

09 April 2015

**Fingolimod (Gilenya): first reported case of progressive multifocal leukoencephalopathy (PML) in a multiple sclerosis patient taking Fingolimod without previous treatment by natalizumab or other immunosuppressive medicines**

Dear Healthcare Professional,

In agreement with European Medicines Agency (EMA) and the Health Products Regulatory Authority (HPRA), Novartis would like to inform you of a first case report of PML in a patient taking fingolimod for multiple sclerosis without previous treatment by natalizumab or other immunosuppressive medicines

**Summary**

- A case of PML was reported in February 2015 in a patient who had been taking fingolimod for more than 4 years.
- This is the first case report of PML in a multiple sclerosis patient taking fingolimod who had not previously received natalizumab (Tysabri) or other immunosuppressive medicines.
- PML was suspected on a routine brain MRI scan and confirmed by positive JC virus DNA in cerebrospinal fluid (CSF) using quantitative PCR. Fingolimod was stopped immediately and to date, the patient has not experienced any clinical signs or symptoms related to PML.
- Prescribers are recommended to be vigilant for the risk of PML in patients treated with fingolimod. The treatment should be permanently discontinued in case of PML.

**Further information**

*Case details*

This is the first case report receive of PML in a multiple sclerosis patient taking fingolimod who had not received natalizumab (Tysabri) or other immunosuppressive medicines. A 49 year old patient with multiple sclerosis developed PML while taking fingolimod in February 2015. The patient had received interferon-beta for 10 months until September 2010. Fingolimod 0.5 mg/day was started in October 2010. Between October 2010 and May 2014, the patient had lymphocyte counts between 0.59 and 0.89 x 10<sup>9</sup>/L. On 9 December 2014, the absolute lymphocyte count was 0.24 x 10<sup>9</sup>/L.

On 23 January 2015, the patient had a routine magnetic resonance imaging (MRI) scan. Lesions compatible with PML were detected. The patient stopped taking fingolimod on 26 January 2015. The diagnosis was confirmed by a CSF sample which was positive for JC virus in a quantitative polymerase chain reaction (PCR) test. Of note, the patient did not experience any clinical signs or symptoms of PML. On 5 February 2015, absolute lymphocyte counts were 0.64 x 10<sup>9</sup>/L.

PML is a rare and serious brain disease caused by reactivation of the JC virus. This virus is commonly found in the general population but only leads to PML if the immune system has been weakened. PML can present with similar features to multiple sclerosis as both are demyelinating diseases.

#### *Indication*

Fingolimod (Gilenya) is indicated as single disease-modifying therapy in highly active relapsing-remitting multiple sclerosis for the following adult patient groups:

- patients with high disease activity despite treatment with at least one disease modifying therapy;
- patients with rapidly evolving severe relapsing-remitting multiple sclerosis defined by 2 or more disabling relapses in one year, and with 1 or more gadolinium-enhancing lesions on brain MRI or a significant increase in T2 lesion load as compared to a previous recent MRI.

Novartis is working with regulatory authorities to evaluate the evidence for the risk of PML and consider if further guidance on managing the risk of PML is needed. Any new advice will be communicated promptly.

#### Call for reporting

Please report any suspect adverse reactions associated with the use of fingolimod in accordance with the national requirements via the national spontaneous reporting system, to:

Healthcare professionals are asked to report any suspected adverse reactions via HPRA Pharmacovigilance, Health Products Regulatory Authority, Kevin O'Malley House, Earlsfort Centre, Earlsfort Terrace, Dublin 2, Ireland; Tel: +353 1 6764971; Fax: +353 1 6762517. Website: [www.hpra.ie](http://www.hpra.ie); E-mail: [medsafety@hpra.ie](mailto:medsafety@hpra.ie).

#### Company contact point

Should you require any further information please contact Novartis Ireland Limited, Beech House, Beech Hill Office Campus, Clonskeagh, Dublin 4. Tel: 01-2601255, Fax: 01-2601263

Yours faithfully,



Eva Lindgren

Chief Scientific Officer