DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 022527/S-015

SUPPLEMENT APPROVAL
REMS ASSESSMENT ACKNOWLEDGMENT
REMS ASSESSMENT PLAN REVISION

Novartis Pharmaceuticals Corporation
Attention: Mara Stiles
Global Program Regulatory Manager
One Health Plaza
East Hanover, NJ 07936-1080

Dear Ms. Stiles:

Please refer to your Supplemental New Drug Application (sNDA) dated June 27, 2014, received June 27, 2014, 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 submitted December 19, 2014, January 13, 2015, January 19, 2015, January 22, 2015, February 17, 2015, May 8, 2015, and May 12, 2015, and your risk evaluation and mitigation strategy (REMS) assessment dated September 19, 2014.

This supplemental new drug application provides for proposed modifications to the approved REMS. In addition, we have found the REMS assessment to be complete.

RISK EVALUATION AND MITIGATION STRATEGY REQUIREMENTS

The REMS for Gilenya (fingolimod) was originally approved on September 21, 2010, and REMS modifications were approved on March 1, 2012, and May 28, 2013. 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:

- Inclusion of the risk of posterior reversible encephalopathy syndrome (PRES) to the REMS, including the goals and relevant REMS materials, to inform healthcare providers about the risk;
- Revisions to the REMS and appended materials to align with labeling approved under Supplement 13 on May 1, 2015;
- Revisions to all the appended REMS materials to include reformatting of the information pertaining to re-initiation of therapy following discontinuation of Gilenya;
- Revision to the duration of the REMS website;
- Revision to the distribution schedule of the Dear Healthcare Professional letters;

- Revision to the timetable for submission of assessments to add a submission of an assessment 11 months from the date of approval of the May 2015 REMS Modification.

Your proposed modified REMS, submitted on May 12, 2015 and appended to this letter, is approved.

Our May 28, 2013, REMS modification approval letter described the REMS assessment plan. The REMS assessment plan should be revised to focus on an assessment of prescribers' understanding of PRES and respiratory risks, as prior assessments have demonstrated that the other risks included in the REMS appear to be reasonably well understood by prescribers.

The revised REMS assessment plan should include but is not limited to the following items.

a. With regard to assessment of the communication plan activities:
    i. An evaluation of healthcare providers' understanding of the serious risks of PRES and respiratory effects associated with GILENYA (fingolimod) as outlined in the REMS materials.
    ii. The date(s) of mailing and number of recipients of the Dear Healthcare Professional (DHCP) letter, Dear Professional Society 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.

b. A summary from all Periodic Safety Update Reports (PSURs) submitted during the assessment period of serious adverse event reports of symptomatic and asymptomatic bradyarrhythmia and atrioventricular blocks, infections, macular edema, PRES, respiratory effects, liver injury, and fetal risk.

c. A summary of pregnancies in women exposed to fingolimod, and maternal and fetal outcomes during the assessment period, including updates from fingolimod pregnancy exposure registry.

d. Specification of measures that would be taken to increase awareness if surveys of healthcare providers indicate that provider awareness is not adequate.

e. 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 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 022527 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 022527 REMS ASSESSMENT

NEW SUPPLEMENT FOR NDA 022527
PROPOSED REMS MODIFICATION

NEW SUPPLEMENT (NEW INDICATION FOR USE)
FOR NDA 022527
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 Hamet Touré, PharmD MPH, Regulatory Project Manager, at (301) 796-7534.

Sincerely,

{See appended electronic signature page}

Alice Hughes, MD
Deputy Director for Safety
Division of Neurology Products
Office of Drug Evaluation I
Center for Drug Evaluation and Research

ENCLOSURE:
REMS

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

/s/

ALICE HUGHES
05/14/2015