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29 April 2015

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

Dear Healthcare Professional,

In agreement with European Medicines Agency (EMA) and Medicines and Healthcare products Regulatory Agency, Novartis would like to inform you of a first case report of PML in a patient taking fingolimod for multiple sclerosis without previous treatment with 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 received natalizumab (Tysabri) or other immunosuppressive medicines.**
- **PML was suspected on a routine brain MRI scan and confirmed by a quantitative PCR test that detected JC virus DNA in cerebrospinal fluid (CSF). 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 the 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 10^9/L. On 9 December 2014, the absolute lymphocyte count was 0.24 x 10^9/L.

On 23 January 2015, the patient had a routine magnetic resonance imaging (MRI) brain 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 10^9/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.

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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 continue to report suspected adverse drug reactions (ADRs) to the MHRA through the Yellow Card Scheme. Please report

- all suspected ADRs that are serious or result in harm. (Serious reactions are those that are fatal, life-threatening, disabling or incapacitating, those that cause a congenital abnormality or result in hospitalisation, and those that are considered medically significant for any other reason.)
- all suspected ADRs associated with new drugs and vaccines identified by the black triangle ▼

It is easiest and quickest to report ADRs online via the Yellow Cards website: www.mhra.gov.uk/yellowcard

Alternatively, prepaid Yellow Cards for reporting are available:

- by writing to FREEPOST YELLOW CARD (no other address details necessary)
- by emailing yellowcard@mhra.gsi.gov.uk
- at the back of the British National Formulary (BNF)
- by telephoning the Commission on Human Medicines (CHM) free phone line: 0800-731-6789
- or by downloading and printing a form from the Yellow Card section of the MHRA website

When reporting please provide as much information as possible, including information about medical history, any concomitant medication, onset, treatment dates, and product brand name. Adverse events should also be reported to Novartis on 01276 698 370 or via the following link: https://psi.novartis.com

Reports of suspected problems or incidents involving medical devices, defective medicines (those that are not of an acceptable quality) and counterfeit medicines and devices can also be submitted at www.mhra.gov.uk/yellowcard

Company contact point

If you have any questions or require further information, please contact Novartis Medical Information department on 01276 698370 or email medinfo.uk@novartis.com.

Yours faithfully,

Dr Dimitrios Georgiopoulos, MD
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