Drug Coverage Policy

Effective Date.....10/15/2024
Coverage Policy Number.....IP0131
Policy Title..... Deflazacort

Muscular Dystrophy – Deflazacort

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

INSTRUCTIONS FOR USE
The following Coverage Policy applies to health benefit plans administered by Cigna Companies. Certain Cigna Companies and/or lines of business only provide utilization review services to clients and do not make coverage determinations. References to standard benefit plan language and coverage determinations do not apply to those clients. Coverage Policies are intended to provide guidance in interpreting certain standard benefit plans administered by Cigna Companies. Please note, the terms of a customer's particular benefit plan document [Group Service Agreement, Evidence of Coverage, Certificate of Coverage, Summary Plan Description (SPD) or similar plan document] may differ significantly from the standard benefit plans upon which these Coverage Policies are based. For example, a customer's benefit plan document may contain a specific exclusion related to a topic addressed in a Coverage Policy. In the event of a conflict, a customer's benefit plan document always supersedes the information in the Coverage Policies. In the absence of a controlling federal or state coverage mandate, benefits are ultimately determined by the terms of the applicable benefit plan document. Coverage determinations in each specific instance require consideration of 1) the terms of the applicable benefit plan document in effect on the date of service; 2) any applicable laws/regulations; 3) any relevant collateral source materials including Coverage Policies and; 4) the specific facts of the particular situation. Each coverage request should be reviewed on its own merits. Medical directors are expected to exercise clinical judgment and have discretion in making individual coverage determinations. Coverage Policies relate exclusively to the administration of health benefit plans. Coverage Policies are not recommendations for treatment and should never be used as treatment guidelines. In certain markets, delegated vendor guidelines may be used to support medical necessity and other coverage determinations.

Cigna Healthcare Coverage Policy

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]

Medical Necessity Criteria

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.

Deflazacort is considered medically necessary when the following criteria are met:

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

Any other use is considered experimental, investigational, or unproven (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.

Revision Details

Type of Revision	Summary of Changes	Date
Annual Revision	• Deleted "…or likely pathogenic variant" for genetic testing criteria in regard to dystrophin gene.	05/01/2024

	• Replaced "time to run or walk 30 feet" with "time to run or walk 10 meters" for Emflaza improvements. • Added 6-minute walk test to motor function tests for Emflaza improvements.	
Selected Revision	Emflaza tablets are available as generic deflazacort tablets. Within the policy changed Emflaza to deflazacort wherever applicable.	06/01/2024
Early Annual Revision	**Removed** "generic for tablets only" from policy heading since the oral suspension is now available as a generic. **Duchenne Muscular Dystrophy:** **Updated** the diagnosis to require confirmation by genetic testing with a confirmed pathogenic variant in the dystrophin gene. **Removed** the criteria requiring a muscle biopsy showing the absence of, or marked decrease in, dystrophin protein for diagnosis confirmation. **Added** the requirement that the patient has tried prednisone or prednisolone for ≥ 6 months and according to the prescriber, experienced at least one significant intolerable adverse effect: Cushingoid appearance, central (truncal) obesity, undesirable weight gain (≥ 10% body weight increase over 6 months), or difficult-to-manage diabetes and/or hypertension. **Updated** the requirement that the patient has experienced significant adverse effects while on prednisone or prednisolone therapy to now state that "according to the prescriber, the patient has experienced significant a severe behavioral adverse effects event while on prednisone or prednisolone therapy that has or would require a prednisone or prednisolone dose reduction." **Added** "documentation required" for use of deflazacort as noted in the criteria.	10/15/2024

The policy effective date is in force until updated or retired.