

PRIOR AUTHORIZATION POLICY

POLICY: Muscular Dystrophy – Emflaza Prior Authorization Policy
• Emflaza™ (deflazacort tablets and oral suspension – PTC Therapeutics, Inc.)

REVIEW DATE: 01/20/2021

OVERVIEW

Emflaza is a corticosteroid indicated for the treatment of patients \geq 2 years of age with **Duchenne muscular dystrophy** (DMD).¹ The efficacy and safety of Emflaza 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 Females 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 Emflaza were established in two pivotal trials in boys with DMD who were \geq 5 years of age.⁴⁻⁵ In one study, treatment consisted of Emflaza 0.9 mg/kg/day, Emflaza 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: Emflaza 0.9 mg/kg/day (0.25 vs. -0.1, P = 0.17), Emflaza 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 Emflaza 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 Emflaza. Central obesity was reported in a statistically significant greater proportion of patients treated with prednisone vs. Emflaza. Psychiatric AEs were generally reported at a higher rate in the prednisone group compared with both Emflaza 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 generic 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 Emflaza. All approvals are provided for the duration noted below. Because of the specialized skills required for evaluation and diagnosis of patients treated with Emflaza as well as the monitoring required for adverse events and long-term efficacy, approval requires Emflaza to be prescribed by or in consultation with a physician who specializes in the condition being treated.

Documentation: Documentation is required for use of Emflaza 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.

Automation: None.

RECOMMENDED AUTHORIZATION CRITERIA

Coverage of Emflaza is recommended in those who meet the following criteria:

FDA-Approved Indications

1. **Duchenne Muscular Dystrophy (DMD).** Approve for 1 year if the patient meets the following criteria (A or B):
 - A) Initial Therapy. Approve if the patient meets the following criteria (i, ii, and iii):
 - i. Patient is 2 years of age and older; AND
 - ii. Patient meets ONE of the following conditions (a or b):
 - a) Patient has tried prednisone/prednisolone for \geq 6 months [documentation required] AND according to the prescriber, the patient has had at least one of the following significant intolerable adverse effects (AEs) [1, 2, 3, or 4]:
 - 1) Cushingoid appearance [documentation required]; OR
 - 2) Central (truncal) obesity [documentation required]; OR
 - 3) Undesirable weight gain defined as \geq 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 (AE) while on prednisone/prednisolone therapy that has or would require a prednisone/prednisolone dose reduction [documentation required].
 - iii. 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 Emflaza. Approve if the patient meets the following criteria (i, ii, and iii):
 - i. Patient has tried prednisone/prednisolone [documentation required]; AND
 - ii. According to the prescriber, the patient has responded to or continues to have improvement or benefit from Emflaza therapy [documentation required]; AND
Note: Examples of improvement or benefit from Emflaza therapy would include improvements in motor function (time from supine to standing, time to climb four stairs, time to run or walk 30 feet), improvement in muscle strength, improve pulmonary function, etc.
 - iii. 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 RECOMMENDED FOR APPROVAL

Coverage of Emflaza is not recommended in the following situations:

- 1.** Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

REFERENCES

1. Emflaza™ tablets and oral suspension [prescribing information]. South Plainfield, NJ: PTC Therapeutics, Inc.; July 2020.
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.