DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 22334/S-40
NDA 203985/S-13

SUPPLEMENT APPROVAL

Novartis Pharmaceuticals Corporation
Attention: Yanina Katz, PharmD
Director, Regulatory Affairs
One Health Plaza
East Hanover, NJ 07936

Dear Dr. Katz:

Please refer to your supplemental New Drug Applications (sNDAs) dated March 10, 2017, received March 10, 2017, and your amendments, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA), for AFINITOR (everolimus) tablets and AFINITOR DISPERZ (everolimus tables for oral suspension).

We acknowledge receipt of your major amendment dated November 17, 2017, which extended the goal date by three months.

The Prior Approval supplemental new drug application for NDA 203985/S-13 provides for a new indication for AFINITOR DISPERZ for the adjunctive treatment of adult and pediatric patients age 2 years and older with tuberous sclerosis complex (TSC)-associated partial-onset seizures. In addition, the WARNINGS AND PRECAUTIONS, Infections (5.2) subsection was updated to provide information on the incidence of serious infections in patients < 6 years of age and the USE IN SPECIFIC POPULATIONS, Pediatric Use (8.4) subsection was updated to describe safety and efficacy in pediatric patients in the indicated population.

The Prior Approval supplemental new drug application for NDA 22334/S-40 revises the WARNINGS AND PRECAUTIONS, Infections (5.2) subsection to provide information on the incidence of serious infections in patients < 6 years of age and revises the USE IN SPECIFIC POPULATIONS, Pediatric Use (8.4) subsection to describe safety and efficacy in pediatric patients with TSC-associated partial-onset seizures.

In addition, the package insert for AFINITOR/AFINITOR DISPERZ was revised to comply with current regulations and guidances and for clarity, including re-organization of information in the DOSAGE AND ADMINISTRATION (2) section, deletion of the OVERDOSAGE (10) section, and moving existing information to new or alternative sections of labeling.

APPROVAL & LABELING

We have completed our review of this supplemental application, as amended. It is approved, effective on the date of this letter, for use as recommended in the enclosed, agreed-upon labeling text.

WAIVER OF HIGHLIGHTS SECTION

Please note that we have previously granted a waiver of the requirements of 21 CFR 201.57(d)(8) regarding the length of Highlights of prescribing information.

CONTENT OF LABELING

As soon as possible, but no later than 14 days from the date of this letter, submit the content of labeling [21 CFR 314.50(l)] in structured product labeling (SPL) format using the FDA automated drug registration and listing system (eLIST), as described at http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm. Content of labeling must be identical to the enclosed labeling text for the package insert, patient package insert, and the Instructions for Use, with the addition of any labeling changes in pending "Changes Being Effected" (CBE) supplements, as well as annual reportable changes not included in the enclosed labeling.

Information on submitting SPL files using eList may be found in the guidance for industry titled "SPL Standard for Content of Labeling Technical Qs and As" at http://www.fda.gov/downloads/DrugsGuidanceComplianceRegulatoryInformation/Guidances/UCM072392.pdf.

The SPL will be accessible from publicly available labeling repositories.

Also within 14 days, amend all pending supplemental applications that include labeling changes for this NDA, including CBE supplements for which FDA has not yet issued an action letter, with the content of labeling [21 CFR 314.50(l)(1)(i)] in MS Word format, that includes the changes approved in this supplemental application, as well as annual reportable changes and annotate each change. To facilitate review of your submission, provide a highlighted or marked-up copy that shows all changes, as well as a clean Microsoft Word version. The marked-up copy should provide appropriate annotations, including supplement number(s) and annual report date(s).

REQUIRED PEDIATRIC ASSESSMENTS

Under the Pediatric Research Equity Act (PREA) (21 U.S.C. 355c), all applications for new active ingredients, new indications, new dosage forms, new dosing regimens, or new routes of administration are required to contain an assessment of the safety and effectiveness of the product for the claimed indication(s) in pediatric patients unless this requirement is waived, deferred, or inapplicable.

Because this drug product for this indication has an orphan drug designation, you are exempt from this requirement

POSTMARKETING COMMITMENTS SUBJECT TO REPORTING REQUIREMENTS UNDER SECTION 506B

We remind you of your postmarketing commitment:

PMC #3355-1: Submit the clinical report and datasets once all patients have completed the Extension phase of Trial M2304, entitled "A Three-Arm, Randomized, Double-Blind, Placebo-Controlled Study of the Efficacy and Safety of Two Trough-Ranges of Everolimus as Adjunctive Therapy in Patients with Tuberous Sclerosis Complex (TSC) Who Have Refractory Partial-Onset Seizures", to provide additional data regarding the activity of everolimus as an anti-seizure medication in patients with TSC.

The timetable you submitted on March 13, 2018, states that you will conduct this study according to the following schedule:

Final Report Submission: August 2018

PROMOTIONAL MATERIALS

You may request advisory comments on proposed introductory advertising and promotional labeling. To do so, submit the following, in triplicate, (1) a cover letter requesting advisory comments, (2) the proposed materials in draft or mock-up form with annotated references, and (3) the package insert(s) to:

OPDP Regulatory Project Manager
Food and Drug Administration
Center for Drug Evaluation and Research
Office of Prescription Drug Promotion (OPDP)
5901-B Ammendale Road
Beltsville, MD 20705-1266

You must submit final promotional materials and package insert(s), accompanied by a Form FDA 2253, at the time of initial dissemination or publication [21 CFR 314.81(b)(3)(i)]. Form FDA 2253 is available at http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM083570.pdf. Information and Instructions for completing the form can be found at http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM375154.pdf. For more information about submission of promotional materials to the Office of Prescription Drug Promotion (OPDP), see http://www.fda.gov/AboutFDA/CentersOffices/CDER/ucm090142.htm.

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, please call Ms. Sharon Sickafuse, Senior Regulatory Health Project Manager, at (301) 796-2320.

Sincerely,

{See appended electronic signature page}

Patricia Keegan, M.D.
Director
Division of Oncology Products 2
Office of Hematology and Oncology Products
Center for Drug Evaluation and Research

ENCLOSURE:
Content of Labeling

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

/s/

PATRICIA KEEGAN
04/10/2018