able to speak, manipulate objects using upper extremities, ambulate)

**Denial Criteria**

- Therapy will be denied if no approval criteria are met

**Required Documentation**

<table>
<thead>
<tr>
<th>Laboratory Results:</th>
<th>X</th>
</tr>
</thead>
<tbody>
<tr>
<td>Progress Notes:</td>
<td>X</td>
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<tr>
<td>MedWatch Form:</td>
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</tr>
<tr>
<td>Other:</td>
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</table>

**Disposition of Edit**

Denial: Exception code “682” (Clinical Edit)
Rule Type: CE

**Default Approval Period**

6 months

**References**


