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22nd January 2016

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

Dear Healthcare Professional,

In agreement with the European Medicines Agency (EMA) and the Medicines and Healthcare products Regulatory Agency, 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.

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- 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.

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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

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,

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