biogen idec

Health Canada Endorsed Important Safety Information on TYSABRI® (natalizumab)

February 13, 2009

Dear Healthcare Professional:

Subject: **Updated Safety Information regarding Progressive Multifocal Leukoencephalopathy (PML) associated with TYSABRI® (natalizumab)**

Biogen Idec Canada Inc., in consultation with Health Canada, would like to inform you that previously communicated safety information regarding post-marketing reports of PML in patients receiving TYSABRI® (natalizumab) monotherapy is now included in the Canadian Product Monograph. PML is a known risk of TYSABRI therapy.

TYSABRI is a humanized monoclonal antibody and is currently authorized as monotherapy (i.e. single disease-modifying agent) for the treatment of patients with relapsing-remitting multiple sclerosis (MS) to reduce the frequency of clinical exacerbations, to decrease the number and volume of active brain lesions identified on magnetic resonance imaging (MRI) scans and to delay the progression of physical disability.

- TYSABRI has been associated with an increased risk of progressive multifocal leukoencephalopathy (PML) as described in the Canadian Product Monograph.
- During post-marketing experience to date, five confirmed cases of PML have been reported in patients receiving TYSABRI monotherapy. Four cases were reported in the European Union and one case was reported in the United States. One case had a fatal outcome.
- Clinical vigilance to the possibility of PML was important in identifying these cases.
- Therefore, these cases underline the importance of continued clinical vigilance and prompt discontinuation of TYSABRI when PML is suspected with subsequent appropriate evaluation including magnetic resonance imaging (MRI) and cerebrospinal fluid (CSF) testing for JC Viral DNA.

PML is a rare, progressive, demyelinating disease of the central nervous system. It is caused by reactivation of the JC virus. PML can cause severe disability or death. The JC virus typically causes PML in immune compromised patients. There have been reported cases of PML in HIV-positive patients, immune suppressed cancer patients, transplantation patients and patients with autoimmune diseases.

During pre-marketing clinical trials, two cases of PML in MS patients receiving TYSABRI in combination with beta-interferon were reported. A third case was reported in an investigational trial of TYSABRI in the treatment of Crohn's disease. Based on these cases, combination therapy of TYSABRI is contraindicated. TYSABRI is generally recommended as monotherapy in patients who have had an inadequate response to, or are unable to tolerate, other therapies for multiple sclerosis. As of the end of December 2008, approximately 37,600 patients were receiving TYSABRI worldwide.

As a result of these post-marketing reports, the Warnings and Precautions section as well as the Consumer Information section of the Product Monograph has been updated to include the occurrence of reports of PML in the post-marketing monotherapy setting, including additional clarification of the typical symptoms

of PML as follows:

> "There have been rare reports of PML in patients who received TYSABRI monotherapy."
> "Typical symptoms of 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."
> "Patients being treated with TYSABRI should be instructed to report any new neurological signs or symptoms to their physician."

Managing marketed health product-related adverse reactions depends on health care professionals and consumers reporting them. Any case of serious or unexpected adverse reactions in patients receiving TYSABRI should be reported to the Tysabri Care Program™ or Health Canada at the following addresses:

Tysabri Care Program™
Phone: 1-888-827-2827

Biogen Idec Canada Inc.
3 Robert Speck Parkway, Suite 300
Mississauga, ON L4Z 2G5

Any suspected adverse reaction can also be reported to:

Canada Vigilance Program
Marketed Health Products Directorate
HEALTH CANADA
Address Locator: 0701C
Ottawa, Ontario, K1A 0K9
Tel: 613-957-0337 or Fax: 613-957-0335
To report an Adverse Reaction, consumers and health professionals may call toll free:
Tel: 866-234-2345
Fax: 866-678-6789
CanadaVigilance@hc-sc.gc.ca

The AR Reporting Form and the AR Guidelines can be found on the Health Canada web site or in *The Canadian Compendium of Pharmaceuticals and Specialties.*

http://www.hc-sc.gc.ca/dhp-mps/medeff/report-declaration/ar-ei_form_e.html
http://www.hc-sc.gc.ca/dhp-mps/medeff/report-declaration/guide/ar-ei_guide-ldir_e.html

For other inquiries related to this communication, please contact Health Canada at:
Marketed Health Products Directorate (MHPD)
E-mail: MHPD_DPSC@hc-sc.gc.ca
Tel: 613-954-6522
Fax: 613-952-7738

Should you have any questions regarding TYSABRI® or require a copy of the revised TYSABRI Product Monograph, please contact the Tysabri Care Program™ at 1-888-827-2827.

Sincerely,

original signed by

Len Walt, M.D., MBA
Medical Director