Emflaza (deflazacort)

NOTICE

This policy contains information which is clinical in nature. The policy is not medical advice. The information in this policy is used by Wellmark to make determinations whether medical treatment is covered under the terms of a Wellmark member's health benefit plan. Physicians and other health care providers are responsible for medical advice and treatment. If you have specific health care needs, you should consult an appropriate health care professional. If you would like to request an accessible version of this document, please contact customer service at 800-524-9242.

BENEFIT APPLICATION

Benefit determinations are based on the applicable contract language in effect at the time the services were rendered. Exclusions, limitations or exceptions may apply. Benefits may vary based on contract, and individual member benefits must be verified. Wellmark determines medical necessity only if the benefit exists and no contract exclusions are applicable. This medical policy may not apply to FEP. Benefits are determined by the Federal Employee Program.

DESCRIPTION

The indications below including FDA-approved indications and compendial uses are considered covered benefits provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications

Emflaza is indicated for the treatment of Duchenne muscular dystrophy (DMD) in patients 2 years of age and older.

All other indications are considered experimental/investigational and are not a covered benefit.

POLICY

Required Documentation

The following information is necessary to initiate the prior authorization review:

1. Laboratory confirmation of DMD diagnosis by genetic testing.
2. Submission of medical records documenting persistent psychiatric/behavioral issues with previous prednisone treatment.
3. Submission of medical records (e.g., chart notes, pulmonary function tests, MRC score, 6MWT distance, etc.) demonstrating clinical benefit from therapy

Criteria for Initial Approval

A) Duchenne Muscular Dystrophy

1. Authorization of 6 months may be granted for treatment of DMD when all of the following criteria are met:
   a.) The diagnosis of DMD was confirmed by genetic testing demonstrating a mutation in the DMD gene.
   b.) The member is 2 years of age or older.
   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
   d.) The member has tried prednisone and experienced persistent, unmanageable, and clinically significant psychiatric/behavioral issues (eg, abnormal behavior, aggression, irritability).
   AND
   - A change in BOTH dosage and timing of prednisone administration (eg, afternoon or evening) has been attempted but was unsuccessful.

   e.) The dose requested is within FDA labeled dosing based on the patient's weight (i.e., 0.9 mg/kg/day)

Continuation of Therapy

A) Duchenne Muscular Dystrophy

1. Authorization of 12 months may be granted for members (including new members) when all of the following criteria are met:
   a.) The member meets initial authorization criteria
   b.) The member demonstrates improved tolerance (i.e. improvement in neuropsychiatric symptoms) to the requested drug as compared to treatment with prednisone
   c.) The member is experiencing a positive response to therapy with the requested drug (see appendix for examples)

Emflaza (deflazacort) is considered **not medically necessary** for members with a diagnosis of DMD who do not meet the criteria set forth above. All other indications are considered experimental/investigational and are not a covered benefit.

Dosing and Administration

Approvals may be subject to dosing limits in accordance with FDA-approved labeling, accepted compendia, and/or evidence-based practice guidelines.

- 0.9 mg/kg once daily

APPENDIX

Appendix: Clinical Response

Positive Response	Clinical Outcome	Assessment Examples
Stabilization or Improvement	Muscle strength	Medical Research Council (MRC) scale for muscle strength with 0 being no movement and 5 being normal strength
Stabilization or Improvement	Pulmonary function	Forced vital capacity (FVC), maximal expiratory pressure
Stabilization or Improvement	Motor function	6 minute walk test (6MWT) distance, timed tests (standing from lying position, climbing 4 stairs, running/walking 30 feet, propelling wheelchair 30 feet)

CLINICAL RATIONALE

Emflaza (deflazacort) is a corticosteroid indicated for the treatment of Duchenne muscular dystrophy (DMD). Specifically, deflazacort is a corticosteroid prodrug, whose active metabolite, 21-desDFZ, acts through the glucocorticoid receptor to exert anti-inflammatory and immunosuppressive effects. The precise mechanism by which Emflaza (deflazacort) exerts its therapeutic effect in patients with DMD is unknown.

The approval of Emflaza by the FDA was based on two trials that evaluated the safety and efficacy of Emflaza. One trial that compared Emflaza with placebo was unable to conclude a significant difference in muscle strength at two years due to disease progression and high dropout rates. Another trial compared Emflaza with prednisone and placebo on muscle strength and motor function in patients with DMD. Over 1 year of treatment, Emflaza was better tolerated and resulted in a lower incidence of weight gain and psychiatric adverse events, which are the most common reasons for discontinuing treatment when compared with prednisone. However, the trial had several limitations resulting in a low quality of evidence.

In a study by McDonald et al, published in Lancet 2017, the authors showed that glucocorticoid treatment for 1 year or longer was associated with increased median age at loss of mobility milestones by 2.1-4.4 years and upper limb milestones by 2.8-8.0 years compared with treatment for less than 1 month. Deflazacort was associated with increased median age at loss of three milestones by 2.1-2.7 years in comparison with prednisone or prednisolone (log-rank $p< 0.012$). Authors noted that their analyses include comparison of multiple glucocorticoid agents and regimens (such as daily vs intermittent dosing) to estimate differences in functional outcomes, and in-depth analysis of specific doses or schedules is not feasible in a long-term prospective natural history study, but requires a randomized clinical trial. For example, differences between deflazacort and prednisone observed long term are possibly attributed to dose or schedule issues. It is possible that dose reductions occurred more commonly with prednisolone or prednisone treatment than with deflazacort treatment because of different frequencies of side-effects. Alternatively, daily regimens of deflazacort might be used more commonly than daily regimens of prednisone or prednisolone because there is more literature pertaining to intermittent prednisolone and prednisone regimens.

Since Emflaza (deflazacort) is a corticosteroid prodrug, the warnings of Emflaza (deflazacort) use are similar to those found with other corticosteroids. Side effects or intolerance to generic corticosteroids are expected with Emflaza (deflazacort) use given the medication is converted to active corticosteroid in the body. Based on a review of the randomized clinical trials, systematic reviews and treatment guidelines, there is very low quality evidence that prednisone is associated with more weight gain than deflazacort but clinical significance has not been studied. Based on the available evidence, the safety of deflazacort (Emflaza) relative to other therapies is unknown at this time.

Corticosteroids, including Emflaza (deflazacort), are effective in the management of DMD. DMD treatment guidelines from the American Academy of Neurology recommend corticosteroid prednisone or deflazacort for the short term benefit of muscle strength and function. Although Emflaza (deflazacort) is FDA approved for DMD, there is insufficient evidence to establish superiority to prednisone therapy. Prednisone is a less costly alternative and appears to be equally effective.

The FOR-DMD randomized clinical trial comparing daily prednisone, daily deflazacort, and intermittent prednisone will provide important data on the safety and efficacy of these regimens in patients 4–6 years of age with Duchenne muscular dystrophy using a composite primary outcome measure containing the time to stand from supine measure and percentage FVC (NCT01603407). The clinical significance of deflazacort over prednisone will not be known until those study results are available. The study was completed in November 2019 but the results have not been published.

PROCEDURES AND BILLING CODES

To report provider services, use appropriate CPT* codes, Alpha Numeric (HCPCS level 2) codes, Revenue codes, and/or ICD diagnostic codes.

REFERENCES

- Emflaza [package insert]. Northbrook, IL: Marathon Pharmaceuticals, LLC; June 2020.
- Bushby K, Finkel R, Birnkrant DJ, et al. Diagnosis and management of Duchenne muscular dystrophy, part 1: diagnosis and pharmacological and psychosocial management. Lancet Neurol. 2010;9:77-93.
- Gloss D, Moxley RT, Ashwal S, Oskoui M. Practice guideline update summary: Corticosteroid treatment of Duchenne muscular dystrophy: Report of the Guideline Development Subcommittee of the American Academy of Neurology. Neurology. 2016;86(5):465-472.
- Griggs RC, Miller JP, Greenberg CR, et al. Efficacy and safety of deflazacort vs prednisone and placebo for Duchenne muscular dystrophy. Neurology. 2016;87(20):2123-2131.
- McDonald CM, Henricson EK, Abresch RT, Duong T, Joyce NC, Hu F, Clemens PR, Hoffman EP, Cnaan A, Gordish-Dressman H; CINRG Investigators. Long-term effects of glucocorticoids on function, quality of life, and survival in patients with Duchenne muscular dystrophy: a prospective cohort study. Lancet. 2017 Nov 22. pii: S0140-6736(17)32160-8. doi: 10.1016/S0140-6736(17)32160-8. [Epub ahead of print]

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