VENTURA COUNTY
HEALTH CARE PLAN

PRIOR AUTHORIZATION POLICY

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

TAC APPROVAL DATE: 03/13/2019; selected revision 6/26/2019

OVERVIEW

Emflaza is a corticosteroid indicated for the treatment of patients 2 years of age and older with Duchenne muscular dystrophy (DMD).[1] The efficacy and safety of Emflaza have not been established in patients < 2 years of age. The Emflaza oral suspension contains benzyl alcohol as a preservative and therefore carries a warning about the risk of gasping syndrome which can occur in neonates and low birth weight infants.

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 ≥ 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. 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. All approvals are provided for 1 year.

Documentation: Documentation is required where noted in the criteria as **[documentation required]**. Documentation may include, but is not limited to, chart notes and/or laboratory data.

Automation: None.

RECOMMENDED AUTHORIZATION CRITERIA

Coverage 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 ALL of the following criteria (A, B, and C):
   - **A)** The patient is 2 years of age and older[1]; AND
   - **B)** The patient meets ONE of the following conditions (i or ii):
     - **i.** The patient has tried prednisone for ≥ 6 months **[documentation required]** AND according to the prescribing physician, the patient has had at least one of the following significant intolerable adverse effects (AEs) [a, b, c, or d]:
       - **a)** Cushingoid appearance **[documentation required]**; OR
       - **b)** Central (truncal) obesity **[documentation required]**; OR
       - **c)** Undesirable weight gain defined as ≥ 10% of body weight gain increase over a 6-month period **[documentation required]**; OR
       - **d)** Diabetes and/or hypertension that is difficult to manage according to the prescribing physician] **[documentation required]**.
     - **ii.** According to the prescribing physician, the patient has experienced a severe behavioral adverse event (AE) while on prednisone therapy that has or would require a prednisone dose reduction **[documentation required]**.
   - **C)** The medication is prescribed by or in consultation with a physician who specializes in the treatment of Duchenne muscular dystrophy (DMD) and/or neuromuscular disorders.

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Emflaza has not been shown to be effective, or there are limited or preliminary data or potential safety concerns that are not supportive of general approval for the following conditions.

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 Therapetuics, Inc.; June 2019.
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.

OTHER REFERENCES UTILIZED

- McDonald CM, Henricson EK, Abresch RT, et al. Long-term effects of glucocorticoids on function, quality of life, and survival in patients with Duchenne muscular dystrophy: a prospective cohort study. *Lancet.* 2018; 391(1011): 451-461.
- Guglieri M, Bushby K, McDemott MP, et al. Developing standardized corticosteroid treatment for Duchenne muscular dystrophy. *Contemp Clin Trials.* 2017; 58:34-39.
- Shieh PB, Mcintosh J, Souza M, et al. : A post HOC analysis from the ACT DMD trial. *Muscle Nerve. 2018;58(5):639-645.*

HISTORY

Type of Revision	Summary of Changes*	TAC Approval Date
New Policy	--	2/15/2017
Annual Revision	No criteria changes	3/07/2018
DEU Revision	Updated documentation section. Documentation required for each review.	5/23/2018
Annual Revision	No criteria changes	3/13/2019
Selected Revision	For Duchenne Muscular Dystrophy, the FDA-approved age for use was updated to patients 2 years of age and older. Previously the approved age was ≥ to 5 years of age.	6/26/2019

* For a further summary of criteria changes, refer to respective TAC minutes available at: http://esidepartments/sites/Dep043/Committees/TAC/Forms/AllItems.aspx; TAC – Therapeutic Assessment Committee.