DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 50-722/S-026
NDA 50-723/S-025
NDA 50-758/S-024
NDA 50-759/S-031

SUPPLEMENT APPROVAL

Roche Palo Alto, LLC.
c/o Genentech, Inc.
Attention: Becky Prokipcak
Regulatory Agent of behalf of Roche
1 DNA Way MS #241B
South San Francisco, CA 94080-4900

Dear Ms. Prokipcak:

Please refer to your Supplemental New Drug Application (sNDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for the following:

NDA Number	Drug Product	Supplement Number	Date of Supplement	Date of Receipt
50-722	CellCept® (mycophenolate mofetil) Capsules, 250 mg	S-026	December 9, 2011	December 9, 2011
50-723	CellCept® (mycophenolate mofetil) Tablets, 500 mg	S-025	December 9, 2011	December 9, 2011
50-758	CellCept® (mycophenolate mofetil hydrochloride for injection) Intravenous, 500 mg/ 20 mL	S-024	December 9, 2011	December 9, 2011
50-759	CellCept® (mycophenolate mofetil for oral suspension) Oral Suspension, 200 mg/mL	S-031	December 9, 2011	December 9, 2011

We also acknowledge your amendment dated June 1, 2012.

These "Prior Approval" supplemental new drug applications propose a new subsection titled Proton Pump Inhibitors (PPIs) in the **PRECAUTIONS: Drug Interactions** section of the Package Insert and the addition of information on Proton Pump Inhibitors (PPIs) in the Medication Guide as follows (~~strikethrough text~~ = deletions, <u>underlined text</u> = additions):

1. PACKAGE INSERT
PRECAUTIONS/Drug Interactions

Antacids With Magnesium and Aluminum Hydroxides

Absorption of a single dose of mycophenolate mofetil (2 g) was decreased when administered to ten rheumatoid arthritis patients also taking Maalox® TC (10 mL qid). The C_{max} and AUC(0-24h) for MPA were 33% and 17% lower, respectively, than when mycophenolate mofetil was administered alone under fasting conditions. CellCept may be administered to patients who are also taking antacids containing magnesium and aluminum hydroxides; however, it is recommended that CellCept and the antacid not be administered simultaneously.

Proton Pump Inhibitors (PPIs)

Coadministration of PPIs (e.g., lansoprazole, pantoprazole) in single doses to healthy volunteers and multiple doses to transplant patients receiving CellCept has been reported to reduce the exposure to mycophenolic acid (MPA). An approximate reduction of 30 to 70% in the C_{max} and 25% to 35% in the AUC of MPA has been observed, possibly due to a decrease in MPA solubility at an increased gastric pH. The clinical impact of reduced MPA exposure on organ rejection has not been established in transplant patients receiving PPIs and CellCept. Because clinical relevance has not been established, PPIs should be used with caution when coadministered to transplant patients being treated with CellCept.

2. MEDICATION GUIDE

What should I tell my healthcare provider before taking CellCept?

……..Tell your healthcare provider about all of the medicines you are taking including prescription and nonprescription medicines, vitamins and herbal supplements. Some medicines may affect the way CellCept works, and CellCept may affect how some medicines work. Especially tell your healthcare provider if you take:

- birth control pills (oral contraceptives). See **"What is the most important information I should know about CellCept?"**
- sevelamer (Renagel®, Renvela™). These products should be taken 2 hours after taking CellCept
- acyclovir (Zovirax®), valacyclovir (Valtrex®), ganciclovir (CYTOVENE®IV, Vitrasert®), valganciclovir (VALCYTE®)
- rifampin (Rifater®, Rifamate®, Rimactane®, Rifadin®)
- antacids that contain magnesium and aluminum (CellCept and the antacid should not be taken at the same time)
- proton pump inhibitors (PPIs) (Prevacid®, Protonix®)
- sulfamethoxazole/trimethoprim (BACTRIM™, BACTRIM DS™)

- norfloxacin (Noroxin®) and metronidazole (Flagyl®, Flagyl® ER, Flagyl® IV, Metro IV, Helidac®, Pylera™)
- ciprofloxacin (Cipro®, Cipro® XR, Ciloxan®, Proquin® XR) and amoxicillin plus clavulanic acid (Augmentin®, Augmentin XR™)
- azathioprine (Azasan®, Imuran®)
- cholestyramine (Questran Light®, Questran®, Locholest Light, Locholest, Prevalite®)

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.

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, 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).

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 contact Hyun J. Son Pharm.D., Safety Regulatory Project Manager, at (301)796-1600.

Sincerely,

{See appended electronic signature page}

Ozlem Belen, M.D., MPH
Deputy Director for Safety
Division of Transplant and Ophthalmology Products
Office of Antimicrobial Products
Center for Drug Evaluation and Research

ENCLOSURE(S):
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
06/08/2012