

## Tecfidera (dimethyl fumarate) Drug Use Criteria

Created: July 13, 2021

Reviewed:

Includes:

| <b>Brand®</b> | <i>Generic</i>                          |
|---------------|---|
| Tecfidera     | dimethyl fumarate 120mg, 240mg capsules |

### GUIDELINE FOR USE:

#### Initial Request:

1. Is medication being prescribed by or in consultation with a neurologist?
  - a. Yes, go to #2.
  - b. No, deny as criteria not met. Please resubmit prior authorization request with current neurology note.
2. Is medication to be used to treat a relapsing form of multiple sclerosis, including clinically isolated syndrome, relapsing-remitting disease, and active secondary progressive disease and is member 18 years or older?
  - a. Yes, go to #3.
  - b. No, and deny as criteria not met. Off-label use of a medication is not a covered benefit on OHP.
3. Is member on concurrent treatment with a disease modifying drug (i.e interferon beta-1b, glatiramer acetate, interferon beta-1a, natalizumab, ofatumumab, ocrelizumab, or mitoxantrone)?
  - a. Yes, deny as criteria not met. Dimethyl fumarate is not to be used with other disease modifying drugs for MS.
  - b. No, go to #4.
4. Have baseline safety assessments been completed (i.e Does documentation include liver function tests and a baseline CBC with lymphocyte count greater than 500/ $\mu$ L)?
  - a. Yes, approve for 6 months. Initial dose: dimethyl fumarate 120mg #14/7day supply. Maintenance dose: dimethyl fumarate 240mg #60/30 day supply.
  - b. No, deny as criteria not met. Please resubmit request with current CBC results, including lymphocyte count and/or liver function test.

### Renewal Request:

1. Has the member's condition improved as assessed by the prescribing physician and physician attests to patient's improvement?
  - a. Yes, approve for 12 months.
  - b. No, forward to MD for review.

### Fumarate Salts (Dimethyl Fumarate, Monomethyl Fumarate, Diroximel Fumarate) Clinical Notes:

- Fumarate salts may decrease a patient's white blood cell count. In the clinical trials the mean lymphocyte counts decreased by approximately 30% during the first year of treatment with dimethyl fumarate and then remained stable. The incidence of infections (60% vs. 58%) and serious infections (2% vs. 2%) was similar in patients treated with dimethyl fumarate or placebo, respectively. There was no increased incidence of serious infections observed in patients with lymphocyte counts  $<0.8 \times 10^3$  cells/mm<sup>3</sup> (equivalent to  $<0.8$  cells/ $\mu$ L). A transient increase in mean eosinophil counts was seen during the first 2 months of therapy.
- Fumarate salts should be held if the WBC falls below  $2 \times 10^3$  cells/mm<sup>3</sup> or the lymphocyte count is below  $0.5 \times 10^3$  cells/mm<sup>3</sup> (cells/ $\mu$ L) and permanently discontinued if the WBC did not increase to over  $2 \times 10^3$  cells/mm<sup>3</sup> or lymphocyte count increased to over  $0.5 \times 10^3$  cells/mm<sup>3</sup> after 4 weeks of withholding therapy.
- Patients should have a CBC with differential monitored every 6 to 12 months.

### Rationale:

**FDA Approved Indication: Multiple sclerosis, relapsing:** Treatment of patients with relapsing forms of multiple sclerosis, including clinically isolated syndrome, relapsing-remitting disease, and active secondary progressive disease.

**Mechanism of Action:** Dimethyl fumarate and its active metabolite, monomethyl fumarate (MMF), have been shown to activate the nuclear factor (erythroid-derived 2)-like 2 (Nrf2) pathway, which is involved in cellular response to oxidative stress. The mechanism by which dimethyl fumarate (DMF) exerts a therapeutic effect in MS is unknown, although it is believed to result from its anti-inflammatory and cytoprotective properties via activation of the Nrf2 pathway.

**Dosing: Multiple sclerosis, relapsing:** Oral: Initial: 120 mg twice daily; after 7 days, increase to the maintenance dose: 240 mg twice daily.

**Contraindications:** Known hypersensitivity (eg, anaphylaxis, angioedema) to dimethyl fumarate or any component of the formulation.

**References:**

1. American Academy of Neurology. <https://www.aan.com/Guidelines/home/GuidelineDetail/898>
2. UpToDate. [https://www.uptodate.com/contents/indications-for-switching-or-stopping-disease-modifying-therapy-for-multiple-sclerosis?search=multiple%20sclerosis%20treatment&topicRef=129091&source=see\\_link](https://www.uptodate.com/contents/indications-for-switching-or-stopping-disease-modifying-therapy-for-multiple-sclerosis?search=multiple%20sclerosis%20treatment&topicRef=129091&source=see_link)
3. Oregon Medicaid FFS Drug Class List - Dimethyl fumarate. [https://www.orpdl.org/durm/PA\\_Docs/multiplesclerisoralagents.pdf](https://www.orpdl.org/durm/PA_Docs/multiplesclerisoralagents.pdf)
4. Drug information: Tecfidera FDA-approved prescribing information. [https://www.tecfidera.com/content/dam/commercial/tecfidera/pat/en\\_us/pdf/full-prescribing-info.pdf](https://www.tecfidera.com/content/dam/commercial/tecfidera/pat/en_us/pdf/full-prescribing-info.pdf)