BLA 761285
BLA 761331

BLA APPROVAL

Amgen Inc.
Attention: Renee Martin, PhD
Director Global Regulatory Affairs, Biosimilars
601 13th Street NW, Suite 1100 N
Washington, DC 20005

Dear Dr. Martin:

Please refer to your biologics license applications (BLAs) dated and received October 31, 2022, and your amendments, submitted under section 351(k) of the Public Health Service Act (PHS Act) for Wezlana (ustekinumab-auub) injection, 45 mg/0.5 mL and 90 mg/mL for subcutaneous use and 130 mg/26 mL for intravenous use. The corresponding reference products are US-licensed Stelara (ustekinumab) injection, 45 mg/0.5 mL and 90 mg/mL for subcutaneous use and 130 mg/26 mL for intravenous use, respectively. This BLA proposes:

- The single-dose presentations of Wezlana (ustekinumab-auub) injection, 45 mg/0.5 mL pre-filled syringe, 45 mg/0.5 mL vial, and 90 mg/mL pre-filled syringe for subcutaneous use as interchangeable with the corresponding presentations of US-licensed Stelara (ustekinumab) injection, 45 mg/0.5 mL and 90 mg/mL for subcutaneous use, respectively, and

- The single-dose vial presentation of Wezlana (ustekinumab-auub) injection,130 mg/26 mL for intravenous use as interchangeable with the corresponding presentation of US-licensed Stelara (ustekinumab) injection, 130 mg/26 mL for intravenous use.

LICENSING

We have approved your BLAs for Wezlana (ustekinumab-auub) effective this date. You are hereby authorized to introduce or deliver for introduction into interstate commerce, Wezlana under your existing Department of Health and Human Services U.S. License No. 1080. Wezlana is indicated for the treatment of:

Adult patients with:

- moderate to severe plaque psoriasis (Ps), who are candidates for phototherapy or systemic therapy

- active psoriatic arthritis (PsA)
- moderately to severely active Crohn's disease (CD)
- moderately to severely active ulcerative colitis

Pediatric patients 6 years and older with:

- moderate to severe plaque psoriasis, who are candidates for phototherapy or systemic therapy
- active psoriatic arthritis (psA).

MANUFACTURING LOCATIONS

Under this license, you are approved to manufacture Wezlana (ustekinumab-auub) at [redacted] (b) (4) The final formulated drug product will be manufactured, filled, labeled, and packaged at Amgen Technology Ireland UC, Dun Laoghaire, Ireland (FEI 3002808497). You may label your product with the proprietary name, Wezlana, and market it as 45 mg/0.5 mL and 90 mg/mL injection in a single-dose prefilled syringe, 45 mg/0.5 mL injection in a single-dose vial, and 130 mg/26 mL injection in a single-dose vial.

DATING PERIOD

The dating period for Wezlana 45 mg/0.5 mL prefilled syringe and 90 mg/mL prefilled syringe shall be 36 months from the date of manufacture when stored at 2 – 8 °C. The dating period for Wezlana 45 mg/0.5 mL vial and 130 mg/26 mL vial shall be 24 months from the date of manufacture when stored at 2 – 8 °C. 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 [redacted] (b) (4) months from the date of manufacture when stored at [redacted] (b) (4) °C.

EXCLUSIVITY FOR FIRST INTERCHANGEABLE BIOLOGICAL PRODUCT

Section 351(k)(6) of the PHS Act provides:

> The Secretary shall not make approval as an interchangeable biological product effective with respect to an application submitted under this subsection that relies on the same reference product for which a prior biological product has received a determination of interchangeability for any condition of use, until the earlier of—

(A) 1 year after the first commercial marketing of the first interchangeable biosimilar biological product to be approved as interchangeable for that reference product;

(B) 18 months after—

(i) a final court decision on all patents in suit in an action instituted under subsection (*l*)(6) against the applicant that submitted the application for the first approved interchangeable biosimilar biological product; or

(ii) the dismissal with or without prejudice of an action instituted under subsection (*l*)(6) against the applicant that submitted the application for the first approved interchangeable biosimilar biological product; or

(C)

(i) 42 months after approval of the first interchangeable biosimilar biological product if the applicant that submitted such application has been sued under subsection (*l*)(6) and such litigation is still ongoing within such 42-month period; or

(ii) 18 months after approval of the first interchangeable biosimilar biological product if the applicant that submitted such application has not been sued under subsection (*l*)(6).

For purposes of this paragraph, the term "final court decision" means a final decision of a court from which no appeal (other than a petition to the United States Supreme Court for a writ of certiorari) has been or can be taken and the term "first interchangeable biosimilar biological product" means any interchangeable biosimilar biological product that is approved on the first day on which such a product is approved as interchangeable with the reference product.

Wezlana (ustekinumab-auub) injection, 45 mg/0.5 mL and 90 mg/mL for subcutaneous use and 130 mg/26 mL for intravenous use are the first products relying on their respective reference products to receive a determination of interchangeability for any condition of use. Therefore, with this approval, these three interchangeable biosimilar biological products are eligible for a period of first interchangeable exclusivity under section 351(k)(6) of the PHS Act.

For each interchangeable biosimilar biological product approved by this letter, submit a general correspondence to these 351(k) BLAs informing the Agency of the date of the first commercial marketing within 30 days of such date. Submit a duplicate copy of the correspondence via email to PurpleBook@fda.hhs.gov.

If applicable, submit a general correspondence to these 351(k) BLAs informing the Agency of the date of any final court decision on all patents in suit in an action instituted

under section 351(*l*)(6) of the PHS Act or the date of dismissal with or without prejudice of any action instituted under section (*l*)(6) within 30 days of such date or within 30 days of this approval if such date occurred prior to approval. Submit a duplicate copy of the correspondence via email to PurpleBook@fda.hhs.gov.

FDA LOT RELEASE

You are not currently required to submit samples of future lots of Wezlana 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 Wezlana, 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 these applications, as amended. They are approved, effective on the date of this letter, for use as recommended in the enclosed agreed-upon labeling.

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.[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]

[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.

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 761285 and BLA 761331**." 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.

Because none of these criteria apply to your application, you are exempt from this requirement.

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

We remind you of your postmarketing commitment:

4540-1 To develop a Monocyte Activation Test (MAT) for reliable endotoxin detection of the 130 mg drug product vial presentation and, if applicable, perform method validation with three batches of drug product. In addition, to concurrently develop an alternative endotoxin detection method which is not subject to low endotoxin recovery for the 130 mg drug product vial presentation as a mitigation, in case the MAT method proves infeasible and, if applicable, perform method validation with three batches of the 130 mg drug product vial presentation. Method feasibility study (MAT or alternative method) will be submitted to the Agency by the end of July 2024.

The timetable you submitted on June 29, 2023, states that you will conduct this study according to the following schedule:

Final Report Submission: 06/25

Submit nonclinical and chemistry, manufacturing, and controls protocols and all postmarketing final reports to these BLAs. 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 these BLAs. 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**."

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

[3] For the most recent version of a guidance, check the FDA guidance web page at https://www.fda.gov/media/128163/download.

[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]

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

[4] http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM083570.pdf
[5] http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM375154.pdf

If you have any questions, call Kimberle Searcy, Regulatory Project Manager at 240-402-4454.

Sincerely,

{See appended electronic signature page}

Shari L. Targum, MD, MPH, FACP, FACC
Deputy Director
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/

SHARI L TARGUM
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