BLA 761338/Original 1

BLA APPROVAL

CELLTRION, Inc.
c/o Parexel International
Attention: Ally Danta
Regulatory Affairs Consultant
2520 Meridian Parkway, Suite 100
Durham, NC 27713

Dear Ally Danta:

Please refer to your biologics license application (BLA) dated and received June 30, 2023, and your amendments, under section 351(k) of the Public Health Service Act for Steqeyma (ustekinumab-stba) injection. We acknowledge receipt of your amendment dated October 16, 2024, which constituted a complete response to our September 30, 2024, action letter.

BLA 761338 seeks licensure of:

- Steqeyma (ustekinumab-stba) injection 45 mg/0.5 mL single-dose prefilled syringe for subcutaneous use as biosimilar to [redacted] (b) (4) Stelara (ustekinumab) injection 45 mg/0.5 mL single-dose prefilled syringe for subcutaneous use,

- Steqeyma (ustekinumab-stba) injection 90 mg/mL single-dose prefilled syringe for subcutaneous use as biosimilar to [redacted] (b) (4) Stelara (ustekinumab) injection 90 mg/mL single-dose prefilled syringe for subcutaneous use, and

- Steqeyma (ustekinumab-stba) injection 130 mg/26 mL single-dose vial for intravenous use as biosimilar to [redacted] (b) (4) Stelara (ustekinumab) injection 130 mg/26 mL single-dose vial for intravenous use.

For administrative purposes, we have split BLA 761338 as follows:

- BLA 761338/Original 1 – biosimilarity [redacted] (b) (4)

The subject of this action letter is BLA 761338/Original 1. [redacted] (b) (4) [redacted] (b) (4)

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

LICENSING

We have approved your BLA for Steqeyma (ustekinumab-stba), effective this date. You are hereby authorized to introduce or deliver for introduction into interstate commerce, Steqeyma under your existing Department of Health and Human Services U.S. License No. 1996. Steqeyma (ustekinumab-stba) is indicated for treatment of:

Adult patients with:

- moderate to severe plaque psoriasis (PsO) 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 (UC)

Pediatric patients 6 years and older with:

- moderate to severe plaque psoriasis (PsO) who are candidates for phototherapy or systemic therapy
- active psoriatic arthritis (PsA)

MANUFACTURING LOCATIONS

Under this license, you are approved to manufacture ustekinumab-stba drug substance at CELLTRION, Inc. (b) (4) Incheon, Republic of Korea (FEI 3005241015). The final formulated product will be manufactured, filled, labeled, and packaged at CELLTRION Pharm, Inc., Cheongju, Republic of Korea (FEI 3012279978) (b) (4) (b) (4) You may label your product with the proprietary name, Steqeyma, and market it in 45 mg/0.5 mL injection, 90 mg/1.0 mL injection and 130 mg/26 mL injection.

DATING PERIOD

The dating period for Steqeyma shall be 36 months from the date of manufacture when stored at 5±3 °C. 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 Steqeyma 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 Steqeyma, or in the manufacturing facilities, will require the submission of information to your biologics license application for our review and written approval, consistent with 21 CFR 601.12.

APPROVAL AND 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 with minor editorial revisions listed below and reflected in the enclosed labeling.

HIGHLIGHTS OF PRESCRIBING INFORMATION

- Update the Initial U.S. Approval to 2024.
- Update the Revised date to 12/2024.

MEDICATION GUIDE

- Add Steqeyma website.
- Update the Approved date to 12/2024.

INSTRUCTIONS FOR USE

- Update the Approved date to 12/2024.

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] 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.*[2]

The SPL will be accessible via publicly available labeling repositories.

[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 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 *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 761338/Original 1** 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.

Plaque Psoriasis and Psoriatic Arthritis

At this time, we have determined that, with respect to plaque psoriasis and 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 plaque psoriasis and psoriatic arthritis in pediatric patients 6 years of age and older who weigh 60 kg or more. We are deferring the required pediatric assessment for patients < 60 kg. See Deferred Pediatric Assessments below.

Crohn's Disease and Ulcerative Colitis

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 and with moderately to severely active ulcerative colitis, no pediatric studies will be required under PREA for your BLA.

Age-appropriate presentation

The presentations of Steqeyma being approved are not designed to allow for accurate and safe administration of doses less than 45 mg, which impacts children who weigh less than 60 kg. For accurate weight-based dosing, an age-appropriate formulation (presentation) is required.

We are deferring the required pediatric assessment for patients < 60 kg as described below.

Deferred Pediatric Assessments
Your deferred pediatric study required under section 505B(a) of the Federal Food, Drug, and Cosmetic Act is required postmarketing study(ies). 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.

4765-1 Develop a presentation that can be used to accurately administer Steqeyma (ustekinumab-stba) to pediatric patients who weigh less than 60 kg.

Final Report Submission: 06/2025

Reports of this required pediatric postmarketing study must be submitted as a supplement to BLA 761338 with the proposed labeling changes you believe are warranted based on the data derived from this study. 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 COMMITMENTS NOT SUBJECT TO THE REPORTING REQUIREMENTS UNDER SECTION 506B

We remind you of your postmarketing commitments:

4765-2 To repeat the bacterial retention study (b) (4) with CT-P43 drug product (5 mg/mL) to verify that the bacterial retention performance (b) (4) is not impacted by contact with the drug product solution (b) (4)

The timetable you submitted on December 10, 20242024, states that you will conduct this study according to the following schedule:

Final report submission: 03/2025

Submit clinical protocols to your IND 146085 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]

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

You must submit adverse experience reports under the adverse experience reporting requirements for licensed biological products (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 for licensed biological products (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:

[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

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.

If you have any questions, contact H. F. Van Horn III, PharmD, MBA, Senior Regulatory Project Manager, at Howard.VanHornIII@fda.hhs.gov.

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

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/

TATIANA OUSSOVA
12/17/2024 03:59:49 PM