deflazacort (Emflaza™)

Policy # 00554
Original Effective Date: 04/19/2017
Current Effective Date: 10/12/2020

Applies to all products administered or underwritten by Blue Cross and Blue Shield of Louisiana and its subsidiary, HMO Louisiana, Inc.(collectively referred to as the "Company"), unless otherwise provided in the applicable contract. Medical technology is constantly evolving, and we reserve the right to review and update Medical Policy periodically.

When Services May Be Eligible for Coverage

Coverage for eligible medical treatments or procedures, drugs, devices or biological products may be provided only if:

- *Benefits are available in the member's contract/certificate, and*
- *Medical necessity criteria and guidelines are met.*

Based on review of available data, the Company may consider deflazacort (Emflaza™)‡ for the treatment of Duchenne muscular dystrophy to be **eligible for coverage.****

Patient Selection Criteria

Coverage eligibility for deflazacort (Emflaza) will be considered when the following criteria (A, B, and C) are met:

A. Patient has a diagnosis of Duchenne muscular dystrophy; AND
B. Patient is at least 2 years of age; AND
C. Patient meets one of the following conditions (I or II):
    I. Patient has tried generic prednisone for ≥ 6 months 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; OR
        b) Central (truncal) obesity; OR
        c) Undesirable weight gain defined as a ≥ 10% of body weight gain increase over a 6-month period; OR
        d) Diabetes and/or hypertension that is difficult to manage according to the prescribing physician; OR
    II. According to the prescribing physician, the patient has experienced a severe behavioral AE while on generic prednisone therapy that has or would require a prednisone dose reduction.

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*(Note: Criterion "C" is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met)*

When Services Are Considered Not Medically Necessary

Based on review of available data, the Company considers the use of deflazacort (Emflaza) when the patient has NOT tried and failed generic prednisone OR does NOT have valid reasoning as to why generic prednisone has not/will not be sufficient to be **not medically necessary.****

When Services Are Considered Investigational

Coverage is not available for investigational medical treatments or procedures, drugs, devices or biological products.

Based on review of available data, the Company considers the use of deflazacort (Emflaza) when the patient selection criteria are not met (EXCEPT those denoted as **not medically necessary**)** to be **investigational.***

Background/Overview

Emflaza is a corticosteroid indicated for the treatment of Duchenne muscular dystrophy in patients 2 years of age and older. The recommended dose of Emflaza is 0.9 mg/kg/day administered once daily by mouth. Emflaza is available in 6 mg, 18 mg, 30 mg, and 36 mg tablets as well as an oral suspension.

Duchenne Muscular Dystrophy

Duchenne muscular dystrophy is a genetic condition and is the most common type of muscular dystrophy. DMD is caused by a lack of dystrophin, which is a protein that helps keep muscle cells intact. This disease most commonly affects boys, but in rare cases, it can affect girls. It is estimated that DMD occurs in 1 of every 3,600 male infants worldwide. Glucocorticoids are currently the only medications available that slow the decline in muscle strength and function in patients with DMD. Prior to the approval of Emflaza, there were no other corticosteroids that carried an official indication for the treatment of DMD, however prednisone has been the mainstay of therapy for quite some time. In fact, there are data available to support the use of prednisone. In comparative trials, Emflaza and prednisone have shown similar efficacy. According to guidelines from the American Academy

of Neurology, patients that experience Cushingoid appearance or obesity with prednisone may be switched to Emflaza. Currently, Emflaza seems to be a therapeutic alternative to prednisone.

FDA or Other Governmental Regulatory Approval

U.S. Food and Drug Administration (FDA)
Emflaza is a corticosteroid indicated for the treatment of Duchenne muscular dystrophy in patients 2 years of age and older.

Rationale/Source

This medical policy was developed through consideration of peer-reviewed medical literature generally recognized by the relevant medical community, U.S. FDA approval status, nationally accepted standards of medical practice and accepted standards of medical practice in this community, Blue Cross and Blue Shield Association technology assessment program (TEC) and other non-affiliated technology evaluation centers, reference to federal regulations, other plan medical policies, and accredited national guidelines.

The effectiveness of Emflaza for the treatment of DMD was established in a multicenter, randomized, double-blind, placebo-controlled, 52 week study conducted in the US and Canada. Patients were randomized to therapy with Emflaza (0.9 or 1.2 mg/kg/day), an active comparator (prednisone), or placebo. A comparison to placebo was made after 12 weeks of treatment. After 12 weeks, placebo patients were re-randomized to receive either Emflaza or the active comparator (prednisone). All patients continued treatment for an additional 40 weeks. Emflaza 0.9 mg/kg/day and prednisone showed a significant difference in muscle strength at week 12 relative to placebo. Improvement in motor function was also noted in both groups. From weeks 12 to 52, there was a significant improvement in average muscle strength score in the Emflaza 0.9 mg/kg/day group compared to the prednisone group. The prednisone group experienced central obesity and Cushingoid experience more often than the Emflaza group (25% vs. 43% for central obesity, 60% vs. 78% for Cushingoid appearance). Cataracts occurred in 4.4% of patients in the Emflaza group vs. 1.6% in the prednisone group.

An additional randomized, double-blind, placebo-controlled study evaluated Emflaza vs. placebo. The results of the analysis of the primary endpoint of average muscle strength scores in study 2 at 2 years were not statistically significant. The lack of statistical significance could possibly be due to

only a limited number of patients remaining in the placebo arm (subjects were discontinued when they lost ambulation). Regardless, muscle strength scores at month 6 and 12, as well as the average time to loss of ambulation, numerically favored Emflaza in comparison with placebo.

Even though there was shown to be a statistical difference between Emflaza and prednisone, there was only a slight decrease in the MRC (medical research council) scale scores. The clinical meaningfulness of the difference is difficult to interpret as both treated groups had positive changes in MRC from baseline. The main difference in the therapies likely lies within the adverse reactions. As noted above, Emflaza currently stands as a therapeutic alternative to prednisone. This is supported in guidelines from the American Academy of Neurology, patients that experience Cushingoid appearance or obesity with prednisone may be switched to Emflaza.

References

1. Emflaza [package insert]. Marathon Pharmaceuticals, LLC. Northbrook, Illinois. Updated June 2019.
2. Emflaza Drug Evaluation. Express Scripts.
3. Gloss D, Moxley RT 3rd, 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.

Policy History

Original Effective Date: 04/19/2017
Current Effective Date: 10/12/2020

04/06/2017	Medical Policy Committee review
04/19/2017	Medical Policy Implementation Committee approval. New policy.
04/05/2018	Medical Policy Committee review
04/18/2018	Medical Policy Implementation Committee approval. No change to coverage.
04/04/2019	Medical Policy Committee review
04/24/2019	Medical Policy Implementation Committee approval. No change to coverage.
09/05/2019	Medical Policy Committee review
09/11/2019	Medical Policy Implementation Committee approval. Updated age requirement to reflect FDA approval for ages 2 years and older.
09/03/2020	Medical Policy Committee review

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09/09/2020 Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
Next Scheduled Review Date: 09/2021

*Investigational – A medical treatment, procedure, drug, device, or biological product is Investigational if the effectiveness has not been clearly tested and it has not been incorporated into standard medical practice. Any determination we make that a medical treatment, procedure, drug, device, or biological product is Investigational will be based on a consideration of the following:

A. Whether the medical treatment, procedure, drug, device, or biological product can be lawfully marketed without approval of the U.S. Food and Drug Administration (FDA) and whether such approval has been granted at the time the medical treatment, procedure, drug, device, or biological product is sought to be furnished; or
B. Whether the medical treatment, procedure, drug, device, or biological product requires further studies or clinical trials to determine its maximum tolerated dose, toxicity, safety, effectiveness, or effectiveness as compared with the standard means of treatment or diagnosis, must improve health outcomes, according to the consensus of opinion among experts as shown by reliable evidence, including:
    1. Consultation with the Blue Cross and Blue Shield Association technology assessment program (TEC) or other nonaffiliated technology evaluation center(s);
    2. Credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community; or
    3. Reference to federal regulations.

**Medically Necessary (or "Medical Necessity") - Health care services, treatment, procedures, equipment, drugs, devices, items or supplies that a Provider, exercising prudent clinical judgment, would provide to a patient for the purpose of preventing, evaluating, diagnosing or treating an illness, injury, disease or its symptoms, and that are:

A. In accordance with nationally accepted standards of medical practice;
B. Clinically appropriate, in terms of type, frequency, extent, level of care, site and duration, and considered effective for the patient's illness, injury or disease; and
C. Not primarily for the personal comfort or convenience of the patient, physician or other health care provider, and not more costly than an alternative service or sequence of services at least as likely to produce equivalent therapeutic or diagnostic results as to the diagnosis or treatment of that patient's illness, injury or disease.

For these purposes, "nationally accepted standards of medical practice" means standards that are based on credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community, Physician Specialty Society recommendations and the views of Physicians practicing in relevant clinical areas and any other relevant factors.

‡ Indicated trademarks are the registered trademarks of their respective owners.

NOTICE: If the Patient's health insurance contract contains language that differs from the BCBSLA Medical Policy definition noted above, the definition in the health insurance contract will be relied upon for specific coverage determinations.

NOTICE: Medical Policies are scientific based opinions, provided solely for coverage and informational purposes. Medical Policies should not be construed to suggest that the Company recommends, advocates, requires, encourages, or discourages any particular treatment, procedure, or service, or any particular course of treatment, procedure, or service.