DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 022334/S-021, S-023, S-024
NDA 203985/S-002, S-004, S-005

SUPPLEMENT APPROVAL

Novartis Pharmaceuticals Corp.
Attention: Lincy Thomas, Pharm.D., MBA
Director, Drug Regulatory Affairs
One Health Plaza
East Hanover, NJ 07936

Dear Dr. Thomas:

Please refer to your supplemental new drug applications identified below, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Afinitor (everolimus) Tablets, 2.5 mg, 5 mg, 7.5 mg, and 10 mg, and Afinitor Disperz (everolimus) Tablets for Oral Suspension, 2 mg, 3 mg, and 5 mg.

SUPPLEMENT	PRODUCT	LETTER DATE	RECEIPT DATE	PROPOSES:
022334/S-021	Afinitor (everolimus) Tablets, 2.5 mg, 5 mg, 7.5 mg, and 10 mg	May 10, 2013	May 10, 2013	These "Prior Approval" supplemental new drug applications propose to add impaired wound healing to the WARNINGS AND PRECAUTIONS section of the Package Insert and to the Patient Package Insert.
203985/S-002	Afinitor Disperz (everolimus) Tablets for Oral Suspension, 2 mg, 3 mg, and 5 mg	June 18, 2013	June 18, 2013	
022334/S-023	Afinitor (everolimus) Tablets, 2.5 mg, 5 mg, 7.5 mg, and 10 mg	May 31, 2013	May 31, 2013	These "Prior Approval" supplemental new drug applications propose to add a Postmarketing Experience subsection to the ADVERSE REACTIONS section of the Package Insert and to add acute pancreatitis to this subsection.
203985/S-004	Afinitor Disperz (everolimus) Tablets for Oral Suspension, 2 mg, 3 mg, and 5 mg	June 19, 2013	June 19, 2013	

022334/S-024	Afinitor (everolimus) Tablets, 2.5 mg, 5 mg, 7.5 mg, and 10 mg	May 31, 2013	May 31, 2013	These "Prior Approval" supplemental new drug applications propose to revise the DOSAGE AND ADMINISTRATION, WARNINGS AND PRECAUTIONS, ADVERSE REACTIONS, DRUG INTERACTIONS, USE IN SPECIFIC POPULATIONS, CLINICAL PHARMACOLOGY, NONCLINICAL TOXICOLOGY, CLINICAL STUDIES, HOW SUPPLIED and STORAGE AND HANDLING sections of the Package Insert.
203985/S-005	Afinitor Disperz (everolimus) Tablets for Oral Suspension, 2 mg, 3 mg, and 5 mg	June 20, 2013	June 21, 2013	

We also refer to our approval letter dated February 20, 2013, which contained the following errors:

The Approval letter references an incorrect NDA number for Afinitor. On page 1 of the Approval letter and in the Header on pages 2, 3, and 4:

NDA 022234/S-021, S-023, S-024
NDA 203985/S-002, S-004, S-005

should be:

NDA 022334/S-021, S-023, S-024
NDA 203985/S-002, S-004, S-005

In addition, Table 9 of Section 6.4 of the Package Insert incorrectly duplicates the 'Hematology' section header.

This replacement approval letter incorporates the correction of the errors. The effective approval date will remain February 20, 2013, the date of the original approval letter.

We acknowledge receipt of your amendments to NDA 022334/S-021 dated August 23, 2013; November 1, 2013; November 13, 2013; November 25, 2013; and January 10, 2014, and your amendments to NDA 203985/S-002 dated August 23, 2013; November 1, 2013; November 13, 2013; November 25, 2013; and January 10, 2014.

In addition, we acknowledge receipt of your amendments to NDA 022334/S-023 dated August 23, 2013; August 27, 2013; November 1, 2013; November 13, 2013; November 25, 2013; and January 10, 2014, and your amendments to NDA 203985/S-004 dated

August 23, 2013; August 28, 2013; November 1, 2013; November 13, 2013; November 25, 2013; and January 10, 2014.

Also, we acknowledge receipt of your amendments to NDA 022334/S-024 dated August 23, 2013; October 8, 2013; November 1, 2013; November 13, 2013; November 25, 2013; and January 10, 2014, and your amendments to NDA 203985/S-005 dated August 23, 2013; October 8, 2013; October 18, 2013; November 1, 2013; November 13, 2013; November 25, 2013; and January 10, 2014.

APPROVAL & LABELING

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

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, text for the patient package insert), 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 includes 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).

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:

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.

All promotional materials that include representations about your drug product must be promptly revised to be consistent with the labeling changes approved in this supplement, including any new safety information [21 CFR 314.70(a)(4)]. The revisions in your promotional materials should include prominent disclosure of the important new safety information that appears in the revised package labeling. Within 7 days of receipt of this letter, submit your statement of intent to comply with 21 CFR 314.70(a)(4) to the address above or by fax to 301-847-8444.

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 Frank Cross, Jr., Senior Regulatory Health Project Manager, at (301) 796-0876.

Sincerely,

{See appended electronic signature page}

Amna Ibrahim, M.D.
Deputy Division Director
Division of Oncology Products 1
Office of Hematology and Oncology Products
Center for Drug Evaluation and Research

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/

AMNA IBRAHIM
02/20/2014

PATRICIA KEEGAN
02/20/2014