CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

125472Orig1s000

PROPRIETARY NAME REVIEW(S)

Department of Health and Human Services
Public Health Service
Food and Drug Administration
Center for Drug Evaluation and Research
Office of Surveillance and Epidemiology
Office of Medication Error Prevention and Risk Management

Proprietary Name Review

Date:	August 9, 2013
Reviewer:	Teresa McMillan, PharmD Division of Medication Error Prevention and Analysis
Team Leader:	Lubna Merchant, PharmD, M.S. Division of Medication Error Prevention and Analysis
Division Director:	Carol Holquist, RPh Division of Medication Error Prevention and Analysis
Drug Name:	Actemra (Tocilizumab) Injection
Strength:	162 mg/0.9 mL
Application Type/Number:	BLA 125472
Applicant/Sponsor:	Genetech
OSE RCM #:	2013-1208

*** This document contains proprietary and confidential information that should not be released to the public.***

CONTENTS

1 INTRODUCTION

This review evaluates the proposed proprietary name, Actemra, for Tocilizumab (BLA 125472), from a safety and promotional perspective. The applicant is proposing to add a new fixed dose syringe that requires a different route of administration and different frequency of administration. Additionally, this new packaging configuration is only indicated for one of the approved indications of use, adult Rheumatoid Arthritis patients. The Applicant proposes to market the syringe under the same proprietary name, Actemra.

2 PRODUCT INFORMATION

Actemra is currently marketed as an intravenous injection in different vial sizes at a concentration of 20 mg per mL. The proposed fixed dose syringe provides for a more concentrated solution 162 mg/0.9 mL that is given subcutaneously weekly or every other week. Table 1 below provides a comparison of the proposed product to the marketed product.[1]

Table 1. Comparison of the Proposed Product With the Marketed Product

Product Name	***Actemra (proposed)***	***Actemra (marketed)***
Approval Year	---	2010
Active Ingredient	Tocilizumab	Tocilizumab
Indication of Use	Treatment of Adult Rheumatoid Arthritis (RA)	• Treatment of Adult Rheumatoid Arthritis (RA) • Systemic Juvenile Idiopathic Arthritis (SJIA),
Route of Administration	Subcutaneous	Intravenous
Dosage Form and Packaging	Injection [Single-use pre-filled syringe]	Injection [Single-use vial]
Strength and Concentration	162 mg/0.9 mL	• 80 mg/4 mL [20 mg/mL] • 200 mg/10 mL [20 mg/mL] • 400 mg/20 mL [20 mg/mL]
Dose and Frequency	**RA** • **Less than 100 kg**: 162 mg every other week, followed by an increase to every week based on clinical response • **Greater than or equal to 100 kg**: 162 mg every week	• **RA**:4 mg/kg once every four weeks followed by an increase to 8 mg/kg once every four weeks based on clinical response • **SJIA**:12 mg/kg once every two weeks if patient less than 30 kg or 8 mg/kg once every two weeks if patient is at or above 30 kg
How Supplied	Sterile preservative-free liquid solution in a single-use pre-filled syringe supplied individually	Sterile concentrate, preservative-free single-use vial (20 mg/mL) solution for intravenous infusion. Supplied individually or in box of four single-use vials.
Preparation and Administration	• Training prior to administration • May be self-injected or administered by a caregiver or healthcare provider following the instructions for use	• Must be diluted in an infusion bag prior to administration • Administered by healthcare professional only

[1] Information obtained from BLA 125472 December 21, 2012 and May 16, 2013 submissions.

3 FAERS DATABASE SEARCH

A FAERS search was not conducted for this review because we completed a FDAAA Section 915 New Molecular Entity (NME) Postmarketing Safety Evaluation (#2010-601 dated March 5, 2013) for Actemra. In that review, we did not identify any name confusion associated with the proprietary name Actemra.

4 PROPRIETARY NAME ASSESSMENT

4.1 PROMOTIONAL ASSESSMENT

The Office of Prescription Drug Promotion OPDP determined the proposed name is acceptable from a promotional perspective. DMEPA and the Division of Pulmonary, Allergy and Rheumatology Products (DPARP) concurred with the findings of OPDP's promotional assessment of the proposed name.

4.2 SAFETY ASSESSMENT

This product is (b) (4) Actemra. However, it requires more frequent administration (weekly vs. monthly) and is packaged in a subcutaneous fixed dose syringe. Although these are important differences between the proposed product and the marketed Actemra, we agree with the applicant's proposal to use the same proprietary name for the following reasons:

- There is no difference in active ingredient, inactive ingredients or manufacturer.
- Although the proposed product is (b) (4) if given intravenously there is limited risk because 162 mg is a dose that falls within the weight based dosing range of the marketed Actemra.
- Because this product will be provided in a prefilled syringe, there is a risk it may be administered by intravenous push. According to the clinical reviewer the outcome of such an event is unknown. However, this risk is inherent for all drug products that are packaged in vials and syringes when the routes of administration differ. Conversely, if a practitioner attempted to use the vial to administer a 162 mg dose subcutaneously because they were unaware of the availability of the pre-filled syringe, the dose could not be administered because the volume needed for this dose exceeds the allowable volume for subcutaneous administration.
- The product will be added to the marketed Actemra insert. This combined insert will delineate the product differences and there will be statements added to the container labels and carton labeling highlighting the difference in dosing and routes of administration.
- Other options for naming this product such as utilizing a different proprietary name or adding a modifier to the name Actemra are also error prone. Pursing a different name for the same product from the same manufacturer could lead to concomitant therapy between this product and the currently marketed Actemra if healthcare practitioners and patients fail to recognize that both products contain Tocilizumab. With respect to the addition of a modifier, it would be difficult to find an appropriate modifier that would convey the product differences (e.g.

packaging configuration, frequency and route of administration) and distinguish it from the marketed Actemra.

- Although this nomenclature approach is not free from the risk of error, it offers a safer approach to naming this product.

4.2.1 Communication of DMEPA's Analysis at Midpoint of Review

DMEPA communicated our findings to the Division of Pulmonary, Allergy, and Rheumatology Products (DPARP) via e-mail on July 19, 2013. At that time we also requested additional information or concerns that could inform our review. Per e-mail correspondence from the (DPARP) on July 22, 2013, they stated no additional concerns with the proposed proprietary name, Actemra.

5 CONCLUSIONS

The proposed proprietary name is acceptable from both a promotional and safety perspective.

If you have further questions or need clarifications, please contact Nichelle Rashid, OSE project manager, at 301-796-3904.

5.1 COMMENTS TO THE APPLICANT

We have completed our review of the proposed proprietary name, Actemra, and have concluded that this name is acceptable.

The proposed proprietary name must be re-reviewed 90 days prior to approval of the BLA. The results are subject to change. If any of the proposed product characteristics as stated in your December 21, 2012 and May 16, 2013 submissions are altered, the name must be resubmitted for review.

APPENDIX A – DATABASE DESCRIPTION

FDA Adverse Event Reporting System (FAERS)

The FDA Adverse Event Reporting System (FAERS) is a database that contains information on adverse event and medication error reports submitted to FDA. The database is designed to support the FDA's post-marketing safety surveillance program for drug and therapeutic biologic products. The informatic structure of the database adheres to the international safety reporting guidance issued by the International Conference on Harmonisation. Adverse events and medication errors are coded to terms in the Medical Dictionary for Regulatory Activities (MedDRA) terminology. The suspect products are coded to valid trade names or active ingredients in the FAERS Product Dictionary (FPD).

FDA implemented FAERS on September 10, 2012, and migrated all the data from the previous reporting system (AERS) to FAERS. Differences may exist when comparing case counts in AERS and FAERS. FDA validated and recoded product information as the AERS reports were migrated to FAERS. In addition, FDA implemented new search functionality based on the date FDA initially received the case to more accurately portray the follow up cases that have multiple receive dates.

FAERS data have limitations. First, there is no certainty that the reported event was actually due to the product. FDA does not require that a causal relationship between a product and event be proven, and reports do not always contain enough detail to properly evaluate an event. Further, FDA does not receive reports for every adverse event or medication error that occurs with a product. Many factors can influence whether or not an event will be reported, such as the time a product has been marketed and publicity about an event. Therefore, FAERS data cannot be used to calculate the incidence of an adverse event or medication error in the U.S. population.

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/s/

TERESA S MCMILLAN
08/09/2013

CAROL A HOLQUIST
08/09/2013