



NDA 022527/S-010

**SUPPLEMENT APPROVAL**

Novartis Pharmaceutical Corporation  
Attention: Mara Stiles  
Regional Branch Regulatory Manager  
One Health Plaza  
East Hanover, NJ 07936-1080

Dear Ms. Stiles:

Please refer to your Supplemental New Drug Application (sNDA) dated September 7, 2012, received September 10, 2012, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Gilenya (fingolimod) 0.5 mg capsules.

We acknowledge receipt of your amendments dated April 1, 2013, April 9, 2013, and April 25, 2013, and your risk evaluation and mitigation strategy (REMS) assessment dated September 10, 2012.

This Prior Approval supplemental new drug application provides for a proposed modification to the approved REMS for Gilenya (fingolimod).

We have completed our review of this supplemental application, as amended. It is approved, effective on the date of this letter.

**RISK EVALUATION AND MITIGATION STRATEGY REQUIREMENTS**

The REMS for Gilenya (fingolimod) was originally approved on September 21, 2010, and a REMS modification was approved on March 1, 2012. The REMS consists of a communication plan and a timetable for submission of assessments of the REMS. Your proposed modifications to the REMS consist of revisions to your communication plan materials (including revisions to your Dear Healthcare Professional Letter, Dear Professional Society letter, and Guide to Important Safety Information brochure) to reflect the labeling changes we approved for Gilenya (fingolimod) on May 9, 2012. In addition, the timetable for submission of assessments of the REMS has been revised to add an assessment four years following the original approval date of the REMS (i.e., on September 21, 2014).

Your proposed modified REMS, submitted on April 25, 2013, and appended to this letter, is approved.

The revised REMS assessment plan should include, but is not limited to, the following:

- a. An evaluation of healthcare providers' understanding of the serious risks of GILENYA (fingolimod)
- b. With regard to assessment of the communication plan:
  - i. The date of product launch and the launch of the communication plan
  - ii. The date(s) of mailing and number of recipients of the Dear Healthcare Professional (DHCP) letter and the Guide to Important Safety Information; Using Gilenya in Patients with Relapsing Forms of Multiple Sclerosis.
  - iii. The number of mailings returned.
  - iv. The sources of the recipient lists
  - v. Describe (or provide a list of) the information sources Novartis used to create the "Novartis Target List," the source of addresses for the communication plan.
  - vi. Periodic summaries of serious adverse event reports of symptomatic and asymptomatic bradyarrhythmia and atrioventricular blocks, infections, macular edema, respiratory effects, hepatic effects, and fetal risk.
  - vii. Periodic summaries of pregnancies in women exposed to fingolimod and maternal and fetal outcomes, including updates from fingolimod pregnancy exposure registry.
  - viii. Specification of measures that would be taken to increase awareness if surveys of healthcare providers indicate that provider awareness is not adequate.

The requirements for assessments of an approved REMS under section 505-1(g)(3) include with respect to each goal included in the strategy, an assessment of the extent to which the approved strategy, including each element of the strategy, is meeting the goal or whether 1 or more such goals or such elements should be modified.

In addition to the assessments submitted according to the timetable included in the approved REMS, you must submit a REMS assessment and may propose a modification to the approved REMS when you submit a supplemental application for a new indication for use as described in section 505-1(g)(2)(A) of the FDCA.

If the assessment instruments and methodology for your REMS assessments are not included in the REMS supporting document, or if you propose changes to the submitted assessment instruments or methodology, you should update the REMS supporting document to include specific assessment instrument and methodology information at least 90 days before the assessments will be conducted. Updates to the REMS supporting document may be included in a new document that references previous REMS supporting document submission(s) for unchanged portions. Alternatively, updates may be made by modifying the complete previous REMS supporting document, with all changes marked and highlighted. Prominently identify the submission containing the assessment instruments and methodology with the following wording in bold capital letters at the top of the first page of the submission:

**NDA 22527 REMS CORRESPONDENCE**  
**(insert concise description of content in bold capital letters, e.g.,**  
**UPDATE TO REMS SUPPORTING DOCUMENT - ASSESSMENT**  
**METHODOLOGY**

An authorized generic drug under this NDA must have an approved REMS prior to marketing. Should you decide to market, sell, or distribute an authorized generic drug under this NDA, contact us to discuss what will be required in the authorized generic drug REMS submission.

Prominently identify the submission containing the REMS assessments or proposed modifications of the REMS with the following wording in bold capital letters at the top of the first page of the submission as appropriate:

**NDA 22527 REMS ASSESSMENT**

**NEW SUPPLEMENT FOR NDA 22527**  
**PROPOSED REMS MODIFICATION**

**NEW SUPPLEMENT (NEW INDICATION FOR USE)**  
**FOR NDA 22527 REMS ASSESSMENT**  
**PROPOSED REMS MODIFICATION (if included)**

If you do not submit electronically, please send 5 copies of REMS-related submissions.

**REPORTING REQUIREMENTS**

We remind you that you must comply with reporting requirements for an approved NDA (21 CFR 314.80 and 314.81).

If you have any questions, contact LCDR Hamet Touré, PharmD MPH, Regulatory Project Manager, at (301) 796-7534.

Sincerely,

*{See appended electronic signature page}*

Eric Bastings, M.D.  
Deputy Director  
Division of Neurology Products  
Office of Drug Evaluation I  
Center of Drug Evaluation and Research

ENCLOSURE:  
REMS

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**This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.**  
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/s/  
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ERIC P BASTINGS  
05/28/2013