BLA 761449

BLA APPROVAL

Fresenius Kabi USA, LLC
Attention: Ama Berko, PharmD
Director, Global Regulatory Affairs
Three Corporate Dr
Lake Zurich, IL 60047

Dear Dr. Ama Berko:

Please refer to your biologics license application (BLA) dated and received July 17, 2024, and your amendments, submitted under section 351(k) of the Public Health Service Act for Tyenne (tocilizumab-aazg) injection.

This BLA seeks licensure of:

- Tyenne (tocilizumab-aazg) injection 162 mg/0.9 mL single-dose prefilled syringe for subcutaneous use as biosimilar to US-licensed Actemra (tocilizumab) injection 162 mg/0.9 mL single-dose prefilled syringe for subcutaneous use; and

- Tyenne (tocilizumab-aazg) injection 162 mg/0.9 mL single-dose prefilled autoinjector for subcutaneous use as biosimilar to US-licensed Actemra (tocilizumab) injection 162 mg/0.9 mL single-dose prefilled autoinjector for subcutaneous use.

LICENSING

We have approved your BLA for Tyenne (tocilizumab-aazg) effective this date. You are hereby authorized to introduce or deliver for introduction into interstate commerce, Tyenne under your existing Department of Health and Human Services U.S. License No. 2146. Under BLA 761449, Tyenne is indicated for the treatment of:

- Rheumatoid Arthritis (RA)
- Giant Cell Arteritis (GCA)
- Polyarticular Juvenile Idiopathic Arthritis (PJIA) in patients ≥ 2 years of age
- Systemic Juvenile Idiopathic Arthritis (SJIA) in patients ≥ 2 years of age

MANUFACTURING LOCATIONS

Under this license, you are approved to manufacture tocilizumab-aazg drug substance at (b) (4). The final formulated drug product in single-dose prefilled syringe and single-dose prefilled autoinjector will be manufactured and filled at (b) (4)

(b) (4). The final device assembly, labeling and secondary packaging will be performed at Fresenius Kabi Austria GmbH, Werndorf, Austria. You may label your product with the proprietary name, Tyenne, and market it in 162 mg/0.9 mL single-dose prefilled syringe and single-dose prefilled autoinjector, injection.

DATING PERIOD

The dating period for Tyenne single-dose prefilled syringe and autoinjector shall be 36 months from the date of manufacture when stored at 5 ± 3 °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.

We have approved the stability protocols in your license application for the purpose of extending the expiration dating of your drug substance and drug product under 21 CFR 601.12.

FDA LOT RELEASE

You are not currently required to submit samples of future lots of Tyenne 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 Tyenne, or in the manufacturing facilities, will require the submission of information to your BLA 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.

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.[1] Content of labeling must be identical to the enclosed labeling (text for the Prescribing Information, Instructions for Use, and Medication Guide). Information on submitting SPL files using

[1] See http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm

eLIST may be found in the guidance for industry *SPL Standard for Content of Labeling Technical Qs and As (October 2009)*.[2]

The SPL will be accessible via publicly available labeling repositories.

CARTON AND CONTAINER LABELING

Submit final printed carton and container labeling that are identical to the enclosed carton and container labeling, as soon as they are available, but no more than 30 days after they are printed. Please submit these labeling electronically according to the guidance for industry *SPL Standard for Content of Labeling Technical Qs & As.* For administrative purposes, designate this submission "**Final Printed Carton and Container Labeling for approved BLA 761449**." Approval of this submission by FDA is not required before the labeling is used.

REQUIRED PEDIATRIC ASSESSMENTS

Under the Pediatric Research Equity Act (PREA) (21 U.S.C. 355c), all applications for new active ingredients (which includes new salts and new fixed combinations), 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.

Rheumatoid arthritis, Giant Cell Arteritis, Polyarticular Juvenile Idiopathic Arthritis, and Systemic Juvenile Idiopathic Arthritis:

At this time, we have determined that no pediatric assessments will be required under PREA for your BLA.

POSTMARKETING COMMITMENTS NOT SUBJECT TO REPORTING REQUIREMENTS UNDER SECTION 506B

We remind you of your postmarketing commitments:

PMC 4821-1: Re-evaluate the drug substance and drug product lot release and stability acceptance criteria for the degree of coloration after release data from 30 drug substance lots and corresponding drug product lots are available, and with consideration of available stability data. The final report should include the corresponding data, the analysis thereof, and any proposed changes to the drug

[2] We update guidances periodically. For the most recent version of a guidance, check the FDA Guidance Documents Database at https://www.fda.gov/RegulatoryInformation/Guidances/default.htm.

substance and drug product release or stability specifications resulting from the assessment.
Final Report Submission: 01/2027

PMC 4821-2: Re-evaluate lot release and stability acceptance criteria for the device performance attributes of the prefilled syringe (b) (4) (PFS (b) (4)) after release data from 30 PFS (b) (4) and PFS-AI lots are available, and with consideration of available stability data. The final report should include the corresponding data, the analysis thereof, and any proposed changes to the drug product release or stability specifications resulting from the assessment.
Final Report Submission: 09/2026

PMC 4821-3: Re-evaluate lot release and stability acceptance criteria for the device performance attributes of the prefilled syringe assembled in autoinjector device (PFS-AI) after release data from 30 PFS (b) (4) and PFS-AI lots are available, and with consideration of available stability data. The final report should include the corresponding data, the analysis thereof, and any proposed changes to the drug product release or stability specifications resulting from the assessment.
Final Report Submission: 03/2026

Submit clinical protocols to your IND 129965 for this product. Submit nonclinical and chemistry, manufacturing, and controls protocols and all postmarketing final reports to this BLA. In addition, under 21 CFR 601.70 you should include a status summary of each commitment in your annual progress report of postmarketing studies to this BLA. The status summary should include expected summary completion and final report submission dates, any changes in plans since the last annual report, and, for clinical studies/trials, number of patients entered into each study/trial. All submissions, including supplements, relating to these postmarketing commitments should be prominently labeled "**Postmarketing Commitment Protocol**," "**Postmarketing Commitment Final Report**," or "**Postmarketing Commitment Correspondence**."

PROMOTIONAL MATERIALS

You may request advisory comments on proposed introductory advertising and promotional labeling. For information about submitting promotional materials, see the final guidance for industry *Providing Regulatory Submissions in Electronic and Non-Electronic Format-Promotional Labeling and Advertising Materials for Human Prescription Drugs*.[3]

You must submit final promotional materials and Prescribing Information, accompanied by a Form FDA 2253, at the time of initial dissemination or publication

[3] For the most recent version of a guidance, check the FDA guidance web page at https://www.fda.gov/media/128163/download.

[21 CFR 314.81(b)(3)(i)]. Form FDA 2253 is available at FDA.gov.[4] Information and Instructions for completing the form can be found at FDA.gov.[5]

REPORTING REQUIREMENTS

You must submit adverse experience reports under the adverse experience reporting requirements at 21 CFR 600.80.

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

You must submit distribution reports under the distribution reporting requirements at 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 4207
Silver Spring, MD 20903

Your product is a Part 3 combination product (21 CFR 3.2(e)); therefore, you must also comply with postmarketing safety reporting requirements for an approved combination product (21 CFR 4, Subpart B). Additional information on combination product postmarketing safety reporting is available at FDA.gov.

If you have any questions, contact Chau Nguyen, Regulatory Project Manager, at (240)-402-0022 or chau.nguyen@fda.hhs.gov.

[4] http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM083570.pdf
[5] http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM375154.pdf

Sincerely,

{See appended electronic signature page}

Raj Nair
Division Director
Division of Rheumatology and Transplant Medicine
Office of Immunology and Inflammation
Office of New Drugs
Center for Drug Evaluation and Research

ENCLOSURES:

- Content of Labeling
  - Prescribing Information
  - Medication Guide
  - Instructions for Use
- Carton and Container Labeling

This is a representation of an electronic record that was signed electronically. Following this are manifestations of any and all electronic signatures for this electronic record.

/s/

RAJ NAIR
03/14/2025 01:19:03 PM