Emflaza (deflazacort) Prior Authorization with Quantity Limit Program Summary

POLICY REVIEW CYCLE

Effective Date **Date of Origin**
3/1/2023

FDA APPROVED INDICATIONS AND DOSAGE

Agent(s)	FDA Indication(s)	Notes	Ref#
Emflaza (deflazacort) Tablet Oral suspension	Treatment of Duchenne muscular dystrophy (DMD) in patients 2 years of age and older		1

See package insert for FDA prescribing information: https://dailymed.nlm.nih.gov/dailymed/index.cfm

CLINICAL RATIONALE

Duchenne Muscular Dystrophy(2-4)	Duchenne muscular dystrophy (DMD) is one of nine primary types (greater than 30 forms known) of muscular dystrophy. Prevalence in the United States is not exactly known but is estimated to be approximately 1 in 3500 male births worldwide. It is an X-linked recessive inherited genetic disorder primarily affecting boys, but in rare cases it can affect girls. Specifically, the dystrophin gene is affected. Dystrophin is located on the cytoplasmic face of the plasma membrane of muscle fibers and provides mechanical reinforcement to the sarcolemma and stabilizes the glycoprotein complex. This helps stave off degradation and digestion of the glycoprotein complex by proteases. Mutations in the dystrophin gene, and subsequent lack of dystrophin in the glycoprotein complex, result in a rapidly progressing disease involving muscle degeneration and weakness. Symptom onset is in early childhood and many are using a wheelchair in some capacity by 7-12 years of age. Beyond muscle weakness, some common symptoms are pseudohypertrophy of the calf muscles, cardiomyopathy, and poor respiratory function. Currently, there is no cure for DMD, and therapies are supportive in nature. Physical therapy, occupational therapy, respiratory care, speech therapy, braces/wheelchairs/contractures and glucocorticoid therapy are among the most common therapies.
Guidelines(5,6)	The American Academy of Neurology (AAN) indicates that glucocorticoids are the only medication currently available that slows the decline in muscle strength and function in DMD, which in turn reduces the risk of scoliosis and stabilizes pulmonary function. Cardiac function might also improve, with limited data to date indicating a slower decline in echocardiographic measures of cardiac dysfunction, although these measures are not necessarily predictive of the delay in cardiac symptoms, signs, or cardiac-related mortality. Initial randomized controlled trials in patients treated with prednisone for up to 6 months showed an improvement in muscle strength, with 0.75 mg/kg daily having the most favorable profile. The goal of the use of glucocorticoids in the ambulatory child is the preservation of ambulation and the minimization of later respiratory, cardiac, and orthopedic complications, taking into account the well-described risks associated with chronic glucocorticoid administration.

	In patients who have used glucocorticoids while ambulatory, many experts continue medication after loss of ambulation, with the goal of preserving upper limb strength, reducing progression of scoliosis, and delaying decline in respiratory and cardiac function. Indications for initiation of glucocorticoids in non-ambulatory patients are more relative than absolute. The effectiveness of glucocorticoid treatment in preventing scoliosis or in stabilizing cardiac or respiratory function in this setting is not known; this issue thus warrants further study. However, limited data from trials suggest short-term stabilization of pulmonary function in the early non-ambulatory patient. Prednisone (prednisolone) and deflazacort are believed to work similarly and neither one has a clearly superior effect on altering the decline in motor, respiratory, or cardiac function in DMD. The choice of which glucocorticoid to use depends on cost, formulation, and perceived side-effect profiles. Prednisone is inexpensive and available in a tablet and liquid formulation. Deflazacort is more expensive and available in fewer tablet sizes. The updated AAN practice guidelines concluded that prednisone and deflazacort are possibly equally effective for improving motor function in patients with DMD (2 Class III studies). There is insufficient evidence to directly compare the effectiveness of prednisone vs deflazacort in cardiac function in patients with DMD (1 Class III study of a combined cohort). Additionally, prednisone is possibly associated with greater weight gain in the first 12 months of treatment, with no significant difference in weight gain with longer-term use compared with deflazacort (2 Class III studies). Deflazacort is possibly associated with an increased risk of cataracts compared with prednisone, although most are not vision-impairing (2 Class III studies).(7) The AAN states that deflazacort could be offered as an intervention for patients with DMD to improve strength and timed motor function and delay the age at loss of ambulation by 1.4–2.5 years (Level C), improve pulmonary function (Level C), reduce the need for scoliosis surgery (Level C), delay the onset of cardiomyopathy by 18 years of age (Level C), increase survival at 5 and 15 years of follow-up (Level C). There is insufficient evidence to establish a difference in effect on cardiac function (Level U).
Efficacy(1)	Emflaza (deflazacort) is a corticosteroid prodrug whose active metabolite acts through the glucocorticoid receptor to exert anti-inflammatory and immunosuppressive effects. The precise mechanism by which deflazacort exerts its therapeutic effects in patients with Duchenne muscular dystrophy (DMD) is unknown. The effectiveness of Emflaza for the treatment of DMD was established in one multicenter, randomized, double-blind, placebo-controlled, 52-week study. 196 male patients between the ages of 5 and 15 years old with documented mutation of the dystrophin gene, onset of weakness before 5 years of age, and serum creatinine kinase activity at least 10 times the upper limit of normal at some stage in their illness were enrolled. Patients were randomized to receive Emflaza (0.9 or 1.2 mg/kg/day), an active comparator, or placebo. After 12 weeks, placebo patients were re-randomized to receive either Emflaza or the active comparator. Efficacy was evaluated by assessing the change between Baseline and Week 12 in average strength of 18 muscle groups. The change in average muscle strength score between Baseline and Week 12 was significantly greater for the deflazacort 0.9 mg/kg/day dose group than for the placebo group. (p-value 0.017).
Safety(1)	Emflaza is contraindicated in patients with known hypersensitivity to deflazacort or to any of the inactive ingredients. Instances of hypersensitivity, including anaphylaxis, have occurred in patients receiving corticosteroid therapy.

	Dosing: The recommended oral dosage of Emflaza is approximately 0.9 mg/kg/day once daily. If tablets are used, round up to the nearest possible dose. Any combination of the four Emflaza tablet strengths can be used to achieve this dose. If the oral suspension is used, round up to the nearest tenth of a milliliter (mL).

REFERENCES

Number	Reference
1	Emflaza prescribing information. Marathon Pharmaceuticals. June 2021.
2	Muscular Dystrophy Association (MDA). Duchenne Muscular Dystrophy. https://www.mda.org/disease/duchenne-muscular-dystrophy.
3	Centers for Disease Control and Prevention (CDC). Muscular Dystrophy. http://www.cdc.gov/ncbddd/musculardystrophy/data.html.
4	National Institutes of Health (NIH). Muscular Dystrophy Information Page. https://www.ninds.nih.gov/Disorders/All-Disorders/Muscular-Dystrophy-Information-Page.
5	Gloss, David MD, et al. American Academy of Neurology (AAN) Practice guideline update summary: Corticosteroid treatment of Duchenne muscular dystrophy. Neurology. February 2, 2016;86:465-472.
6	Gloss MD, David, et al. Practice guideline update summary: Corticosteroid treatment of Duchenne muscular dystrophy. Report of the Guideline Development Subcommittee of the American Academy of Neurology. Neurology February 2, 2016 vol.86 no. 5 465-472. doi: http://dx.doi.org/10.1212/WNL.0000000000002337.

POLICY AGENT SUMMARY PRIOR AUTHORIZATION

Target Brand Agent(s)	Target Generic Agent(s)	Strength	Targeted MSC	Available MSC	Preferred Status	Effective Date
Emflaza	deflazacort susp ; deflazacort tab	18 MG ; 22.75 MG/ML ; 30 MG ; 36 MG ; 6 MG	M ; N ; O ; Y	N		

POLICY AGENT SUMMARY QUANTITY LIMIT

Target Brand Agent Name(s)	Target Generic Agent Name(s)	Strength	QL Amount	Dose Form	Days Supply	Duration	Addtl QL Info	Allowed Exceptions	Targeted NDCs When Exclusions Exist	Effective Date
Emflaza	Deflazacort Tab 18 MG	18 MG	30.0	TABS	30	Days				
Emflaza	Deflazacort Tab 6 MG	6 MG	60.0	TABS	30	Days				

CLIENT SUMMARY – PRIOR AUTHORIZATION

Target Brand Agent Name(s)	Target Generic Agent Name(s)	Strength	Client Formulary
Emflaza	deflazacort susp ; deflazacort tab	18 MG ; 22.75 MG/ML ; 30 MG ; 36 MG ; 6 MG	Commercial ; HIM ; ResultsRx

CLIENT SUMMARY – QUANTITY LIMITS

Target Brand Agent Name(s)	Target Generic Agent Name(s)	Strength	Client Formulary
Emflaza	Deflazacort Tab 18 MG	18 MG	Commercial ; HIM ; ResultsRx
Emflaza	Deflazacort Tab 6 MG	6 MG	Commercial ; HIM ; ResultsRx

PRIOR AUTHORIZATION CLINICAL CRITERIA FOR APPROVAL

Module	Clinical Criteria for Approval
	Initial Evaluation **Target agent** will be approved when ALL of the following are met: 1. The patient has a diagnosis of Duchenne Muscular Dystrophy confirmed by genetic analysis (i.e., dystrophin deletion or duplication mutation) (genetic test must be submitted) **AND** 2. ONE of the following: A. The patient's age is within FDA labeling for the requested indication for the requested agent **OR** B. The prescriber has provided information supporting the use of the requested agent for the patient's age for the requested indication **AND** 3. ONE of the following: A. The prescriber has provided information that the patient has tried and failed a generic prednisone (or prednisolone) used for at least 6 months **OR** B. The prescriber has provided information that the patient has an intolerance or hypersensitivity to generic prednisone (or prednisolone) that is NOT expected to occur with the requested agent **OR**

Module	Clinical Criteria for Approval
	C. The patient has an FDA labeled contraindication to generic prednisone (or prednisolone) **AND** 4. The prescriber is a specialist in the area of the patient's diagnosis (e.g., pediatric neurologist) or the prescriber has consulted with a specialist in the area of the patient's diagnosis **AND** 5. The patient does NOT have any FDA labeled contraindications to the requested agent **AND** 6. The requested quantity (dose) does NOT exceed the maximum FDA labeled dose based on the patient's weight (i.e., 0.9 mg/kg/day) **Length of Approval:** 12 months NOTE: Quantity Limit applies, please refer to Quantity Limit Criteria section below. **Renewal Evaluation** **Target agent** will be approved when ALL of the following are met: 1. The patient has been previously approved for the requested agent through the plan's Prior Authorization process **AND** 2. Information has been provided demonstrating that the patient has had improvement, stabilization of the patient's disease, or clinical benefit (e.g., improved strength and timed motor function, improved pulmonary function, reduced the need for scoliosis surgery) **AND** 3. The patient does NOT have any FDA labeled contraindications to the requested agent **AND** 4. The requested quantity (dose) does NOT exceed the maximum FDA labeled dose based on the patient's weight (i.e., 0.9 mg/kg/day) **Length of Approval:** 12 months NOTE: Quantity Limit applies, please refer to Quantity Limit Criteria section below.

QUANTITY LIMIT CLINICAL CRITERIA FOR APPROVAL

Module	Clinical Criteria for Approval
	Quantity Limit for the Target Agent(s) will be approved when ONE of the following is met: 1. The requested agent is Emflaza suspension **OR** 2. The requested agent strength does not have a program quantity limit **OR** 3. The requested quantity (dose) does not exceed the program quantity limit **OR** 4. BOTH of the following: A. The requested quantity (dose) is greater than the program quantity limit **AND** B. The requested quantity (dose) cannot be achieved with a lower quantity of any combination of the four Emflaza tablet strengths **Approval Length:** 12 months