

**Health Canada Endorsed Important Safety Information on  
TECFIDERA™ (dimethyl fumarate)**

biogen idec®

February 6, 2015

Dear Healthcare Professional:

**Subject:   TECFIDERA™ (dimethyl fumarate): New Safety Information  
              Regarding the Risk of Progressive Multifocal  
              Leukoencephalopathy (PML)**

Biogen Idec Canada Inc., in consultation with Health Canada, would like to inform you that new safety information regarding the risk of PML is being added to the TECFIDERA Canadian Product Monograph. The update was prompted by a fatal case of PML reported in a clinical trial patient receiving TECFIDERA.

TECFIDERA is approved for the treatment of relapsing remitting multiple sclerosis (MS) to reduce the frequency of clinical exacerbations and to delay the progression of disability.

- A fatal case of PML was reported in a patient with severe and prolonged lymphopenia (lymphocyte counts predominantly  $<0.5 \times 10^9/L$  for 3.5 years). The patient had no other medical conditions that could have compromised immune system functions and had not been taking any other immunosuppressive or immunomodulatory medications concomitantly.
- The Product Monograph for TECFIDERA is being updated to include the risk of PML. Given that a contributory role of TECFIDERA-induced lymphopenia in the development of PML cannot be excluded, the Product Monograph update will also recommend close lymphocyte monitoring.
- Complete blood counts, including lymphocyte counts, should be obtained prior to treatment with TECFIDERA, then every 6 to 12 months and as clinically indicated. Interruption of TECFIDERA should be considered in patients with lymphocyte counts  $<0.5 \times 10^9/L$  persisting for more than 6 months. After the interruption of TECFIDERA, lymphocyte counts should be followed until recovery.

The fatal case of PML was reported in October 2014. The patient was participating in the open-label ENDORSE study and received 4.5 years of TECFIDERA therapy. During treatment with TECFIDERA, the patient experienced severe and prolonged lymphopenia (over 3.5 years in duration), which is associated with an increased risk of PML.

PML is an opportunistic viral infection of the brain caused by the John Cunningham (JC) virus that occurs typically in patients who are immunocompromised and can lead to severe disability or death. Some symptoms of PML are similar to those of

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

A copy of this letter can be accessed on the [Health Canada Web site](#) and on the [Biogen Idec Canada Inc. Web site](#).

Managing marketed health product-related adverse reactions depends on health care professionals and consumers reporting them. Reporting rates determined on the basis of spontaneously reported post-marketing adverse reactions are generally presumed to underestimate the risks associated with health product treatments. Any case of prolonged lymphopenia, PML or other serious or unexpected adverse reactions in patients receiving TECFIDERA should be reported to Biogen Idec Canada Inc. or Health Canada.

Biogen Idec Canada Inc.  
90 Burnhamthorpe Rd. W., Suite 1100  
Mississauga, ON L5B 3C3  
1-855-676-6300

**To correct your mailing address or fax number, contact Biogen Idec Canada Inc.**

You can report any suspected adverse reactions associated with the use of health products to Health Canada by:

- Calling toll-free at 1-866-234-2345; or
- Visiting MedEffect Canada's Web page on [Adverse Reaction Reporting \(http://www.hc-sc.gc.ca/dhp-mps/medeff/repodeclaration/index-eng.php\)](http://www.hc-sc.gc.ca/dhp-mps/medeff/repodeclaration/index-eng.php) for information on how to report online, by mail or by fax

For other health product inquiries related to this communication, contact Health Canada at:  
Marketed Health Products Directorate  
E-mail: MHPD\_DPSC.public@hc-sc.gc.ca  
Telephone: 613-954-6522  
Fax: 613-952-7738

Sincerely,

***Original signed by***

Len Walt, M.D., MBA  
Medical Director