DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 21083/S-053
NDA 21110/S-067

SUPPLEMENT APPROVAL

Wyeth Pharmaceuticals, Inc.
a subsidiary of Pfizer, Inc.
Attention: Nhu M. Tran, PharmD
Director, WRS
P. O. Box 8299
Philadelphia, PA 19101-8299

Dear Dr. Tran:
Please refer to your Supplemental New Drug Applications (sNDAs) dated and received September 24, 2012, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Rapamune (sirolimus), Oral Solution, 1 mg/mL (NDA 21083) and Rapamune (sirolimus), Tablets, 1 mg, 2mg, and 5 mg (NDA 21110).

We acknowledge receipt of your amendments dated March 4, 2013.

These "Changes Being Effected" supplemental new drug applications provide for the following revisions to the package insert (additions are noted as underlined text).

6 ADVERSE REACTIONS

6.1 Clinical Studies Experience in Prophylaxis of Organ Rejection Following Renal Transplantation

… The following adverse reactions were reported less frequently (≥ 3%, but < 20%

- ***Urogenital System*** – Pyelonephritis, decline in renal function (creatinine increas)ed) in long-term combination of cyclosporine with Rapamune [see *Warnings and Precautions (5.8)*], ovarian cysts, menstrual disorders (including amenorrhea and menorrhagia).

6.6 Postmarketing Experience

…

- ***Urogenital*** – Nephrotic syndrome, proteinuria, focal segmental glomerulosclerosis, ovarian cysts, menstrual disorders (including amenorrhea and menorrhagia). Azoospermia has been reported with the use of Rapamune and has been reversible upon discontinuation of Rapamune in most cases.

We have completed our review of these applications, as amended. They are approved, effective on the date of this letter, for use as recommended in the agreed-upon labeling text, submitted as Final Printed Labeling on March 4, 2013.

DRUG REGISTRATION AND LISTING

All drug establishment registration and drug listing information is to be submitted to FDA electronically, via the FDA automated system for processing structured product labeling (SPL) files (eLIST). At the time that you submit your final printed labeling (FPL), the content of labeling (Drug Facts) should be submitted in SPL format as described at http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm. 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/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM072392.pdf. In addition, representative container or carton labeling, whichever includes Drug Facts, (where differences exist only in the quantity of contents statement) should be submitted as a JPG file.

REPORTING REQUIREMENTS

We remind you that you must comply with reporting requirements for approved NDAs (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: Package Insert

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
03/07/2013