Drug Therapy Guidelines	Applicable	Emflaza™ (deflazacort)
Medical Benefit		**Effective:** 1/30/20
Pharmacy- Formulary 1	x	**Next Review:** 12/20
Pharmacy- Formulary 2	x	**Date of Origin:** 4/17
Pharmacy- Formulary 3/Exclusive	x	**Review Dates:** 3/17, 12/17, 12/18, 12/19
Pharmacy- Formulary 4/AON	x	

I. Medication Description

Emflaza (deflazacort) is a corticosteroid prodrug that is indicated for the treatment of Duchenne muscular dystrophy (DMD) in patients ≥5 years of age**.** Deflazacort's active metabolite, 21-desDFZ, 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.

II. Position Statement

Coverage is determined through a prior authorization process with supporting clinical documentation for all requests.

III. Policy

Coverage of Emflaza is provided when the following criteria are met:

- Medication is prescribed by a neurologist or a provider who specializes in the treatment of Duchenne Muscular Dystrophy (DMD) and/or neuromuscular disorders **AND**
- The diagnosis of DMD was confirmed by one of the following:
  - Genetic testing demonstrating a pathologic mutation of the dystrophin gene **OR**
  - Absence of dystrophin protein confirmed by muscle biopsy **AND**
- Member must be at least 2 years of age **AND**
- At least one of the following are true:
  - The member has experienced a severe behavioral or neuropsychiatric adverse effect (AE) while on prednisone therapy that has or would require a prednisone dose reduction **OR**
  - The member has tried prednisone for ≥ 6 months and has had at least one of the following significant intolerable adverse effects (AEs) that is unable to be managed:
    - Cushingoid appearance
    - Central (truncal) obesity
    - Weight gain of at least 10% of body weight over 6-month period
    - Diabetes and/or hypertension that is difficult to manage.

IV. Quantity Limitations

- Suspension: allow up to 2 bottles per month (2 x 13ml bottles)

- 6mg, 18mg, 30mg, 36mg tablets: 30 per month overall
- Additional quantities can be reviewed for coverage as needed due to patient's weight. Factors such as ability to use suspension or lowest cost tablet combinations to obtain desired dose will be considered.

V. Coverage Duration

Coverage may be provided for up to 6 months and may be renewed.

VI. Coverage Renewal Criteria

Coverage can be renewed when the following criteria have been met:

- The member is receiving a clinical benefit from Emflaza therapy, such as improvement or stabilization of muscle strength or pulmonary function (supporting chart notes must be provided) **AND**
- A clear benefit to the use of Emflaza has been shown compared to other available corticosteroids (e.g. reduction in Cushingoid appearance, reduction in the rate of weight gain compared to baseline, etc) which may include one or more of the following:
    - When approved due to excessive weight gain with prednisone: member must have experienced a return to baseline growth curve/weight expectations or remained on the same growth curve/weight that was in effect when Emflaza was initiated **AND**
    - When approved due to behavioral or neuropsychiatric side effects: member has shown improvement in symptoms while on Emflaza therapy.

VII. Billing/Coding Information

Available as:

- 6mg, 18mg, 30mg, and 36mg oral tablets
- 22.75mg/ml oral suspension
    - Available as 13ml bottles
    - Must be dispensed as full, unbroken bottles

VIII. Summary of Policy Changes

- 4/10/17: new policy
- 1/1/18: no policy changes
- 2/15/19: clarified: specialist, documentation required for DMD diagnosis, and renewal criteria
- 1/30/20: updated age requirement

IX. References

1. Emflaza™ tablets and oral suspension [prescribing information]. Northbrook, IL: Marathon Parmaceuticals, LLC; Revised June, 2019.
2. 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.

3. Angelini C, Pegoraro E, Turella E, et al. Emflaza in Duchenne dystrophy: study of long-term effect. *Muscle Nerve*. 1994;17(4):386-391.
4. Griggs RC, Bushby K. Finding the optimum regimen for Duchenne muscular dystrophy (FOR-DMD). In: Clinicaltrials.gov. Bethesda, MD; National Library of Medicine; 2000. Available at: https://clinicaltrials.gov/ct2/show/NCT01603407?term=NCT01603407&rank=1
5. Biggar WD, Harris VA, Eliasoph L, and Alman B. Long-term benefits of Emflaza treatment for boys with Duchenne muscular dystrophy in their second decade. Neuromuscul Disord. 2006;16(4):249-255.
6. King WM, Ruttencutter R, Nagaraja HN, et al. Orthopedic outcomes of long-term daily corticosteroid treatment in Duchenne muscular dystrophy. Neurology. 2007;68(19):1607-13.
7. Annexstad EJ, Lund-Petersen I, Rasmussen M. Duchenne muscular dystrophy. Tidsskr Nor Laegeforen. 2014;134(14):1361-1364
8. Wood MJA. To skip or not to skip: that is the question for Duchenne muscular dystrophy. Mol Ther. 2013;21(12):2131-2132.
9. 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(1):77-93.
10. 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.
11. Bonifati MD, Ruzza G, Bonometto P, et al. A multicenter, double-blind, randomized trial of Emflaza versus prednisone in Duchenne muscular dystrophy. Muscle Nerve. 2000;23:1344-1347.
12. Bello L, Gordish-Dressman H, Morgenroth LP, et al. Prednisone/prednisolone and Emflaza regimens in the CINRG Duchenne natural history study. *Neurology*. 2015;85:1-8.
13. Houde S, Filiatrault M, Fournier A, et al. Emflaza use in Duchenne muscular dystrophy: an 8-year follow-up. Pediatr Neurol. 2008;38(3):200-206.
14. Mesa LE, Dubrovsky AL, Corderi J, et al. Steroids in Duchenne muscular dystrophy. Neuromuscular Disorders. 1991;1(4):261-266.
15. Prednisone tablets, oral solution, and intensol™ solution [prescribing information]. Eatontown, NJ: West-Ward Pharmaceuticals; October 2016.
16. Parente L. Emflaza: therapeutic index, relative potency and equivalent doses versus other corticosteroids. BMC Pharmacol Toxicol. 2017;18(1):1.
17. Markham LW, Spicer RL, Khoury PR, et al. Steroid therapy and cardiac function in Duchenne muscular dystrophy. Pediatr Cardiol. 2005;26:768-771.
18. Balban B, Matthews DJ, Clayton GH, and Carry T. Corticosteroid treatment and functional improvement in Duchenne muscular dystrophy. Am J Phys Med Rehabil. 2005;84:843-850.
19. Matthews E, Brassington R, Kuntzer T, Jichi F, and Manzur AY. Corticosteroids for the treatment of Duchenne muscular dystrophy. Cochrane Database Syst Rev. 2016;(5):CD003725. doi: 10.1002/14651858.CD003725.
20. University of Rochester; Newcastle University, University Medical Center Freiburg, National Institute of Neurological Disorders and Stroke (NINDS). Finding the optimum regimen for Duchenne muscular dystrophy (FOR-DMD). In: ClinicalTrials.gov [Internet]. Bethesda (MD): National Library of Medicine (US). 2017- [cited 2017 Feb 16]. Available at: https://clinicaltrials.gov/ct2/show/record/NCT01603407?term=FOR+DMD&rank=1. NLM Identifier: NCT01603407.

21. Darras B.T.(2018). Duchenne and Becker muscular dystrophy: Clinical features and diagnosis. In: UpToDate, Post TW (Ed), UpToDate, Waltham, MA. (Accessed on November 28, 2018)

The Plan fully expects that only appropriate and medically necessary services will be rendered. The Plan reserves the right to conduct pre-payment and post-payment reviews to assess the medical appropriateness of the above-referenced therapies.

The preceding policy is a guideline to allow for coverage of the pertinent medication/product, and is not meant to serve as a clinical practice guideline.