EMA confirms recommendations to minimise risk of brain infection PML with Tysabri

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Information on Tysabri®

- Tysabri (natalizumab) is a medicine used to treat adults with highly active multiple sclerosis (MS) specifically in the type of MS known as 'relapsing-remitting' MS.
- Tysabri was authorized in the European Union in June 2006 and is available in Malta via centralized procedure for hospital use

EMA confirms that more frequent MRI scans should be considered for patients at higher risk

The Committee for Medicinal Products for Human (CHMP) at the EMA has confirmed the PRAC recommendations aimed at minimizing the risk of progressive multifocal leukoencephalopathy (PML) brain infection with Tysabri. In summary the new evidence highlights the need for more frequent MRI scans for patients at higher risk and also re-stratifies patients' risk of PML. Patients are at higher risk of developing PML if they:

- Have tested positive for John Cunningham (JC) virus, and
- Have been treated with Tysabri for more than 2 years, and
- Either have used an immunosuppressant before starting Tysabri, or have not used immunosuppressants but have a high JC virus antibody index

In higher risk patients, treatment with Tysabri should only be continued if benefits outweigh the risks and Tysabri treatment must be stopped if PML is suspected. Readers are encouraged to refer to safety circulars P17/2015 and P01/2016 for more information on the risk of PML and Tysabri.

The CHMP opinion will now be forwarded to the European Commission, which will issue a final legally binding decision applicable in all EU Member States in due course.

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For Healthcare Professionals

Based on this emergent data more detailed information on the risk stratification, diagnosis and treatment of PML will be included in the updated Physician Information and Management Guidelines for Tysabri.

In the mean time HCPs should follow these recommendations as issued by the EMA:

- Before starting treatment with Tysabri, patients and carers should be advised about the risk of PML. Patients should be instructed to seek medical advice if they think their disease is getting worse, or if they notice any new or unusual symptoms.
- Before starting treatment, a baseline MRI should be available (usually within 3 months) as a reference, and a baseline anti-JCV antibody test should be performed to support PML risk stratification.
- During treatment with Tysabri, patients should be monitored at regular intervals for signs and symptoms of new neurological dysfunction, and a full brain MRI should be performed at least once a year for the duration of treatment.
- For patients at higher risk of PML, more frequent MRIs (e.g. every 3-6 months) using an abbreviated protocol (e.g. FLAIR, T2-weighted and DW imaging) should be considered, as earlier detection of PML in asymptomatic patients is associated with improved PML outcomes.
- PML should be considered in the differential diagnosis of any patient presenting with neurological symptoms and/or new brain lesions on MRI. Cases of asymptomatic PML based on MRI and positive JC virus DNA in the CSF have been reported.
- If PML is suspected, the MRI protocol should be extended to include contrast-enhanced T1-weighted imaging and testing of CSF for the presence of JC virus DNA using ultrasensitive PCR should be considered.
- If PML is suspected at any time, treatment with Tysabri must be stopped until PML has been excluded.
- Anti-JC virus antibody testing should be done every 6 months in antibody-negative patients. Patients who have low index values and no history of prior immunosuppressant use should also be retested every 6 months once they reach the 2-year treatment point.
- After 2 years of treatment, patients should be informed again about the risk of PML with Tysabri.
- Patients and carers should be advised to continue to be vigilant about the risk of PML for up to 6 months following discontinuation of Tysabri.

Prescribers of Tysabri are encouraged to refer to the Summary of Product Characteristics (SmPC) and Physician Information and Management Guidelines for Multiple Sclerosis patients on Tysabri therapy which will be updated in due course.

Information for patients

Progressive multifocal leukoencephalopathy (PML) is a serious brain infection which is known to be an uncommon risk of Tysabri. New recommendations have been issued which may help early detection of PML and improve patients' outcomes.

- Your doctor will be able to advise you about your risk of developing PML based on blood levels of anti-JC virus antibodies, Tysabri treatment duration and prior use of medicines that suppress your immune system.
- Before starting treatment with Tysabri, and then regularly during treatment, your doctor will do blood tests to measure the level of antibodies for JC virus and MRI scans to monitor your condition. Your doctor will also check for signs and symptoms suggestive of PML. These tests may be done more often if you are considered at higher risk for PML.
- If PML is suspected, your doctor will stop treatment with Tysabri until PML can be ruled out.
- Symptoms of PML may be similar to those of a multiple sclerosis attack, and include progressive weakness, speech and communication difficulties, vision problems, and sometimes changes in mood or behaviour. Patients who believe their disease is getting worse or notice any new or unusual symptoms while using Tysabri and for up to 6 months after stopping Tysabri are encouraged to speak to their doctor as soon as possible.
- Patients are encouraged to refer to the Patient Alert Card supplied by their doctors for more information about the risk of PML with Tysabri
- Patients who have any questions or concerns can speak to their doctor, nurse or pharmacist.

For more information on the CHMP's opinion on this issue please refer to the press release issued by the European Medicines Agency

Reporting Adverse Drug Reactions

Healthcare professionals and patients are encouraged to maintain vigilance on Tysabri®. Suspected Adverse Drug Reactions (side effects) or medication errors may be reported using the Medicines Authority ADR reporting form or online at http://www.medicinesauthority.gov.mt/adrportal or to the marketing authorisation holder or their local representatives.

Prof. John J Borg PhD (Bristol)
Post-licensing Director

Healthcare professionals and patients are encouraged to regularly check the Medicine Authority website for product safety updates as these are issued on an ongoing basis.