BLA 761244/S-003

SUPPLEMENT APPROVAL

Boehringer Ingelheim Pharmaceuticals, Inc.
Attention: Christopher Dougherty, PhD, MS
Director, Regulatory Affairs
900 Ridgebury Road
P.O. Box 368
Ridgefield, CT 06877

Dear Dr. Dougherty:

Please refer to your supplemental biologics license application (sBLA), dated and received May 18, 2023, and your amendments, submitted under section 351(a) of the Public Health Service Act for Spevigo (spesolimab-sbzo) 150 mg/mL single-dose prefilled syringe for subcutaneous use and 450 mg/7.5 mL single-dose vial for intravenous use.

This Prior Approval supplemental biologics license application provides for the treatment of generalized pustular psoriasis (GPP) in adults and pediatric patients 12 years of age and older and weighing at least 40 kg.

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.

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]

[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.

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 carton and container labeling submitted on February 26, 2024, 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 761244/S-003**." 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 this drug product for this indication has an orphan drug designation, you are exempt from this requirement.

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

We remind you of your postmarketing commitments:

4588-1 To establish and validate an appropriate method for determining number and size of potential product-related visible particles in spesolimab prefilled syringe with needle safety device (PFS-NSD-1) and implement the method for evaluation of visible particles in spesolimab PFS-NSD-1 stability testing with re-evaluation and/or establishment of acceptance criteria related to visible particles.

The timetable you submitted on January 29, 2024, states that you will conduct this study according to the following schedule:

Final Report Submission: 10/2024

4588-2 To re-establish the operating ranges for (b) (4) spesolimab drug substance during manufacture of spesolimab PFS-1/PFS-NSD-1 with appropriate supporting data.

The timetable you submitted on January 29, 2024, states that you will conduct this study according to the following schedule:

Final Report Submission: 10/2024

Submit clinical protocols to your IND 131311 for this product. 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]

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

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

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.

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). Under 21 CFR 600(c)(2)(i), quarterly periodic safety reports must be submitted for the first 3 years post-approval of the original BLA (i.e., through August 31, 2025 for BLA 761244).

Per 21 CFR 600.80(c)(2)(i), we are reestablishing the quarterly periodic safety reporting requirement for this application to extend the third-year period post-approval of this supplement. Therefore, you must submit periodic safety reports on a quarterly basis through March 17, 2027, then on an annual basis thereafter. We note, in our August 8, 2023 response to your waiver request, we waived you of the requirement to submit the periodic adverse experience report (PAER) required under 21 CFR 600.80(c)(2)(i) and instead allowed you to submit periodic safety reports in the ICH E2C(R2) Periodic Benefit-Risk Evaluation Report (PBRER) format, as outlined in our letter. We request that you review the periodic safety report submission schedule for BLA 761244. If modifications to the submission schedule are necessary to ensure that there are no gaps in reporting resulting from the extension of the quarterly reporting requirement, you should submit a request to BLA 761244 for a modification to your previously granted periodic safety reporting waiver.

REQUESTED ENHANCED PHARMACOVIGILANCE (EPV)

We are modifying our previous EPV request included in our September 1, 2022, approval letter for BLA 761244, as follows:

1. Guillain-Barre Syndrome (GBS)

    a. For Spevigo, we request that you submit all serious and non-serious domestic and/or foreign cases of GBS as 15-day Alert reports (described under 21 CFR 600.80(c)(1)) through the 3rd year following the supplement's U.S. approval date.

[4] http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM083570.pdf
[5] http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM375154.pdf

b. We request that you provide a narrative summary including analyses of cases reporting GBS cases as part of your required periodic safety reports (i.e., PAER required under 21 CFR 600.80(c)(2) or the ICH E2C PBRER format), quarterly during the first 3 years post-supplement approval and annually thereafter, through the 5th year following the supplement's U.S. approval date.

2. Exposure in pregnant patients, patients who are lactating, and infants exposed through breastmilk or infants who were exposed while in utero.

   a. For Spevigo, we request that you submit all reported cases of possible exposure in pregnant patients, patients who are lactating, and infants exposed through breastmilk or infants who were exposed while in utero as 15-day Alert reports (described under 21 CFR 600.80(c)(1)) through the 3rd year following the supplement's U.S. approval date.

   b. We request that you provide a narrative summary including analyses of cases reporting possible exposure in pregnant patients, patients who are lactating, and infants exposed through breastmilk or infants who were exposed while in utero as part of your required periodic safety reports (i.e., PAER required under 21 CFR 600.80(c)(2) or the ICH E2C PBRER format), quarterly during the first 3 years post-supplement approval and annually thereafter, through the 5th year following the supplement's U.S. approval date.

In addition to the above modifications, we also request the following:

Your analyses should include interval and cumulative data relative to the date of approval of Spevigo. Your analyses should provide an assessment of causality, with documentation of indication, temporal association, duration of therapy, associated signs and symptoms, confounders, underlying risk factors, treatment given for the event, outcome, and dechallenge/rechallenge.

If you have any questions, call Susan Rhee, Chief of Project Management Staff, at susan.rhee@fda.hhs.gov or 301-796-2402.

Sincerely,

{See appended electronic signature page}

Jill Lindstrom, MD, FAAD
Director
Division of Dermatology and Dentistry
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/

JILL A LINDSTROM
03/18/2024 05:52:29 PM