DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 22527 / S-005

SUPPLEMENT APPROVAL
REMOVE REMS ELEMENT

Mara Stiles
Global Program Regulatory Manager,
Neuroscience and Ophthalmology
Novartis Pharmaceuticals Corporation
One Health Plaza
East Hanover, NJ 07936-1080

Dear Ms.Stiles:

Please refer to your Supplemental New Drug Application (sNDA) dated August 22, 2011, received August 22, 2011, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Gilenya (fingolimod) capsules.

We acknowledge receipt of your amendments dated October 3 and 19, 2011 and December 16, 2011. We also acknowledge your risk evaluation and mitigation strategy (REMS) assessment dated August 22, 2011.

This Prior Approval supplemental new drug application proposes to eliminate the Medication Guide as an element of the approved Gilenya (fingolimod) REMS.

We have completed our review of this supplemental application. 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. The REMS consists of a Medication Guide, communication plan, and a timetable for submission of assessments of the REMS.

Your proposed modification to the REMS consists of eliminating the requirement for the Medication Guide as an element of the REMS.

We have determined that maintaining the Medication Guide as part of the approved labeling is adequate to address the serious and significant public health concern and meets the standard in 21 CFR 208.1. Therefore, it is no longer necessary to include the Medication Guide as an element of the approved REMS to ensure that the benefits of the Gilenya (fingolimod) outweigh the risks.

Therefore, a Medication Guide and is no longer required as part of the REMS for Gilenya (fingolimod).

Your proposed modified REMS, submitted on August 22, 2011, and appended to this letter, is approved.

The modified REMS consists of a communication plan and a timetable for submission of assessments of the REMS.

We remind you that the Medication Guide will continue to be part of the approved labeling for Gilenya (fingolimod) in accordance with 21 CFR 208.

The timetable for submission of assessments of the REMS will remain the same as that approved on September 21, 2010.

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

a. An evaluation of healthcare providers' (HCPs') 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. 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.
    vi. Periodic summaries of pregnancies in women exposed to fingolimod and maternal and fetal outcomes, including updates from fingolimod pregnancy exposure registry.
c. Based on the information submitted, an assessment of and conclusion regarding whether the REMS is meeting its goals, and whether modifications to the REMS are needed.
d. Specification of measures that would be taken to increase awareness if surveys of HCPs indicate that provider awareness is not adequate.
e. Information on the status of any postapproval study or clinical trial required under section 505(o)(3) or otherwise undertaken to investigate a safety issue. With respect to any such postapproval study, you must include the status of such study, including whether any difficulties completing the study have been encountered. With respect to any such postapproval clinical trial, you must include the status of such clinical trial, including whether enrollment has begun, the number of participants enrolled, the expected completion date, whether any difficulties completing the clinical trial have been encountered, and registration information with respect to requirements under

subsections (i) and (j) of section 402 of the Public Health Service Act. You can satisfy these requirements in your REMS assessments by referring to relevant information included in the most recent annual report required under section 506B and 21 CFR 314.81(b)(2)(vii) and including any material or significant updates to the status information since the annual report was prepared. Failure to comply with the REMS assessments provisions in section 505-1(g) could result in enforcement action.

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 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
REMS ASSESSMENT

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, call LCDR Hamet Touré, Regulatory Project Manager, at (301) 796-7534.

Sincerely,

{See appended electronic signature page}

Russell G. Katz, M.D.
Director
Division of Neurology Products
Office of Drug Evaluation I
Center for Drug Evaluation and Research

ENCLOSURES:
REMS
REMS materials

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

RUSSELL G KATZ
03/01/2012