BLA 761058/S-011

SUPPLEMENT APPROVAL
FULFILLMENT OF POSTMARKETING REQUIREMENT

Boehringer Ingelheim
900 Ridgebury Rd
PO Box 368
Ridgefield, CT 06877-0368

Attention: Christopher Dougherty, PhD, MS
Director, Regulatory Affairs

Dear Dr. Dougherty:

Please refer to your supplemental biologics license application (sBLA) dated and received November 19, 2021, and your amendments, submitted under section 351(k) of the Public Health Service Act for Cyltezo (adalimumab-adbm).

This Prior Approval sBLA provides for the addition of a Cyltezo (adalimumab-abdm) 10 mg/0.2 mL prefilled syringe (PFS) manufactured at Boehringer Ingelheim Freemont, Inc.,California (FEI# 3005925062) as interchangeable with US-licensed Humira 10 mg/0.2 mL PFS.

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.

EXCLUSIVITY FOR FIRST INTERCHANGEABLE BIOLOGICAL PRODUCT

Cyltezo (adalimumab-adbm) 10 mg/0.2 mL PFS is the first biological product relying on its reference product, to receive a determination of interchangeability for any condition of use. Therefore, with this approval, Boehringer Ingelheim is eligible for a period of first interchangeable exclusivity under section 351(k)(6) of the Public Health Service Act for the Cyltezo (adalimumab-adbm) 10 mg/0.2 mL PFS.

As provided by section 351(k), "the Secretary shall not make a determination under paragraph (4) that the second or subsequent biological product is interchangeable for any condition of use until the earlier of—

(A) 1 year after the first commercial marketing of the first interchangeable biosimilar biological product to be approved as interchangeable for that reference product;

(B) 18 months after—

(i) a final court decision on all patents in suit in an action instituted under subsection (*l*)(6) against the applicant that submitted the application for the first approved interchangeable biosimilar biological product; or

(ii) the dismissal with or without prejudice of an action instituted under subsection (*l*)(6) against the applicant that submitted the application for the first approved interchangeable biosimilar biological product; or

(C) (i) 42 months after approval of the first interchangeable biosimilar biological product if the applicant that submitted such application has been sued under subsection (*l*)(6) and such litigation is still ongoing within such 42-month period; or

(ii) 18 months after approval of the first interchangeable biosimilar biological product if the applicant that submitted such application has not been sued under subsection (*l*)(6).

For purposes of this paragraph, the term "final court decision" means a final decision of a court from which no appeal (other than a petition to the United States Supreme Court for a writ of certiorari) has been or can be taken."

For each interchangeable biosimilar biological product approved by this letter, please submit a general correspondence to this 351(k) BLA informing the Agency of the date of first commercial marketing within 30 days of such date. Please also submit a duplicate copy of the correspondence via email to PurpleBook@fda.hhs.gov. Additionally, if applicable, please submit a general correspondence to this 351(k) BLA informing the Agency of the date of any final court decision (as defined in section 351(k)(6)) on all patents in suit in an action instituted under subsection *(l)*(6) or the date of dismissal with or without prejudice of any action instituted under subsection (*l*)(6) within 30 days of such date or within 30 days of this approval if such date occurred prior to approval. Please also submit a duplicate copy of the correspondence via email to PurpleBook@fda.hhs.gov.

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] that is identical to the enclosed labeling (text for the Prescribing Information, Instructions for Use, Medication Guide) and include the labeling changes proposed in any pending "Changes Being Effected" (CBE) supplements.

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

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.

Also within 14 days, amend all pending supplemental applications that include labeling changes for this BLA, including pending "Changes Being Effected" (CBE) supplements, for which FDA has not yet issued an action letter, with the content of labeling [21 CFR 601.12(f)] in Microsoft Word format that includes the changes approved in this supplemental application, as well as annual reportable changes. To facilitate review of your submission, provide a highlighted or marked-up copy that shows all changes, as well as a clean Microsoft Word version. The marked-up copy should provide appropriate annotations, including supplement number(s) and annual report date(s).

CARTON AND CONTAINER LABELING

Submit final printed carton and container labeling that are identical to the enclosed carton and container labeling and carton and container labeling submitted on February 16, 2022, 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 *Providing Regulatory Submissions in Electronic Format — Certain Human Pharmaceutical Product Applications and Related Submissions Using the eCTD Specifications*. For administrative purposes, designate this submission "**Product Correspondence – Final Printed Carton and Container Labeling for approved BLA 761058/ S-011**." Approval of this submission by FDA is not required before the labeling is used.

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

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

Instructions for completing the form can be found at FDA.gov.[5]

FULFILLMENT OF POSTMARKETING REQUIREMENT(S)/COMMITMENT(S)

We refer to your supplemental biologics license application (sBLA) under section 351 of the Public Health Service Act for Cyltezo (adalimumab-adbm).

We have received your submission dated November 19, 2021, containing the final report for the following postmarketing requirement listed in the August 25, 2017, approval letter for BLA 761058.

3260-4 Develop a presentation that can be used to accurately administer Cyltezo (adalimumab-adbm) to pediatric patients who weigh less than 30 kg.

We have reviewed your submission and conclude that the above requirement was fulfilled.

We remind you that there is a postmarketing commitment listed in the August 25, 2017, approval letter that is still open.

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.

Because none of these criteria apply to your supplemental biologics license application, you are exempt from this requirement.

This information will be included in your biologics license application file.

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

If you have any questions, call Sadaf Nabavian, Sr. Regulatory Project Manager, at 301-796-2777.

Sincerely,

{See appended electronic signature page}

Nikolay P. Nikolov, MD
Director
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
- 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/

NIKOLAY P NIKOLOV
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