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Direct Healthcare Professional Communication

Gilenya (fingolimod) – New contraindication in pregnant women and in women of childbearing potential not using effective contraception

Dear Healthcare professional,

Novartis, in agreement with the European Medicines Agency and the Malta Medicines Authority, 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 %; EUROCAT).
- **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 (sphingosine1-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 %; EUROCAT[1]).

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 provided in the "Physician Information Pack," will include 3 educational materials to facilitate the regular counselling of patients regarding the risk of reproductive toxicity[2]:

- 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 by dialling +35621222872 or visiting www.report.novartis.com, in order to allow monitoring of these patients through the Pregnancy Outcomes Intensive Monitoring Program (PRIM). Physicians may also enrol a pregnant MS patient under their care in the fingolimod pregnancy registry by visiting www.gilenyapregnancyregistry.com

Reporting suspected adverse reactions after authorization of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are reminded to continue to report suspected adverse reactions associated with fingolimod in accordance with the national spontaneous reporting system. Report forms can be downloaded from www.medicinesauthority.gov.mt/adrportal and posted to Post-licensing directorate, Medicines Authority, Sir Temi Żammit Buildings, Malta Life Sciences Park, San Ġwann SĠN 3000, Malta or sent by email to postlicensing.medicinesauthority@gov.mt.

[1] EUROCAT: European surveillance of congenital anomalies (http://www.eurocat-network.eu).
[2] The current educational material will be updated. Current educational material can be found on the Malta Medicines Authority website at http://www.medicinesauthority.gov.mt/rmm

Alternatively, to Novartis Patient Safety Malta via web: www.report.novartis.com or via e-mail: drug_safety.malta@novartis.com or via phone on: +356 21222872.

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

Company contact point

Should you have any questions or require additional information, please call Medical Information at:

Company	Product name	Email	Phone
Novartis Pharma Services Inc., Representative Office, Malta	Gilenya	novartis.malta@novartis.com	+356 21222872

Yours faithfully,

Post-Licensing Directorate

Medicines Authority

Disclaimer

This Direct Healthcare Professional Communication has been submitted to you on behalf of Novartis Pharma Services Inc., Representative Office, Malta.