PUBLIC COMMUNICATION
Health Canada Endorsed Important Safety Information on
PrGILENYA* (fingolimod)

NOVARTIS

August 23, 2012

Subject: **GILENYA* (fingolimod) – Stronger safety recommendations regarding first-dose heart monitoring and use in patients with heart conditions**

Novartis Pharmaceuticals Canada Inc. ("Novartis"), in collaboration with Health Canada, would like to inform you about important new safety information for the multiple sclerosis drug GILENYA* (fingolimod).

GILENYA* causes the heart rate to slow down in the first hours and return to baseline after about one month of treatment. GILENYA* can also cause an irregular heartbeat, especially after the first dose. Isolated cases of serious side effects on the heart, including temporary, but serious irregularity in heart beat and one case of unexplained death, have also been observed within 24 hours of the first dose, possibly associated with GILENYA*. A number of Canadians have reported side effects on the heart with the majority having occurred within 6 hours of the first dose. There have been international reports of deaths in patients treated with GILENYA*, some of which were considered possibly associated with GILENYA*. No deaths have been reported in Canada.

In response to these safety concerns, new recommendations to reduce the risk of effects on the heart in patients taking GILENYA* have been included in the Product Monograph.

- GILENYA* can cause the heart rate to decrease and may affect heart rhythm after the first dose. Serious heart complications and one unexplained death have been observed following the first dose of GILENYA*.
- Due to the heart-related side effects of GILENYA*, the following is now required when you start treatment with GILENYA* or after a break in the treatment:
  - An electrocardiogram (ECG) to check the health of your heart before you start GILENYA* and 6 hours after your first dose.
  - Stay in the clinic or office for at least 6 hours after taking your first dose of GILENYA* so your heart rate and blood pressure can be checked hourly during that time and appropriate measures taken if heart-related side effects occur.
  - In case of serious heart side effects at the end of the 6-hour observation period, you will need to be observed longer, possibly overnight, in a health care facility.
- GILENYA* should not be used in patients with certain heart-related conditions.

Therefore, before you use GILENYA*, talk to your doctor or pharmacist if you have current or past heart problems, if you are taking medicines for cardiac problems or high blood pressure, or you have a history of sudden loss of consciousness.

GILENYA* is a prescription medicine to treat the relapsing and remitting form of multiple sclerosis (MS). GILENYA* is generally recommended for MS patients who have not responded well to, or cannot tolerate one or more of the other therapies for multiple sclerosis.

Heart-related side effects are a known risk with GILENYA* use and the previous Canadian Product Monograph already contained several warnings to this effect. Following a safety review, the Product Monograph warnings have been strengthened with respect to heart-related side effects and new recommendations for close patient monitoring have been added.

The effects of GILENYA* on the heart may be greater in patients with certain heart-related conditions. Before you use GILENYA* talk to your doctor or pharmacist if:

- You have heart problems or a history of heart problems, such as irregular or abnormal heartbeat (arrhythmia), severe cardiac disease, uncontrolled high blood pressure, a history of stroke or other diseases related to blood vessels in the brain, a history of sudden loss of consciousness, severe untreated sleep apnea (a condition in which breathing is difficult during sleep), or if you are at risk for, or if you have heart rhythm disturbances.

- You are taking medicines for irregular heartbeat, for high blood pressure or for other cardiac problems.

If you experience any symptoms of a possible heart rhythm disturbance, such as dizziness, palpitations (sensation of rapid, pounding, or irregular heart beat), fainting, or seizures, at any time during treatment with GILENYA*, you should seek immediate medical attention.

Do not stop taking GILENYA* or change your dose without talking with your doctor.

On February 27, 2012, Health Canada issued an information update related to the ongoing safety review on the risk of heart-related side effects with GILENYA* use (see http://www.hc-sc.gc.ca/ahc-asc/media/advisories-avis/_2012/2012_28-eng.php). Novartis has also sent a letter to all multiple sclerosis healthcare professionals to inform them of this new safety information. A copy of that letter is available on the Health Canada website at: *http://www.hc-sc.gc.ca/dhp-mps/medeff/advisories-avis/prof/_2012/index-eng.php*

Managing marketed health product-related adverse reactions depends on health care professionals and consumers reporting them. Reporting rates determined on the basis of spontaneously reported post-marketing adverse reactions are generally presumed to underestimate the risks associated with health product treatments. Any case of serious side effects on the heart or other serious or unexpected adverse reactions in patients

receiving GILENYA* should be reported to Novartis or Health Canada.

Novartis Pharmaceuticals Canada Inc.
385 Bouchard Blvd.
Dorval, (QC) H9S 1A9
Phone: 1-800-363-8883 (Medical Information)

You can report any suspected adverse reactions associated with the use of health products to the Canada Vigilance Program by one of the following 3 ways:

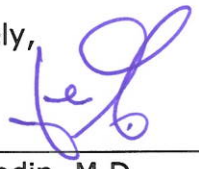
- Report online at www.healthcanada.gc.ca/medeffect
- Call toll-free at 1-866-234-2345
- Complete a Reporting Form and:
  - Fax toll-free to 1-866-678-6789, or
  - Mail to: Canada Vigilance Program
    Health Canada
    Postal Locator 0701E
    Ottawa, Ontario K1A 0K9

The Reporting Forms, postage paid labels, and Guidelines can be found on the MedEffect™ Canada Web site in the Adverse Reaction Reporting section (http://hc-sc.gc.ca/dhp-mps/medeff/report-declaration/index-eng.php).

For other health product inquiries related to this communication, please contact Health Canada at:
Marketed Health Products Directorate
E-mail: mhpd_dpsc@hc-sc.gc.ca
Telephone: 613-954-6522
Fax: 613-952-7738

Should you have any questions or require additional information regarding the use of GILENYA*, please contact Novartis Pharmaceuticals Canada Inc., Medical Information Department at 1-800-363-8883.

Sincerely,



Jean Godin, M.D.
Chief Scientific Officer and Vice-President Clinical and Regulatory Affairs

*GILENYA is a registered trademark.