Bafiertam®
(monomethyl fumarate) delayed-release capsules 95mg

Go Direct With BAFIERTAM® (monomethyl fumarate)

The only oral fumarate FDA-approved to treat patients with relapsing forms of multiple sclerosis that does not require metabolic conversion[1-3] and has no dietary restrictions.

INDICATIONS AND USAGE

BAFIERTAM is indicated for the treatment of relapsing forms of multiple sclerosis (MS), to include clinically isolated syndrome, relapsing-remitting disease, and active secondary progressive disease, in adults.

SELECT IMPORTANT SAFETY INFORMATION

CONTRAINDICATIONS

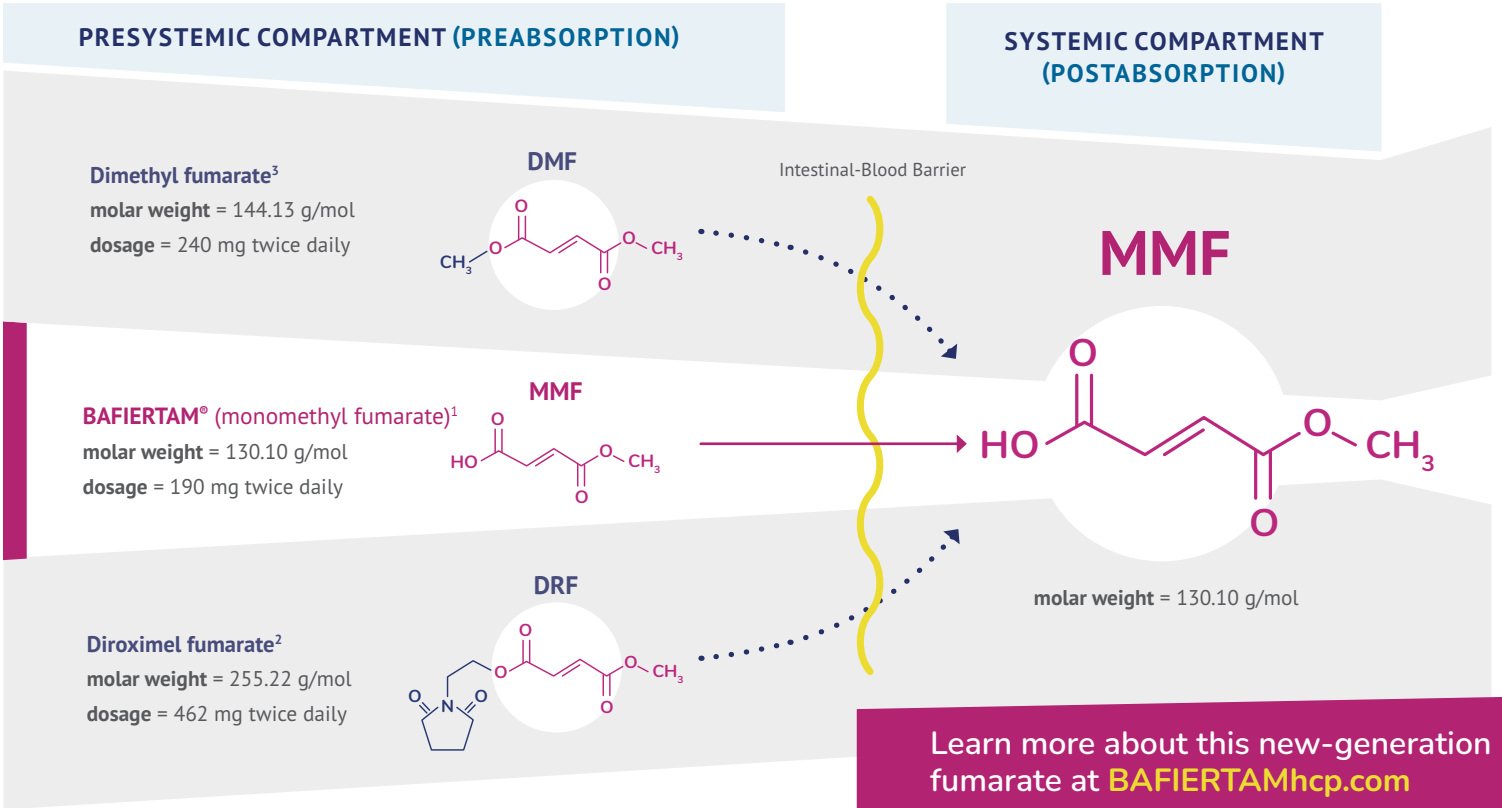
BAFIERTAM is contraindicated in patients

- With known hypersensitivity to monomethyl fumarate, dimethyl fumarate, diroximel fumarate, or to any of the excipients of BAFIERTAM. Reactions may include anaphylaxis or angioedema
- Taking dimethyl fumarate or diroximel fumarate

Please see the additional Important Safety Information at the end of this brochure and in the enclosed full Prescribing Information.

Three Oral Fumarates. One Goes Direct

A comparative view of the absorption of fumarates



Bafiertam® (monomethyl fumarate) and diroximel fumarate are bioequivalent to Tecfidera® (dimethyl fumarate). BAFIERTAM was approved based on bioequivalence studies vs Tecfidera.

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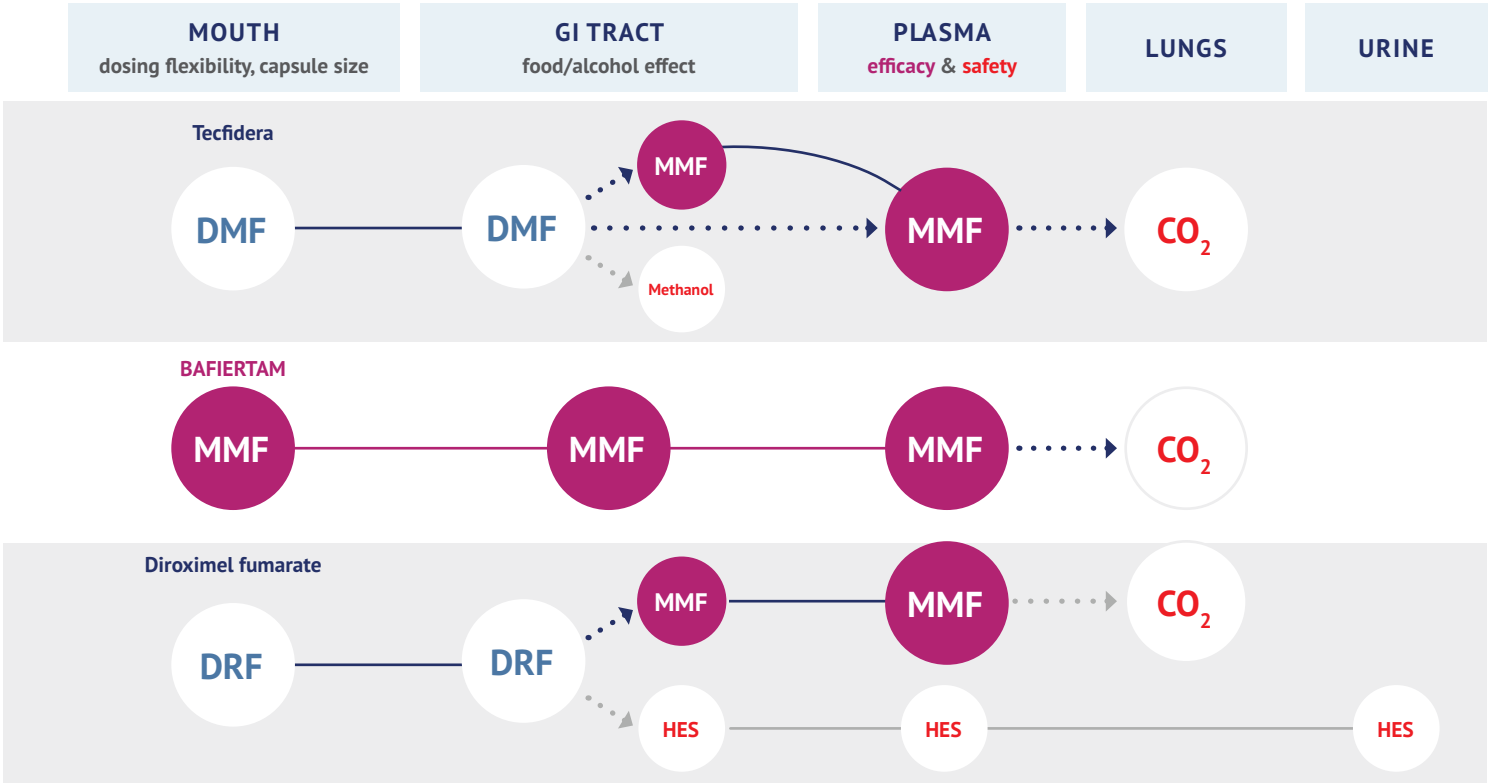
Upon oral administration, the prodrugs, DMF and DRF, are metabolized to produce the active metabolite MMF. BAFIERTAM, by contrast, does not require conversion to deliver this active agent directly to the systemic circulation.*



HES = 2-hydroxyethyl succinamide.

*Palte MJ, Wehr A, Tawa M, et al. Improving the gastrointestinal tolerability of fumaric acid esters: early findings on gastrointestinal events with diroximel fumarate in patients with relapsing-remitting multiple sclerosis from the phase 3, open-label EVOLVE-MS-1 Study. *Adv Ther*. 2019;36(11):3154-3165.

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Important Safety Information

WARNINGS AND PRECAUTIONS

Anaphylaxis and Angioedema

- BAFIERTAM can cause anaphylaxis and angioedema after the first dose or at any time during treatment. Signs and symptoms in patients taking dimethyl fumarate (the prodrug of BAFIERTAM) have included difficulty breathing, urticaria, and swelling of the throat and tongue. Patients should be instructed to discontinue BAFIERTAM and seek immediate medical care should they experience signs and symptoms of anaphylaxis or angioedema.

Progressive Multifocal Leukoencephalopathy (PML)

- PML has occurred in patients with MS treated with dimethyl fumarate (the prodrug of BAFIERTAM). PML is an opportunistic viral infection of the brain caused by the JC virus (JCV) that typically only occurs in patients who are immunocompromised, and that usually leads to death or severe disability. A fatal case of PML occurred in a patient who received dimethyl fumarate (the prodrug of BAFIERTAM) for 4 years while enrolled in a clinical trial.
- PML has also occurred in patients taking dimethyl fumarate in the postmarketing setting in the presence of lymphopenia ($<0.9 \times 10^9$/L). While the role of lymphopenia in these cases is uncertain, the PML cases have occurred predominantly in patients with lymphocyte counts $<0.8 \times 10^9$/L persisting for more than 6 months.
- At the first sign or symptom suggestive of PML, withhold BAFIERTAM and perform an appropriate diagnostic evaluation. Typical symptoms associated with PML are diverse, progress over days to weeks, and include progressive weakness on one side of the body or clumsiness of limbs, disturbance of vision, and changes in thinking, memory, and orientation leading to confusion and personality changes.
- Magnetic resonance imaging (MRI) findings may be apparent before clinical signs or symptoms. Monitoring with MRI for signs consistent with PML may be useful, and any suspicious findings should lead to further investigation to allow for an early diagnosis of PML, if present.

Herpes Zoster and Other Serious Opportunistic Infections

- Serious cases of herpes zoster have occurred with dimethyl fumarate (the prodrug of BAFIERTAM), including disseminated herpes zoster, herpes zoster ophthalmicus, herpes zoster meningoencephalitis, and herpes zoster meningomyelitis. These events may occur at any time during treatment. Monitor patients on BAFIERTAM for signs and symptoms of herpes zoster. If herpes zoster occurs, appropriate treatment for herpes zoster should be administered.
- Other serious opportunistic infections have occurred with dimethyl fumarate (the prodrug of BAFIERTAM), including cases of serious viral (herpes simplex virus, West Nile virus, cytomegalovirus), fungal (Candida and Aspergillus), and bacterial (Nocardia, Listeria monocytogenes, Mycobacterium tuberculosis) infections. These infections have been reported in patients with reduced absolute lymphocyte counts (ALC) as well as in patients with normal ALC. These infections have affected the brain, meninges, spinal cord, gastrointestinal tract, lungs, skin, eye, and ear. Patients with symptoms and signs consistent with any of these infections should undergo prompt diagnostic evaluation and receive appropriate treatment.
- Consider withholding BAFIERTAM treatment in patients with herpes zoster or other serious infections until the infection has resolved.

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Lymphopenia

- BAFIERTAM may decrease lymphocyte counts. In the MS placebo-controlled trials with dimethyl fumarate (the prodrug of BAFIERTAM), mean lymphocyte counts decreased by approximately 30% during the first year of treatment with dimethyl fumarate and then remained stable. Four weeks after stopping dimethyl fumarate, mean lymphocyte counts increased, but did not return to baseline. Six percent (6%) of dimethyl fumarate patients and <1% of placebo patients experienced lymphocyte counts <0.5x10^9/L (lower limit of normal 0.91x10^9/L). 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 <0.8x10^9/L or <0.5x10^9/L in controlled trials, although one patient in an extension study developed PML in the setting of prolonged lymphopenia (lymphocyte counts predominantly <0.5x10^9/L for 3.5 years).
- In controlled and uncontrolled clinical trials with dimethyl fumarate, 2% of patients experienced lymphocyte counts <0.5x10^9/L for at least 6 months, and in this group, the majority of lymphocyte counts remained <0.5x10^9/L with continued therapy. Neither BAFIERTAM nor dimethyl fumarate have been studied in patients with preexisting low lymphocyte counts.
- Obtain a CBC, including lymphocyte count, before initiating treatment with BAFIERTAM, 6 months after starting treatment, and then every 6 to 12 months thereafter, and as clinically indicated. Consider interruption of BAFIERTAM in patients with lymphocyte counts less than 0.5x10^9/L persisting for more than 6 months. Given the potential for delayed recovery of lymphocyte counts, continue to obtain lymphocyte counts until their recovery if BAFIERTAM is discontinued or interrupted because of lymphopenia. Consider withholding treatment from patients with serious infections until resolution. Decisions about whether or not to restart BAFIERTAM should be individualized based on clinical circumstances.

Liver Injury

- Clinically significant cases of liver injury have been reported in patients treated with dimethyl fumarate (the prodrug of BAFIERTAM) in the postmarketing setting. The onset has ranged from a few days to several months after initiation of treatment. Signs and symptoms of liver injury, including elevation of serum aminotransferases to greater than 5-fold the upper limit of normal and elevation of total bilirubin to greater than 2-fold the upper limit of normal 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 upper limit of normal) were observed during controlled trials.
- Obtain serum aminotransferase, alkaline phosphatase, and total bilirubin levels before initiating BAFIERTAM and during treatment, as clinically indicated. Discontinue BAFIERTAM if clinically significant liver injury induced by BAFIERTAM is suspected.

Important Safety Information (continued)

Flushing

- BAFIERTAM may cause flushing (e.g., warmth, redness, itching, and/or burning sensation). In clinical trials of dimethyl fumarate (the prodrug of BAFIERTAM), 40% of dimethyl fumarate-treated patients experienced flushing. Studies with dimethyl fumarate show that administration of non-enteric coated aspirin (up to a dose of 325 mg) 30 minutes prior to dosing may reduce the incidence or severity of flushing. In the BAFIERTAM studies, the presence of food did not impact the incidence of flushing.

ADVERSE REACTIONS

- The most common adverse reactions (incidence ⩾10% and ⩾2% more than placebo) for dimethyl fumarate (the prodrug of BAFIERTAM) were flushing, abdominal pain, diarrhea, and nausea.
- Gastrointestinal adverse reactions: Dimethyl fumarate caused GI events (e.g., nausea, vomiting, diarrhea, abdominal pain, and dyspepsia). In clinical trials, the incidence of GI events was higher early in the course of treatment (primarily during the first month) and usually decreased over time in patients treated with dimethyl fumarate compared with placebo. Four percent (4%) of patients treated with dimethyl fumarate and less than 1% of patients on placebo discontinued due to gastrointestinal events. The incidence of serious GI events was 1% in patients treated with dimethyl fumarate.
- Hepatic transaminases: An increased incidence of elevations of hepatic transaminases in patients treated with dimethyl fumarate in clinical trials was seen primarily during the first 6 months of treatment, and most patients with elevations had levels <3 times the upper limit of normal (ULN). Elevations of alanine aminotransferase and aspartate aminotransferase to ⩾3 times the ULN occurred in a small number of patients treated with both dimethyl fumarate and in patients on placebo, and were balanced between the groups. There were no elevations in transaminases ⩾3 times the ULN with concomitant elevations in total bilirubin >2 times the ULN. Discontinuations due to elevated hepatic transaminases were <1%, and were similar in patients treated with dimethyl fumarate or placebo.
- Eosinophilia adverse reactions: A transient increase in mean eosinophil counts was seen during the first 2 months of therapy with dimethyl fumarate.

Please see the enclosed full Prescribing Information.

References: 1. BAFIERTAM. Prescribing information. Banner Life Sciences LLC; 2021. **2.** Vumerity. Prescribing information. Biogen Inc; 2022. **3.** Tecfidera. Prescribing information. Biogen Inc; 2022.

BANNER LIFE SCIENCES