BLA 761343

BLA APPROVAL

Alvotech USA Inc.
PharmaLex US Corporation
c/o AmerisourceBergen
Attention: Sheela J. Mitta
US Agent for Alvotech USA Inc.
1 West 1st Avenue
Conshohocken, PA 19428

Dear Vandan Patel:

Please refer to your biologics license application (BLA) dated October 11, 2022, received October 11, 2022, and your amendments, submitted under section 351(k) of the Public Health Service Act for Selarsdi (ustekinumab-aekn) injection.

This BLA seeks licensure of Selarsdi (ustekinumab-aekn) injection 45 mg/0.5 mL for subcutaneous use in a single-dose prefilled syringe as biosimilar to Stelara (ustekinumab) injection 45 mg/0.5 mL for subcutaneous use in a single-dose prefilled syringe, and Selarsdi (ustekinumab-aekn) injection 90 mg/mL for subcutaneous use in a single-dose prefilled syringe as biosimilar to Stelara (ustekinumab) injection 90 mg/mL for subcutaneous use in a single-dose prefilled syringe.

We acknowledge receipt of your resubmission dated October 16, 2023, which constituted a complete response to our October 11, 2023, action letter.

LICENSING

We have approved your BLA for Selarsdi (ustekinumab-aekn) effective this date. You are hereby authorized to introduce or deliver for introduction into interstate commerce, Selarsdi under your existing Department of Health and Human Services U.S. License No. 2225. Selarsdi is indicated for the treatment of:

Adult patients with:

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

Pediatric patients 6 years of age 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-aekn drug substance at Alvotech hf, in Sæmundargata 15-19, Reykjavik, 102, Iceland. The final formulated drug product will be manufactured and filled at Alvotech hf, Sæmundargata 15-19, Reykjavik, 102, Iceland and assembled, labeled, and packaged at (b) (4) You may label your product with the proprietary name, Selarsdi, and market it in 45 mg/0.5 mL and 90 mg/mL injection in a single-dose pre-filled syringe (PFS).

DATING PERIOD

The dating period for Selarsdi shall be 24 months from the date of manufacture when stored at 5°C ±3°C, including out of fridge storage at 30°C (b) (4) for a maximum of 30 days at once. 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.

We have approved the stability protocols in your license application for the purpose of extending the expiration dating period of your drug substance and drug product under 21 CFR 601.12.

FDA LOT RELEASE

You are not currently required to submit samples of future lots of Selarsdi 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 Selarsdi, or in the manufacturing facilities, will require the submission of information to your BLA for our review and written approval, consistent with 21 CFR 601.12.

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.[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 (October 2009)*.[2]

The SPL will be accessible via publicly available labeling repositories.

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 *SPL Standard for Content of Labeling Technical Qs & As.* For administrative purposes, designate this submission "**Final Printed Carton and Container Labeling for approved BLA 761343**." 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.

Psoriatic Arthritis
At this time, we have determined that, with respect to 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 psoriatic arthritis in pediatric patients 6 years of age and older, and nothing further is required at this time.

Plaque Psoriasis
At this time, we have determined that, with respect to plaque psoriasis in pediatric patients 0 to less than 6 years of age, no pediatric studies will be required under PREA for your BLA.

[1] See 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.

You have provided a pediatric assessment for plaque psoriasis in pediatric patients 6 years of age and older, and nothing further is required at this time.

Age-appropriate presentation
We are deferring the required pediatric assessment for patients < 60 kg. See Deferred Pediatric Assessments below.

Deferred Pediatric Assessments
Your deferred pediatric studies required under section 505B(a) of the Federal Food, Drug, and Cosmetic Act are required postmarketing studies. The status of these postmarketing studies must be reported annually according to 21 CFR 601.28 and section 505B(a)(3)(C) of the Federal Food, Drug, and Cosmetic Act. These required studies are listed below.

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.

Final Report Submission: 10/2024

Submit the protocols to your IND 148203, with a cross-reference letter to this BLA. Reports of these required pediatric postmarketing studies must be submitted as a BLA or as a supplement to your approved BLA with the proposed labeling changes you believe are warranted based on the data derived from these studies. 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.

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]

[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

REPORTING REQUIREMENTS

You must submit adverse experience reports under the adverse experience reporting requirements at 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 at 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:

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, call Sascha Randolph, Regulatory Project Manager, at (301) 796-8546.

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
  - 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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