

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

761373Orig2s000

761425Orig2s000

OTHER ACTION LETTERS



BLA 761373/Original 2
BLA 761425/Original 2

CORRECTED PROVISIONAL DETERMINATION

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 (BLAs) dated and received March 30, 2023, and January 29, 2024, and your amendments, submitted under section 351(k) of the Public Health Service (PHS) Act for Pyzchiva (ustekinumab-ttwe) injection.

We also refer to our Provisional Determination 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 interchangeable with 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 interchangeable with Stelara (ustekinumab) injection 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 interchangeable with Stelara (ustekinumab) injection 130 mg/26 mL single-dose vial for intravenous use.

These BLAs collectively propose the use of Pyzchiva (ustekinumab-ttwe) injection for adult and pediatric patients 6 years and older with moderate to severe plaque psoriasis (Ps) who are candidates for phototherapy or systemic therapy, adult and pediatric patients 6 years and older with active psoriatic arthritis (PsA), adult patients with

moderately to severely active Crohn's disease (CD), and adult patients with moderately to severely active ulcerative colitis.

For administrative purposes, we have split BLAs 761373 and 761425 as follows:

- BLA 761373/Original 1 – biosimilarity
- BLA 761373/Original 2 – interchangeability
- BLA 761425/Original 1 – biosimilarity
- BLA 761425/Original 2 – interchangeability

The subjects of this correspondence are BLA 761373/Original 2 and BLA 761425/Original 2. A separate correspondence was issued for BLA 761373/Original 1 and BLA 761425/Original 1.

All future submissions to these BLAs should specify the BLA number and the Original number to which each submission pertains.

We have completed a provisional review of this application, as amended. A final determination under sections 351(i) and 351(k) of the PHS Act that:

- Pyzchiva (ustekinumab-ttwe) injection 45 mg/0.5 mL single-dose prefilled syringe for subcutaneous use would be interchangeable with Stelara (ustekinumab) injection 45 mg/0.5 mL single-dose prefilled syringe for subcutaneous use
- Pyzchiva (ustekinumab-ttwe) injection 90 mg/mL single-dose prefilled syringe for subcutaneous use would be interchangeable with Stelara (ustekinumab) injection 90 mg/mL single-dose prefilled syringe for subcutaneous use
- Pyzchiva (ustekinumab-ttwe) injection 130 mg/26 mL (5 mg/mL) single-dose vial for intravenous use would be interchangeable with Stelara (ustekinumab) injection 130 mg/26 mL (5 mg/mL) single-dose vial for intravenous use

is currently subject to an unexpired period of exclusivity for the first interchangeable biosimilar biological products, and thus may not be made before the exclusivity period has expired. See section 351(k)(6) of the PHS Act. We have not identified any deficiencies that would justify a complete response action at this time; however, we also cannot approve your application because of the unexpired period of first interchangeable exclusivity. We have therefore provisionally determined that your 351(k) application meets the interchangeability criteria under section 351(k) of the PHS Act.

This provisional determination is based upon information available to the Agency at this time (i.e., information in your application and that the manufacturing of the biological product complies with the standards established in the BLA as well as the requirements

in applicable regulations). This determination is subject to change on the basis of any new information that may come to our attention.

To obtain approval of this application, submit an amendment no more than six months prior to the date you believe that your application will be eligible for approval. In your cover letter, clearly identify your amendment as “**REQUEST FOR APPROVAL**”. This amendment should provide the legal/regulatory basis for your request for approval and should include a copy of any relevant supporting documentation, as appropriate. In addition to a safety update, the amendment should also identify changes, if any, in the application, i.e., updated labeling; chemistry, manufacturing, and controls data; and risk evaluation and mitigation strategy (REMS). If there are no changes, clearly state so in your cover letter. Any changes require our review before approval, and the goal date for our review will be set accordingly.

BLA 761373/Original 2 and BLA 761425/Original 2 are not approved and Pyzchiva (ustekinumab-ttwe) cannot be legally marketed as an interchangeable biosimilar product unless and until you have been notified in writing that BLA 761373/Original 2 and BLA 761425/Original 2 are approved after any necessary additional review. Enclosed are the currently agreed upon labeling (text for the Prescribing Information, Medication Guide, Instructions for Use, Carton and Container labeling). If you believe that there are grounds for issuing the approval letter before the expiration of the exclusivity period, you should amend your application accordingly.

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 in pediatric patients unless this requirement is waived, deferred, or inapplicable.

Refer to the BLA Approval letter for BLA 761373/Original 1 and BLA 761425/Original 1 for required pediatric assessments.

**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 clinical protocols to your IND 136959 for this product. 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.**”

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
 - o Prescribing Information
 - o Medication Guide
 - o 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 11:57:54 AM