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Emflaza (Deflazacort) for Children with Duchenne Muscular Dystrophy: Comparative Effectiveness versus Prednisone

Individual Topic Request

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Policy Context

Deflazacort, under the brand name Emflaza, was approved by the Food and Drug Administration (FDA) in February 2017 for treatment of Duchenne muscular dystrophy (DMD) in patients ages five and older (Marathon Pharmaceuticals, 2017). The drug was granted fast-track approval under the FDA's rare pediatric disease priority review voucher program (FDA, 2016). Regulatory approval was based on the results of a randomized, placebo-controlled trial (Griggs et al., 2016). Deflazacort has been used for decades in Canada (McAdam, Mayo, Alman, & Biggar, 2012) and Europe, but it had not previously been approved for use in the United States. State Medicaid officials are interested in the comparative effectiveness and safety of deflazacort compared to prednisone.

Key Findings

- Four randomized controlled trials of poor methodological quality showed *very low-quality evidence* (i.e., we have very little confidence in the effect estimate; the true effect is likely to be substantially different from the estimate of effect) of the following:
 - Deflazacort and prednisone do not significantly differ on muscle strength and motor outcomes.
 - Deflazacort is associated with significantly less weight gain but more cataracts than prednisone.
- We found no comparative evidence for deflazacort and prednisone beyond two years of follow-up.
- The trial used to establish FDA approval of deflazacort was completed in 1995, and its results might not be generalizable to individuals who currently have DMD.

Table 1 summarizes the quality of the evidence for the comparative effectiveness of deflazacort and prednisone for children with DMD. We assigned outcomes a summary judgment for the overall quality of evidence based on the Grading of Recommendations, Assessment, Development, and Evaluation (GRADE) system (Guyatt et al., 2008).

Table 1. Summary of Findings for Comparative Effectiveness of Deflazacort vs. Prednisone in Children with DMD

Outcome	Quality of the evidence	Explanation
Muscle strength and motor outcomes	Very low	Downgraded for risk of bias, imprecision, and lack of applicability
Weight gain	Very low	Downgraded for risk of bias, imprecision, and lack of applicability
Cataracts	Very low	Downgraded for risk of bias, imprecision, and lack of applicability

Background

Muscular dystrophy refers to a group of disorders caused by a mutation in one of several genes required for muscle function (Darras, 2017a). It is classified as Duchenne, Becker, or intermediate type. DMD is the most severe form, and also the most common (Darras, 2017a). Diagnosis is based on clinical signs of muscle weakness, family history, and elevated creatinine kinase levels (Darras, 2017a). Genetic testing or muscle biopsy can confirm the diagnosis (Darras, 2017a).

Children with DMD typically experience progressive muscle weakness starting between ages two and three, loss of independent ambulation often occurring by age 12, and eventual death from cardiomyopathy or respiratory failure in their late teens or early twenties (Darras, 2017a).

Orthopedic complications including fractures and scoliosis also commonly occur (Darras, 2017a).

There is no cure for DMD. Treatment is aimed at managing symptoms and slowing disease progression. In children over age five, glucocorticoids are prescribed to improve motor and pulmonary function and reduce the risk of scoliosis (Darras, 2017b).

PICO

Population

Children (under age 21 years) with DMD

Intervention

Deflazacort

Comparator

Prednisone

Outcomes

Muscle strength, motor function, quality of life, mortality, adverse events

Objective

The objective is to assess the evidence for the comparative effectiveness and safety of deflazacort versus prednisone in children with DMD.

Methods

We searched core evidence and guideline sources for systematic reviews and meta-analyses and randomized controlled trials of deflazacort versus other glucocorticoids for patients with DMD. Search strategies are detailed in Appendix A. Electronic searches were supplemented with manual searches of reference lists of included articles. To identify ongoing trials, we searched the website ClinicalTrials.gov.

We assessed the methodological quality of included studies and the quality of the body of evidence for specific outcomes using the criteria described in Appendix A. Results were synthesized narratively.

Findings

Controlled Trials

Searches identified four randomized controlled trials, reported in seven publications, of deflazacort versus prednisone for children with DMD (Bonifati et al., 2000a; Bonifati et al., 2000b; Brooke, 1996; Dubowitz, 2000; Griggs et al., 2016; Karimzadeh & Ghavazi, 2012; Reitter, 1995). Appendix B and Tables 1 and 2 summarize the quality of the body of evidence for specific outcomes and study characteristics, methodological quality, and results of the included comparative trials. We rated all of the studies as having poor methodological quality (Bonifati et al., 2000a; Bonifati et al., 2000b).

The four trials, as described in the seven publications, had similar eligibility criteria: boys over five years old with a confirmed diagnosis of DMD. Two trials specified that the children were still ambulatory, and two excluded those with any previous or recent steroid use. All of the trials included a comparison of deflazacort 0.9 mg/kg/day to prednisone 0.75 mg/kg/day. The follow-up periods ranged from 12 weeks to two years.

The randomized controlled trial recently published by Griggs et al. (2016) and submitted to the FDA for regulatory approval of Emflaza was completed in 1995 and first presented at the 75th American Academy of Neurology annual meeting in 1996 (Brooke, 1996). Boys over age five with either Duchenne or Becker muscular dystrophy were eligible. A total of 196 boys were randomized to receive deflazacort 0.9 mg/kg/day (n = 51), deflazacort 1.2 mg/kg/day (n = 49), prednisone 0.75 mg/kg/day (n = 46), or a placebo (n = 50).

The primary outcome was change in muscle strength from baseline to week 12, as measured by the Medical Research Council (MRC) scale score. Secondary outcomes included change in muscle strength from week 12 to one year, motor function, pulmonary function, the physician's global assessment of disease severity, adverse events, weight gain, and change in growth (Griggs et al., 2016). The results were presented as the mean difference from the baseline. Both deflazacort and prednisone significantly improved muscle strength and motor function compared to a placebo, but there was no significant difference between the deflazacort and prednisone groups on the primary outcome of change in MRC score up to week 12 (0.15; 95% CI, 0.01 to 0.28 vs. 0.27; 0.13 to 0.41). Similarly, there was no significant difference between groups on the mean change in MRC score from baseline to one year (0.39; 95% CI, 0.25 to 0.54 vs. 0.23; 0.07 to 0.38) or on tests of timed motor functioning. Patients in the deflazacort group had less weight gain after one year (mean difference 5.05 kg; 95% CI, 4.08 to 6.01 kg vs. 8.45 kg; 7.41 to 9.49 kg; $p < 0.0001$) but more developed cataracts (6.6% vs. 4.4%; p value not reported) (Griggs et al., 2016). Change from baseline to one year in body mass index was also tested and found to be significantly greater with prednisone (2.29; 95% CI, 1.71 to 2.87 vs. 3.60; 95% CI, 2.97 to 4.24; $p = 0.0024$) (Griggs et al., 2016).

We rated this trial as having poor methodological quality for several reasons. There was no information on randomization and allocation concealment methods, and baseline data on

disease severity was not reported. Although it was recently published, the trial was completed in 1995, and thus might not be generalizable to current treatment. For example, the study included children with either Duchenne or Becker muscular dystrophy because at the time the distinction between the different types of muscular dystrophy was less clear than it is today (Griggs et al., 2013).

Another trial, which ultimately enrolled 100 patients, was first published as a preliminary report on 67 patients in 1995 (Reitter, 1995). In that publication, the authors presented the results graphically and did not report data by intervention group. According to the authors, the preliminary data showed that both prednisone and deflazacort improved the course of disease, but did not point to any differences by medication group (Reitter, 1995). The trial's final results were briefly described in a conference workshop summary published in 2000 (Dubowitz, 2000). Of 100 boys enrolled, 80 completed two years of treatment with no protocol violations. Fourteen boys withdrew from treatment because of weight gain; "the majority" of them were in the prednisone group (Dubowitz, 2000). There were no significant differences between groups on measures of muscle strength and motor function, although no data were reported. Weight gain was significantly higher in boys who received prednisone (no data), but more boys on deflazacort developed cataracts (36% vs. 3%). The study's final results have never been fully published. We rated this study poor quality because of very limited reporting of methods and high and differential loss to follow-up without the use of intention-to-treat analysis.

A trial of 18 patients conducted in Italy was described in two publications reporting outcomes at one year (Bonifati et al., 2000a) and two years (Bonifati et al., 2000b). Intervention groups were stratified by age and disease severity, and patients and evaluators were blinded to treatment allocation. Muscle strength and motor outcomes results were presented graphically only. The authors found no significant difference in functional score at three, six, or nine months. However, they did find an improvement in functional score in the prednisone group from month 9 to month 12, but attributed this finding to participants discontinuing the study who had more severe scores. After two years, no significant differences were found between the two groups in the MRC score or functional scores (Bonifati et al., 2000b). More weight gain was observed in the prednisone group at one year (mean difference from baseline 2.17 kg vs. 5.08 kg), and continued into the second year (4.6 kg vs. 8.7 kg; $p < 0.05$). We rated this study as having poor methodological quality because of its small sample size and lack of reporting of randomization and allocation concealment methods.

Karimzadeh and Ghavazi (2012) conducted a randomized controlled trial in Iran enrolling 34 participants. The authors found a greater mean increase in the motor function index in the deflazacort group at 12 months (15.0% vs. 18.1%; $p = 0.001$) and 18 months, but the difference was not statistically significant at 18 months (24.5% vs. 29.2%; $p = 0.128$). Muscle strength was not measured. There was significantly more weight gain with prednisone from baseline to 12 months (mean increase from baseline 13.0% vs. 21.7%; $p = 0.001$) and 18 months (21.7% vs. 32.0%; $p = 0.046$). Four patients in the prednisone group withdrew from treatment because of

uncontrollable weight gain. We rated this trial as having poor methodological quality because of a high and differential loss to follow-up (17.6% deflazacort, 29.4% prednisone) without the use of intention-to-treat analysis. The authors also did not provide information on randomization, allocation concealment, blinding methods, or baseline characteristics by intervention group.

Table 2 briefly summarizes the main findings of these trials (See Appendix B for data). Taken together, they do not provide sufficient evidence to conclude that one drug is safer or more effective than another for children with DMD. This body of evidence suggests that deflazacort and prednisone demonstrate no significant differences in efficacy but have different adverse effect profiles. For deflazacort, less weight gain was observed, but cataracts were more common. However, the trials were of poor methodological quality and outcome reporting was incomplete. Two of the trials were conducted more than 20 years ago, and the more recent ones had very small sample sizes.

Table 2. Summary of Controlled Trials of Deflazacort vs. Prednisone in Children with DMD

Study citations (Quality)	Number enrolled	Duration	Muscle strength/ Motor outcomes	Adverse effects
Brooke, 1996; Griggs, 2016 (Poor)	196	3 months (primary outcome) 1 year (additional analyses)	Both deflazacort and prednisone better than placebo More improvement in muscle strength with deflazacort between week 12 and one year, but no difference between groups at week 12 or one year	More weight gain with prednisone More cataracts with deflazacort
Reiter, 1995; Dubowitz, 2000 (Poor)	100	2 years	Not significantly different between groups	More weight gain with prednisone More cataracts with deflazacort
Bonifati, 2000a; Bonifati, 2000b (Poor)	18	2 years	Not significantly different between groups	More weight gain with prednisone More cataracts with deflazacort
Karimzadeh, 2012 (Poor)	34	18 months	Better with deflazacort at 12 months; no difference at 18 months	More weight gain with prednisone

Systematic Reviews

Three good methodological quality systematic reviews (Campbell & Jacob, 2003; Matthews, Brassington, Kuntzer, Jichi, & Manzur, 2016; Wong & Christopher, 2002), one with a meta-analysis (Matthews et al., 2016), included a comparison of deflazacort to prednisone in children with DMD. No review included all four of the trials that we identified for this report. Because the reviews were conducted during different time periods and varied in their study inclusion criteria

(e.g., whether to include abstracts), the body of evidence they considered differed. No review included the fully published Griggs trial (Griggs et al., 2016), although the abstract (Brooke, 1996) was included in two (Campbell & Jacob, 2003; Wong & Christopher, 2002). Despite these differences, the reviewers reached similar conclusions, as shown in Table 3. The authors of two of the three reviews concluded that deflazacort and prednisone were similarly effective in improving strength and functional outcomes, and that deflazacort leads to less weight gain than prednisone (Campbell & Jacob, 2003; Wong & Christopher, 2002). The authors of the third review (Matthews et al., 2016) did not make conclusions about motor outcomes because of a lack of reporting in the trials they included. They concluded that evidence from two trials (Bonifati et al., 2000a; Karimzadeh & Ghavazi, 2012) indicated that deflazacort causes less weight gain than prednisone after one year. Using GRADE Working Group methods (Schünemann, Brozek, Guyatt, & Oxman, 2014), the review authors downgraded the quality of this evidence to “very low quality” (very little confidence in the effect estimate) based on a high risk of bias in trials, evidence of publication bias, and imprecision of the estimate (Matthews et al., 2016).

Table 3. Systematic Reviews of Deflazacort vs. Prednisone in Children with DMD

Author, year	Active control trial publications included	Authors’ conclusions on comparative effectiveness
Matthews, 2016	Bonifati, 2000a; Karimzadeh, 2012	Very low-quality evidence from two trials indicates that deflazacort causes less weight gain than prednisone after one year of treatment.
Campbell, 2003	Bonifati, 2000a; Brooke, 1996	The authors’ examination of individual studies found that deflazacort appears to improve strength and functional outcomes compared to a placebo, but it remains unclear whether deflazacort has a benefit over prednisone on similar outcomes. Two trials found that deflazacort causes less weight gain than prednisone.
Wong, 2001	Reitter, 1995 Brooke, 1996 Bonifati, 2000a	The authors found that (1) prednisone/prednisolone and deflazacort were of definite benefit in improving muscle strength and delaying the loss of independent ambulation by at least 3 years; (2) long-term prednisone/prednisolone and deflazacort improved pulmonary function; and (3) weight gain and growth suppression were the main side effects; deflazacort caused less weight gain.

Clinical Practice Guideline

We identified a recent, good methodological quality clinical practice guideline of corticosteroid treatment for DMD (Gloss, Moxley, Ashwal, & Oskoui, 2016). Only one controlled trial (Bonifati et al., 2000a) was included. The guideline differed from the systematic reviews in that the authors included observational studies of the comparative effectiveness of deflazacort and prednisone, in addition to the controlled trial. Table 4 summarizes the sections of the guideline related to

the use of prednisone and deflazacort. The guideline authors did not recommend one drug over another, and their recommendations regarding the comparative effectiveness of deflazacort and prednisone reflected low confidence in the quality of the evidence (Gloss et al., 2016).

Table 4. American Academy of Neurology Practice Guideline on Corticosteroid Treatment of DMD (2016 update)

Prednisone	Deflazacort	Comparative effectiveness
<p>Should be used to</p> <ul style="list-style-type: none"> • Improve strength (Level B) • Improve pulmonary function (Level B) <p>May be used to</p> <ul style="list-style-type: none"> • Reduce the need for scoliosis surgery (Level C) • Improve timed motor function (Level C) • Delay the onset of cardiomyopathy by age 18 (Level C) 	<p>May be used to</p> <ul style="list-style-type: none"> • 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 age 18 (Level C) • Increase survival at 5 and 15 years of follow-up (Level C) 	<ul style="list-style-type: none"> • Deflazacort and prednisone may be equivalent in improving motor function (Level C) • Insufficient evidence to establish a difference in effect on cardiac function (Level U) • Prednisone may be associated with greater weight gain in the first years of treatment than deflazacort (Level C) • Deflazacort may be associated with a greater risk of cataracts than prednisone (Level C)

Note: Explanation of Recommendation Levels

	Level U	Level C	Level B	Level A
Value of benefit relative to risk	Too close to call	Small	Moderate	Large
Confidence in evidence	Very low	Low	Moderate	High
Strength of inferences	Not plausible	Plausible	Convincing	Compelling

Source: Adapted from Gloss et al. (2016)

Summary and Conclusions

We found very low-quality evidence that deflazacort and prednisone do not significantly differ on muscle strength or motor outcomes in children with DMD. We also found very low-quality evidence that deflazacort leads to significantly less weight gain than prednisone, and that deflazacort is associated with more cataracts than prednisone. Although four randomized trials have included a comparison of the two drugs, all were small and had serious methodological flaws. Additionally, two of the trials were conducted more than 20 years ago and only one was conducted in the United States, limiting their generalizability to current practice. Three recent systematic reviews and a clinical practice guideline were consistent in not recommending one drug over the other.

Because of the very low quality of the body of evidence, well-designed studies with complete reporting of all relevant outcomes are needed. Rigorously designed comparative trials will help clinicians make better-informed decisions about which treatments to consider in children with DMD. A search of ClinicalTrials.gov identified one ongoing trial of deflazacort versus prednisone for DMD (ClinicalTrials.gov, 2017). This double-blind, randomized controlled trial, sponsored by the University of Rochester, will enroll boys with DMD ages four to seven years and will compare daily deflazacort (0.9 mg/kg) to two prednisone regimens (0.75 mg/kg daily or 10 days on and 10 days off treatment). Participants will be followed for three years. The primary outcome is a composite of three measures (time to stand from lying, forced vital capacity, and parents' and children's reported global satisfaction with treatment). The record gives an estimated trial completion date of October 2019 and a planned sample size of 196 patients.

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Appendix A. Methods

Search Strategies

Database: Ovid MEDLINE(R) <1946 to March Week 1 2017>

Search Strategy:

- 1 Muscular Dystrophy, Duchenne/dt [Drug Therapy] (564)
- 2 limit 1 to (english language and humans) (406)
- 3 limit 2 to (clinical trial, all or controlled clinical trial or randomized controlled trial) (95)
- 4 Glucocorticoids/ (56636)
- 5 3 and 4 (17)

Database: Ovid MEDLINE(R) <1946 to February Week 4 2017>

Search Strategy:

- 1 Emflaza.mp. (0)
- 2 deflazacort.mp. (480)
- 3 duchenne muscular dystrophy.mp. (7068)
- 4 1 or 2 (480)
- 5 3 and 4 (72)
- 6 limit 5 to yr="2007 -Current" (46)
- 7 limit 6 to english language (46)
- 8 humans/ (16442539)
- 9 animals/ (5992793)
- 10 9 not (8 and 9) (4291970)
- 11 7 not 10 (43)

Quality Assessment

We assessed the methodological quality of the included controlled trials and systematic reviews using standard instruments developed and adapted by the Center for Evidence-based Policy researchers, these instruments are modifications of the systems in use by NICE and SIGN (National Institute for Health and Care Excellence, 2009; Scottish Intercollegiate Guidelines Network, 2009).

Systematic Reviews

One rater assigned each study a rating of good, fair, or poor based on its adherence to recommended methods and its potential for biases. In brief, good-quality systematic reviews include a clearly focused question, a literature search sufficiently rigorous to identify all relevant studies, and criteria used to select studies for inclusion (e.g., randomized controlled trials), and they assess study quality and similarities between studies to determine whether combining them is appropriate for evidence synthesis. Fair-quality systematic reviews have incomplete information about methods that might mask important limitations or a meaningful conflict of interest. Poor-quality systematic reviews have clear flaws that could introduce significant bias.

Randomized Controlled Trials

One rater assigned the study a rating of good, fair, or poor based on its adherence to recommended methods and potential for biases. Good-quality randomized controlled trials include a clear description of the population, setting, intervention, and comparison groups; a random and concealed allocation of patients to study groups; low dropout rates; and intention-to-treat analyses. Good-quality randomized controlled trials also have low potential for bias from conflicts of interest and funding source(s). Fair-quality randomized controlled trials have incomplete information about methods that might mask important limitations or a meaningful conflict of interest. Poor-quality randomized controlled trials have clear flaws that could introduce significant bias.

Quality of Evidence Assessment

We assigned outcomes a summary judgment for the overall quality of evidence based on the system developed by the Grading of Recommendations, Assessment, Development, and Evaluation Working Group (GRADE) (Guyatt et al., 2008; Schünemann et al., 2014). The GRADE system defines the overall quality of a body of evidence for an outcome in the following manner:

- **High quality:** We are very confident that the true effect lies close to that of the estimate of the effect
- **Moderate quality:** We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different
- **Low quality:** Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect
- **Very low quality:** We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect

Appendix B. Summary of Randomized Controlled Trials of Deflazacort vs. Prednisone

Table B1. Study Design Characteristics

Study Citations	Setting/ Eligibility criteria	Number enrolled	Duration	Intervention	Comparator	Quality assessment and notes
Bonifati, 2000a; Bonifati, 2000b	Italy, 2 neuromuscular centers Diagnosis of DMD confirmed by dystrophin immunohistochemistry, age over 5 years, preserved ability to ambulate independently, and no previous steroid therapy.	18	2 years	Deflazacort 0.9 mg/kg/day	Prednisone 0.75 mg/kg/day	Poor Randomization and allocation method not described. Baseline characteristics not reported other than age. Authors reported that functional parameters were similar between groups but no data were given. One patient excluded from analysis (6%).
Karimzadeh, 2012	Iran, single center Muscle weakness before age 5, male, proximal muscle weakness, increase in creatinine kinase >40 times normal limit at start of symptoms. Diagnosis confirmed by muscle biopsy to prove dystrophin deficiency or genetic evaluation to confirm dystrophin gene deletion.	34	18 months	Deflazacort 0.9 m/kg/day decreased to 0.5 mg/kg/day if complications	Prednisone 0.75 mg/kg/day decreased to 0.3 mg/kg/day if complications	Poor Randomization and allocation concealment methods not reported; baseline characteristics not reported by group, described as single-blind, but no details. High and differential loss to follow-up (3 deflazacort, 5 prednisone).
Reiter, 1995; Dubowitz, 2000	Germany, single center Boys between age 5 and age at loss of ambulation, diagnosis confirmed by cDNA analysis,	100	2 years	Deflazacort 0.9 mg/kg/day	Prednisone 0.75 mg/kg/day	Poor Very little detail on study methods. Final study results were

Study Citations	Setting/ Eligibility criteria	Number enrolled	Duration	Intervention	Comparator	Quality assessment and notes
	muscle biopsy, and dystrophin Western blot.					never fully published. Randomization and allocation concealment methods not reported, baseline characteristics not reported, no detail on blinding.
Griggs, 2016; Brooke, 1996	US and Canada, multicenter Boys ages 5 to 15, with onset of weakness before age 5; increased serum creatinine kinase activity at least 10 times the upper limit of normal; and either genetic analysis of the dystrophin gene or biopsy that demonstrated a clear alteration in dystrophin amount or distribution in the muscle. Exclusion criteria: Previous long-term use (>1 year) of oral glucocorticoids, active peptic ulcer disease or history of gastrointestinal bleeding or perforation, any use of oral steroids for >1 month within 6 months of study entry, any use of oral steroids for <1 month within 2 months of study entry, normal muscle biopsy or muscle biopsy evidence of denervation or glycogen storage disease, or skin rash suggestive of dermatomyositis.	196	3 months (primary outcome) 1 year (additional unplanned analyses)	Deflazacort 0.9 mg/kg/day 1.2 mg/kg/day	Prednisone 0.75 mg/kg/day Placebo	Poor Randomization and allocation concealment methods not reported. Only baseline age, race, and BMI reported. No data on disease severity at baseline. Short (12-week) follow-up on primary outcome. Potential conflict of interest: first author is consultant for Marathon pharmaceuticals. This study was completed over 20 years ago but just recently published in full.

Table B2. Results of Trials of Deflazacort vs. Prednisone

	Deflazacort 0.9 mg/kg/day vs. Prednisone 0.75 mg/kg/day			
Study citations (Quality)	Muscle strength	Motor function	Weight gain	Other outcomes
Bonifati, 2000a; Bonifati, 2000b (Fair)	(Graph only) No significant difference in MRC score at 3, 6, or 9 months	(Graph only) No significant difference in functional score at 3, 6, or 9 months Improvement in functional score in prednisone group from month 9 to 12, but attributed to drop out of a patient with more severe scores	Mean increase at 1 year: 2.17 kg vs. 5.08 kg p-value not reported % increase at 6 months (no data) P < 0.05 % increase at 1 year: 9% vs. 21.3% p-value not reported Increase of over 20% body weight at 1 year: 1 vs. 4 patients p-value not reported At 2 years: 4 vs. all patients p-value not reported	1 vs. 0 traumatic bone fracture 3 vs. 1 cataract at 2 years p-values not reported
Griggs, 2016; Brooke, 1996 (Poor)	MRC score Mean difference (95% CI) Change from baseline to week 12 (primary outcome): 0.15 (0.01, 0.28) vs. 0.27 (0.13, 0.41); nonsignificant	No differences between groups in timed functional testing (Supine to standing; climb 4 stairs; run or walk 30 feet; propel wheelchair 30 feet)	Mean difference (95% CI) Weight change from baseline to week 12: 1.72 kg (0.51, 2.93) vs. 3.23 kg (1.94, 4.52); nonsignificant From week 12 to one year: 3.64 kg (2.90, 4.38) vs. 5.57 kg (4.76, 6.37); p = 0.0003 From baseline to one year:	Discontinuation due to adverse events: 3/51 (6%) vs. 4/46 (7%); nonsignificant Deaths: 1/51 vs. 1/46; nonsignificant Cushingoid appearance: 60.3% vs. 77.8%; p = 0.0385

Deflazacort 0.9 mg/kg/day vs. Prednisone 0.75 mg/kg/day				
Study citations (Quality)	Muscle strength	Motor function	Weight gain	Other outcomes
	Change from week 12 to week 52: 0.17 (0.03, 0.31) vs. -0.12 (-0.26, 0.03); p = 0.044 Change from baseline to one year: 0.39 (0.25, 0.54) vs. 0.23 (0.07, 0.38); nonsignificant		5.05 kg (4.08, 6.01) vs. 8.45 kg (7.41, 9.49); p < 0.0001 Change in body mass index from baseline to one year: 2.29 (1.71, 2.87) vs. 3.60 (2.97, 4.24); p = 0.0024	Physician's global assessment of disease severity: nonsignificant
Karimzadeh, 2012 (Poor)	Not measured	Motor function index mean percentage change at one year: 15.0% vs. 18.1%; p = 0.001 At 18 months: 24.5% vs. 29.2%: (p = 0.128)	Percent increase in weight at 1 year: 13.0% vs. 21.7%; p = 0.001 Withdrawal due to uncontrollable weight loss: 0 vs. 4 patients Mean weight gain at 18 months: 21.7% vs. 32.0%; p = 0.046	No other adverse events observed
Reiter, 1995; Dubowitz, 2000 (Poor)	Data presented graphically only; no differences between groups	Data presented graphically only; no differences between groups	More weight gain with prednisone (no data) 14 boys withdrew from treatment due to weight gain, "the majority" in the prednisone group p-value not reported	Cataracts: 16/44 (36%) vs. 1/36 (3%) p-value not reported

Suggested citation: Carson, S., Driver, R., & Harrod, C. (2017). *Emflaza (deflazacort) for children with Duchenne muscular dystrophy: Comparative effectiveness versus prednisone*. Portland, OR: Center for Evidence-based Policy, Oregon Health & Science University.

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