Cross-Discipline Team Leader and Multidisciplinary Evaluation and Review Memo

Date	See Electronic Stamp Date
From	Carol Kim, Pharm.D. (Clinical Reviewer, OTBB) Cristina Ausin, Ph.D. (CDTL, OTBB) Oussova, Tatiana, M.D. (Division Signatory, DDD)
Application Type	BLA Supplement
Application Number	761338-S003
Received Date	February 14, 2025
BsUFA Goal Date	June 13, 2025
Division/Office	Division of Dermatology and Dentistry (DDD) Office of Immunology and Inflammation (OII) in collaboration with the Division of Rheumatology and Transplant Medicine (DRTM)/OII and Division of Gastroenterology (DG)/OII
Review Completion Date	See DARRTS stamp date
Product Code Name	CT-P43
Nonproprietary Name	ustekinumab-stba
Proprietary Name	Steqeyma
Pharmacologic Class	IL12/23 ANTAGONIST
Applicant	Celltrion Inc.
Applicant Proposed Indication(s)	• Moderate to severe plaque psoriasis (PsO) in adult patients and pediatric patients 6 years of age and older who are candidates for phototherapy or systemic therapy; • Active psoriatic arthritis (PsA) in adult patients and pediatric patients 6 years of age and older; • Moderately to severely active Crohn's Disease (CD) in adults • Moderately to severely active Ulcerative Colitis (UC) in adults
Recommendation on Regulatory Action	Approval of Steqeyma (ustekinumab-stba) 45 mg/0.5 mL injection for subcutaneous use in a single dose-vial as interchangeable with U.S.-Stelara (ustekinumab) 45 mg/0.5 mL injection for subcutaneous use in a single-dose vial to fulfill the PMR requirement that the Applicant develop a presentation that can be used to accurately administer Steqeyma to pediatric patients who weigh less than 60 kg.

1. Introduction

Steqeyma (ustekinumab-stba) is a human interleukin-12 and -23 antagonist biosimilar interchangeable to US-Stelara (ustekinumab).

On December 17, 2024, under section 351(k) of the Public Health Service (PHS) Act, the Agency approved CT-P43 (Steqeyma) under Original 1 as a biosimilar to US-Stelara for the following strengths and presentations:

- Steqeyma (ustekinumab-stba) 45 mg/0.5 mL injection for subcutaneous use in a PFS as biosimilar to US-Stelara 45 mg/0.5 mL injection for subcutaneous use in a PFS,
- Steqeyma (ustekinumab-stba) 90 mg/mL injection for subcutaneous use in a PFS as biosimilar to US-Stelara 90 mg/mL injection for subcutaneous use in a PFS,
- Steqeyma (ustekinumab-stba) 130 mg/26 mL injection for subcutaneous use in a single-dose vial as biosimilar to US-Stelara 130 mg/26 mL injection for intravenous use in single-dose vial.

In addition, on December 17, 2024, FDA made a provisional determination under Original 2 that:

- Steqeyma (ustekinumab-stba) 45 mg/0.5 mL injection for subcutaneous use in a PFS would be interchangeable with US-Stelara 45 mg/0.5 mL injection for subcutaneous use in a PFS,
- Steqeyma (ustekinumab-stba) 90 mg/mL injection for subcutaneous use in a PFS would be interchangeable with US-Stelara 90 mg/mL injection for subcutaneous use in a PFS,
- Steqeyma (ustekinumab-stba) 130 mg/26 mL injection for subcutaneous use in a single-dose vial would be interchangeable with US-Stelara 130 mg/26 mL injection for intravenous use in single-dose vial, but for unexpired first interchangeable exclusivity.

On February 14, 2025, the Applicant submitted supplement 003 in response to PREA PMR 4765-01 seeking licensure of Steqeyma (ustekinumab-stba) 45 mg/0.5 mL injection for subcutaneous use in a single-dose vial as biosimilar to and interchangeable with US-Stelara (ustekinumab) 45mg/0.5 mL injection for subcutaneous use in a single-dose vial. With this submission, the Applicant submitted the following rationale with their prior approval supplement (PAS) to BLA 761338:

> *"…to add 45 mg/0.5 mL single-dose vial for subcutaneous use as biosimilar to and interchangeable with Stelara (ustekinumab) injection 45 mg/0.5 mL single-dose vial for subcutaneous use. Addition of 45 mg/0.5 mL single-dose vial presentation can be used to accurately administer Steqeyma (ustekinumab-stba) to pediatric patients who weigh less than 60 kg".*

No new clinical information is included in the Applicant's sBLA submission, which is the subject of this review.

On May 28, 2025, the following interchangeable products were approved under Original 2. For details, refer to Action Package dated April 30, 2025 in DARRTS:

- Steqeyma (ustekinumab-stba) 45 mg/0.5 mL and 90 mg/mL injection, for subcutaneous use in a single-dose prefilled syringe (PFS) as interchangeable to US-Stelara (ustekinumab) 45 mg/0.5 mL and 90 mg/mL injection, for subcutaneous use in a PFS, respectively
- Steqeyma (ustekinumab-stba) 130 mg/26 mL injection for intravenous use in a single-dose vial as interchangeable to US-Stelara (ustekinumab) 130 mg/26 mL injection for intravenous use in a single-dose vial

The "Biosimilar Multidisciplinary Evaluation and Review" (BMER) documenting the Agency's review of the original application (Original 1) dated December 17, 2024, and the CDTL memo documenting the Agency's review of Original 2 dated April 30, 2025, are incorporated herein by reference. Refer to them for additional information.

2. Product Quality

The Office of Pharmaceutical Manufacturing Assessment (OPMA) team in the Office of Pharmaceutical Quality (OPQ) reviewed the submission regarding the addition of new presentation 45 mg/0.5 mL vial for subcutaneous use and stated the following:

> *"This BLA supplement was reviewed from a sterility assurance perspective and is recommended for Approval.*
> *• Manufacturing Facility Assessment Recommendation: Approval*
> *• Product quality aspects not related to microbial control and facilities should be reviewed by OPQAIII."*

The Office of Product Quality Assessment III (OPQA III) team OPQ reviewed the submission and stated the following:

> *"This BLA supplement is recommended for approval from a product quality perspective. OPMA performed a separate assessment of this submission from microbiology and facility perspectives and recommend approval of the supplement."*

The OPQ team has determined that the Applicant has provided adequate data and information in the BLA, including this supplement, to support a demonstration that CT-P43 (Steqeyma) 45 mg/0.5 mL injection for subcutaneous use in a single-dose vial is

highly similar to US-Stelara 45 mg/0.5 mL injection for subcutaneous use in a single-dose vial, notwithstanding minor differences in clinically inactive components.

OPQ recommends approval of this PAS from a product quality perspective.

3. Nonclinical Pharmacology/Toxicology

No new nonclinical pharmacology/toxicology information was submitted nor required for this sBLA. There are no nonclinical pharmacology/toxicology issues that would preclude approval of this supplement.

4. Clinical Pharmacology

No new clinical pharmacology information was submitted nor required under this sBLA. There are no clinical pharmacology issues that would preclude approval this supplement.

5. Clinical/Statistical- Efficacy

No new clinical information was submitted under this sBLA. There are no clinical/statistical efficacy issues that would preclude approval of this supplement.

6. Safety

No new clinical information was submitted under this sBLA. There are no clinical safety issues that would preclude approval of this supplement.

7. Advisory Committee Meeting

Not applicable.

8. Other Relevant Regulatory Issues

Not applicable

9. Labeling

DDD consulted the Division of Medical Policy Programs (DMPP) and the Office of Prescription Drug Promotion (OPDP) regarding patient labeling on February 21, 2025,

Division of Medical Policy Programs (DMPP) review team, provided a collaborative patient labeling review of the Medication Guide (MG) and Instructions for Use (IFU). The MG and IFUs are acceptable with recommended changes. [Reference ID: 5586987]

The review team evaluated updated labeling (5/28/2025 and 6/4/2025 submissions) for BLA 761338/S003 and found it to be acceptable.

Other Labeling Recommendations

It has been determined that the proposed labeling is compliant with Physician Labeling Rule (PLR) and Pregnancy and Lactation Labeling Rule (PLLR), is clinically meaningful and scientifically accurate, and conveys the essential scientific information needed for safe and effective use of the product.

10. Pediatrics

A presentation that could be used to directly and accurately administer Steqeyma to pediatric patients over 6 years of age and with a body weight of less than 60 kg (as required by PREA) was not included in the original 351(k) biosimilar application. At that time, only the 45 mg/0.5 mL PFS for subcutaneous use, 90 mg/mL PFS for subcutaneous use, and the 130 mg/26 mL vial for intravenous use were available, and development of the pediatric presentation for patients weighing less than 60 kg was deferred. At the time of the approval of the original BLA, a postmarketing requirement (PMR) for a pediatric presentation was issued, PMR 4765-1.

On February 14, 2025, the Applicant submitted supplement 003 to add a 45 mg/0.5 mL single-dose vial for subcutaneous use for weight-based dosing of pediatric patients with a body weight of less than 60 kg and to fulfill the PREA PMR. The applicant also included the latest version of “Revised Agreed Amended Initial Pediatric Study Plan (iPSP)” dated August 30, 2024 (version 6.0, IND SN0046) reviewed by the FDA (refer to Amended Initial Pediatric Study Plan-Written Response dated 1/17/2023 in DARRTs). According to Pediatric Study Plan (PSP) Closure Form dated December 12, 2024, the plan was previously discussed at the PeRC on June 4, 2024, and there has not been a change to the pediatric plan for the current supplement.

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.

The Applicant has fulfilled the PREA PMR with the development and submission of the current supplement for Steqeyma, 45 mg/0.5 mL injection for subcutaneous use in a single-dose vial.

PREA PMR 4765-1: Develop a presentation that can be used to accurately administer CT-P43 to pediatric patients who weigh less than 60 kg.

Regarding PREA Requirements at the time of approval for CT-P43 (Steqeyma) BLA 761338, the Agency determined the following:

- The Applicant provided pediatric assessments for psoriatic arthritis and plaque psoriasis in pediatric patients 6 years of age and older, and nothing further was required at the time;
- With respect to psoriatic arthritis and plaque psoriasis in pediatric patients 0 to less than 6 years of age, no pediatric studies were required under PREA for the BLAs;

The labeling for US-Stelara does not include adequate pediatric information and is not licensed for the treatment of:

- Plaque psoriasis in pediatric patients < 6 years of age
- Psoriatic arthritis in pediatric patients < 6 years of age
- Crohn's disease in pediatric patients 0-17 years of age
- Ulcerative colitis in pediatric patients 0-17 years of age

Therefore, no pediatric studies would be required under PREA for this sBLA at this time.

On April 29, 2025, PeRC agreed with the team's assessment that the Applicant fulfilled the PREA PMR requirement with the development of a presentation that can be used to accurately administer Steqeyma (CT-P43) to pediatric patients who weigh less than 60 kg.

11. Postmarketing Requirements

The Applicant has fulfilled the following PMR:

PREA PMR 4765-1: Develop a presentation that can be used to accurately administer CT-P43 to pediatric patients who weigh less than 60 kg.

12. Recommended Regulatory Action

FDA has determined that the applicant has provided adequate data and information in the BLA, including this supplement, to satisfy PREA PMR 4765-1 and demonstrated that Steqeyma (CT-P43) 45 mg/0.5 mL injection for subcutaneous use in a single-

dose vial is highly similar to US-Stelara 45 mg/0.5 mL injection for subcutaneous use in a single-dose vial, notwithstanding minor differences in clinically inactive components. FDA has further determined that the data and information provided by the applicant in the BLA and this supplement support a demonstration of no clinically meaningful differences between Steqeyma (CT-P43) 45 mg/0.5 mL injection for subcutaneous use in a single-dose vial and US-Stelara 45 mg/0.5 mL injection for subcutaneous use in a single-dose vial. The conditions of use for Steqeyma (CT-P43) 45 mg/0.5 mL single-dose vial have been previously approved for US-Stelara, and the strength, dosage form, and route of administration of Steqeyma 45 mg/0.5 mL single-dose vial are the same as those of US-Stelara 45 mg/0.5 mL single-dose vial. The Applicant has provided adequate data and information to support a demonstration that Steqeyma 45 mg/0.5 mL single-dose vial can be expected to produce the same clinical results as those of US-Stelara 45 mg/0.5 mL single-dose vial in any given patient. The risk in terms of safety or diminished efficacy of alternating or switching between use of the Steqeyma 45 mg/0.5 mL single-dose vial and US-Stelara 45 mg/0.5 mL single-dose vial is not greater than the risk of using US-Stelara 45 mg/0.5 mL single-dose vial without such alternation or switch.

The FDA review team recommends Approval of the sBLA 761338-003 for Steqeyma (CT-P43) 45 mg/0.5 mL injection for subcutaneous use in a single-dose vial as interchangeable with US-Stelara 45 mg/0.5 mL injection for subcutaneous use in a single-dose vial.

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/

CAROL Y KIM
06/12/2025 07:38:43 AM

CRISTINA AUSIN
06/12/2025 07:39:50 AM

TATIANA OUSSOVA
06/12/2025 08:45:33 AM