



FOOD AND DRUG ADMINISTRATION
CENTER FOR DRUG EVALUATION AND RESEARCH
Division of Pulmonary, Allergy, and Rheumatology Products
10903 New Hampshire Avenue
Building 22
Silver Spring, MD 20993

Medical Officer Review

BLA/Supplement: 125472/32; 125276/117

Drug Name: Actemra (tocilizumab)

Sponsor: Genentech, Inc.

Indications: Rheumatoid Arthritis

Type of Submission: Changes Being Effected (CBE) Labeling Supplement

Date of Submission: May 14, 2018

Review Date: May 17, 2018

Reviewer: Rachel L. Glaser, M.D.

Team Leader: Nikolay P. Nikolov, M.D.

Synopsis: This review outlines the Division's review and general agreement with the proposed labeling changes to the 'Recent Major Changes' section, Section 2.8 'Preparation and Administration Instructions for Subcutaneous Injection,' and Section 14.3, 'Giant Cell Arteritis - Subcutaneous Administration.' The proposed labeling changes are acceptable. The recommended regulatory action is Approval.

Review

1. Recommendations for Regulatory Action

Our overall conclusion is that these CBE Supplements should be approved.

2. Regulatory History

TCZ is a recombinant humanized anti-human interleukin 6 (IL-6) receptor monoclonal antibody. It is available and marketed in the United States as an IV formulation (original BLA 125276, approved January 2010) and as a SC formulation (original BLA

125472, approved October 2013). IV TCZ is approved for treatment of moderate to severely active rheumatoid arthritis (RA) in adults, systemic juvenile idiopathic arthritis (SJIA) in children 2 years of age and older, polyarticular juvenile idiopathic arthritis (PJIA) in children 2 years of age and older, and Cytokine Release Syndrome in adults and in children 2 years of age and older. SC TCZ is approved for moderate to severely active RA in adults, giant cell arteritis (GCA) in adults, and PJIA in children 2 years of age and older. The BLAs share one product label.

After approval of BLA 125472s28 for treatment of PJIA with SC TCZ on May 11, 2018, it was noted by the applicant that the 'Recent Major Changes' section had not been updated to reflect the new information in the Dosage and Administration section. It was additionally noted, that the numbering for the reference to Table 8 in Section 14.3 was not updated.

3. Proposed Changes to the Label

The proposed modifications to 'Recent Major Changes' include reference to the changes to the Dosage and Administration Sections 2.3 and 2.8 in 5/2018, as follows:

----- RECENT MAJOR CHANGES -----	
Indications and Usage (1.2)	05/2017
Indications and Usage (1.5)	08/2017
Dosage and Administration (2.2, 2.8)	05/2017
Dosage and Administration (2.5, 2.6, 2.7, 2.9)	08/2017
<u>Dosage and Administration (2.3, 2.8)</u>	<u>05/2018</u>

In Section 2.8 'Preparation and Administration Instructions for Subcutaneous Injection', reference to supportive information within the supplement, for use during the review cycle, was removed as follows:

caregiver may administer ACTEMRA if a healthcare practitioner determines that it is appropriate. PJIA patients may self-inject with ACTEMRA or the patient's caregiver may administer ACTEMRA if both the healthcare practitioner and the parent/legal guardian determines it is appropriate. ~~[Module 2.5 CO Section 5.6]~~ Patients, or patient caregivers, should be instructed to follow the directions provided in the Instructions for Use (IFU) for additional details on medication administration.

There are no other proposed changes to the Dosage and Administration Section.

In Section 14.3, 'Giant Cell Arteritis - Subcutaneous Administration,' the textual reference to the table "Efficacy Results from Study WA28119" was corrected from "Table 7" to "Table 8."

4. Summary of Changes and Recommendations

The Applicant proposes minor modifications to the label to present the updated information under the 'Recent Major Changes' section, and includes correction of numbering of Table 8 in Section 14.3, 'Giant Cell Arteritis – Subcutaneous Administration' and removal of a reference intended for Agency use during review in Section 2.8 'Preparation and Administration Instructions for Subcutaneous Injection.' The proposed modifications are acceptable. Thus, we recommend approval of these supplements.

Recommended Regulatory Action

The recommended regulatory action is Approval of CBE supplement 117 to BLA 125276 and CBE supplement 32 to BLA 125472.

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/s/

RACHEL GLASER
05/17/2018

NIKOLAY P NIKOLOV
05/17/2018