



NDA 022334/S-004

**SUPPLEMENT APPROVAL**

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

Dear Ms. Thomas:

Please refer to your Supplemental New Drug Application (sNDA) listed below, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Afinitor® (everolimus) Tablets.

This Prior Approval Supplement provides for revising the package insert (PI) to include text for hepatitis B reactivation with fatal outcome in an ongoing clinical study (CRAD001C2324). This supplement proposes revisions to the following sections of the PI: 5 Warnings and Precautions, 5.2 Infections, 5.5 Drug-drug Interactions; 6 Adverse Reactions; 17 Patient Counseling Information, 17.2 Infections, and Patient Information.

We have completed our review of this supplemental application. 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, using the FDA automated drug registration and listing system (eLIST), the content of labeling [21 CFR 314.50(l)] in structured product labeling (SPL) format, as described at <http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm>, that is identical to the enclosed labeling text for the package insert and patient package insert, and include the labeling changes proposed in any pending "Changes Being Effected" (CBE) supplements. 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 pending "Changes Being Effected" (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.

### **PROMOTIONAL MATERIALS**

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

Food and Drug Administration  
Center for Drug Evaluation and Research  
Division of Drug Marketing, Advertising, and Communications  
5901-B Ammendale Road  
Beltsville, MD 20705-1266

As required under 21 CFR 314.81(b)(3)(i), you must submit final promotional materials, and the package insert(s), at the time of initial dissemination or publication, accompanied by a Form FDA 2253. For instruction on completing the Form FDA 2253, see page 2 of the Form. For more information about submission of promotional materials to the Division of Drug Marketing, Advertising, and Communications (DDMAC), see <http://www.fda.gov/AboutFDA/CentersOffices/CDER/ucm090142.htm>.

### **LETTERS TO HEALTH CARE PROFESSIONALS**

If you decide to issue a letter communicating important safety-related information about this drug product (i.e., a "Dear Health Care Professional" letter), we request that you submit, at least 24 hours prior to issuing the letter, an electronic copy of the letter to this NDA, to [CDERMedWatchSafetyAlerts@fda.hhs.gov](mailto:CDERMedWatchSafetyAlerts@fda.hhs.gov), and to the following address:

MedWatch  
Food and Drug Administration  
Suite 12B-05  
5600 Fishers Lane  
Rockville, MD 20857

### **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, Amy Tilley, Regulatory Project Manager, at 301-796-3994.

Sincerely,

*{See appended electronic signature page}*

Robert L. Justice, M.D., M.S.

Director

Division of Drug Oncology Products

Office of Oncology Drug Products

Center for Drug Evaluation and Research

ENCLOSURE(S):

Content of Labeling

Application  
Type/Number

Submission  
Type/Number

Submitter Name

Product Name

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NDA-22334

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SUPPL-4

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NOVARTIS  
PHARMACEUTICA  
LS CORP

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AFFINITOR

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**This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.**  
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/s/  
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ROBERT L JUSTICE

07/09/2010