DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 21083/S056
NDA 21110/S074

SUPPLEMENT APPROVAL

PF PRISM, C.V.
c/o Pfizer, Inc
Attention: Deneen Stewart, PhD
Director, Worldwide Safety and Regulatory
500 Arcola Road
Collegeville, PA 19426

Dear Dr. Stewart:
Please refer to your Supplemental New Drug Applications (sNDAs), submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) as follows:

NDA Number	Supplement #	Drug Name	Dated and Received on
21083	056	Rapamune (sirolimus) Oral Solution	December 24, 2014
21110	074	Rapamune (sirolimus) Tablets	December 24, 2014

We acknowledge receipt of your amendments dated February 12, 2015.

These "Changes Being Effected" supplemental new drug applications provide for the following changes to the Package Insert and Medication Guide (additions are noted by underlined text).

1. In the **6.1 Clinical Studies Experience in Prophylaxis of Organ Rejection Following Renal Transplantation** section, under the header "The following adverse reactions were reported less frequently (≥ 3%, but < 20%), *Metabolic/Nutritional* bullet, the words "diabetes mellitus" are added to read:

   - ***Metabolic/Nutritional*** – Abnormal healing, increased lactic dehydrogenase (LDH), hypokalemia, diabetes mellitus

2. **In the 6.6 Postmarketing Experience** section, under ***Metabolic/Nutritional***, the words "diabetes mellitus" are added to read:

    - ***Metabolic/Nutritional***-Liver function test abnormal, AST/SGOT increased, ALT/SGPT increased, hypophosphatemia, hyperglycemia, diabetes mellitus

3. **In the 6.6 Postmarketing Experience** section, a new bullet is added as follows:

    - ***Nervous system*** - Posterior reversible encephalopathy syndrome.

4. **In the MEDICATION GUIDE,** the **Common side effects with RAPAMUNE** subsection, a new bullet is added as follows:

    - high blood sugar (diabetes)

We also note numerous editorial changes, including the sequential numbering of the tables all throughout the labeling.

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, which is identical to the labeling text submitted on February 12, 2015.

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 and 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 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).

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 Judit Milstein, Chief, Project Management Staff at 301-796-0763.

Sincerely,

{See appended electronic signature page}

Ozlem Belen, MD, MPH
Deputy Director for Safety
Division of Transplant and Ophthalmology Products
Office of Antimicrobial 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/

OZLEM A BELEN
03/06/2015