DEMONSTRATED SAFETY PROFILE[1]

Contraindication

TECFIDERA is contraindicated in patients with known hypersensitivity to dimethyl fumarate or to any of the excipients of TECFIDERA. Reactions have included anaphylaxis and angioedema[1]

Warnings and Precautions

Warning

Can occur after the first dose or anytime during treatment with TECFIDERA

Signs and symptoms

Include difficulty breathing, urticaria, and swelling of the throat and tongue

Guidance

Discontinue TECFIDERA and seek immediate medical care

Warning

- Has occurred in patients with MS treated with TECFIDERA
- 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

Details

A fatal case of PML occurred in a patient who received TECFIDERA for 4 years while enrolled in a clinical trial

Patient experienced prolonged lymphopenia (lymphocyte counts predominantly $<0.5 \times 10^9$/L for 3.5 years) while taking TECFIDERA

(<0.8x10^9/L)
persisting for more than 6 months

While the role of lymphopenia in these cases is uncertain, the majority of cases occurred in patients with lymphocyte counts <0.5x10^9/L

Signs and symptoms

Diverse and progress over days to weeks

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

MRI findings may be apparent before clinical signs or symptoms

Guidance

At the first sign or symptom suggestive of PML, withhold TECFIDERA and perform an appropriate diagnostic evaluation

For additional information, please see full Prescribing Information.

Warning

TECFIDERA may decrease lymphocyte counts

Details

- During the first year in clinical trials, mean lymphocyte counts decreased by approximately 30% and then remained stable
- Four weeks after stopping TECFIDERA, mean lymphocyte counts increased but did not return to baseline
- Six percent (6%) of TECFIDERA patients and <1% of placebo patients experienced lymphocyte counts <0.5x10^9/L (lower limit of normal 0.91x10^9/L)
- In controlled and uncontrolled clinical trials, 2% of patients experienced lymphocyte counts <0.5x10^9/L for at least six months, and in this group, the majority of lymphocyte counts remained <0.5x10^9/L with continued therapy
- TECFIDERA has not been studied in patients with pre-existing low lymphocyte counts

Guidance

- Obtain a CBC, including lymphocyte count, before initiating treatment with TECFIDERA, 6 months after starting treatment, and then every 6 to 12 months thereafter, and as clinically indicated
- Consider interruption of TECFIDERA in patients with lymphocyte counts <0.5x10^9/L

- Given the potential for delayed recovery of lymphocyte counts, continue to obtain lymphocyte counts until their recovery if TECFIDERA is discontinued or interrupted due to lymphopenia
- Restart TECFIDERA based on individual and clinical circumstances
- Please see **Infections** below for additional details

Warning

- 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
- None of the reported cases resulted in liver failure, liver transplant, or death. Some cases required hospitalization
- 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

Signs and symptoms

Include 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

Guidance

- Obtain serum aminotransferase, alkaline phosphatase, and total bilirubin levels prior to treatment with TECFIDERA and during treatment, as clinically indicated
- Discontinue TECFIDERA if clinically significant liver injury induced by TECFIDERA is suspected

Warning

- May occur during treatment with TECFIDERA. In clinical trials, 40% experienced flushing
- 3% of patients discontinued TECFIDERA because of flushing and <1% had serious flushing symptoms that were not life-threatening but led to hospitalization

Signs and symptoms

- Generally began soon after initiating treatment and usually improved or resolved over time
- Include warmth, redness, itching, and/or burning sensation

Guidance

Taking TECFIDERA with food may help with flushing

Alternatively, taking non-enteric coated aspirin (up to a dose of 325 mg) 30 minutes prior to TECFIDERA dosing may reduce the incidence and severity of flushing

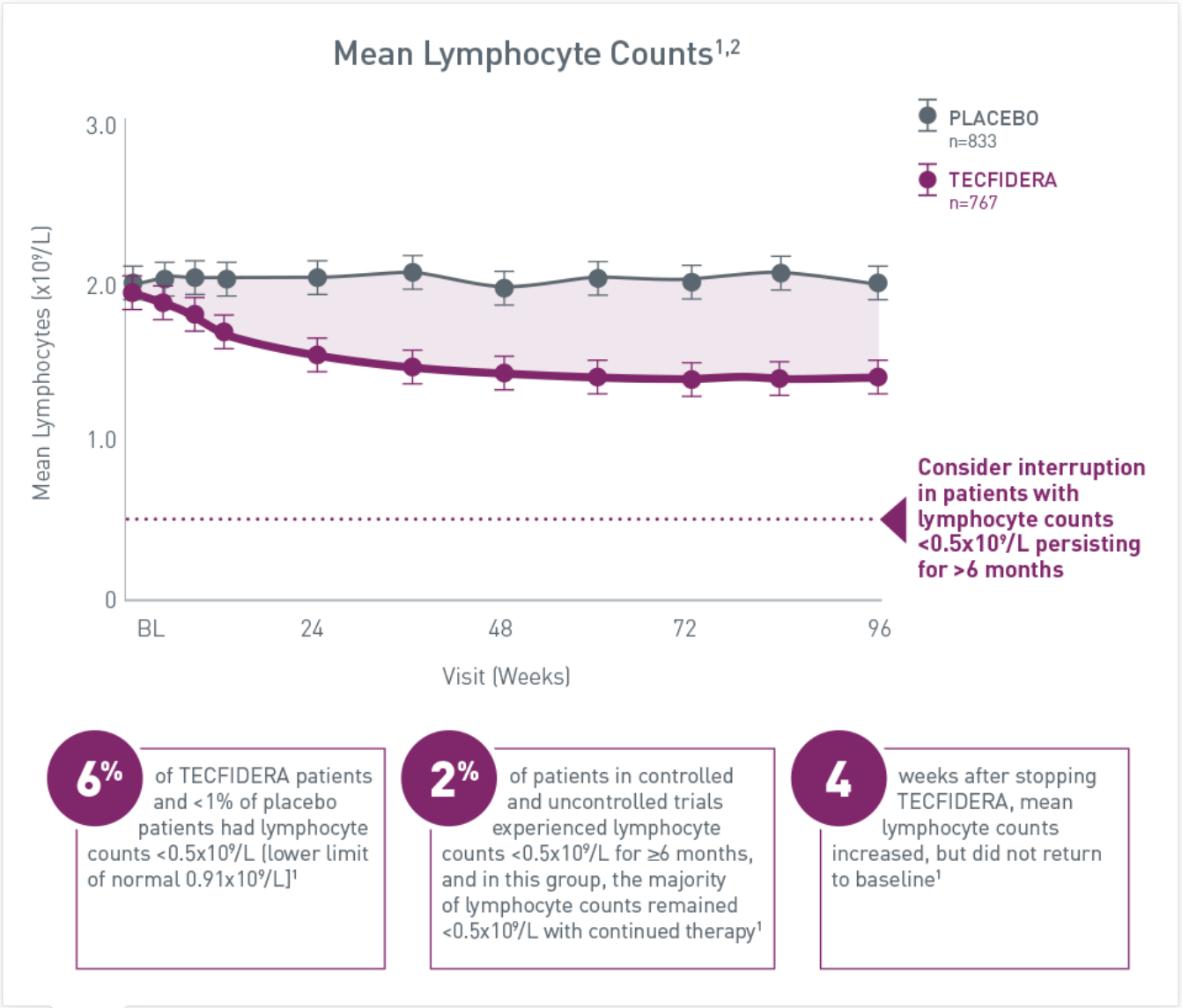
Advise patients to contact their healthcare provider if they experience persistent and/or severe flushing

ROUTINE MONITORING FOR YOUR PATIENTS[1]

OBTAIN PRIOR TO INITIATION[1]	AFTER INITIATION[1]	
	At 6 months	Every 6-12 months thereafter, and as clinically indicated
✓ CBC with lymphocyte count		
✓ Liver tests (serum aminotransferase, alkaline phosphatase, and total bilirubin)	Repeat as clinically indicated	

WATCH how MS experts help patients make the most of TECFIDERA >

TECFIDERA MAY DECREASE LYMPHOCYTE COUNTS[1,2]



see proven strategies to help guide patients' treatment experiences ›

Indication

Tecfidera® (dimethyl fumarate) is indicated for the treatment of patients with relapsing forms of multiple sclerosis.

Important Safety Information

TECFIDERA is contraindicated in patients with known hypersensitivity to dimethyl fumarate or any of the excipients of TECFIDERA. TECFIDERA can cause anaphylaxis and angioedema after the first dose or at any time during treatment. Patients experiencing signs and symptoms of

DOCKET ALARM

Explore Litigation Insights

Docket Alarm provides insights to develop a more informed litigation strategy and the peace of mind of knowing you're on top of things.

Real-Time Litigation Alerts

Keep your litigation team up-to-date with **real-time alerts** and advanced team management tools built for the enterprise, all while greatly reducing PACER spend.

Our comprehensive service means we can handle Federal, State, and Administrative courts across the country.

Advanced Docket Research

With over 230 million records, Docket Alarm's cloud-native docket research platform finds what other services can't. Coverage includes Federal, State, plus PTAB, TTAB, ITC and NLRB decisions, all in one place.

Identify arguments that have been successful in the past with full text, pinpoint searching. Link to case law cited within any court document via Fastcase.

Analytics At Your Fingertips

Learn what happened the last time a particular judge, opposing counsel or company faced cases similar to yours.

Advanced out-of-the-box PTAB and TTAB analytics are always at your fingertips.

API

Docket Alarm offers a powerful API (application programming interface) to developers that want to integrate case filings into their apps.

LAW FIRMS
Build custom dashboards for your attorneys and clients with live data direct from the court.

Automate many repetitive legal tasks like conflict checks, document management, and marketing.

FINANCIAL INSTITUTIONS
Litigation and bankruptcy checks for companies and debtors.

E-DISCOVERY AND LEGAL VENDORS
Sync your system to PACER to automate legal marketing.