NDA 50722/S-048
NDA 50723/S-048
NDA 50758/S-045
NDA 50759/S-053

SUPPLEMENT APPROVAL

Roche Palo Alto LLC
c/o Genentech Inc.
1 DNA Way
South San Francisco, CA 94080-4900

Attention: Elizabeth Wishart
Regulatory Agent on behalf of Roche

Dear Ms. Wishart:

Please refer to your supplemental new drug applications (sNDAs) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA or the Act) for the following:

NDA Number	Supplement Number	Drug Name	Dated and Received
50722	048	CellCept (mycophenolate mofetil) Capsules, 250 mg	June 21, 2021
50723	048	CellCept (mycophenolate mofetil) Tablets, 500 mg	June 21, 2021
50758	045	CellCept (mycophenolate mofetil hydrochloride) Intravenous	June 21, 2021
50759	053	CellCept (mycophenolate mofetil) Oral suspension	June 21, 2021

These Changes Being Effected supplemental new drug applications provide for proposed modifications to the approved Mycophenolate risk evaluation and mitigation strategy (REMS).

RISK EVALUATION AND MITIGATION STRATEGY (REMS) REQUIREMENTS

The Shared System REMS for the mycophenolate products, of which CellCept (mycophenolate mofetil) is a member, was originally approved on September 25, 2012, and the most recent REMS modification was approved on April 21, 2021. The REMS consists of elements to assure safe use, and a timetable for submission of assessments of the REMS.

Your proposed modification to the REMS consist of changes to the Mycophenolate risk evaluation and mitigation strategy (REMS) website screenshots (non-CE and CE) to align the data insights section of the Patient Overview page with the data insights from the Patient Brochure.

Your proposed modified REMS, submitted to Drug Master File (DMF) 031030 on June 16, 2021, appended to this letter, is approved.

This shared system, known as the Mycophenolate Shared System REMS, currently includes products listed on the FDA REMS website: http://www.fda.gov/rems.

Other products may be added in the future if additional NDAs or ANDAs are approved.

We remind you that you must include an adequate rationale to support a proposed REMS modification for the addition, modification, or removal of any goal or element of the REMS, as described in section 505-1(g)(4) of the FD&C Act.

The timetable for submission of assessments of the REMS remains the same as that approved on January 15, 2021.

There are no changes to the REMS assessment plan described in our January 15, 2021 letter.

We remind you that in addition to the REMS assessments submitted according to the timetable in the approved REMS, you must include an adequate rationale to support a proposed REMS modification for the addition, modification, or removal of any goal or element of the REMS, as described in section 505-1(g)(4) of the FDCA.

We also remind you that you must submit a REMS assessment when you submit a supplemental application for a new indication for use, as described in section 505-1(g)(2)(A) of the FDCA. This assessment should include:

a) An evaluation of how the benefit-risk profile will or will not change with the new indication;

b) A determination of the implications of a change in the benefit-risk profile for the current REMS;

c) *If the new indication for use introduces unexpected risks*: A description of those risks and an evaluation of whether those risks can be appropriately managed with the currently approved REMS.

d) *If a REMS assessment was submitted in the 18 months prior to submission of the supplemental application for a new indication for use*: A statement about whether the REMS was meeting its goals at the time of that last assessment and if any modifications of the REMS have been proposed since that assessment.

e) *If a REMS assessment has not been submitted in the 18 months prior to submission of the supplemental application for a new indication for use:* Provision of as many of the currently listed assessment plan items as is feasible.

f) *If you propose a REMS modification based on a change in the benefit-risk profile or because of the new indication of use, submit an adequate rationale to support the modification, including*: Provision of the reason(s) why the proposed REMS modification is necessary, the potential effect on the serious risk(s) for which the REMS was required, on patient access to the drug, and/or on the burden on the health care delivery system; and other appropriate evidence or data to support the proposed change. Additionally, include any changes to the assessment plan necessary to assess the proposed modified REMS. *If you are not proposing REMS modifications*, provide a rationale for why the REMS does not need to be modified.

If the assessment instruments and methodology for your REMS assessments are not included in the REMS supporting document, or if you propose changes to the submitted assessment instruments or methodology, you should update the REMS supporting document to include specific assessment instrument and methodology information at least 90 days before the assessments will be conducted. Updates to the REMS supporting document may be included in a new document that references previous REMS supporting document submission(s) for unchanged portions. Alternatively, updates may be made by modifying the complete previous REMS supporting document, with all changes marked and highlighted. Prominently identify the submission containing the assessment instruments and methodology with the following wording in bold capital letters at the top of the first page of the submission:

NDA ###### REMS ASSESSMENT METHODOLOGY
(insert concise description of content in bold capital letters, e.g., ASSESSMENT METHODOLOGY, PROTOCOL, SURVEY METHODOLOGIES, AUDIT PLAN, DRUG USE STUDY)

An authorized generic drug under this NDA must have an approved REMS prior to marketing. Should you decide to market, sell, or distribute an authorized generic drug under this NDA, contact us to discuss what will be required in the authorized generic drug REMS submission.

We remind you that section 505-1(f)(8) of the FD&C Act prohibits holders of an approved covered application with elements to assure safe use from using any element to block or delay approval of an application under section 505(b)(2) or (j). A violation of this provision in 505-1(f) could result in enforcement action.

Prominently identify any submission containing the REMS assessments or proposed modifications of the REMS with the following wording in bold capital letters at the top of the first page of the submission as appropriate:

NDA ###### REMS ASSESSMENT
CROSS REFERENCE TO THE REMS DMF

or

NEW SUPPLEMENT FOR NDA ######/S-000
CHANGES BEING EFFECTED IN 30 DAYS
PROPOSED MINOR REMS MODIFICATION
CROSS REFERENCE TO THE REMS DMF

or

NEW SUPPLEMENT FOR NDA ######/S-000
PRIOR APPROVAL SUPPLEMENT
PROPOSED MAJOR REMS MODIFICATION
CROSS REFERENCE TO THE REMS DMF

or

NEW SUPPLEMENT FOR NDA ######/S-000
PRIOR APPROVAL SUPPLEMENT
PROPOSED REMS MODIFICATIONS DUE TO SAFETY LABELING CHANGES SUBMITTED IN SUPPLEMENT XXX
CROSS REFERENCE TO THE REMS DMF

or

NEW SUPPLEMENT (NEW INDICATION FOR USE)
FOR NDA ######/S-000
REMS ASSESSMENT
PROPOSED REMS MODIFICATION (if included)
CROSS REFERENCE TO THE REMS DMF

Should you choose to submit a REMS revision, prominently identify the submission containing the REMS revisions with the following wording in bold capital letters at the top of the first page of the submission:

REMS REVISIONS FOR NDA
CROSS REFERENCE TO THE REMS DMF

SUBMISSION OF REMS DOCUMENT IN SPL FORMAT

FDA can accept the REMS document in Structured Product Labeling (SPL) format. If you intend to submit the REMS document in SPL format, as soon as possible, but no later than 14 days from the date of this letter, submit the REMS document in SPL format using the FDA automated drug registration and listing system (eLIST).

For more information on submitting REMS in SPL format, please email FDAREMSwebsite@fda.hhs.gov.

PROMOTIONAL MATERIALS

You may request advisory comments on proposed introductory advertising and promotional labeling. For information about submitting promotional materials, see the final guidance for industry *Providing Regulatory Submissions in Electronic and Non-Electronic Format-Promotional Labeling and Advertising Materials for Human Prescription Drugs.*[1]

You must submit final promotional materials and Prescribing Information, accompanied by a Form FDA 2253, at the time of initial dissemination or publication [21 CFR 314.81(b)(3)(i)]. Form FDA 2253 is available at FDA.gov.[2] Information and Instructions for completing the form can be found at FDA.gov.[3]

REPORTING REQUIREMENTS

We remind you that you must comply with reporting requirements for an approved NDA (21 CFR 314.80 and 314.81).

[1] For the most recent version of a guidance, check the FDA guidance web page at https://www.fda.gov/media/128163/download.
[2] http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM083570.pdf
[3] http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM375154.pdf

If you have any questions, call Ms. June Germain, Safety Regulatory Project Manager, at 301-796-4024.

Sincerely,

{See appended electronic signature page}

Ozlem Belen, MD, MPH
Deputy Director
Division of Rheumatology and Transplant Medicine
Office of Immunology and Inflammation
Center for Drug Evaluation and Research

ENCLOSURE: REMS

This is a representation of an electronic record that was signed electronically. Following this are manifestations of any and all electronic signatures for this electronic record.

/s/

OZLEM A BELEN
08/11/2021 09:53:30 AM