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Revised: 01/15/24

Subject: Deflazacort (Emflaza)

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DESCRIPTION:

Muscular dystrophy includes a group of genetic disorders that cause muscle weakness and progressive disability. Duchenne muscular dystrophy (DMD) is the most common and progresses most rapidly. This X-linked recessive disorder is caused by mutations (mainly deletions) in the dystrophin gene that lead to an absence or defect in the dystrophin protein.

Dystrophin is thought to maintain the structural integrity of the muscle cell membrane by connecting the cytoskeleton to the underlying extracellular matrix, and acting as a scaffold for several molecules that also contribute to normal muscle physiology. Absence of dystrophin leads to mitochondrial dysfunction and damage, with inflammatory processes also appearing to contribute to muscle pathology. Muscle fibers ultimately undergo necrosis with replacement by adipose and connective tissue. Principal disease manifestations include progressive degeneration of skeletal and cardiac muscle, leading to loss of physical function in childhood and adolescence with premature death from respiratory and/or cardiac failure in the second to fourth decade.

As males have only one X chromosome, and thus one single copy of the dystrophin gene, they have a much higher probability of developing DMD. A small number of females are also affected, but remain asymptomatic and only rarely present with a mild form of the disease. DMD has an estimated incidence of 1 in 3,500 male births. Available data suggests around 83% of DMD patients have genotypes amenable to exon skipping, and that 13% of DMD patients have genotypes that are amenable to exon 51 skipping.

Treatment options for DMD predominantly focus on management of symptoms and secondary complications. Glucocorticoids are the only pharmacological treatments that have been shown to improve skeletal muscle strength and function in reproducible randomized controlled trials; they also reduce the risk of scoliosis, stabilize pulmonary function, and may also improve cardiac function. Current

guidelines recommend initiation of glucocorticoids (such as prednisolone) once patients reach a plateau of motor skill development, generally at age 4-6 years, but prior to onset of motor decline.

Other pharmacologic therapies for DMD are primarily aimed at the management of comorbidities such as cardiomyopathy, osteoporosis, pain management, and respiratory failure. These treatment options include: angiotensin-converting-enzyme (ACE) inhibitors, beta-blockers, calcium and vitamin D supplements, muscle relaxants, and non-steroidal anti-inflammatory drugs.

Deflazacort (Emflaza), an oral corticosteroid prodrug, was approved by the U.S. Food and Drug Administration (FDA) in 2017 for treatment of DMD in patients 5 years of age and older. Deflazacort's active metabolite acts through the glucocorticoid receptor to exert anti-inflammatory and immunosuppressive effects. The exact mechanism by which deflazacort exerts its therapeutic effects in DMD is not known.

The approval of deflazacort was based on study by Griggs, et al completed in 1995 and later published 2016. Subjects (n=196) were included if between the ages of 5 and 15 years, with onset of weakness before 5 years of age; increased serum creatine kinase ($\geq 10\times$ ULN); and either genetic analysis of the dystrophin gene or biopsy that demonstrated an alteration in dystrophin amount or distribution. Seven of the 196 participants were later determined to have Becker muscular dystrophy (instead of DMD) due to a less definitive understanding of the differences between the two diseases at that time. Prior oral corticosteroid use for longer than 1 year or within 6 months of study entry was not permitted.

Participants were randomized to therapy with deflazacort (0.9 or 1.2 mg/kg/day), prednisone (0.75 mg/kg/day), or placebo. The primary clinical efficacy endpoint was the change in average muscle strength score from baseline to week 12 using a modified Medical Research Council (MRC) 11-point scale. A score of 0 was consistent with no movement of the muscle, while a score of 10 indicated normal strength. After the initial 12 weeks, participants in the placebo group were randomized to 1 of the 3 active treatment groups and continued treatment for an additional 40 weeks.

At week 12, the primary efficacy analysis demonstrated a significant LS mean difference in change in muscle strength in favor of all treatment groups vs placebo (Table 1). The secondary endpoint of change in muscle strength from week 12 to week 52 demonstrated a significant improvement in the lower dose deflazacort group vs prednisone, but no difference in the higher dose deflazacort group vs prednisone (Table 1).

Pulmonary function tests, including forced vital capacity (FVC) and maximum voluntary ventilation (MVV), were also assessed. Some measures showed or trended toward statistical significance. At week 12, there was a significant increase in weight vs placebo in the prednisone group, but not the deflazacort group – although, all treatment and control groups reported weight gains. The mean weight increase over 12 months was 16.8% (LS mean difference: 5.05 kg, 95%CI 4.08-6.01) and 18.3% (LS mean difference: 5.60 kg, 95%CI 4.59-6.61) in deflazacort low and high dose respectively, and 26.7% (LS mean difference: 8.45 kg, 95%CI 7.41-9.49) in prednisone. Cataract occurred at a higher rate with daily deflazacort (0.9 mg/kg, 4.4%; 1.2 mg/kg, 1.5%) than prednisone (1.6%),

Table 1

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| Primary and Secondary Endpoints, Changes in weight |
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| | deflazacort 0.9 mg/kg/d | deflazacort 1.2 mg/kg/d | prednisone 0.75 mg/kg/d |
|---|--|--|--|
| LS Mean change in average muscle strength vs placebo at week 12 | 0.25 vs -0.1 p=0.017 95% CI 0.04-0.46 | 0.36 vs -0.1 p=0.0003 95% CI 0.14-0.57 | 0.37 vs -0.1 p=0.0002 95% CI 0.15-0.59 |
| LS Mean change in average muscle strength vs prednisone from week 12 to week 52 | 0.17 vs -0.12 p=0.044 95% CI 0.08-0.49 | 0.04 vs -0.12 p=0.18 95% CI -0.06-0.37 | |
| LS Mean change in average weight (kg) vs placebo at week 12 | 1.72 vs 1.23 No significant differences | 1.71 vs 1.23 No significant differences | 3.23 vs 1.23 p=0.0459 95% CI 0.03–3.97 |

In 2016, the American Academy of Neurology (AAN) released their guideline update Corticosteroid treatment of Duchene muscular dystrophy. The guidelines recommend offering either prednisone and deflazacort as an intervention for patients with DMD. However, the recommendation for use of prednisone to improve strength, timed motor function, and pulmonary function is associated with a higher level of evidence (Level B, moderate) compared to deflazacort (Level C, weak) for the same measures.

Additionally the guidelines include the following statement:

“Deflazacort and prednisone may be equivalent in improving motor function (Level C). There is insufficient evidence to establish a difference in effect on cardiac function (Level U). Prednisone may be associated with increased weight gain in the first years of treatment compared with deflazacort (Level C). Deflazacort may be associated with increased risk of cataracts compared with prednisone (Level C).”

POSITION STATEMENT:

Comparative Effectiveness

The FDA has deemed the drug(s) or biological product(s) in this coverage policy to be appropriate for self-administration or administration by a caregiver (i.e., not a healthcare professional). Therefore, coverage (i.e., administration) in a provider-administered setting such as an outpatient hospital, ambulatory surgical suite, physician office, or emergency facility **does not meet the definition of medical necessity.**

Initiation of deflazacort (Emflaza) **meets the definition of medical necessity** when **ALL** of the following criteria are met:

1. Member is diagnosed with Duchenne Muscular Dystrophy (DMD)
2. Member’s DMD diagnosis is confirmed by genetic testing – laboratory results must be provided
3. Member’s DMD symptom onset occurred prior to 5 years of age
4. Member meets one of the following:
 - a. Member has been receiving treatment with prednisone for at least 6 months – documentation from the medical record must be provided

- b. Member was previously approved for deflazacort by another health plan – documentation of a recent (within 90 days prior to authorization request) health plan-paid claim for deflazacort must be provided
- 5. Member has experienced prednisone-related weight gain of more than 20% from baseline (i.e., prior to initiation of prednisone) – documentation from the medical record must be provided
- 6. Member provides a baseline score from a 6- minute walk test – documentation from the medical record must be provided
- 7. Member is 2 years of age or older
- 8. Dose does not exceed 0.9 mg/kg/day – dosage will be achieved using the fewest number of tablets (or volume of solution) per day

Approval duration: 6 months

Continuation of deflazacort (Emflaza) **meets the definition of medical necessity** when **ALL** of the following criteria are met:

- 1. Authorization/reauthorization has been previously approved by Florida Blue in the past two years for treatment of DMD, OR the member has previously met all indication-specific initiation criteria
- 2. Member meets **ONE** of the following
 - a. Member demonstrates a clinically meaningful response to treatment with deflazacort as evidenced by any of the following:
 - i. Improvement or maintenance of score from 6-minute walk test compared to baseline (i.e., immediately prior to initiation of deflazacort) – documentation from the medical record must be provided
 - ii. Weight loss of approximately 10% from baseline (i.e., prior to initiation of deflazacort) – documentation from the medical record must be provided
 - b. Member has been receiving treatment for a minimum of 1 year and demonstrates a clinically meaningful response to treatment with deflazacort as evidenced by any of the following:
 - i. Improvement or maintenance of score from 6-minute walk test compared to baseline (i.e., immediately prior to initiation of deflazacort) – documentation from the medical record must be provided
 - ii. Weight or body mass index (BMI) for age falls below the 85th percentile based on CDC growth charts– documentation from the medical record must be provided
- 3. Member has been evaluated by an ophthalmologist for development of deflazacort-related adverse effects (e.g., cataracts) since initiation of deflazacort or within the past year (whichever is more recent) – documentation from the medical record must be provided
- 4. Dose does not exceed 0.9 mg/kg/day – dosage will be achieved using the fewest number of tablets (or volume of solution) per day

Approval duration: 1 year

DOSAGE/ADMINISTRATION:

THIS INFORMATION IS PROVIDED FOR INFORMATIONAL PURPOSES ONLY AND SHOULD NOT BE USED AS A SOURCE FOR MAKING PRESCRIBING OR OTHER MEDICAL DETERMINATIONS. PROVIDERS SHOULD REFER TO THE MANUFACTURER'S FULL PRESCRIBING INFORMATION FOR DOSAGE GUIDELINES AND OTHER INFORMATION RELATED TO THIS MEDICATION BEFORE MAKING ANY CLINICAL DECISIONS REGARDING ITS USAGE.

FDA-approved

- The recommended once-daily dosage is approximately 0.9 mg/kg/day administered orally (2.1)
- Discontinue gradually when administered for more than a few days

Dose Adjustments

- CYP3A4 Inhibitors - Give one third of the recommended dosage when administered with moderate or strong CYP3A4 inhibitors. For example, a 36 mg per day dose would be reduced to a 12 mg per day dose when used with moderate or strong CYP3A4 inhibitors.
- CYP3A4 Inducers - Avoid use with moderate or strong CYP3A4 inducers

Drug Availability

- Tablets: 6 mg, 18 mg, 30 mg, and 36 mg
- Oral Suspension: 22.75 mg/mL

PRECAUTIONS:

Boxed Warning

- None

Contraindications

- Hypersensitivity to deflazacort or any of the inactive ingredients

Precautions/Warnings

- Alterations in Endocrine Function: Hypothalamic-pituitary-adrenal axis suppression, Cushing's syndrome, and hyperglycemia can occur; Monitor patients for these conditions with chronic use
- Immunosuppression and Increased Risk of Infection: Increased risk of new, exacerbation, dissemination, or reactivation of latent infections, which can be severe and at times fatal; Signs and symptoms of infection may be masked
- Alterations in Cardiovascular/Renal Function: Monitor for elevated blood pressure and sodium, and for decreased potassium levels
- Gastrointestinal Perforation: Increased risk in patients with certain GI disorders; Signs and symptoms may be masked
- Behavioral and Mood Disturbances: May include euphoria, insomnia, mood swings, personality changes, severe depression, and psychosis
- Effects on Bones: Monitor for decreases in bone mineral density with chronic use
- Ophthalmic Effects: May include cataracts, infections, and glaucoma; Monitor intraocular pressure if continued for more than 6 weeks

- Vaccination: Do not administer live or live attenuated vaccines to patients receiving immunosuppressive doses of corticosteroids
- Serious Skin Rashes: Discontinue at the first sign of rash, unless the rash is clearly not drug related

BILLING/CODING INFORMATION:

The following codes may be used to describe:

HCPCS Coding

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| J3490 | Unclassified drugs |
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ICD-10 Diagnosis Codes That Support Medical Necessity

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|--------|---------------------------------------|
| G71.01 | Duchenne or Becker muscular dystrophy |
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REIMBURSEMENT INFORMATION:

Refer to section entitled [POSITION STATEMENT](#).

PROGRAM EXCEPTIONS:

Federal Employee Program (FEP): Follow FEP guidelines.

State Account Organization (SAO): Follow SAO guidelines.

Medicare Part D: Florida Blue has delegated to Prime Therapeutics authority to make coverage determinations for the Medicare Part D services referenced in this guideline.

Medicare Advantage: No National Coverage Determination (NCD) and/or Local Coverage Determination (LCD) were found at the time of the last guideline review date.

DEFINITIONS:

6 minute walk test: assesses distance walked over 6 minutes as a sub-maximal test of aerobic capacity/endurance

9 Hole Peg Test: a brief, standardized quantitative test of upper extremity function

Maximum Voluntary Isometric Contraction Test: assesses muscle strength

North Star Ambulatory Assessment: a functional scale designed for ambulant boys affected by DMD

RELATED GUIDELINES:

[Eteplirsen \(Exondys 51\), 09-J2000-69](#)

OTHER:

None

REFERENCES:

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COMMITTEE APPROVAL:

This Medical Coverage Guideline (MCG) was approved by the Florida Blue Pharmacy Policy Committee on 12/13/23.

GUIDELINE UPDATE INFORMATION:

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| 06/15/17 | New Medical Coverage Guideline. |
| 01/15/19 | Review and revision; updated references. |
| 12/15/19 | Revision to guideline; updated position statement |
| 01/15/20 | Review and revision; updated coding and references. |
| 04/15/21 | Review and revision; updated references, position statement. |
| 02/15/22 | Revision; updated position statement. |
| 01/15/24 | Review and revision; updated references. |