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DEPARTMENT OF HEALTH
DRUG OFFICE
DRUG REGISTRATION AND IMPORT/EXPORT CONTROL DIVISION
3/F., Public Health Laboratory Centre,
382 Nam Cheong Street, Kowloon, Hong Kong

15 February 2016

Dear Healthcare Professionals,

Tysabri (natalizumab): Updated recommendations to minimise the risk of the rare brain infection PML

Your attention is drawn to the European Medicines Agency's (EMA) announcement regarding updated recommendations to minimise the risk of the rare brain infection progressive multifocal leukoencephalopathy (PML) with Tysabri. New advice may help early detection of PML and improve patients' outcomes.

EMA's Pharmacovigilance Risk Assessment Committee (PRAC) has completed its review of the risk of PML with the multiple sclerosis medicine Tysabri (natalizumab) and has recommended new measures to minimise this risk. PML is a rare and very serious brain infection caused by John Cunningham (JC) virus.

Tysabri is a medicine used to treat adults with highly active 'relapsing-remitting' multiple sclerosis (MS). It is used when the disease has failed to respond to treatment with a beta-interferon or glatiramer acetate, or is severe and getting worse rapidly.

The active substance in Tysabri, natalizumab, is a monoclonal antibody that has been designed to recognise and attach to a specific part of a protein called 'α4β1 integrin'. This is found on the surface of most leucocytes. By blocking the integrin, natalizumab stops the leucocytes from going from the blood into the brain. This reduces the inflammation and nerve damage caused by MS.

Recent studies suggest that early detection and treatment of PML when the disease is asymptomatic are critically important in limiting the degree of brain damage and resulting disability caused by the disease. Asymptomatic cases of PML can be detected on an MRI scan. On the basis of this data, the PRAC concluded that for patients at higher risk of PML more frequent MRI scans (e.g. every 3 to 6 months) should be considered.

Known risk factors for the development of PML in patients treated with Tysabri are the presence of antibodies against JC virus, treatment with Tysabri for more than two years, and use of immunosuppressant medicines before starting Tysabri. Patients who have all three risk factors are considered at higher risk of PML.

New data from clinical studies suggest that, in patients who have not been treated with immunosuppressants before starting Tysabri, the level of antibodies (index) relates to the level of risk for PML. More specifically, current evidence suggests that the risk of PML is small, and lower than previously estimated, at antibody index values of 0.9 or less, and increases substantially in patients with index values above 1.5 who have been treated with Tysabri for longer than 2 years. Therefore, the PRAC concluded that patients with a high antibody index who have not used immunosuppressants before Tysabri and have been treated with Tysabri for more than 2 years are also considered at higher risk of PML.

Healthcare professionals are advised of the following:

- In patients at higher risk of developing PML, treatment with Tysabri should only be continued if benefits outweigh the risks.

- For patients who have a low antibody index and have not used immunosuppressant medicines before starting Tysabri, the PRAC recommends repeating the antibody test every 6 months once they have taken Tysabri for longer than 2 years.
- In patients who tested negative for JC virus antibodies, the antibody test should be repeated every 6 months.
- If PML is suspected at any time, treatment with Tysabri must be stopped until PML has been excluded.

Please refer to the EMA's website for details:

http://www.ema.europa.eu/ema/index.jsp?curl=pages/news_and_events/news/2016/02/news_detail_002471.jsp&mid=WC0b01ac058004d5c1

In Hong Kong, Tysabri Concentrate for Solution for Infusion 300mg (HK-61519) is a pharmaceutical product registered by UCB Pharma (Hong Kong) Limited, and is a prescription only medicine. News on the start of review of Tysabri was previously issued by the EMA, and was posted on the Drug Office website on 12 October 2015. The local package insert of the product has already included the warning on PML. So far, the Department of Health has not received any adverse drug reaction case related to the product. In view of the completion of the EMA's review with updated recommendations to minimise the risk of PML, the matter will be discussed by the Registration Committee of the Pharmacy and Poisons Board. Healthcare professionals are advised to balance the risk of possible adverse effects against the benefit of treatment.

Please report any adverse events caused by drugs to the Pharmacovigilance Unit of the DH (tel. no.: 2319 2920, fax: 2319 6319 or email: adr@dh.gov.hk). For details, please refer to the website at Drug Office under "ADR Reporting": http://www.drugoffice.gov.hk/adr.html. You may wish to visit the Drug Office's website for subscription and browsing of "Drug News" which is a monthly digest of drug safety news and information issued by Drug Office.

Yours faithfully,

(Grant NG)
for Assistant Director (Drug)