Tecfidera® (dimethyl fumarate) – New Warning

- On January 19, 2017, the FDA approved a new update to the *Warnings and Precautions* section of the Tecfidera (dimethyl fumarate) drug label regarding liver injury.

- Tecfidera is indicated for the treatment of patients with relapsing forms of multiple sclerosis.

- Clinically significant cases of liver injury have been reported in patients treated with Tecfidera in the postmarketing setting. The onset has ranged from a few days to several months after initiation of treatment with Tecfidera.

- Signs and symptoms of liver injury, including elevation of serum aminotransferases to greater than 5-fold the upper limit of normal (ULN) and elevation of total bilirubin to greater than 2-fold the ULN have been observed. These abnormalities resolved upon treatment discontinuation.

- Some cases required hospitalization. None of the reported cases resulted in liver failure, liver transplant, or death. However, the combination of new serum aminotransferase elevations with increased levels of bilirubin caused by drug-induced hepatocellular injury is an important predictor of serious liver injury that may lead to acute liver failure, liver transplant, or death in some patients.

- Elevations of hepatic transaminases (most no greater than 3 times the ULN) were observed during controlled trials.

- Serum aminotransferases such as alkaline phosphatase and total bilirubin levels should be obtained prior to treatment with Tecfidera and during treatment, as clinically indicated. Tecfidera should be discontinued if clinically significant liver injury induced by Tecfidera is suspected.

- In support of the new warning, the *Dosage and Administration* section was also updated with information stating that serum aminotransferase, alkaline phosphatase, and total bilirubin levels should be obtained prior to treatment with Tecfidera.

- A new *Overdose* section was added to the Tecfidera drug label stating that cases of overdose have occurred. Symptoms described in these cases were consistent with the known adverse event profile of Tecfidera.

    — There are no known therapeutic interventions to enhance Tecfidera elimination nor is there a known antidote. In the event of an overdose, symptomatic supportive treatment should be initiated.

- The *Pharmacokinetics* section was updated with new information regarding the use of Tecfidera in conjunction with oral contraceptives.

- The coadministration of Tecfidera with a combined oral contraceptive (norelgestromin/ethinyl estradiol) did not elicit any relevant effects in oral contraceptives exposure. No interaction studies have been performed with oral contraceptives containing other progestogens.

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