

Direct Healthcare Professional Communication:**Gilenya ▼ (fingolimod) – New contraindication in pregnant women and in women of childbearing potential not using effective contraception**

Dear Healthcare professional,

In agreement with European Medicines Agency (EMA) and Medicines and Healthcare products Regulatory Agency (MHRA), Novartis would like to inform you of the following:

Summary

- **Due to the risk of congenital malformations in fetuses exposed to fingolimod (Gilenya ▼), fingolimod is now contraindicated in:**
 - **pregnant women**
 - **women of childbearing potential not using effective contraception**
- **Post-marketing data suggest that infants born to mothers who have been exposed to fingolimod during pregnancy have a two-fold increased risk for congenital malformations compared with the rate observed in the general population (2-3 %; EUROCAT¹).**
- **For women of childbearing potential, ensure before treatment initiation and during the treatment that:**
 - **the patient is informed on the risk of harmful effects to the foetus associated with fingolimod treatment,**
 - **a negative pregnancy test result is available before any treatment initiation,**
 - **effective contraception is used during treatment and for 2 months after treatment discontinuation,**
 - **fingolimod treatment is stopped 2 months before planning a pregnancy.**
- **If a woman becomes pregnant during treatment:**
 - **fingolimod must be discontinued,**
 - **medical advice should be given to the patient regarding the risk of harmful effects to the foetus,**
 - **the pregnancy should be closely monitored, and ultrasonography examinations should be performed.**

Background

Gilenya ▼ is indicated as disease-modifying therapy in highly active relapsing-remitting multiple sclerosis for the following groups of adults and children aged 10 years and older:

- patients with highly active disease despite a full and adequate course of treatment with at least one disease-modifying therapy , or
- 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.

The receptor affected by fingolimod (sphingosine 1-phosphate receptor) is involved in vascular formation during embryogenesis. Animal studies have shown reproductive toxicity in rats.

Based on human experience, post-marketing data suggest that use of fingolimod is associated with a 2 fold increased risk of major congenital malformations when administered during pregnancy compared with the rate observed in the general population (2-3 %; EUROCAT¹).

¹ European network of population-based registries for the epidemiological surveillance of congenital anomalies (<http://www.eurocat-network.eu>)

The most frequently reported major malformations are:

- congenital heart disease such as atrial and ventricular septal defects, tetralogy of Fallot;
- renal abnormalities;
- musculoskeletal abnormalities.

Information is provided in the “Physician Information Pack,” which includes 3 educational materials to facilitate the regular counselling of patients regarding the risk of reproductive toxicity²:

- **Physician’s checklist**
- **Patient / Parent / Caregiver guide**
- **Pregnancy-specific patient reminder card**

Call for reporting

Physicians are encouraged to continue reporting on pregnant patients who may have been exposed to fingolimod at any time during pregnancy (from 8 weeks prior to last menstrual period onward) to Novartis online through the patient safety information (PSI) tool at <https://psi.novartis.com>, or by visiting uk.patientsafety@novartis.com, in order to allow monitoring of these patients through the Pregnancy Outcomes Intensive Monitoring Program (PRIM). Physicians may also enroll a pregnant MS patient under their care in the fingolimod pregnancy registry by dialling 0808 2345424 or visiting www.gilenyapregnancyregistry.com or www.gpregnancy.com, or by email to gpr@quintiles.com.

Gilenya ▼ is subject to additional monitoring to allow quick identification of new safety information. Healthcare professionals are asked to report any suspected adverse reactions.

Please continue to report suspected adverse drug reactions (ADRs) to the MHRA through the Yellow Card Scheme. It is easiest and quickest to report ADRs online via the Yellow Cards website - <https://yellowcard.mhra.gov.uk/> or via the Yellow Card app available from the Apple App Store or Google Play Store.

Alternatively, prepaid Yellow Cards for reporting are available by writing to FREEPOST YELLOW CARD (no other address details necessary); by emailing yellowcard@mhra.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 website.

Adverse events should also be reported to Novartis online through the patient safety information (PSI) tool at <https://psi.novartis.com> or via uk.patientsafety@novartis.com.

Further copies of this letter can be obtained via the electronic medicines compendium (eMC) website by visiting <https://www.medicines.org.uk/emc>.

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 Mark Toms, MBChB

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² The current educational materials will be updated.