DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

BLA 125276/22
BLA 125276/23

SUPPLEMENT BLA APPROVAL
REMOVE REMS ELEMENT
April 15, 2011

Genentech, Inc. A Member of the Roche Group
c/o Hoffman-La Roche, Inc.
340 Kingsland Street
Nutley, New Jersey 07110-1199

Attention: Alan J. Mart
Director, Drug Regulatory Affairs

Dear Mr. Mart:

Please refer to your Supplemental Biologics License Applications (sBLA), dated October 14, and 29, 2010, received October 15, and 29, 2010, submitted under section 351 of the Public Health Service Act for Actemra (tocilizumab).

We acknowledge receipt of your amendments to supplement 22 dated January 4, 11, 14, and 26, March 28, and 31, and April 6, 7, 8, 14, and 15, 2011, your risk evaluation and mitigation strategy (REMS) assessment dated October 14, 2010, and your amendments to supplement 23 dated January 14, and April 15 (2), 2011.

"Prior Approval" efficacy supplement 22 to your biologics license application provides for the treatment of active systemic juvenile idiopathic arthritis in patients 2 years of age and older and a proposed modification to the approved REMS. "Prior Approval" supplement 23 provides for hypersensitivity reactions information to be added to the HIGHLIGHTS, WARNINGS, and ADVERSE REACTIONS sections of the package insert and the Medication Guide.

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. In addition, we have found the REMS assessment to be adequate.

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 CFR 601.14(b)] in structured product labeling (SPL) format, as described at

http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm, that is identical to the enclosed labeling (text for the package insert, text for the patient package insert, Medication Guide) and include the labeling changes proposed in any pending "Changes Being Effected" (CBE) supplements. 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. For administrative purposes, please designate this submission "**Product Correspondence – Final SPL for approved BLA STN 125276/22 and 125276/23**."

Also within 14 days, amend all pending supplemental applications for this BLA, including pending "Changes Being Effected" (CBE) supplements, for which FDA has not yet issued an action letter, with the content of labeling [21 CFR 601.12(f)] in MS Word format that includes the changes approved in this supplemental application.

The SPL will be accessible via publicly available labeling repositories.

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

REQUIRED PEDIATRIC ASSESSMENTS

Under the Pediatric Research Equity Act (PREA) (21 U.S.C. 355c), all applications for new active ingredients, 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(s) in pediatric patients unless this requirement is waived, deferred, or inapplicable.

We are deferring submission of your pediatric study for ages 0 to less than 2 years for supplement 22 because pediatric studies should be delayed until additional safety or effectiveness data have been collected. The biological product will be ready for approval for use in 2-17 years of age before pediatric studies with zero to less than 2 years of age are complete.

Your deferred pediatric study required by section 505B(a) of the Federal Food, Drug, and Cosmetic Act is a required postmarketing study. The status of this postmarketing study must be reported annually according to 21 CFR 601.28 and section 505B(a)(3)(B) of the Federal Food, Drug, and Cosmetic Act. This required study is listed below.

1. A pharmacokinetic and safety study of tocilizumab (TCZ) in patients less than 2 years old with active systemic juvenile idiopathic arthritis (sJIA)

   Final Protocol Submission: 07/2011
   Study Completion: 03/2014
   Final Report Submission: 10/2014

Submit final reports to this BLA. For administrative purposes, all submissions related to this required pediatric postmarketing study must be clearly designated "**Required Pediatric Assessment(s)**".

We note that you have fulfilled the pediatric study requirement for ages 2 to 17 years in supplement 22.

RISK EVALUATION AND MITIGATION STRATEGY REQUIREMENTS

The REMS for Actemra (tocilizumab) was originally approved on January 8, 2010. The REMS consists of a Medication Guide, communication plan, and a timetable for submission of assessments of the REMS.

We have determined that it is no longer necessary to include the Medication Guide as an element of the approved to ensure that the benefits of the drug outweigh the risks.

Your proposed modified REMS, submitted on April 8, 2011, and appended to this letter, is approved.

The modified REMS consists of communication plan and a timetable for submission of assessments of the REMS.

We remind you that the Medication Guide will continue to be part of the approved labeling for Actemra (tocilizumab) in accordance with 21 CFR 208.

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 letter dated January 8, 2010.

We remind you that assessments of an approved REMS must also include, under section 505-1(g)(3)(B) and (C), information on the status of any postapproval study or clinical trial required under section 505(o) or otherwise undertaken to investigate a safety issue. With respect to any such postapproval study, you must include the status of such study, including whether any difficulties completing the study have been encountered. With respect to any such postapproval clinical trial, you must include the status of such clinical trial, including whether enrollment has begun, the number of participants enrolled, the expected completion date, whether any difficulties completing the clinical trial have been encountered, and registration information with respect to requirements under subsections (i) and (j) of section 402 of the Public Health Service Act. You can satisfy these requirements in your REMS assessments by referring to relevant information included in the most recent annual report required under section 506B and 21 CFR 601.70 and including any material or significant updates to the status information since the annual report was prepared. Failure to comply with the REMS assessments provisions in section 505-1(g) could result in enforcement action.

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 FDCA.

Prominently identify the 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:

BLA 125276 REMS ASSESSMENT

NEW SUPPLEMENT FOR BLA 125276
PROPOSED REMS MODIFICATION
REMS ASSESSMENT

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

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

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 package insert(s) to:

Food and Drug Administration
Center for Drug Evaluation and Research
Division of Drug Marketing, Advertising, and Communications
5901-B Ammendale Road
Beltsville, MD 20705-1266

As required under 21 CFR 601.12(f)(4), you must submit final promotional materials, and the package insert(s), at the time of initial dissemination or publication, accompanied by a Form FDA 2253. For instruction on completing the Form FDA 2253, see page 2 of the Form. For more information about submission of promotional materials to the Division of Drug Marketing, Advertising, and Communications (DDMAC), 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 BLA (in 21 CFR 600.80 and in 21 CFR 600.81).

If you have any questions, call Colette Jackson, Senior Regulatory Health Project Manager, at (301) 796-1230.

Sincerely,

/Badrul A. Chowdhury, M.D., Ph.D./
Badrul A. Chowdhury, M.D., Ph.D.
Director
Division of Pulmonary, Allergy, and Rheumatology Products
Office of Drug Evaluation II
Center for Drug Evaluation and Research

ENCLOSURES:
- Package Insert
- Medication Guide
- REMS
- REMS Materials