



NDA 22334/S-029

SUPPLEMENT APPROVAL

Novartis Pharmaceuticals Corporation
Attention: Lincy Thomas, Pharm.D., MBA
Director, Drug Regulatory Affairs
One Health Plaza
East Hanover, NJ 07936-1080

Dear Dr. Thomas:

Please refer to your Supplemental New Drug Application (sNDA) dated July 23, 2014, received July 23, 2014, 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.

We acknowledge receipt of your amendments dated December 17, 2014; January 2, 2015; and January 9, 2015.

Prior Approval Supplement NDA 022334/SLR-029, provides for revising the Package Insert to add:

- new Section 5.3 Warnings and Precautions: Angioedema with Concomitant Use of Angiotensin-Converting Enzyme (ACE) Inhibitors
- angioedema to Section 6 Adverse Reactions and Section 6.3 Adverse Reactions: Advanced RCC
- ovarian cyst, gingivitis and angioedema to Section 6.4 Adverse Reactions: Renal AML with TSC
- gingivitis to Section 6.5 Adverse Reactions: Renal AML with TSC
- eukaryotic initiation factor to Section 12.1 Clinical Pharmacology – Mechanism of Action
- results from food-effect study with AFINITOR DISPERZ to Section 12.3 Pharmacokinetics Absorption
- addition of new Section: Angioedema with Concomitant use of Angiotensin-Converting Enzyme (ACE) Inhibitors to Section 17 Patient Counseling Information

In addition, Prior Approval Supplement NDA 022334/SLR-029, provides for revising the Patient Package Insert to add:

- “Wear gloves to avoid possible contact with everolimus when preparing suspensions of AFINITOR DISPERZ for another person.”
- Minor textual and editorial revisions

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.

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).

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 none of these criteria apply to your application, you are exempt from this requirement.

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.
Acting Director
Division of Oncology Products 1
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/

GEOFFREY S KIM
01/23/2015
for Dr. Ibrahim