DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 210115
NDA 50708/S047
NDA 50709/S040

NDA APPROVAL
SUPPLEMENT APPROVALS

Astellas Pharma US, Inc.
Attention: Mary Jo Pritza, MPH, PharmD
Senior Director, Regulatory Affairs
1 Astellas Way
Northbrook, Illinois 60062

Dear Dr. Pritza:

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

NDA/ Supplement Number	**Product Name**	**Date of Submission and Receipt**
NDA 210115	PROGRAF Granules (tacrolimus for oral suspension) Strengths: 0.2 mg and 1 mg	7/26/2017
NDA 50708/S047	PROGRAF (tacrolimus) capsules Strengths: 0.5 mg, 1 mg, and 5 mg	2/21/2018
NDA 50709/S040	PROGRAF (tacrolimus) injection Strength: 5 mg/mL	2/21/2018

NDA 210115 provides for the use of PROGRAF Granules (tacrolimus for oral suspension) for the prevention of rejection in heart, kidney or liver transplant in pediatric patients.

The prior approval supplemental new drug applications, NDA 50708/S047 and NDA 50709/S040, provide for the addition of information pertaining to PROGRAF Granules to harmonize the labeling for the three PROGRAF formulations.

We have completed our review of these applications, as amended. These applications are approved, effective on the date of this letter, for use as recommended in the enclosed agreed-upon

labeling text (labeling for NDA 210115, NDA 50708/S047 and NDA 50709/S040, submitted and received on May 22, 2018), which includes the Prescribing Information for PROGRAF Granules, PROGRAF capsules and PROGRAF injection, Patient Package Insert for PROGRAF Granules and PROGRAF capsules, and Information for Use for PROGRAF Granules, with minor editorial changes.

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 to all three applications 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 Prescribing Information, text for the Patient Package Insert, and Instructions for Use). Information on submitting SPL files using eLIST may be found in the guidance for industry *SPL Standard for Content of Labeling Technical Qs and As*, available at http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM072392.pdf

The SPL will be accessible via publicly available labeling repositories.

CARTON AND IMMEDIATE CONTAINER LABELS

We acknowledge your May 9, 2018, submission containing draft printed carton and container labels for NDA 210115.

Submit final printed carton and immediate container labels for NDA 210115 that are identical to the carton and immediate container labels submitted on May 9, 2018, as soon as they are available, but no more than 30 days after they are printed. Please submit these labels electronically according to the guidance for industry titled *Providing Regulatory Submissions in Electronic Format — Certain Human Pharmaceutical Product Applications and Related Submissions Using the eCTD Specifications (May 2015, Revision 3)*. For administrative purposes, designate this submission "**Final Printed Carton and Container Labels for approved NDA 210115**." Approval of this submission by FDA is not required before the labeling is used.

MARKET PACKAGE

Please submit one market package of the drug product when it is available to the following address:

Wendy Streight, PhD
Regulatory Project Manager
Food and Drug Administration
Center for Drug Evaluation and Research
White Oak Building 22, Room: 6349

10903 New Hampshire Avenue
Silver Spring, Maryland
Use zip code **20903** *if shipping via United States Postal Service (USPS).*
Use zip code **20993** *if sending via any carrier other than USPS (e.g., UPS, DHL, FedEx).*

REQUIRED PEDIATRIC ASSESSMENTS

Under the Pediatric Research Equity Act (PREA) (21 U.S.C. 355c), all applications for new active ingredients (which includes new salts and new fixed combinations), 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 in pediatric patients unless this requirement is waived, deferred, or inapplicable. As the product for NDA 210115, tacrolimus for oral suspension, has an orphan drug designation, PREA does not apply to your application.

FULFILMENT OF PREA POST MARKETING REQUIREMENT (PMR)

We have also reviewed your submission dated July 26, 2017, containing the final report for the following postmarketing requirement listed in the July 19, 2013, NDA 204096 approval letter:

2061-1 Deferred requirement for development of an age appropriate formulation: Develop an age appropriate formulation to allow for dosing for ages 1 to <5 years.

Final Report Submission: 12/2020

We have concluded that the above requirement was fulfilled.

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 prescribing information, Medication Guide, and patient PI (as applicable) to:

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

Alternatively, you may submit a request for advisory comments electronically in eCTD format. For more information about submitting promotional materials in eCTD format, see the draft Guidance for Industry (available at: http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM443702.pdf).

As required under 21 CFR 314.81(b)(3)(i), you must submit final promotional materials, and the prescribing information, at the time of initial dissemination or publication, accompanied by a Form FDA 2253. Form FDA 2253 is available at http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM083570.pdf. Information and Instructions for completing the form can be found at http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM375154.pdf. For more information about submission of promotional materials to the Office of Prescription Drug Promotion (OPDP), see http://www.fda.gov/AboutFDA/CentersOffices/CDER/ucm090142.htm.

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 Wendy Streight, PhD, Regulatory Project Manager, at (301) 796-1600.

Sincerely,

{See appended electronic signature page}

Renata Albrecht, MD
Director
Division of Transplant and Ophthalmology Products
Office of Antimicrobial Products
Center for Drug Evaluation and Research

Enclosures: Content of Labeling: Prescribing Information, Patient Package Insert and Instructions for Use for NDA 210115; NDA 50708/S047; NDA 50709/S040
Carton and Container Labels: NDA 210115

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

RENATA ALBRECHT
05/24/2018