BLA 761066/S-001

SUPPLEMENT APPROVAL

Samsung Bioepis Co., Ltd.
c/o MMS Holdings, Inc.
Attention: Andrew Zelar
Technical Specialist, Regulatory Strategy
6880 Commerce Boulevard
Canton, MI 48187

Dear Andrew Zelar:

Please refer to your supplemental biologics license application (sBLA), dated and received November 3, 2023, and your amendments, submitted under section 351(k) of the Public Health Service Act for Eticovo (etanercept-ykro) injection.

We acknowledge receipt of your amendment dated November 3, 2023, which constituted complete responses to our March 23, 2020, and August 9, 2023, action letters.

This Prior Approval supplemental biologics license application seeks licensure of Eticovo (etanercept-ykro) 50 mg/mL injection for subcutaneous use in an autoinjector pen as biosimilar to US-licensed Enbrel (etanercept) 50 mg/mL injection for subcutaneous use in an autoinjector.

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,[1] that is identical to the enclosed labeling (Prescribing Information, Instructions

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

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).

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 761066/S-001**." 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 application, you are exempt from this requirement.

[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.

POSTMARKETING COMMITMENTS NOT SUBJECT TO THE REPORTING REQUIREMENTS UNDER SECTION 506B

We remind you of your postmarketing commitments:

4633-1 Perform supplemental validation studies for the FlowCam method to more accurately determine the number of visible particles in your drug product (DP). The supplemental validation studies for the FlowCam method should include, but not limited to, (b) (4) as recommended in USP <1790>. This additional validation can include re-evaluation and/or re-establishment of acceptance criteria related to visible particles, as applicable (e.g., limit of quantification (LOQ)).

The timetable you submitted on April 30, 2024, states that you will conduct this study according to the following schedule:

Final Report Submission: 12/2024

4633-2 Evaluate the size, shape, and identity of the visible particles using the revalidated FlowCam method for particle number determination, along with applicable orthogonal method(s) (i.e., FT-IR) and to conduct a comparative assessment with US-licensed Enbrel samples.

The timetable you submitted on April 30, 2024, states that you will conduct this study according to the following schedule:

Final Report Submission: 06/2025

4633-3 Continue investigation of the root-cause of the visible particle formation using appropriately validated analytical method(s). The study should include an adequate study design with appropriate negative control samples for visible particle formation. The control strategy surrounding visible particles should be updated accordingly based on additional results from the root-cause analysis.

The timetable you submitted on April 30, 2024, states that you will conduct this study according to the following schedule:

Final Report Submission: 12/2025

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/subjects 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 [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

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.

[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

If you have any questions, contact Suprat Saely, Regulatory Project Manager, at suprat.saely@fda.hhs.gov or 240-402-1604.

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
- 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
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