BLA 761343/S-005

SUPPLEMENT APPROVAL
FULFILLMENT OF POSTMARKETING REQUIREMENT

Alvotech USA Inc.
C/O PharmaLex US Corporation
c/o Cencora
Attention: Vandan Patel
Sr. Specialist, Regulatory Affairs
1 West 1st Avenue
Conshohocken, PA 19428

Dear Vandan Patel:

Please refer to your supplemental biologics license application (sBLA) dated and received April 19, 2024, and your amendments, submitted under section 351(k) of the Public Health Service Act for Selarsdi (ustekinumab-aekn) injection.

We acknowledge receipt of your amendment dated October 31, 2024, which constituted a complete response to our October 18, 2024, action letter.

This Prior Approval sBLA provides for the addition of a Selarsdi (ustekinumab-aekn) injection 45 mg/0.5 mL single-dose vial for subcutaneous use as a biosimilar to US-licensed Stelara (ustekinumab) injection 45 mg/0.5 mL single-dose vial for subcutaneous use and updates to labeling for Selarsdi and unbranded biological product labeling for Ustekinumab-aekn.

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, as described at FDA.gov,[1] that is identical to the enclosed labeling (text for the Prescribing Information,

[1] http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm

Instructions for Use, Medication Guide) and include the labeling changes proposed in any pending "Changes Being Effected" (CBE) supplements.

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.

Also within 14 days, amend all pending supplemental applications that include labeling changes for this BLA, including pending "Changes Being Effected" (CBE) supplements, for which FDA has not yet issued an action letter, with the content of labeling [21 CFR 601.12(f)] in Microsoft Word format that includes the changes approved in this supplemental application, as well as annual reportable changes. To facilitate review of your submission, provide a highlighted or marked-up copy that shows all changes, as well as a clean Microsoft Word version. The marked-up copy should provide appropriate annotations, including supplement number(s) and annual report date(s).

CARTON AND CONTAINER LABELING

We acknowledge your December 16, 2024, submission containing final printed carton and container labeling.

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 note that you have fulfilled the pediatric assessment requirement for all relevant pediatric age groups for this application.

FULFILLMENT OF POSTMARKETING REQUIREMENT(S)/COMMITMENT(S)

We have received your submissions dated April 19, 2024, and October 31, 2024, containing the final report(s) for the following postmarketing requirement listed in the April 16, 2024, approval letter for BLA 761343.

4623-1	Develop a presentation that can be used to directly and accurately administer Selarsdi (ustekinumab-aekn) to pediatric patients who weigh less than 60 kg.

[2] We update guidances periodically. For the most recent version of a guidance, check the FDA Guidance Documents Database https://www.fda.gov/RegulatoryInformation/Guidances/default.htm.

We have reviewed your submission and conclude that the above requirement was fulfilled.

We remind you that there are postmarketing commitments listed in the October 18, 2024, approval letter that are still open.

POSTMARKETING COMMITMENTS NOT SUBJECT TO THE REPORTING REQUIREMENTS UNDER SECTION 506B

We remind you of your postmarketing commitments:

4801-01 To implement (b) (4) the control strategy for (b) (4) in the drug product (DP) manufacturing process of AVT04-DP Vial 45. Update Sections 3.2.P.3.3 Description of Manufacturing Process and Process Controls and 3.2.P.3.4 Control of Critical Steps and Intermediate with the appropriate information on DP manufacturing process step (b) (4) Provide justification(s) for the selected process (b) (4) in ensuring consistent (b) (4) concentrations during DP manufacturing process and in the final drug product, AVT04-DP Vial 45.

The timetable you submitted on December 23, 2024, states that you will conduct this study according to the following schedule:

Final Report Submission: 03/25

4801-02 To implement a method for drug product (DP) gross content per vial with upper and lower limits in the DP release specification for AVT04-DP Vial 45. Submit the final study report that will include the description of the analytical method, method verification/validation to support that the method is suitable to test the DP gross content per vial, and data and information to support the specification.

The timetable you submitted on December 23, 2024, states that you will conduct this study according to the following schedule:

Final Report Submission: 10/25

4801-03 Update the acceptance criteria for extractable volume from single to two decimal points for release and shelf-life test results for AVT04-DP Vial 45 to ensure that for each released DP lot the labeled dose of 0.5 mL can be withdrawn and administered to the patients throughout the shelf-life of the product.

The timetable you submitted on December 23, 2024, states that you will conduct this study according to the following schedule:

Final Report Submission: 03/25

4801-04 To provide results from the real-world shipping study for AVT04-DP Vial 45 (b) (4) to ensure that the quality of the drug product and integrity of the container closure system are maintained until it reaches the end-user. Submit the final study report, including data for the product quality attributes and shipping container temperatures (internal, external), from the drug product shipping studies performed per the real time temperature monitoring study protocol for AVT04- (b) (4) vial presentation, (b) (4) to qualify the commercial shipping process.

The timetable you submitted on December 23, 2024, states that you will conduct this study according to the following schedule:

Final Report Submission: 06/25

4801-05 To validate (b) (4) in a new bacterial retention study (b) (4) will be controlled within the (b) (4) limit. (b) (4)

The timetable you submitted on January 21, 2025, states that you will conduct this study according to the following schedule:

Final Report Submission: 10/25

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 601.12(f)(4)]. 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

We remind you that you must comply with reporting requirements for an approved BLA (in 21 CFR 600.80 and in 21 CFR 600.81).

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 Andrew Chi, PharmD, Regulatory Project Manager, at (301) 796-8597 or email at andrew.chi@fda.hhs.gov.

Sincerely,

{See appended electronic signature page}

Gordana Diglisic, MD
Associate Director for Therapeutic Review
Division of Dermatology and Dentistry
Office of Immunology and Inflammation
Office of New Drugs
Center for Drug Evaluation and Research

[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

ENCLOSURE(S):
Branded Product Labeling

- Content of Labeling
  - Prescribing Information
  - Medication Guide
  - Instructions for Use
- Carton and Container Labeling

Unbranded Biological Product Labeling

- 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/

GORDANA DIGLISIC
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