BLA 761343/S-002

SUPPLEMENT APPROVAL

Alvotech USA Inc.
C/O PharmaLex US Corporation, Authorized U.S. Agent
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.

This Category D Prior Approval supplemental biologics license application provides for the addition of:

- Selardsdi (ustekinumab-aekn) injection 130 mg/26 mL single-dose vial for intravenous use as a biosimilar to US-licensed Stelara (US-Stelara) injection 130 mg/26 ml single-dose vial for intravenous use
- (b) (4)
- The following indications: treatment of adult patients with moderately to severely active Crohn's disease (CD) and moderately to severely active ulcerative colitis (UC)

For administrative purposes, we have designated your submission as follows:

- BLA 761343/S-002 – Addition of Selarsdi 130 mg/26 mL in a vial and approval for the treatment of adult patients with moderately to severely active CD and moderately to severely active UC
- (b) (4)

The subject of this action letter is BLA 761343/S-002. (b) (4)

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

- Included revision date in Highlights of Prescribing Information
- Included revision date in Medication Guide

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

[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 https://www.fda.gov/RegulatoryInformation/Guidances/default.htm.

CARTON AND CONTAINER LABELING

We acknowledge your October 10, 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.

Crohn's Disease
At this time, we have determined that, with respect to this indication, no pediatric studies will be required under PREA for your sBLA.

Ulcerative Colitis
At this time, we have determined that, with respect to this indication, no pediatric studies will be required under PREA for your sBLA.

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

We remind you of your postmarketing commitments:

4720-01 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 130. 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 October 1, 2024, states that you will conduct this study according to the following schedule:

Final Report Submission: 10/2025

4720-02 To provide results from the real-world shipping study for AVT04-DP Vial 130 (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, (b) (4)

(b) (4)

The timetable you submitted on October 1, 2024, states that you will conduct this study according to the following schedule:

Final Report Submission: 06/2025

4720-03 To perform a leachables study on AVT04-DP Vial 130 in the commercial container closure system to identify and quantify any potential leachables using the appropriate test methods at 4.5 months (upright, DP batch P125811PV), 17 months (upright, DP batch P125802E) and 18 months (inverted, DP batch P125802E) of storage at 2-8°C. Submit the final study report with the results of the leachables study, toxicological risk assessment for the identified leachables in the drug product and assessment of potential impact of leachable(s) on product quality and safety of the patients.

The timetable you submitted on October 1, 2024, states that you will conduct this study according to the following schedule:

Final Report Submission: 01/2025

4720-04 To perform a real-time leachables study using the commercial container closure system with AVT04-DP Vial 130 engineering lots (P125806PV, P125807PV, and P125808PV) stored at the long-term storage condition of 2-8°C and placed in the worse-case orientation for potential leachables to identify and quantify any potential leachables using the appropriate test methods at initial, the end of the shelf-life and intermediate time points. Submit the final study report with the results of the leachable study, toxicological risk assessment (TRA) for identified leachables in the drug product and assessment of potential impact of leachable(s) on product quality and safety of the patient.

The timetable you submitted on October 1, 2024, states that you will conduct this study according to the following schedule:

Final Report Submissions:
T12 leachables report and corresponding TRA assessment: 02/2026
T36 leachables report and corresponding TRA assessment: 02/2028
T48 leachables report and corresponding TRA assessment: 02/2029

4720-05 To implement [redacted] for the 130mg presentation.

The timetable you submitted on October 18, 2024, states that you will conduct this study according to the following schedule:

Final Report Submission: 10/2025

4720-06 To conduct depyrogenation validation studies [redacted] used for depyrogenation and sterilization.

The timetable you submitted on October 18, 2024, states that you will conduct this study according to the following schedule:

Final Report Submission: 10/2025

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**."

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).

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

ENCLOSURE(S):

- Content of Labeling
  - Prescribing Information
  - Medication Guide
- 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
10/18/2024 02:58:53 PM