

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:
BLA 125276/S049

STATISTICAL REVIEW(S)



U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research
Office of Translational Sciences
Office of Biostatistics

STATISTICAL REVIEW AND EVALUATION CLINICAL STUDIES

NDA/BLA #: BLA 125276/SN49 (Supplement)

Supplement #:

Drug Name: Actemra (tocilizumab)

Indication(s): Treatment of adult patients with [REDACTED] (b) (4)
[REDACTED] (b) (4)

Applicant: Roche

Date(s): Received: 12-20-2011; PDUFA: 10-12-2012

Review Priority: Standard

Biometrics Division: Division of Biometrics 2

Statistical Reviewer: Joan Buenconsejo, PhD

Medical Division: Division of Pulmonary, Allergy, and Rheumatology Products

Clinical Team: Keith Hull, MD
Sarah Yim, MD

Project Manager: Philantha Bowen

Keywords:

1 EXECUTIVE SUMMARY

Hoffman-La Roche, Inc. has proposed supplemental labeling for Actemra, previously approved on January 8, 2010 by the Agency for the treatment of adult patients with moderately to severely active rheumatoid arthritis (RA) who have had an inadequate response to one or more tumor necrosis factors (TNF-IR), as well as for the treatment of active systemic juvenile idiopathic arthritis in patients 2 years of age and older which was approved on April 15, 2011.

Prior to the issuance of the action letter on the original submission, a teleconference between the applicant and the Agency was held on January 5, 2010. The Agency advised the applicant that they had concerns over potential tocilizumab safety issues and, given the availability of other therapies in the market, they believed it was appropriate to limit tocilizumab treatment to the TNF-IR population. The Agency advised that the potential safety signals of tocilizumab would have to be evaluated in the postmarketing setting (with large enough sample and patient years of exposure for signal detection of rare and serious toxicities) before the indication could be expanded to include DMARD-IR patients.

In the present submission, the applicant is seeking to expand the indication in support of the use of Actemra in patients whom have had an inadequate response (b) (4) for the following indication:

Actemra is indicated for adult patients with moderately to severely active rheumatoid arthritis.

The data supporting the application comes from the original randomized placebo-controlled RA trials, the long-term extension safety studies, the postmarketing data from the applicant's global safety database, and epidemiological data.

At the filing meeting, it was decided that statistical review is not necessary given that the current submission does not include new clinical trials to assess efficacy. Furthermore, safety assessments of the data from the long-term extension studies, postmarketing and the epidemiological studies will mainly be descriptive. The reader is referred to Dr. Keith Hull's review regarding the adequacy of the safety data provided by the applicant to support the label change, and his recommendation.

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/s/

JOAN K BUENCONSEJO
08/28/2012