Emflaza (deflazacort) Prior Authorization with Quantity Limit Program Summary

This program applies to FlexRx Closed, FlexRx Open, FocusRx, GenRx Closed, GenRx Open, Health Insurance Marketplace, and KeyRx formularies.

This is a FlexRx Standard and GenRx Standard program.

The BCBS MN Step Therapy Supplement also applies to this program for all Commercial/HIM lines of business.

POLICY REVIEW CYCLE

Effective Date	Date of Origin
2/1/2024	8/1/2017

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	Duchenne muscular dystrophy (DMD) is a genetic disorder characterized by progressive muscle degeneration and weakness due to the alterations of a protein called dystrophin that helps keep muscle cells intact. DMD is the most common childhood form of muscular dystrophy as well as the most common of the muscular dystrophies overall with more than 30 known forms. DMD is an X-linked recessive inherited genetic disorder primarily affecting males, although females who carry the defective gene may show some symptoms. Prevalence is 15.9 per 100,000 live male births in the US and 19.5 per 100,000 live male births in the UK. Dystrophin is the protein associated with this affected gene and provides structural stability to skeletal muscles. Mutations in this gene, and subsequent lack of dystrophin in muscle fiber, result in a rapidly progressing disease involving muscle degeneration and weakness. Symptom onset is in early childhood and many children lose the ability to walk by early adolescence. Beyond muscle weakness, other symptoms include enlargement of the calf muscles, lumbar lordosis, and later on cardiomyopathyand poor respiratory function. Until relatively recently, boys with DMD usually did not survive much beyond their teen years. Thanks to advances in cardiac and respiratory care, life expectancy is increasing and many young adults with DMD are surviving into their early 30s. 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. (2-4) Glucocorticoids are the standard of care for DMD, although they remain non-curative. Their long-term use improves muscle strength, improves timed motor function, delays

	loss of ambulation, improves pulmonary function, reduces the need for scoliosis surgery, delays onset of cardiomyopathy, increases survival, and maintains quality of life. The choice of which glucocorticoid to use depends on cost, formulation, and perceived side-effect profiles.(3) The updated American Academy of Neurology 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). 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). 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).(5)
Efficacy	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. All patients continued treatment for an additional 40 weeks. 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). Although not a pre-specified statistical analysis, compared with placebo, the deflazacort 0.9 mg/kg/day dose group demonstrated at Week 52 the persistence of the treatment effect observed at Week 12.(1) A 2nd study of a randomized, double-blind, placebo-controlled, 104-week clinical trial evaluated deflazacort in comparison to placebo. The study population consisted of 29 male children 6 to 12 years of age with a DMD diagnosis confirmed by the documented presence of abnormal dystrophin or a confirmed mutation of the dystrophin gene. The results of the analysis of the primary endpoint of average muscle strength scores in this 2nd study (graded on a 0-5 scale) at 2 years were not statistically significant, possibly because of a limited number of patients remaining in the placebo arm (subjects were discontinued from the trial when they lost ambulation). Although not statistically controlled for multiple comparisons, average muscle strength scores at Months 6 and 12, as well as the average time to loss of ambulation, numerically favored deflazacort in comparison with placebo.(1)
Safety	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.(1)

REFERENCES

Number	Reference
1	Emflaza prescribing information. Marathon Pharmaceuticals. June 2021.
2	Duchenne muscular dystrophy (DMD). Muscular Dystrophy Association. (2021, April 29). https://www.mda.org/disease/duchenne-muscular-dystrophy

Number	Reference
3	Biggar, W. D., Skalsky, A., & McDonald, C. M. (2022). Comparing deflazacort and prednisone in Duchenne Muscular Dystrophy. Journal of Neuromuscular Diseases, 9(4), 463–476. https://doi.org/10.3233/jnd-210776
4	U.S. Department of Health and Human Services. Muscular dystrophy. National Institute of Neurological Disorders and Stroke. https://www.ninds.nih.gov/health-information/disorders/muscular-dystrophy
5	Gloss, D., Moxley, R. T., Ashwal, S., & Oskoui, M. (2016). Practice guideline update summary: Corticosteroid treatment of Duchenne muscular dystrophy. Neurology, 86(5), 465–472. https://doi.org/10.1212/wnl.0000000000002337
6	Reference no longer used

POLICY AGENT SUMMARY PRIOR AUTHORIZATION

Target Brand Agent(s)	Target Generic Agent(s)	Strength	Targeted MSC	Available MSC	Final Age Limit	Preferred Status
Emflaza	deflazacort susp	22.75 MG/ML	M ; N ; O ; Y	N		
Emflaza	deflazacort tab	18 MG ; 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	Day Supply	Duration	Addtl QL Info	Allowed Exceptions	Targeted NDCs When Exclusions Exist
Emflaza	Deflazacort Tab 18 MG	18 MG	30	Tablets	30	DAYS			
Emflaza	Deflazacort Tab 6 MG	6 MG	60	Tablets	30	DAYS			

CLIENT SUMMARY – PRIOR AUTHORIZATION

Target Brand Agent Name(s)	Target Generic Agent Name(s)	Strength	Client Formulary
Emflaza	deflazacort susp	22.75 MG/ML	FlexRx Closed ; FlexRx Open ; FocusRx ; GenRx Closed ; GenRx Open ; Health Insurance Marketplace/BasicRx ; KeyRx
Emflaza	deflazacort tab	18 MG ; 30 MG ; 36 MG ; 6 MG	FlexRx Closed ; FlexRx Open ; FocusRx ; GenRx Closed ; GenRx Open ; Health Insurance Marketplace/BasicRx ; KeyRx

CLIENT SUMMARY – QUANTITY LIMITS

Target Brand Agent Name(s)	Target Generic Agent Name(s)	Strength	Client Formulary
Emflaza	Deflazacort Tab 18 MG	18 MG	FlexRx Closed ; FlexRx Open ; FocusRx ; GenRx Closed ; GenRx Open ; Health Insurance

Target Brand Agent Name(s)	Target Generic Agent Name(s)	Strength	Client Formulary
			Marketplace/BasicRx ; KeyRx
Emflaza	Deflazacort Tab 6 MG	6 MG	FlexRx Closed ; FlexRx Open ; FocusRx ; GenRx Closed ; GenRx Open ; Health Insurance Marketplace/BasicRx ; KeyRx

PRIOR AUTHORIZATION CLINICAL CRITERIA FOR APPROVAL

Module	Clinical Criteria for Approval
PA	**Initial Evaluation** **Target Agent(s)** 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 required) **AND** 2. If the patient has an FDA approved indication, then 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) **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** C. The patient has an FDA labeled contraindication to generic prednisone (or prednisolone) **OR** D. The patient is currently being treated with the requested agent as indicated by ALL of the following: 1. A statement by the prescriber that the patient is currently taking the requested agent **AND** 2. A statement by the prescriber that the patient is currently receiving a positive therapeutic outcome on requested agent **AND** 3. The prescriber states that a change in therapy is expected to be ineffective or cause harm **OR** E. The prescriber has provided documentation that generic prednisone (or prednisolone) cannot be used due to a documented medical condition or comorbid condition that is likely to cause an adverse reaction, decrease ability of the patient to achieve or maintain reasonable functional ability in performing daily activities or cause physical or mental harm **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: If Quantity Limit applies, please refer to Quantity Limit criteria. **Renewal Evaluation**

Module	Clinical Criteria for Approval
	Target Agent(s) 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. The patient has had clinical benefit or disease stabilization with the requested agent (e.g., improved strength, timed motor function, pulmonary function; reduced need for scoliosis surgery) **AND** 3. 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** 4. The patient does NOT have any FDA labeled contraindications to the requested agent **AND** 5. 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: If Quantity Limit applies, please refer to Quantity Limit criteria.

QUANTITY LIMIT CLINICAL CRITERIA FOR APPROVAL

Module	Clinical Criteria for Approval
QL	**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) exceeds 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