

Date: 04th January 2016

Fingolimod (Gilenya) - Risks related to the effects on the immune system

Dear Sir/Madam,

In agreement with the European Medicines Agency (EMA) and Health Products Regulatory Authority, Novartis would like to inform you of recent product information changes in relation to the immunosuppressive effects of fingolimod (Gilenya) and to take this opportunity to remind you of some important recommendations for use.

Summary

The adverse effects listed below have been reported in patients receiving fingolimod.

- **Basal cell carcinoma**
 - Medical evaluation of the skin before treatment initiation and during treatment is recommended.
- **Progressive multifocal leukoencephalopathy (PML):**
 - Physicians should be alert to the risk of PML. They should inform patients and carers of early symptoms suggestive of PML and instruct them to seek medical advice if such symptoms occur.
 - Before initiating treatment with fingolimod, a baseline MRI should be available (usually within 3 months) as a reference.
 - During routine MRI, physicians should pay close attention to lesions suggestive of PML.
 - If PML is suspected MRI should be performed immediately for diagnostic purposes and treatment with fingolimod should be suspended until PML has been excluded.
- **Other infections with opportunistic pathogens, including infections of the central nervous system**

In the event of infection:

 - Initiation of treatment should be delayed in patients with severe active infection until resolution.
 - Suspension of treatment should be considered if a patient develops a serious infection, and benefit/risk should be carefully considered prior to re-initiation of therapy.
- **Continue following complete blood count (CBC) monitoring requirements**

Further information

Fingolimod is licensed for use as disease-modifying monotherapy in highly active relapsing remitting multiple sclerosis.

Due to its immunosuppressive effects, fingolimod may predispose to serious adverse reactions. In this respect, the product information of fingolimod has been recently updated.

- **Basal cell carcinoma**

Cases of basal cell carcinoma (BCC) have been reported in patients receiving fingolimod. Cases were reported from both the clinical trial programme and the post-marketing setting. Therefore, vigilance for skin lesions is warranted and a medical evaluation of the skin is recommended at treatment initiation, after at least one year and then at least yearly taking into consideration clinical judgement. The patient should be referred to a dermatologist if suspicious lesions are detected.

Patients with known active malignancies (including BCC) must not be treated with fingolimod.

- Opportunistic Infections

The immunosuppressive effects of fingolimod may increase the risk of infections involving the CNS, including opportunistic infections such as viral infections (e.g. herpes simplex virus, varicella zoster virus), fungal infections (e.g. cryptococcal meningitis) or bacterial infections (e.g. atypical mycobacterium).

Prescribers are reminded that:

- Initiation of treatment with fingolimod should be delayed in patients with severe active infection until resolution.
- Suspension of fingolimod should be considered if a patient develops a serious infection and benefit-risk should be carefully considered prior to re-initiation of therapy.
- Elimination of fingolimod following discontinuation of therapy may take up to two months and vigilance for infection should therefore be continued throughout this period.

- ❖ Progressive multifocal leukoencephalopathy (PML)

Cases of PML have been reported during fingolimod treatment. PML is an opportunistic infection caused by JCV which may be fatal or result in severe disability. PML can only occur in the presence of a JCV infection. If JCV testing is undertaken, it should be considered that the influence of lymphopenia on the accuracy of anti-JCV antibody test has not been studied in fingolimod treated patients. It should also be noted that a negative anti JCV antibody test does not preclude the possibility of subsequent JCV infection. Before initiating treatment with fingolimod, a baseline MRI should be available (usually within 3 months) as a reference. During routine MRI (in accordance with national and local recommendations), physicians should pay attention to PML suggestive lesions. MRI may be considered as part of increased vigilance in patients considered at increased risk of PML. If PML is suspected, MRI should be performed immediately for diagnostic purposes and treatment with fingolimod should be suspended until PML has been excluded.

- Lymphoma

Cases of lymphoma have been reported in patients treated with fingolimod.

- Complete blood count monitoring

Finally, healthcare professionals are reminded that a recent (i.e. within 6 months or after discontinuation of prior therapy) complete blood count (CBC) should be available prior to initiation of fingolimod therapy in order to ensure that the effects of the previous therapy on the immune system (i.e. cytopenia) have resolved. Periodic assessments of CBC are also recommended during treatment (i.e. 3 months after starting treatment and at least yearly thereafter), and in case of signs of infection.

For complete information on the safety profile of fingolimod and related recommendations for use, please consult the product information.

Call for reporting

Please report any suspected adverse reactions associated with the use of fingolimod in accordance with the national requirements via the national spontaneous reporting system to **HPRA Pharmacovigilance**, Kevin O'Malley House, Earlsfort Centre, Earlsfort Terrace, Dublin 2, Ireland. Tel: 01 676 4971. Fax 01 676 2517. Website www.hpra.ie. E-mail: medsafety@hpra.ie

Adverse events should also be reported to Novartis on 01 260 1255

Company contact point

If you require any further information, please contact Niamh Murphy, Gilenya Medical Adviser on 0879744114 or email niamh.murphy@novartis.com

~~Yours sincerely~~



Dr. Eva Lindgren
Medical Director