



NDA 22334/S-17

ACCELERATED APPROVAL

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

Dear Dr. Gutman:

Please refer to your Supplemental New Drug Application (sNDA) dated December 19, 2011, received December 19, 2011, 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 tablets.

We acknowledge receipt of your amendments dated February 24, March 29, and April 5, 13, 16, 19, 23, and 24, 2012.

This "Prior Approval" supplemental new drug application provides for the treatment of adults with renal angiomyolipoma and tuberous sclerosis complex (TSC), not requiring immediate surgery.

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(1)] 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, Medication Guide), 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 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).

ACCELERATED APPROVAL REQUIREMENTS

Products approved under the accelerated approval regulations, 21 CFR 314.510, require further adequate and well-controlled studies/clinical trials to verify and describe clinical benefit. Therefore, you are required to conduct the following:

PMR #1892-1 To complete the ongoing clinical trial CRAD001M2302 entitled “A Randomized, Double-blind, Placebo-controlled Study of RAD001 in the Treatment of Angiomyolipoma in Patients with either Tuberous Sclerosis Complex (TSC) or Sporadic Lymphangiomyomatosis (LAM)” to further verify and describe the ultimate clinical outcomes of the duration of objective responses, incidence of nephrectomy and of renal embolization four years after randomization of the last patient in the study, as specified in the original protocol. You will submit the final comprehensive clinical study report, inclusive of all data collected in the clinical trial, as described in ICH E3.

The timetable you submitted on April 23, 2012, states you will conduct this trial according to the following schedule:

Final Protocol Submission:	June 10, 2010
Study/Trial Completion:	January 2015
Final Report Submission:	August 2015

Submit final reports to this NDA as a supplemental application. For administrative purposes, all submissions relating to this postmarketing requirement must be clearly designated “**Subpart H Postmarketing Requirement.**”

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 your request for orphan drug designation was granted, you are exempt from this requirement.

PROMOTIONAL MATERIALS

As required by 21 CFR 314.550, submit all promotional materials at least 30 days before the intended time of initial distribution of labeling or initial publication of the advertisement. Send two copies of all promotional materials directly to:

Food and Drug Administration
Center for Drug Evaluation and Research
Office of Prescription Drug Promotion
5901-B Ammendale Road
Beltsville, MD 20705-1266

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
04/26/2012