BLA 761373/Original 1
BLA 761425/Original 1

CORRECTED BLA APPROVAL

Samsung Bioepis Co., Ltd.
c/o ICON Clinical Research LLC
Attention: Wendy DeSpain, BSc, MBA, RAC
US Agent/Senior Director - Regulatory Affairs
4130 Parklake Avenue, Suite 400
Raleigh, NC 27612

Dear Wendy DeSpain:

Please refer to your biologics license applications (BLA) dated and received March 30, 2023 and January 29, 2024, and your amendments, submitted under section 351(k) of the Public Health Service Act for Pyzchiva (ustekinumab-ttwe) injection.

We also refer to our Approval letter dated June 28, 2024, which contained the following error: the Indications and Usage section was not visible in the Highlights of the Prescribing Information labeling.

This corrected action letter incorporates the correction of the error. The effective action date will remain June 28, 2024, the date of the original letter.

We acknowledge receipt of your major amendment to BLA 761373 dated March 15, 2024, which extended the goal date for BLA 761373 by three months.

BLA 761373 seeks licensure of:

- Pyzchiva (ustekinumab-ttwe) injection 45 mg/0.5 mL single-dose prefilled syringe for subcutaneous use as biosimilar to (b) (4) Stelara (ustekinumab) injection 45 mg/0.5 mL single-dose prefilled syringe for subcutaneous use; and
- Pyzchiva (ustekinumab-ttwe) injection 90 mg/mL single-dose prefilled syringe for subcutaneous use as biosimilar to (b) (4) Stelara (ustekinumab) injection 90 mg/mL single-dose prefilled syringe for subcutaneous use

BLA 761425 seeks licensure of Pyzchiva (ustekinumab-ttwe) injection 130 mg/26 mL single-dose vial for intravenous use as biosimilar to (b) (4) with Stelara (ustekinumab) injection 130 mg/26 mL single-dose vial for intravenous use.

(b) (4)

LICENSING

We have approved the products in your BLA 761373/Original 1 and BLA 761425/Original 1 for Pyzchiva (ustekinumab-ttwe) as biosimilar products effective this date. You are hereby authorized to introduce or deliver for introduction into interstate commerce, Pyzchiva under your existing Department of Health and Human Services U.S. License No. 2046. Pyzchiva is indicated for the treatment of:

Adult patients with:

- moderate to severe plaque psoriasis (Ps), who are candidates for phototherapy or systemic therapy
- active psoriatic arthritis (PsA)
- moderately to severely active Crohn's disease (CD)
- moderately to severely active ulcerative colitis

Pediatric patients 6 years and older with:

- moderate to severe plaque psoriasis, who are candidates for phototherapy or systemic therapy
- active psoriatic arthritis (psA).

MANUFACTURING LOCATIONS

Under this license, you are approved to manufacture ustekinumab-ttwe drug substance at (b) (4). The final

formulated drug product will be manufactured, filled, labeled, and packaged at (b) (4) You may label your product with the proprietary name, Pyzchiva, and market it as 45 mg/0.5 mL injection in a single-dose prefilled syringe and 90 mg/mL injection in a single-dose prefilled syringe for subcutaneous use and in 130 mg/26 mL injection in a single-dose vial for intravenous use.

DATING PERIOD

The dating period for Pyzchiva prefilled syringe shall be 24 months from the date of manufacture when stored at 2°C - 8°C protected from light. The dating period for Pyzchiva vial presentation shall be 18 months from the date of manufacture when stored at 2°C - 8°C protected from light. 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)

We have approved the stability protocols in your license application for the purpose of extending the expiration dating period of your drug substance and drug product under 21 CFR 601.12.

FDA LOT RELEASE

You are not currently required to submit samples of future lots of Pyzchiva 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 Pyzchiva, or in the manufacturing facilities, will require the submission of information to your BLAs for our review and written approval, consistent with 21 CFR 601.12.

APPROVAL & LABELING

We have completed our review of these applications, as amended.They are approved, effective on the date of this letter, for use as recommended in the enclosed agreed-upon labeling.

WAIVER OF ½ PAGE LENGTH REQUIREMENT FOR HIGHLIGHTS

We are waiving the requirements of 21 CFR 201.57(d)(8) regarding the length of Highlights of Prescribing Information. This waiver applies to all future supplements containing revised labeling unless we notify you otherwise.**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.

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 761373/Original 1 and BLA 761425/Original 1**." Approval of these submissions 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.

Psoriatic Arthritis

At this time, we have determined that, with respect to psoriatic arthritis in pediatric patients 0 to less than 6 years of age, no pediatric studies will be required under PREA for your BLA.

You have provided a pediatric assessment for psoriatic arthritis in pediatric patients 6 years of age and older, and nothing further is required at this time.

[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.

Plaque Psoriasis
At this time, we have determined that, with respect to plaque psoriasis in pediatric patients 0 to less than 6 years of age, no pediatric studies will be required under PREA for your BLA.

You have provided a pediatric assessment for plaque psoriasis in pediatric patients 6 years of age and older, and nothing further is required at this time.

Crohn's Disease
At this time, we have determined that, with respect pediatric patients 0 to 17 years of age with moderately to severely active Crohn's disease despite conventional therapy, no pediatric studies will be required under PREA for your BLA.

Ulcerative Colitis
At this time, we have determined that, with respect pediatric patients 0 to 17 years of age with moderately to severely active ulcerative colitis, no pediatric studies will be required under PREA for your BLA.

Age-appropriate presentation
We are deferring the required pediatric assessment for patients < 60 kg. See Deferred Pediatric Assessments below.

Deferred Pediatric Assessments
Your deferred pediatric study required by section 505B(a) of the Federal Food, Drug, and Cosmetic Act is a required postmarketing study. The status of this postmarketing study must be reported annually according to 21 CFR 601.70 and section 505B(a)(4)(C) of the Federal Food, Drug, and Cosmetic Act. This required study is listed below.

4572-1 Develop a presentation that can be used to accurately administer Pyzchiva to pediatric patients who weigh less than 60 kg.

Final Report Submission: 12/2024

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 protocols to your IND 136959 with a cross-reference letter to this BLA. Reports of this required pediatric postmarketing study must be submitted as a BLA or as a supplement to BLA 761373 with the proposed labeling changes you believe are warranted based on the data derived from this study. When submitting the reports,

[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.

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 COMMITMENTS NOT SUBJECT TO THE REPORTING REQUIREMENTS UNDER SECTION 506B

We remind you of your BLA 761425 postmarketing commitment:

4651-1 Develop an endotoxin testing method for the 5 mg/mL drug product that mitigates the low endotoxin recovery (LER) effect, submit method qualification results with 3 lots of 5 mg/mL drug product, and provide results of a LER study performed with the updated method using 3 lots of drug product. The USP <151> pyrogen test will be replaced by a suitable in vitro endotoxin method upon approval of the supplement.

The timetable you submitted on January 9, 2024, states that you will conduct this study according to the following schedule:

Final Report Submission: 01/2026

Submit nonclinical and chemistry, manufacturing, and controls protocols and all postmarketing final reports to the respective 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 the respective 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*.[4]

You must submit final promotional materials and Prescribing Information, accompanied by a Form FDA 2253, at the time of initial dissemination or publication

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

[21 CFR 314.81(b)(3)(i)]. Form FDA 2253 is available at FDA.gov.[5] Information and Instructions for completing the form can be found at FDA.gov.[6]

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.

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

If you have any questions, contact Strother D. Dixon, Senior Regulatory Project Manager at strother.dixon@fda.hhs.gov or (301) 796-1015.

Sincerely,

{See appended electronic signature page}

Tatiana Oussova, MD, MPH
Deputy Director for Safety
Division of Dermatology and Dentistry
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/

TATIANA OUSSOVA
07/04/2024 12:00:33 PM