DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

BLA 125276/92

SUPPLEMENT APPROVAL
REMS MODIFICATION APPROVAL

Genentech, Inc.
A Member of the Roche Group
1 DNA Way
South San Francisco, CA 94080

Attention: Stuart Heminway, Program Director
Regulatory Affairs

Dear Mr. Heminway:

Please refer to your Supplemental Biologics License Application (sBLA), dated October 17, 2013, received October 18, 2013, submitted under section 351(a) of the Public Health Service Act for Actemra (tocilizumab), for intravenous administration and your risk evaluation and mitigation strategy (REMS) assessment dated October 17, 2013.

We acknowledge receipt of your amendment dated October 18, 2013.

This Prior Approval supplemental biologics application proposes revisions to the package insert and Medication Guide, as well as modifications to the approved REMS in order to include information for Actemra (tocilizumab) for subcutaneous administration and updated labeling for hypersensitivity reactions, to assure consistency between the labeling and REMS for both Actemra (tocilizumab) for subcutaneous administration and for Actemra (tocilizumab) for intravenous administration.

We have completed our review of this supplemental application, as amended. It is approved, effective on the date of this letter, for use as recommended in the enclosed, agreed-upon labeling text.

WAIVER OF HIGHLIGHTS SECTION

Please note that we have previously granted a waiver of the requirements of 21 CFR 201.57(d)(8) regarding the length of Highlights of prescribing information.

CONTENT OF LABELING

As soon as possible, but no later than 14 days from the date of this letter, submit, via the FDA automated drug registration and listing system (eLIST), the content of labeling [21 601.14(b)] in structured product labeling (SPL) format, 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, text for the instructions for use, Medication Guide). 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.

The SPL will be accessible via publicly available labeling repositories.

In addition, within 14 days of the date of this letter, amend any pending supplement that includes labeling changes for this BLA with content of labeling in SPL format to include the changes approved in this supplement.

We request that the labeling approved today be available on your website within 10 days of receipt of this letter.

RISK EVALUATION AND MITIGATION STRATEGY REQUIREMENTS

The REMS for Actemra was originally approved on January 8, 2010, and REMS modifications were approved on April 15, 2011, June 20 and October 11, 2012, and last modified on July 2, 2013. The REMS consists of a communication plan and a timetable for submission of assessments of the REMS. Your proposed modifications to the REMS consists of a revised communication plan to include information on Actemra (tocilizumab) for subcutaneous administration and on the updated labeling for hypersensitivity reactions to assure consistency between the REMS for Actemra (tocilizumab) subcutaneous administration and the REMS for Actemra (tocilizumab) for intravenous administration.

The timetable for submission of assessments of the REMS will remain the same as that approved on January 8, 2010.

There are no changes to the REMS assessment plan described in our June 20, 2012, letter.

The requirements for assessments of an approved REMS under section 505-1(g)(3) include with respect to each goal included in the strategy, an assessment of the extent to which the approved strategy, including each element of the strategy, is meeting the goal or whether 1 or more such goals or such elements should be modified.

In addition to the assessments submitted according to the timetable included in the approved REMS, you must submit a REMS assessment and may propose a modification to the approved REMS when you submit a supplemental application for a new indication for use as described in section 505-1(g)(2)(A) of the FDCA.

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:

BLA 125276 REMS CORRESPONDENCE
(insert concise description of content in bold capital letters, e.g.,
UPDATE TO REMS SUPPORTING DOCUMENT - ASSESSMENT METHODOLOGY)

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

BLA 125276 REMS ASSESSMENT

NEW SUPPLEMENT FOR BLA 125276
PROPOSED REMS MODIFICATION

NEW SUPPLEMENT (NEW INDICATION FOR USE)
FORBLA 125276
REMS ASSESSMENT
PROPOSED REMS MODIFICATION (if included)

If you do not submit electronically, please send 5 copies of REMS-related submissions.

REPORTING REQUIREMENTS

We remind you that you must comply with reporting requirements for an approved BLA (in 21 CFR 600.80 and in 21 CFR 600.81).

If you have any questions, call Philantha Bowen, Senior Regulatory Project Management Officer, at (301) 796-2466.

Sincerely,

{See appended electronic signature page}

Sally Seymour, M.D.
Deputy Director for Safety
Division of Pulmonary, Allergy, and Rheumatology Products
Office of Drug Evaluation II

ENCLOSURE:
Content of Labeling
REMS

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

/s/

SALLY M SEYMOUR
10/21/2013