PRIOR AUTHORIZATION POLICY

POLICY: Muscular Dystrophy – Deflazacort Prior Authorization Policy
- Emflaza™ (deflazacort tablets and oral suspension – PTC Therapeutics)

REVIEW DATE: 01/10/2024; selected revision 03/06/2024, 07/03/2024

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CIGNA NATIONAL FORMULARY COVERAGE:

OVERVIEW

Deflazacort, a corticosteroid, is indicated for the treatment of **Duchenne muscular dystrophy** (DMD) in patients ≥ 2 years of age.[1] The efficacy and safety of deflazacort have not been established in patients < 2 years of age.

Disease Overview

DMD is an X-linked recessive disease affecting 1 in 3,600 to 6,000 newborn male infants.[2] The disease is attributed to large frame-shift deletions in the DMD gene (chromosome Xp21) which lead to loss of a structural protein of muscle cells (dystrophin).[3] Female carriers are usually asymptomatic but some may show mild symptoms.[2] Most patients present with symptoms of DMD between the ages of 3 and 5 years. There are wide variances in how quickly DMD progresses, but without intervention, death is at approximately 19 years of age.[2,3] With respiratory, cardiac, orthopedic and rehabilitative interventions and use of corticosteroids, children born today can have a life expectancy of up to 40 years.

Clinical Efficacy

The efficacy and safety of deflazacort were established in two pivotal trials in boys with DMD who were ≥ 5 years of age.[4,5] In one study, treatment consisted of

deflazacort 0.9 mg/kg/day, deflazacort 1.2 mg/kg/day, or prednisone 0.75 mg/kg/day (n = 196).[4] The primary efficacy analysis, mean change from baseline to Week 12 in average muscle strength (assessed by modified Medical Research Council [MRC]), demonstrated a significant least squares (LS) mean difference in favor of active treatment vs. placebo: deflazacort 0.9 mg/kg/day (0.25 vs. -0.1, P = 0.17), deflazacort 1.2 mg/kg/day (0.36 vs. -0.1, P = 0.0003), and prednisone 0.75 mg/kg/day (0.37 vs. -0.1, P = 0.0002). Adverse events (AEs) differed between prednisone and deflazacort treatment groups. Cushingoid appearance (69.4%), erythema (41.8%), and hirsutism (39.3%) were observed in a numerically greater proportion of patients in the prednisone group compared with either dose of deflazacort. Central obesity was reported in a statistically significant greater proportion of patients treated with prednisone vs. deflazacort. Psychiatric AEs were generally reported at a higher rate in the prednisone group compared with both deflazacort groups.

Guidelines

There are guidelines for the diagnosis and management of DMD available from the DMD Care Considerations Working Group (updated 2018).[6] Dystrophin gene deletion and duplication testing are usually the first test done to confirm a diagnosis of DMD. If deletion/duplication testing is negative, dystrophin gene sequencing is done to look for remaining types of mutations. If genetic testing does not confirm a diagnosis of DMD, then a muscle biopsy should be performed to test for the presence of dystrophin protein. These guidelines additionally discuss the benefits of glucocorticoids in patients with DMD. These benefits include the loss of ambulation at a later age, preservation of upper limb and respiratory function, and avoidance of scoliosis surgery. Although the benefits of glucocorticoids are well established, based on available data, there is uncertainty about which specific products and doses are best.[6]

POLICY STATEMENT

Prior Authorization is recommended for prescription benefit coverage of deflazacort. All approvals are provided for the duration noted below. Because of the specialized skills required for evaluation and diagnosis of patients treated with deflazacort as well as the monitoring required for adverse events and long-term efficacy, approval requires deflazacort to be prescribed by or in consultation with a physician who specializes in the condition being treated.

Documentation: Documentation is required for use of deflazacort as noted in the criteria as **[documentation required]**. Documentation may include, but is not limited to, chart notes, prescription claims records, prescription receipts, and/or other information.

- **Emflaza™ (deflazacort tablets and oral suspension (PTC Therapeutics)**

is(are) covered as medically necessary when the following criteria is(are) met for FDA-approved indication(s) or other uses with supportive evidence (if applicable):

FDA-Approved Indication

1. **Duchenne Muscular Dystrophy.** Approve for 1 year if the patient meets ONE of the following (A or B):
   - **A)** Initial Therapy. Approve if the patient meets ALL of the following (i, ii, iii, and iv):
     - **i.** Patient is ≥ 2 years of age; AND
     - **ii.** Patient's diagnosis of Duchenne Muscular Dystrophy is confirmed by genetic testing with a confirmed pathogenic variant in the dystrophin gene **[documentation required]**; AND
     - **iii.** Patient meets ONE of the following conditions (a or b):
       - **a)** Patient has tried prednisone or prednisolone for ≥ 6 months **[documentation required]** AND according to the prescriber, the patient has had at least ONE of the following significant intolerable adverse effects [1, 2, 3, or 4]:
         - **1)** Cushingoid appearance **[documentation required]**; OR
         - **2)** Central (truncal) obesity **[documentation required]**; OR
         - **3)** Undesirable weight gain defined as ≥ 10% of body weight gain increase over a 6-month period **[documentation required]**; OR
         - **4)** Diabetes and/or hypertension that is difficult to manage according to the prescriber **[documentation required]**; OR
       - **b)** According to the prescriber, the patient has experienced a severe behavioral adverse event while on prednisone or prednisolone therapy that has or would require a prednisone or prednisolone dose reduction **[documentation required]**; AND
     - **iv.** The medication is prescribed by or in consultation with a physician who specializes in the treatment of Duchenne muscular dystrophy and/or neuromuscular disorders.
   - **B)** Patient is Currently Receiving Deflazacort. Approve if the patient meets ALL of the following (i, ii, iii, and iv):
     - **i.** Patient is ≥ 2 years of age; AND
     - **ii.** Patient has tried prednisone or prednisolone **[documentation required]**; AND
     - **iii.** According to the prescriber, the patient has responded to or continues to have improvement or benefit from deflazacort therapy **[documentation required]**; AND
       Note: Examples of improvement or benefit from deflazacort therapy would include improvements in motor function (time from supine to standing, time to climb four stairs, time to run or walk 10 meters, 6-minute walk test), improvement in muscle strength, improved pulmonary function, etc.
     - **iv.** The medication is prescribed by or in consultation with a physician who specializes in the treatment of Duchenne muscular dystrophy and/or neuromuscular disorders.

CONDITIONS NOT COVERED

- **Emflaza™ (deflazacort tablets and oral suspension (PTC Therapeutics)**

is(are) considered experimental, investigational or unproven for ANY other use(s) including the following; criteria will be updated as new published data are available.

REFERENCES

1. Emflaza™ tablets and oral suspension [prescribing information]. South Plainfield, NJ: PTC Therapeutics; June 2021.
2. Annexstad EJ, Lund-Petersen I, Rasmussen M. Duchenne muscular dystrophy. *Tidsskr Nor Laegeforen*. 2014;134(14):1361-1364.
3. Wood MJA. To skip or not to skip: that is the question for Duchenne muscular dystrophy. *Mol Ther*. 2013;21(12):2131-2132.
4. Griggs RC, Miller JP, Greenberg CR, et al. Efficacy and safety of Emflaza vs prednisone and placebo for Duchenne muscular dystrophy. *Neurology*. 2016;87(20):2123-2131.
5. Angelini C, Pegoraro E, Turella E, et al. Emflaza in Duchenne dystrophy: study of long-term effect. *Muscle Nerve*. 1994;17(4):386-391.
6. Birnkrandt 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.

HISTORY

Type of Revision	Summary of Changes	Review Date
Annual Revision	No criteria changes.	02/15/2023
Early Annual Revision	**Duchenne Muscular Dystrophy:** In the criteria referring to genetic testing, deleted "…or likely pathogenic" reference to dystrophin gene. Under "Patient is Currently Receiving Emflaza", added age criterion. Under "Note" for improvements with Emflaza therapy, changed "time to run or walk 10 meters" from 30 feet. Also added 6-minute walk test to the list of motor function tests.	01/10/2024
Selected Revision	Emflaza tablets are available as generic deflazacort tablets. Changed policy name to Deflazacort PA. Also, within the policy changed Emflaza to deflazacort wherever applicable.	03/06/2024
Selected Revision	From policy heading deleted "generic for tablets only" since the oral suspension is now available as a generic. **Duchenne Muscular Dystrophy:** For diagnosis confirmation of Duchenne muscular dystrophy, deleted criteria asking for "Muscle biopsy showing the absence of, or marked decrease in, dystrophin protein."	07/03/2024

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