U.S. FOOD & DRUG ADMINISTRATION

BLA 761299/S-007

SUPPLEMENT APPROVAL

Alvotech USA Inc.
c/o PharmaLex US Corporation
c/o Cencora
Attention: Vandan Patel
Senior 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 February 26, 2024, and your amendments, submitted under section 351(k) of the Public Health Service Act for Simlandi (adalimumab-ryvk) injection.

This Prior Approval sBLA seeks licensure of Simlandi (adalimumab-ryvk) injection for subcutaneous use as interchangeable with US-licensed Humira (US-Humira) (adalimumab) injection for subcutaneous use as follows:

(b) (4)

- Simlandi 40 mg/0.4 mL in a PFS as interchangeable with US-Humira 40 mg/0.4 mL in a PFS.

(b) (4)

This sBLA also proposes (b) (4)

Simlandi is licensed as interchangeable to US-licensed Humira for the following indications:

- Rheumatoid Arthritis (RA): reducing signs and symptoms, inducing major clinical response, inhibiting the progression of structural damage, and improving physical function in adult patients with moderately to severely active RA.
- Juvenile Idiopathic Arthritis (JIA): reducing signs and symptoms of moderately to severely active polyarticular JIA in patients 2 years of age and older.

- Psoriatic Arthritis (PsA): reducing signs and symptoms, inhibiting the progression of structural damage, and improving physical function in adult patients with active PsA.
- Ankylosing Spondylitis (AS): reducing signs and symptoms in adult patients with active AS.
- Crohn's Disease (CD): treatment of moderately to severely active Crohn's disease in adults and pediatric patients 6 years of age and older.
- Ulcerative Colitis (UC): treatment of moderately to severely active ulcerative colitis in adult patients.
- Plaque Psoriasis (Ps): treatment of adult patients with moderate to severe chronic plaque psoriasis who are candidates for systemic therapy or phototherapy, and when other systemic therapies are medically less appropriate.
- Hidradenitis Suppurativa (HS): treatment of moderate to severe hidradenitis suppurativa in adult patients.
- Uveitis (UV): treatment of non-infectious intermediate, posterior, and panuveitis in adult patients.

For administrative purposes, we have split S-007 into the following supplements:

- BLA 761299/S-007 – Simlandi (adalimumab-ryvk):
  - Simlandi injection 40 mg/0.4 mL for subcutaneous use in a PFS seeking interchangeability with US-licensed Humira injection 40 mg/0.4 mL for subcutaneous use in a PFS
  - Simlandi injection, 20 mg/0.2 mL and 80 mg/0.8 mL for subcutaneous use in a PFS seeking biosimilarity to US-licensed Humira injection 20 mg/0.2 mL and 80 mg/0.8 mL, for subcutaneous use in a PFS, respectively.

(b) (4)

(b) (4)

The subject of this correspondence is BLA 761299/S-007. (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.

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, Instructions for Use, Medication Guide, and Quick Reference 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

Submit final printed carton and container labeling that are identical to the container labeling submitted February 26, 2024, and carton labeling submitted June 18, 2024, 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 "**Product Correspondence – Final Printed Carton and Container Labeling for approved BLA 761299/ S-007**." Approval of this submission by FDA is not required before the labeling is used.

[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.

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.

Rheumatoid Arthritis
At this time, we have determined that, with respect to Polyarticular Juvenile Idiopathic Arthritis (pJIA) in pediatric patients 0 to less than 2 years of age, no pediatric studies will be required under PREA for your BLA.

Psoriatic Arthritis
At this time, we have determined that, with respect to this indication, no pediatric studies will be required under PREA for your BLA.

Ankylosing Spondylitis
At this time, we have determined that, with respect to this indication, no pediatric studies will be required under PREA for your BLA.

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

Ulcerative Colitis
At this time, we have determined that, with respect to UC in pediatric patients 0 to less than 5 years of age, no pediatric studies will be required under PREA for your BLA. You have provided a pediatric assessment for UC in pediatric patients 5 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 this indication, no pediatric studies will be required under PREA for your BLA.

Hidradenitis Suppurativa
At this time, we have determined that, with respect to HS in pediatric patients 0 to less than 12 years of age, no pediatric studies will be required under PREA for your BLA. You have provided a pediatric assessment for HS in pediatric patients 12 years of age and older, and nothing further is required at this time.

Uveitis
At this time, we have determined that, with respect to uveitis in pediatric patients 0 to less than 2 years of age, no pediatric studies will be required under PREA for your BLA. You have provided a pediatric assessment for uveitis in pediatric patients 2 years of age and older, and nothing further is required at this time.

Deferred Pediatric Assessments:
Your deferred pediatric assessment required by section 505B(a) of the Federal Food, Drug, and Cosmetic Act is a required postmarketing study. The status of this postmarketing assessment must be reported annually according to 21 CFR 601.28 and section 505B(a)(4)(B) of the Federal Food, Drug, and Cosmetic Act. This required study is listed below.

4660-1 Develop a presentation that can be used to accurately administer Simlandi (adalimumab-ryvk) to pediatric patients who weigh less than 15 kg

Final Report Submission: 06/2026

Reports of this required pediatric postmarketing study must be submitted as a supplement to your approved BLA 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.

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

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 products are Part 3 combination products (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.

This information will be included in your biologics license application file.

If you have any questions, call Saharat Patanavanich, Regulatory Project Manager, at (240) 402-0139.

Sincerely,

{See appended electronic signature page}

Rachel Glaser, MD
Associate Director for Therapeutic Review
Division of Rheumatology and Transplant Medicine
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 – prefilled syringe
- Instructions for Use – autoinjector (revised June 14, 2024)
- Quick Reference Guide - prefilled syringe
- Quick Reference Guide - autoinjector (revised May 31, 2024)

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/

RACHEL GLASER
06/26/2024 01:52:12 PM