



BLA 761037

**BLA APPROVAL**

Sanofi US Services Inc.  
55 Corporate Drive  
Bridgewater, NJ 08807

Attention: Sarah Feathers, PharmD  
Global Regulatory Affairs

Dear Dr. Feathers:

Please refer to your Biologics License Application (BLA) dated and received October 30, 2015, and your amendments, submitted under section 351(a) of the Public Health Service Act for Kevzara (sarilumab) injection, 150 mg/1.14 mL and 200 mg/1.14 mL pre-filled syringes.

We acknowledge receipt of your resubmission dated March 22, 2017, which constituted a complete response to our October 28, 2016, action letter.

**LICENSING**

We are issuing Department of Health and Human Services U.S. License No. 1752 to Regeneron Pharmaceutical, Inc., Rensselaer, NY, and Sanofi Winthrop Le Trait, Le Trait, France, under the provisions of section 351(a) of the Public Health Service Act controlling the manufacture and sale of biological products. The license authorizes you to introduce or deliver for introduction into interstate commerce, those products for which your company has demonstrated compliance with establishment and product standards.

Under this license, you are authorized to manufacture the product Kevzara (sarilumab). Kevzara is indicated for adult patients with moderately to severely active rheumatoid arthritis who have had an inadequate response or intolerance to one or more disease-modifying antirheumatic drugs (DMARDs).

**MANUFACTURING LOCATIONS**

Under this license, you are approved to manufacture sarilumab drug substance at Regeneron Pharmaceutical, Inc., Rensselaer, NY. The final formulated product will be manufactured, filled, labeled, and packaged at Sanofi Winthrop Le Trait, Le Trait, France. You may label your product with the proprietary name, Kevzara, and will market it in 150 mg/1.14 mL and 200 mg/1.14 mL pre-filled syringes.

### **DATING PERIOD**

The dating period for Kevzara shall be 24 months from the date of manufacture when stored at 2-8°C. The date of manufacture shall be defined as the date of final sterile filtration of the formulated drug product. The dating period for your drug substance shall be (b) (4) months from the date of manufacture when stored at (b) (4) °C. (b) (4)

### **FDA LOT RELEASE**

You are not currently required to submit samples of future lots of Kevzara to the Center for Drug Evaluation and Research (CDER) for release by the Director, CDER, under 21 CFR 610.2. We will continue to monitor compliance with 21 CFR 610.1, requiring completion of tests for conformity with standards applicable to each product prior to release of each lot.

Any changes in the manufacturing, testing, packaging, or labeling of Kevzara, or in the manufacturing facilities, will require the submission of information to your biologics license application for our review and written approval, consistent with 21 CFR 601.12.

### **APPROVAL & LABELING**

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

FDA issued a final guidance entitled Nonproprietary Naming of Biological Products on January 13, 2017, stating the Agency's intention to designate proper names for certain biological products that include distinguishing suffixes. This 351(a) application is within the scope of this guidance. However, the issuing of the guidance occurred at a point in our review of the application that did not allow for sufficient time for FDA to designate a proper name with a suffix, as described in the guidance. Therefore, in order to avoid delaying the approval of the application and in the interest of public health, we will approve the proper name as designated without a suffix and intend to work with you post-approval to implement a proper name consistent with the principles outlined in the guidance. We would also work with you to minimize the impact this would have to your manufacture and distribution of this product.

### **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, Medication Guide, and text for Instructions for Use). 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.

### **CARTON AND IMMEDIATE CONTAINER LABELS**

Submit final printed carton and container labels that are identical to the enclosed carton and immediate container labels, as soon as they are available, but no more than 30 days after they are printed. Please submit these labels electronically according to the guidance for industry titled *Providing Regulatory Submissions in Electronic Format — Certain Human Pharmaceutical Product Applications and Related Submissions Using the eCTD Specifications (May 2015, Revision 3)*. For administrative purposes, designate this submission “**Final Printed Carton and Container Labels for approved BLA 761037.**” Approval of this submission by FDA is not required before the labeling is used.

### **ADVISORY COMMITTEE**

Your application for Kevzara was not referred to an FDA advisory committee because this biologic is not the first in its class.

### **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 waiving the pediatric study requirement for pediatric patients who are less than 24 months of age because necessary studies are impossible or highly impracticable to conduct, based on the ability to adequately diagnose the disease.

We are deferring submission of your pediatric studies for ages 2-17 years for this application because this product is ready for approval for use in adults and the pediatric studies have not been completed.

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

3218-1: A study to assess the pharmacokinetic and pharmacodynamics (PK/PD) parameters and dosing of sarilumab in children ages  $\geq 2$  years to 17 years with polyarticular juvenile idiopathic arthritis (pJIA) (study DRI3925).

The timetable you submitted on May 18, 2017, states that you will conduct this study according to the following schedule:

|                          |         |
|--------------------------|---------|
| Trial Completion:        | 09/2017 |
| Final Report Submission: | 03/2018 |

3218-2: A study to assess the efficacy and safety of sarilumab in children ages  $\geq 2$  years to 17 years with polyarticular JIA (study EFC11783).

The timetable you submitted on May 18, 2017, states that you will conduct this study according to the following schedule:

|                            |         |
|----------------------------|---------|
| Final Protocol Submission: | 04/2018 |
| Trial Completion:          | 06/2022 |
| Final Report Submission:   | 01/2023 |

Submit the protocol(s) to your IND 100632, with a cross-reference letter to this BLA.

Reports of these required pediatric postmarketing studies must be submitted as a BLA or as a supplement to your approved BLA with the proposed labeling changes you believe are warranted based on the data derived from these studies. When submitting the reports, please clearly mark your submission "**SUBMISSION OF REQUIRED PEDIATRIC ASSESSMENTS**" in large font, bolded type at the beginning of the cover letter of the submission.

### **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 to:

Food and Drug Administration  
Center for Drug Evaluation and Research  
Office of Prescription Drug Promotion  
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, at the time of initial dissemination or publication, accompanied by a Form FDA 2253. Form FDA 2253 is available at

<http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM083570.pdf>.

Information and Instructions for completing the form can be found at

<http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM375154.pdf>. For more information about submission of promotional materials to the Office of Prescription Drug Promotion (OPDP), see <http://www.fda.gov/AboutFDA/CentersOffices/CDER/ucm090142.htm>.

## **REPORTING REQUIREMENTS**

You must submit adverse experience reports under the adverse experience reporting requirements for licensed biological products (21 CFR 600.80). You should submit postmarketing adverse experience reports to:

Food and Drug Administration  
Center for Drug Evaluation and Research  
Central Document Room  
5901-B Ammendale Road  
Beltsville, MD 20705-1266

Prominently identify all adverse experience reports as described in 21 CFR 600.80.

You must submit distribution reports under the distribution reporting requirements for licensed biological products (21 CFR 600.81).

You must submit reports of biological product deviations under 21 CFR 600.14. You should promptly identify and investigate all manufacturing deviations, including those associated with processing, testing, packing, labeling, storage, holding and distribution. If the deviation involves a distributed product, may affect the safety, purity, or potency of the product, and meets the other criteria in the regulation, you must submit a report on Form FDA-3486 to:

Food and Drug Administration  
Center for Drug Evaluation and Research  
Division of Compliance Risk Management and Surveillance  
5901-B Ammendale Road  
Beltsville, MD 20705-1266

Biological product deviations, sent by courier or overnight mail, should be addressed to:

Food and Drug Administration  
Center for Drug Evaluation and Research  
Division of Compliance Risk Management and Surveillance  
10903 New Hampshire Avenue, Bldg. 51, Room 4206  
Silver Spring, MD 20903

## **MEDWATCH-TO-MANUFACTURER PROGRAM**

The MedWatch-to-Manufacturer Program provides manufacturers with copies of serious adverse event reports that are received directly by the FDA. New molecular entities and important new biologics qualify for inclusion for three years after approval. Your firm is eligible to receive copies of reports for this product. To participate in the program, please see the enrollment instructions and program description details at

<http://www.fda.gov/Safety/MedWatch/HowToReport/ucm166910.htm>.

**POST APPROVAL FEEDBACK MEETING**

New molecular entities and new biologics qualify for a post approval feedback meeting. Such meetings are used to discuss the quality of the application and to evaluate the communication process during drug development and marketing application review. The purpose is to learn from successful aspects of the review process and to identify areas that could benefit from improvement. If you would like to have such a meeting with us, call the Regulatory Project Manager for this application.

If you have any questions, call Christine Ford, Regulatory Project Manager, at (301) 796-3420.

Sincerely,

*{See appended electronic signature page}*

Curtis J. Rosebraugh, MD, MPH  
Director  
Office of Drug Evaluation II  
Office of New Drugs  
Center for Drug Evaluation and Research

ENCLOSURE(S):

Content of Labeling  
Carton and Container Labeling

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**This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.**  
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/s/  
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CURTIS J ROSEBRAUGH  
05/22/2017