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® (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), FDA approved in December 2019, and Viltepso® (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. Amondys 45® (casimersen) was FDA approved in February 2021 for the treatment of DMD in patients who have a confirmed mutation of the DMD gene that is amenable to exon 45 skipping.
(approximately 8% of the DMD population). All 4 agents are antisense oligonucleotides delivered by a once weekly IV infusion. Although patients receiving either Exondys 51, Vyondys 53, Villtepso, or Amondys 45 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:

<table>
<thead>
<tr>
<th>Drug</th>
<th>Claims</th>
<th>Spend</th>
<th>Avg Spend per Claim</th>
</tr>
</thead>
<tbody>
<tr>
<td>AMONDYS 45 100 MG/2 ML VIAL</td>
<td>0</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>EMFLAZA 22.75 MG/ML SUSP</td>
<td>4</td>
<td>$39,536.66</td>
<td>$9,884.16</td>
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<tr>
<td>EMFLAZA 6 MG TABLET</td>
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<td>-</td>
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<tr>
<td>EMFLAZA 18 MG TABLET</td>
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<td>$5,197.96</td>
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<tr>
<td>EMFLAZA 30 MG TABLET</td>
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<td>5,904.80</td>
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<tr>
<td>EMFLAZA 36 MG TABLET</td>
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<td>$206,005.83</td>
<td>9,363.90</td>
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<tr>
<td>EXONDYS 51 100 MG/2 ML VIAL</td>
<td>175</td>
<td>$1,076,824.90</td>
<td>6,153.28</td>
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<tr>
<td>EXONDYS 51 500 MG/10 ML VIAL</td>
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<td>49,485.52</td>
</tr>
<tr>
<td>VILTEPSO 250 MG/5 ML</td>
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<td>-</td>
<td>-</td>
</tr>
<tr>
<td>VYONDYS 53 100 MG/2 ML VIAL</td>
<td>0</td>
<td>-</td>
<td>-</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dose based on a 25kg participant</th>
<th>Cost per month (MAC)</th>
</tr>
</thead>
<tbody>
<tr>
<td>AMONDYS 45</td>
<td>750 mg once weekly (8 of 2 ml vials)</td>
<td>$51,200.00 per 28 days</td>
</tr>
<tr>
<td>EMFLAZA SUSP (dose = 22.5 mg/day)</td>
<td>22.75 mg daily (2 bottles of 13 ml)</td>
<td>$8,405.02 per 26 days</td>
</tr>
<tr>
<td>EMFLAZA TABLET (dose = 22.5 mg/day)</td>
<td>18 mg tab daily (18 mg tab + 6 mg tab)</td>
<td>$5,741.40 per 30 days</td>
</tr>
<tr>
<td>EXONDYS 51</td>
<td>750 mg once weekly (3 of 2 ml vials + 10 ml vial)</td>
<td>$51,200.00 per 28 days</td>
</tr>
<tr>
<td>VILTEPSO</td>
<td>2,000 mg once weekly (8 of 5 ml vials)</td>
<td>$45,120.00 per 28 days</td>
</tr>
<tr>
<td>VYONDYS 53</td>
<td>750 mg once weekly (8 of 2 ml vials)</td>
<td>$51,200.00 per 28 days</td>
</tr>
</tbody>
</table>

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:
  o Age ≥ 2 years and older AND
  o Dosed at 0.9 mg/kg/day, rounding up to the nearest possible dose AND
  o Documentation of adequate trial and therapy failure, intolerance, or significant weight gain while on prednisone at a therapeutic dose (at least 0.75 mg/kg/day or 10 mg/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
  o 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, Vyondys 53, Viltepso, or Amondys 45:
  o Age ≥ 4 years and ≤ 19 years AND
  o Documentation of concurrent prednisone or deflazacort therapy, defined as 6 months in the past 9 months AND
  o For Exondys 51:
    ▪ Genetic testing to confirm pathogenic variant of DMD gene amenable to exon 51 skipping AND
    ▪ Dosed at 30 mg/kg once weekly
  o For Vyondys 53:
    ▪ Genetic testing to confirm pathogenic variant of DMD gene amenable to exon 53 skipping AND
    ▪ Dosed at 30 mg/kg once weekly AND
    ▪ Documentation of clinical reason why participant cannot take Viltepso
  o For Viltepso:
    ▪ Genetic testing to confirm pathogenic variant of DMD gene amenable to exon 53 skipping AND
    ▪ Dosed at 80 mg/kg once weekly
  o For Amondys 45:
    ▪ Genetic testing to confirm pathogenic variant of DMD gene amenable to exon 45 skipping AND
    ▪ Dosed at 30 mg/kg once weekly
  o 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, Viltepso, or Amondys 45:
      ▪ 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

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

Disposition of Edit

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

Default Approval Period

6 months

References

- Amondys 45 (casimersen) [package insert]. Cambridge, MA: Sarepta Therapeutics; February 2021