BLA 761151

CORRECTED BLA APPROVAL

UCB, Inc.
Attention: Jason Morgan, PhD
Regulatory Science Lead
1950 Lake Park Drive
Building 2100
Smyrna, GA 30080

Dear Dr. Morgan:

Please refer to your biologics license application (BLA) dated and received July 15, 2020, and your amendments, submitted under section 351(a) of the Public Health Service Act for Bimzelx (bimekizumab-bkzx) injection, for subcutaneous use.

We also refer to our approval letter dated October 17, 2023, which contained the following error: omitted container labeling.

This corrected action letter incorporates the correction of the error. The effective action date will remain October 17, 2023, the date of the original letter.

We acknowledge receipt of your resubmission dated November 21, 2022, which constituted a complete response to our May 12, 2022, action letter.

LICENSING

We have approved your BLA for Bimzelx (bimekizumab-bkzx) effective this date. You are hereby authorized to introduce or deliver for introduction into interstate commerce, Bimzelx under your existing Department of Health and Human Services U.S. License No. 1736. Bimzelx is indicated for the treatment of moderate to severe plaque psoriasis in adults who are candidates for systemic therapy or phototherapy.

MANUFACTURING LOCATIONS

Under this license, you are approved to manufacture bimekizumab-bkzx drug substance at (b) (4) The final formulated drug product will be manufactured, filled, and packaged at UCB Pharma SA, Chemin du Foriest, Braine-l'Alleud, Belgium. Secondary packaging, labeling, and storage of the final formulated drug product will be at (b) (4) You may label your product with the proprietary name, Bimzelx, and market it in 160 mg/mL solution in a prefilled syringe and autoinjector.

DATING PERIOD

The dating period for Bimzelx shall be 36 months from the date of manufacture when stored at 2 to 8°C with storage up to 30 days at 25˚C permitted within the expiry. The date of manufacture shall be defined as the date of final sterile filtration of the formulated drug product. The dating period for your drug substance shall be (b) (4) months from the date of manufacture when stored at (b) (4) °C.

FDA LOT RELEASE

You are not currently required to submit samples of future lots of Bimzelx to the Center for Drug Evaluation and Research (CDER) for release by the Director, CDER, under 21 CFR 610.2. We will continue to monitor compliance with 21 CFR 610.1, requiring completion of tests for conformity with standards applicable to each product prior to release of each lot.

Any changes in the manufacturing, testing, packaging, or labeling of Bimzelx, or in the manufacturing facilities, will require the submission of information to your BLA for our review and written approval, consistent with 21 CFR 601.12.

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.[1] Content of labeling must be identical to the enclosed labeling (text for the Prescribing Information, Instructions for Use, and Medication Guide). 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 (October 2009)*.[2]

The SPL will be accessible via publicly available labeling repositories.

[1] See 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 at 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 *SPL Standard for Content of Labeling Technical Qs & As.* For administrative purposes, designate this submission "**Final Printed Carton and Container Labeling for approved BLA 761151**." Approval of this submission by FDA is not required before the labeling is used.

ADVISORY COMMITTEE

Your application for Bimzelx was not referred to an FDA advisory committee because the clinical trial design is acceptable.

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.

We are waiving the pediatric study requirement for ages 0 to less than 6 years of agebecause the number of pediatric psoriasis patients in the 0 < 6 years age range is so small that the studies would be highly impractical or impossible to conduct. .

We are deferring submission of your pediatric studies for ages 6 to less than 18 years of age for this application because this product is ready for approval for use in adults and the pediatric studies have not been completed.

Your deferred pediatric studies required by section 505B(a) of the Federal Food, Drug, and Cosmetic Act are required postmarketing studies. The status of this postmarketing studies must be reported annually according to 21 CFR 601.28 and section 505B(a)(4)(B) of the Federal Food, Drug, and Cosmetic Act. These required studies are listed below.

4268 – 1 Conduct a multicenter, open-label trial to assess the pharmacokinetics and safety of bimekizumab in adolescents 12 to <18 years of age with moderate to severe plaque psoriasis.

Final Protocol Submission: 12/2021
Study Completion: 05/2025
Final Report Submission: 12/2025

4268 – 2 Conduct a multicenter, randomized, parallel-group, blinded, active-controlled trial to assess the safety and pharmacokinetics of bimekizumab in pediatric subjects 6 to <18 years old with moderate to severe plaque psoriasis.

Draft Protocol Submission: 06/2023
Final Protocol Submission: 06/2024
Study/Trial Completion: 01/2031
Final Report Submission: 08/2031

FDA considers the term *final* to mean that the applicant has submitted a protocol, the FDA review team has sent comments to the applicant, and the protocol has been revised as needed to meet the goal of the study or clinical trial.[3]

Submit the protocol(s) to your IND 128707, with a cross-reference letter to this BLA. Reports of these required pediatric postmarketing studies must be submitted as a biologics license application (BLA) or as a supplement to your approved BLA with the proposed labeling changes you believe are warranted based on the data derived from these studies. When submitting the reports, please clearly mark your submission "**SUBMISSION OF REQUIRED PEDIATRIC ASSESSMENTS**" in large font, bolded type at the beginning of the cover letter of the submission.

POSTMARKETING REQUIREMENTS UNDER 505(o)

Section 505(o)(3) of the Federal Food, Drug, and Cosmetic Act (FDCA) authorizes FDA to require holders of approved drug and biological product applications to conduct postmarketing studies and clinical trials for certain purposes, if FDA makes certain findings required by the statute.

We have determined that an analysis of spontaneous postmarketing adverse events reported under subsection 505(k)(1) of the FDCA will not be sufficient to identify an unexpected serious risk of adverse pregnancy, fetal, infant and fetal outcomes as well as an unexpected serious risk of malignancy (including lymphoma), opportunistic infections, reactivation of Hepatitis B, tuberculosis, serious infections, hypersensitivity, gastrointestinal events (including inflammatory bowel disease, elevated liver enzymes/drug-induced liver injury), Major Adverse Cardiovascular Events (myocardial infarction, stroke, cardiovascular death, and sudden death) and hematologic events.

Furthermore, the active postmarket risk identification and analysis system as available under section 505(k)(3) of the FDCA will not be sufficient to assess these serious risks.

[3] See the guidance for Industry *Postmarketing Studies and Clinical Trials—Implementation of Section 505(o)(3) of the Federal Food, Drug, and Cosmetic Act (October 2019).* https://www.fda.gov/RegulatoryInformation/Guidances/default.htm.

Therefore, based on appropriate scientific data, FDA has determined that you are required to conduct the following studies:

4268 – 3 Conduct a prospective, registry based observational exposure cohort study that compares the maternal, fetal, and infant outcomes of women exposed to bimekizumab during pregnancy to an unexposed control population. The registry should be designed to detect and record major and minor congenital malformations, spontaneous abortions, stillbirths, elective terminations, small for gestational age, preterm birth, and any other adverse pregnancy outcomes. These outcomes will be assessed throughout pregnancy. Infant outcomes, including effects on postnatal growth and development, neonatal deaths, and infections, will be assessed through at least the first year of life.

The timetable you submitted on October 2, 2023, states that you will conduct this study according to the following schedule:

Draft Protocol Submission: 12/2023
Final Protocol Submission: 08/2024
Interim Report Submission: 01/2030
Study Completion: 06/2034

Final Report Submission: 06/2035

4268 – 4 Conduct an additional pregnancy study that uses a different design from the pregnancy registry (for example, a retrospective cohort study using claims or electronic medical record data with outcome validation or a case control study) to assess major congenital malformations, spontaneous abortions, stillbirths, small for gestational age, and preterm birth in women exposed to bimekizumab during pregnancy compared to an unexposed control population.

The timetable you submitted on October 2, 2023, states that you will conduct this study according to the following schedule:

Draft Protocol Submission: 12/2023
Final Protocol Submission: 12/2024
Interim Report Submission: 12/2028
Study Completion: 12/2034
Final Report Submission: 12/2035

4268 – 5 Perform a lactation study (milk only) in lactating women who have received therapeutic doses of bimekizumab to assess concentrations of bimekizumab in breastmilk using a validated assay and to assess the

effects on the breastfed infant. A mother-infant pair study may be required in the future depending on the results of this milk-only study.

The timetable you submitted on October 2, 2023, states that you will conduct this study according to the following schedule:

Draft Protocol Submission: 11/2023
Final Protocol Submission: 11/2024
Study Completion: 05/2027
Final Report Submission: 11/2028

4268 – 6 Conduct a prospective observational study to assess the long-term safety of bimekizumab treatment in US adult patients with moderate to severe plaque psoriasis. Fully ascertain and centrally verify malignancy (including lymphoma), opportunistic infections, reactivation of Hepatitis B, tuberculosis, and serious infections. Other outcomes include hypersensitivity, gastrointestinal events (including inflammatory bowel disease, elevated liver enzymes/drug-induced liver injury), Major Adverse Cardiovascular Events (myocardial infarction, stroke, cardiovascular death, and sudden death) and hematologic events. For each adverse-event outcome separately, compare incidence in bimekizumab-treated patients against reference rates internally derived from analyses conducted in patients treated with other chronic systemic treatments for moderate-to-severe plaque psoriasis. Regardless of treatment discontinuation or switch to a different treatment for plaque psoriasis, continue following patients for malignancy outcomes and possibly other adverse events with delayed onset. Enroll a sufficient number of patients to describe the frequency of the adverse events in representative U.S. patients who start treatment with bimekizumab for plaque psoriasis in the setting of routine clinical practice. Implement a plan that uses rigorous, transparent, and verifiable methods to ascertain and characterize safety events that occur during and after treatment with bimekizumab. Enroll patients over a 4-year period and plan to follow for a minimum of 8 years from time of enrollment.

The timetable you submitted on October 2, 2023, states that you will conduct this study according to the following schedule:

Draft Protocol Submission: 12/2023
Final Protocol Submission: 11/2024
Study Completion: 03/2037
Final Report Submission: 03/2038

FDA considers the term *final* to mean that the applicant has submitted a protocol, the FDA review team has sent comments to the applicant, and the protocol has been revised as needed to meet the goal of the study or clinical trial.[4]

Submit clinical protocols to your IND 128707 with a cross-reference letter to this BLA. Submit nonclinical and chemistry, manufacturing, and controls protocols and all final report(s) to your BLA. Prominently identify the submission with the following wording in bold capital letters at the top of the first page of the submission, as appropriate: **Required Postmarketing Protocol Under 505(o), Required Postmarketing Final Report Under 505(o), Required Postmarketing Correspondence Under 505(o).**

Submission of the protocols for required postmarketing observational studies to your IND is for purposes of administrative tracking only. These studies do not constitute clinical investigations pursuant to 21 CFR 312.3(b) and therefore are not subject to the IND requirements under 21 CFR part 312.

Section 505(o)(3)(E)(ii) of the FDCA requires you to report periodically on the status of any study or clinical trial required under this section. This section also requires you to periodically report to FDA on the status of any study or clinical trial otherwise undertaken to investigate a safety issue. Section 506B(a)(1) of the FDCA, as well as 21 CFR 601.70 requires you to report annually on the status of any postmarketing commitments or required studies or clinical trials.

FDA will consider the submission of your annual report under section 506B(a)(1) and 21 CFR 601.70 to satisfy the periodic reporting requirement under section 505(o)(3)(E)(ii) provided that you include the elements listed in 505(o) and 21 CFR 601.70. We remind you that to comply with 505(o), your annual report must also include a report on the status of any study or clinical trial otherwise undertaken to investigate a safety issue. Failure to submit an annual report for studies or clinical trials required under 505(o) on the date required will be considered a violation of FDCA section 505(o)(3)(E)(ii) and could result in enforcement action.

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*.[5]

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[4] See the guidance for Industry *Postmarketing Studies and Clinical Trials—Implementation of Section 505(o)(3) of the Federal Food, Drug, and Cosmetic Act (October 2019).* https://www.fda.gov/RegulatoryInformation/Guidances/default.htm.

[5] 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.[6] Information and Instructions for completing the form can be found at FDA.gov.[7]

REPORTING REQUIREMENTS

You must submit adverse experience reports under the adverse experience reporting requirements at 21 CFR 600.80.

Prominently identify all adverse experience reports as described in 21 CFR 600.80.

You must submit distribution reports under the distribution reporting requirements at 21 CFR 600.81.

You must submit reports of biological product deviations under 21 CFR 600.14. You should promptly identify and investigate all manufacturing deviations, including those associated with processing, testing, packing, labeling, storage, holding and distribution. If the deviation involves a distributed product, may affect the safety, purity, or potency of the product, and meets the other criteria in the regulation, you must submit a report on Form FDA 3486 to:

Food and Drug Administration
Center for Drug Evaluation and Research
Division of Compliance Risk Management and Surveillance
5901-B Ammendale Road
Beltsville, MD 20705-1266

Biological product deviations, sent by courier or overnight mail, should be addressed to:

Food and Drug Administration
Center for Drug Evaluation and Research
Division of Compliance Risk Management and Surveillance
10903 New Hampshire Avenue, Bldg. 51, Room 4207
Silver Spring, MD 20903

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.

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

POST APPROVAL FEEDBACK MEETING

New biological products qualify for a post approval feedback meeting. Such meetings are used to discuss the quality of the application and to evaluate the communication process during drug development and marketing application review. The purpose is to learn from successful aspects of the review process and to identify areas that could benefit from improvement. If you would like to have such a meeting with us, call the Regulatory Project Manager for this application.

If you have any questions, call Strother D. Dixon, Senior Regulatory Project Manager, at (301) 796-1015.

Sincerely,

{See appended electronic signature page}

Nikolay P. Nikolov, MD
Acting Office Director
Office of Immunology and Inflammation
Office of New Drugs
Center for Drug Evaluation and Research

ENCLOSURES:

- 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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