BLA 761255/Original 2

BLA APPROVAL
FULFILLMENT OF POSTMARKETING
REQUIREMENT/COMMITMENT(S)

Fresenius Kabi USA, LLC
Attention: Navayath Shobana, PhD
Senior Director, Regulatory Affairs
Three Corporate Drive
Lake Zurich, IL 60047

Dear Dr. Shobana:

Please refer to your biologics license application (BLA) dated and received December 13, 2021, and your amendments, submitted under section 351(k) of the Public Health Service Act for Idacio (adalimumab-aacf) injection.

We acknowledge receipt of your resubmission dated July 7, 2023, which constituted a complete response to our December 13, 2022, action letter.

BLA 761255 provides for the use of Idacio (adalimumab-aacf) for the following indications including:

1. Rheumatoid Arthritis (RA): reducing signs and symptoms, inducing major clinical response, inhibiting the progression of structural damage, and improving physical function in adult patients with moderately to severely active RA.
2. Juvenile Idiopathic Arthritis (JIA): reducing signs and symptoms of moderately to severely active polyarticular JIA in patients 2 years and older.
3. Psoriatic Arthritis (PsA): reducing signs and symptoms, inhibiting the progression of structural damage, and improving physical function in adult patients with active PsA.
4. Ankylosing Spondylitis (AS): reducing signs and symptoms in adult patients with active AS.
5. Crohn's Disease (CD): treatment of moderately to severely active Crohn's disease in adult and pediatric patients 6 years of age and older.
6. Ulcerative Colitis (UC): treatment of moderately to severely active ulcerative colitis in adult patients.
7. Plaque Psoriasis (Ps): treatment of adult patients with moderate to severe chronic plaque psoriasis who are candidates for systemic therapy or phototherapy, and when other systemic therapies are medically less appropriate.

8. Hidradenitis Suppurativa: treatment of moderate to severe hidradenitis suppurativa in adult patients
9. Uveitis: treatment of non-infectious intermediate, posterior and panuveitis in adult patients

For administrative purposes, we have designated as follows:

BLA 761255/Original 1 – single-dose prefilled pen and single-dose prefilled glass syringe

BLA 761255/Original 2 – single-dose vial kit for institutional use only

The subject of this action letter is BLA 761255/Original 2. A separate action letter was issued for BLA 761255/Original 1.

LICENSING

We have approved your BLA for Idacio (adalimumab-aacf) effective this date. You are hereby authorized to introduce or deliver for introduction into interstate commerce, Idacio single-dose vial kit under your existing Department of Health and Human Services U.S. License No. 2146.

MANUFACTURING LOCATIONS

Under this license, you are approved to manufacture adalimumab-aacf drug substance at Merck Serono S.A. in Corsier-sur-Vevey, Switzerland. The final formulated product will be manufactured, filled, labeled, and packaged at Merck Serono S.A., Aubonne, Switzerland. You may label your product with the proprietary name, Idacio, and will market it in 40 mg/0.8 mL solution in a single-dose glass vial kit.

DATING PERIOD

The dating period for Idacio single-dose glass vial kit shall be 36 months from the date of manufacture when stored at 36°F to 46°F (2°C to 8°C). This dating period may include a single period up to 28 days at a maximum of 77°F (25°C) with protection from light. 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.

The expiration date for the packaged product, Idacio single-dose vial kit shall be dependent on the shortest expiration date of any component.

FDA LOT RELEASE

You are not currently required to submit samples of future lots of Idacio and each kit component 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 Idacio, 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 AND 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, as described at FDA.gov.[1] Content of labeling must be identical to the enclosed labeling (text for the Prescribing Information and Medication Guide). Information on submitting SPL files using eLIST may be found in the guidance for industry *SPL Standard for Content of Labeling Technical Qs and As.*[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 labeling submitted on December 7, 2023, 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 761255/ Original 2**." Approval of this submission by FDA is not required before the labeling is used.

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

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.

We have received your submission dated July 7, 2023, for the following postmarketing requirement listed in the December 13, 2022, approval letter for BLA 761255/Original-1.

4376-1 Develop a presentation that can be used to accurately administer Idacio (adalimumab-aacf) to pediatric patients weighing 10 kg to less than 40 kg.

We note that you have fulfilled the pediatric study(ies) requirement for all relevant pediatric age groups for this application.

We acknowledge your submissions to address postmarketing commitments listed in the December 13, 2022, approval letter for BLA 761255/Original-1 that are still open. After completion of review, we will notify you whether the commitments have been fulfilled.

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 [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 for licensed biological products (21 CFR 600.80).

[3] For the most recent version of a guidance, check the FDA guidance web page at https://www.fda.gov/media/128163/download.
[4] http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM083570.pdf
[5] http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM375154.pdf

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 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, call Susie Choi, Regulatory Project Manager, at 240-402-2925.

Sincerely,

{See appended electronic signature page}

Raj Nair, MD
Director (Acting)
Division of Rheumatology and Transplant Medicine
Office of Immunology and Inflammation
Office of New Drugs
Center for Drug Evaluation and Research

ENCLOSURE(S):

- Content of Labeling
  - Prescribing Information
  - Medication Guide
  - Instructions for Use (prefilled pen and prefilled syringe)
- 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/

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