Important Safety Information on GILENYA (fingolimod) and the Risk of Congenital Malformations

NOVARTIS

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Audience
Healthcare professionals including neurologists, obstetricians, gynecologists, pediatricians, family physicians, general practitioners, nurses, and pharmacists.

Key messages

- **When used during pregnancy, GILENYA (fingolimod) has been associated with an increased risk of major congenital malformations, including congenital heart disease such as atrial septal defect, and renal and musculoskeletal abnormalities.**
- **GILENYA is now contraindicated in women who are pregnant or in women of childbearing potential who are not using effective contraception.**
- **Healthcare professionals should discuss the following with all female patients of reproductive potential (including female adolescents and their parent/guardian/caregiver) treated with, or to be treated with, GILENYA:**
    - **the risk of harmful effects associated with GILENYA to a fetus during pregnancy;**
    - **the need for a negative pregnancy test before starting treatment with GILENYA, which is then repeated at appropriate intervals during treatment;**
    - **the necessity to use effective contraception during therapy with GILENYA, and for 2 months after stopping GILENYA treatment; and**
    - **the need to discontinue GILENYA 2 months before planning a pregnancy.**
- **The Canadian Product Monograph (CPM) for GILENYA has been updated to include this new contraindication and new safety information.**
- **Health Canada will work with the manufacturers of generic versions of fingolimod to update their respective CPMs.**

What is the issue?
There is a risk of congenital malformations in a fetus exposed to GILENYA. Available human data (post-marketing data and pregnancy registry information) suggest that the use of GILENYA is associated with an increased risk of overall major congenital malformation (approximately 5%) when administered during pregnancy in comparison with the prevalence observed in the general population (2-4%).

Products affected
GILENYA, Fingolimod capsules, 0.25 mg and 0.5 mg (as fingolimod hydrochloride).

Other products affected by this risk information include all generic Fingolimod capsules 0.5 mg (as fingolimod hydrochloride).

Background information
GILENYA is indicated as monotherapy for the treatment of adults with the relapsing-remitting form of multiple sclerosis (MS) to reduce the frequency of relapses and to delay the progression of physical disability. GILENYA is generally recommended in MS patients who have had an inadequate response to, or are unable to tolerate, one or more therapies for multiple sclerosis.

GILENYA is also indicated as monotherapy for the treatment of pediatric patients between 10 years and 18 years of age with relapsing multiple sclerosis to reduce the frequency of clinical exacerbations.

Available human data (post-marketing data and pregnancy registry information) supported by animal data suggest that use of GILENYA is associated with an increased risk of overall major congenital malformation (approximately 5%) when administered during pregnancy in comparison with the prevalence observed in the general population (2-4%).

The pattern of malformation reported for GILENYA is similar to that observed in the general population. However, an increased prevalence of the following specific major malformations was noted:

- congenital heart disease such as atrial septal defects;
- renal abnormalities; and
- musculoskeletal abnormalities.

The *Contraindications*, *Warnings and Precautions*, and *Consumer Information* sections of Canadian Product Monograph (CPM) for GILENYA has been updated to include the new contraindication and new safety information regarding the risk of congenital malformations.

Information for consumers

GILENYA is used to treat adults with the relapsing and remitting form of multiple sclerosis (MS). MS is an unpredictable, often disabling disease of the central nervous system. GILENYA is generally recommended for MS patients who have not responded well to, or cannot tolerate, one or more of the other therapies for MS.

GILENYA is also used to treat children and adolescent patients between 10 and 18 years of age with the relapsing form of MS.

Animal and post-marketing studies have shown that GILENYA can harm an unborn baby if used during pregnancy.

Before starting treatment with GILENYA, women (including female adolescents and their parent/guardian/caregiver) who could become pregnant or are planning to become pregnant should:

- talk with their doctor about the risk to an unborn baby;
- do a pregnancy test to ensure that they are not pregnant, and repeat the pregnancy test at appropriate intervals during treatment;
- use effective contraception while taking GILENYA and for 2 months after they stop taking it; and
- discontinue GILENYA 2 months before planning a pregnancy.

Women who become pregnant while taking GILENYA should inform their doctor immediately.

Patients should discuss any questions or concerns about this information with their healthcare professional.

Information for healthcare professionals

Healthcare professionals are advised to discuss the following with all female patients of reproductive potential (including female adolescents and their parent/guardian/caregiver patients treated with, or to be treated with, GILENYA:

- the risk of harmful effects associated with GILENYA to a fetus during pregnancy;
- the need for a negative pregnancy test before starting treatment with GILENYA, which is then repeated at appropriate intervals during treatment;
- the necessity to use effective contraception during therapy with GILENYA, and for 2 months after stopping GILENYA treatment,
- the need to discontinue GILENYA 2 months before planning a pregnancy.

If a female patient becomes pregnant while taking GILENYA, stop treatment. Alternative therapy for MS should be considered in women stopping GILENYA

treatment due to pregnancy or for planning a pregnancy to avoid the possible return of the disease activity.

Action taken by Health Canada
Health Canada, in collaboration with Novartis Pharmaceuticals Canada Inc., updated the CPM for GILENYA. Health Canada will work with manufacturers of generic versions of fingolimod to update their respective CPMs.

Health Canada is communicating this important safety information to healthcare professionals and Canadians via the Recalls and Safety Alerts Database on the Healthy Canadians Web Site (https://healthycanadians.gc.ca/recall-alert-rappel-avis/index-eng.php). This communication update will be further distributed through the MedEffect™ e-Notice email notification system, as well as through social media channels, including LinkedIn and Twitter.

Report health or safety concerns
Health Canada's ability to monitor the safety of marketed health products depends on healthcare professionals and consumers reporting adverse reactions and medical device incidents. Any case of serious or unexpected side effects in patients receiving GILENYA should be reported to Novartis Pharmaceuticals Canada Inc. or to the respective generic fingolimod manufacturer or Health Canada.

Physicians are also encouraged to report if patients may have been exposed to fingolimod at any time during pregnancy (from 8 weeks prior to last menstrual period onward) to Health Canada and Novartis Pharmaceuticals Canada Inc. by calling 1-855-363-8883 or to the respective generic fingolimod manufacturer.

Novartis Pharmaceuticals Canada Inc.
385 Bouchard Blvd.
Dorval, Québec, H9S 1A9
1-800-363-8883

www.novartis.ca/en/util/contact/product.shtml

To correct your mailing address or fax number, contact Novartis Pharmaceuticals Canada Inc.

You can report any suspected adverse reactions associated with the use of health products to Health Canada by:

- Calling toll-free at 1-866-234-2345; or
- Visiting MedEffect Canada's Web page on Adverse Reaction Reporting (https://www.canada.ca/en/health-canada/services/drugs-health-products/medeffect-canada/adverse-reaction-reporting.html) for information on how to report online, by mail or by fax.

For other health product inquiries related to this communication, contact Health Canada at:

Marketed Health Products Directorate
E-mail: hc.mhpd-dpsc.sc@canada.ca
Telephone: 613-954-6522
Fax: 613-952-7738

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