



BLA 761059/S-005

**SUPPLEMENT APPROVAL**

Samsung Bioepis Co., Ltd  
c/o Cardinal Health 127, Inc.  
7400 West 110<sup>th</sup> Street  
Overland Park, Kansas 66210

Attention: Todd Phillips, PharmD, RAC  
Director, Global Regulatory Affairs

Dear Dr. Phillips:

Please refer to your supplemental biologics license application (sBLA), dated and received October 15, 2021, and your amendments, submitted under section 351(k) of the Public Health Service Act for Hadlima (adalimumab-bwvd) injection.

This Prior Approval supplemental biologics license application provides for:

1. Introduction of 40 mg/0.4 mL Hadlima (adalimumab-bwvd) prefilled syringe (PFS) and prefilled auto-injector (AI) presentations with shelf-life of 24 months
2. Introduction of Samsung Biologics Co. Ltd (SBL) (FEI 3010479596) for the following:
  - a. A manufacturing site for 50 mg/mL (SB5A) drug substance with a shelf-life of (b) (4) months and 100 mg/mL (SB5B) drug substance with a shelf-life of (b) (4) months.
  - b. A release testing site for appearance, protein concentration, endotoxin, and microbial enumeration
  - c. An in-process testing site (b) (4), (b) (4)
3. Introduction of (b) (4) a drug product manufacturing site for 40 mg/0.4 mL Hadlima (adalimumab-bwvd) PFS and AI
4. Introduction of (b) (4) a drug substance in-process testing site (b) (4)
5. Introduction of (b) (4) a drug substance in-process testing site (b) (4)
6. Introduction of Samsung Bioepis Co., Ltd. (FEI 3010031951) as a drug substance in-process testing site (b) (4)
7. Introduction of (b) (4) a drug substance storage site

8. Introduction of (b) (4) a drug product secondary packaging site for 40 mg/0.4 mL Hadlima (adalimumab-bwwd) PFS and AI, functional release testing (b) (4) (b) (4) site for 40 mg/0.4 mL Hadlima (adalimumab-bwwd) AI, and functional stability testing (b) (4) (b) (4) site for 40 mg/0.4 mL Hadlima (adalimumab-bwwd) AI
9. Introduction of (b) (4) a functional release testing (b) (4) (b) (4) site for 40 mg/0.4 mL Hadlima (adalimumab-bwwd) PFS and functional stability testing (b) (4) (b) (4) site for 40 mg/0.4 mL Hadlima (adalimumab-bwwd) PFS
10. Introduction of (b) (4) a functional stability testing site for 40 mg/0.4 mL Hadlima (adalimumab-bwwd) PFS and AI for CCIT testing
11. Introduction of the (b) (4) analytical method for protein concentration determination at SBL (DS release and in-process testing), (b) (4) (in-process DP testing), and (b) (4), for DS stability testing and DP release and stability testing).
12. Protocols for extension of shelf-life for DS (b) (4) for 40 mg/0.4 mL Hadlima (adalimumab-bwwd) PFS and AI presentations
13. A protocol for concurrent validation of the (b) (4) (b) (4) at commercial scale

## **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.

## **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,<sup>1</sup> that is identical to the enclosed labeling (text for the Prescribing Information, Medication Guide, and Instructions for Use) 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*.<sup>2</sup>

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).

## **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 761059/S-005.**” 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.

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<sup>1</sup> <http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm>

<sup>2</sup> 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>.

## **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*.<sup>3</sup>

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.<sup>4</sup> Information and Instructions for completing the form can be found at FDA.gov.<sup>5</sup>

## **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).

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 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  
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

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

<sup>4</sup> <http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM083570.pdf>

<sup>5</sup> <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.**  
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/s/  
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Signing on behalf of Dr. Nikolay Nikolov, Division Director, DRTM