12/2014: The US Food and Drug Administration (FDA) approved a change to the prescription label for dimethyl fumarate (Tecfidera) to include new information:

Dosage and Administration, Dosing Information
The Dosing and Administration section has been changed to include the following:

Section 2.1: Dosing
• Temporary dose reductions to 120 mg twice a day may be considered by individuals who do not tolerate the maintenance dose.
• The recommended dose of 240 mg twice a day should be resumed within 4 weeks.
• Discontinuation of treatment with dimethyl fumarate should be considered for patients unable to tolerate the return to the maintenance dose.
• The incidence or severity of flushing may be reduced by taking dimethyl fumarate with food or by the administration of non-enteric coated aspirin (up to a dose of 325 mg) 30 minutes prior to taking the medication.

Contraindications
Section 4 has changed to include the following:
• Dimethyl fumarate is contraindicated in patients with known hypersensitivity to dimethyl fumarate or to any of the excipients of this medication. Reactions have included anaphylaxis and angioedema.

Warnings and Precautions
The Warnings and Precautions section has been changed to include the following:

• 5.1 Anaphylaxis and Angioedema
  - Dimethyl fumarate can cause anaphylaxis and angioedema after the first dose or at any time during treatment. Signs and symptoms have included difficulty breathing, urticaria and swelling of the throat and tongue.
• 5.2 Progressive Multifocal Leukoencephalopathy (PML)
  - A fatal case of PML occurred in a patient who received dimethyl fumarate for four years while enrolled in a clinical trial.
  - The patient experienced prolonged lymphopenia (counts predominantly <0.5x10⁹/L for 3.5 years) while on the medication; however the role of lymphopenia in this case is not known.
  - The patient had no identified systemic medical conditions resulting in a compromised immune system and had no previous treatment with natalizumab (known to have an association with PML) and no concomitant treatment with an immunosuppressive or immunomodulatory medication.

• 5.3 Lymphopenia
  - Dimethyl fumarate may decrease lymphocyte counts.
  - In the pivotal trials, mean lymphocyte counts decreased by approximately 30% during the first year of treatment and then remained stable.
    ○ Four weeks after stopping the medication, mean lymphocyte counts increased but did not return to baseline.
    ○ 6% of dimethyl fumarate patients and <1% of placebo patients experienced lymphocyte counts <0.5x10⁹/L.
    ○ The incidence of infections did not differ between patients treated with dimethyl fumarate and those who received placebo.
    ○ There was no increased incidence of serious infections in patients with lymphocyte counts <0.8x10⁹/L or 5x10⁹/L in controlled trials, although one patient in an extension study developed PML (see Warnings and Precautions, Section 5.2).
  - In controlled and uncontrolled clinical trials, 2% of patients experienced lymphocyte counts <0.5x10⁹/L for at least six months, and the majority of counts in these patients remained <0.5x10⁹/L with continued therapy.
  - A CBC including lymphocyte count should be obtained before initiating treatment with dimethyl fumarate, as well as six months after treatment, and every 6-12 months thereafter and as clinically indicated.
  - Consider interruption of treatment in patients with lymphocyte counts <0.5x10⁹/L that persist for more than six months.
• Given the potential for delay in lymphocyte recovery after discontinuation of treatment, consider following lymphocyte counts until lymphopenia is resolved.
  - Consider withholding treatment in patients with serious infections until the infection(s) is resolved.

• 5.4 Flushing
  The following information was added to the warning about flushing:
  - Administration of dimethyl fumarate with food may reduce the incidence of flushing.
  - Alternatively, administration of non-enteric coated aspirin (up to a dose of 325 mg) 30 minutes prior to dimethyl fumarate may reduce incidence or severity of flushing.

_The Emerging Therapies Collaborative will continue to post updated information as it becomes available._

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