BLA 761058/S008

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 December 16, 2020, received December 16, 2020, and your amendments, submitted under section 351(k) of the Public Health Service Act for Cyltezo (adalimumab-adbm) injection.

This Prior Approval supplemental biologics application requests approval of Cyltezo (adalimumab-adbm) 20 mg/0.4mL and 40 mg/0.8 mL prefilled syringes (PFS) as interchangeable with US-licensed Humira 20 mg/0.4mL and 40 mg/0.8 mL PFS for the following indications:

- 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.
- Juvenile Idiopathic Arthritis (JIA): reducing signs and symptoms of moderately to severely active polyarticular JIA in patients 2 years of age and older.
- Psoriatic Arthritis (PsA): reducing signs and symptoms, inhibiting the progression of structural damage, and improving physical function in adult patients with active PsA.
- Ankylosing Spondylitis (AS): reducing signs and symptoms in adult patients with active AS.
- Crohn's Disease (CD): treatment of moderately to severely active Crohn's disease in adults and pediatric patients 6 years of age and older.
- Ulcerative Colitis (UC): treatment of moderately to severely active ulcerative colitis in adult patients.

Limitations of Use: Effectiveness has not been established in patients who have lost response to or were intolerant to TNF blockers.

- 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.

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) 20 mg/0.4mL PFS and Cyltezo (adalimumab-adbm) 40 mg/0.8 mL PFS are the first biological products relying on their respective reference products, 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) 20 mg/0.4mL PFS and for the Cyltezo (adalimumab-adbm) 40 mg/0.8 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.

WAIVER OF HIGHLIGHTS ½ PAGE LENGTH REQUIREMENT FOR HIGHLIGHTS

Please note that we have previously granted a waiver of the requirements of 21 CFR 201.57(d)(8) regarding the length of Highlights of Prescribing Information.

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, and Medication Guide) and include the labeling changes proposed in any pending "Changes Being Effected" (CBE) supplements.

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(s), 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).

[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 https://www.fda.gov/RegulatoryInformation/Guidances/default.htm.

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 *Providing Regulatory Submissions in Electronic Format — Certain Human Pharmaceutical Product Applications and Related Submissions Using the eCTD Specifications*. For administrative purposes, designate this submission "**Final Printed Carton and Container Labeling for approved BLA 761058/S-008**." 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.

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

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

We have received your submissions dated September 27, 28, and 29, 2021, containing the final reports for the following postmarketing requirements listed in the August 25, 2017 approval letter for BLA 761058.

> 3260-1 Assessment of Cyltezo (adalimumab-adbm) for the treatment of Polyarticular juvenile idiopathic arthritis (pJIA) in patients 2 years to less than 4 years of age.
>
> 3260-2 Assessment of Cyltezo (adalimumab-adbm) for the treatment of pediatric Crohn's disease in pediatric patients 6 years to 17 years of age.
>
> 3260-3 Assessment of Cyltezo (adalimumab-adbm) for the treatment of pediatric ulcerative colitis in pediatric patients 5 years to 17 years of age.

We have reviewed your submissions and conclude that the above requirements were fulfilled.

We remind you that there is a postmarketing requirement listed in the August 25, 2017 approval letter that remains unfulfilled.

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]

As required under 21 CFR 601.12(f)(4), you must submit final promotional materials, and the Prescribing Information, at the time of initial dissemination or publication, accompanied by a Form FDA 2253. 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

We remind you that you must comply with reporting requirements for an approved BLA (in 21 CFR 600.80 and in 21 CFR 600.81).

If you have any questions, call Sadaf Nabavian, 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
Center for Drug Evaluation and Research

ENCLOSURE(S):

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

[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

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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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