Bishember Kathuria
Chief Scientific Officer

Novartis Ireland Ltd
The Vista Building
Elm Park Business Park
Merrion Road
Dublin 4
D04 A9N6
Tel +353 1 2601255
Fax +353 1 2601263
E-Mail:
bishember.kathuria@novartis.com

Direct Healthcare Professional Communication

26 August 2019

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

Dear Healthcare Professional,

In agreement with the European Medicines Agency (EMA) and the Health Products Regulatory Authority (HPRA), Novartis would like to inform you of the following:

Summary

- **Due to the risk of congenital malformations in foetuses 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 of 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,

Bishember Kathuria
Chief Scientific Officer

Novartis Ireland Ltd
The Vista Building
Elm Park Business Park
Merrion Road
Dublin 4
D04 A9N6
Tel +353 1 2601255
Fax +353 1 2601263
E-Mail:
bishember.kathuria@novartis.com

- the pregnancy should be closely monitored, and ultrasonography examinations should be performed.

We request that you cascade this letter to all members of your team.

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 %; EUROCAT1).

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 will be provided in the "Physician Information Pack," which will include 2 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

[1] European network of population-based registries for the epidemiological surveillance of congenital anomalies (http://www.eurocat-network.eu)
[2] The current educational materials will be updated.

Bishember Kathuria
Chief Scientific Officer

Novartis Ireland Ltd
The Vista Building
Elm Park Business Park
Merrion Road
Dublin 4
D04 A9N6
Tel +353 1 2601255
Fax +353 1 2601263
E-Mail:
bishember.kathuria@novartis.com

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 dialing 01-2080 612 or by email to drugsafety.dublin@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 visiting www.gilenyapregnancyregistry.com, by dialing +800 6882 6637 or by email to gpr@quintiles.com.

▼This medicinal product is subject to additional monitoring. This will allow quick identification of new safety information. Adverse events should be reported. Healthcare professionals are asked to report any suspected adverse reactions via HPRA Pharmacovigilance, Earlsfort Terrace, IRL - Dublin 2; Tel: +353 1 6764971; Fax: +353 1 6762517; Website: www.hpra.ie; E-mail:medsafety@hpra.ie. Adverse events should also be reported to Novartis Ireland by calling 01-2080 612 or by email to drugsafety.dublin@novartis.com.

Company contact point

Dr. Bishember Kathuria MB BS, MBA

Chief Scientific Officer | Novartis Ireland Ltd.

Vista Building, Elm Park Business Park | Merrion Road, Dublin 4, D04 A9N6, Ireland

Mail: bishember.kathuria@novartis.com | P: +353(0)12204909 | M: +353(0)873898581