BLA 761399

BLA APPROVAL

Celltrion, Inc.
c/o Parexel International
Attention: Laya Keyvan, MS, MBA
Senior Consultant
2520 Meridian Parkway
Suite 100
Durham, NC 27713

Dear Laya Keyvan:

Please refer to your biologics license application (BLA) dated and received March 8, 2024, and your amendments, submitted under section 351(k) of the Public Health Service Act for Omlyclo (omalizumab-igec) injection, 75 mg/0.5 mL and 150 mg/mL for subcutaneous use.

BLA 761399 seeks licensure of Omlyclo (omalizumab-igec) injection as interchangeable with US-licensed Xolair (omalizumab) as follows:

- 75 mg/0.5 mL injection in a single-dose prefilled syringe for subcutaneous use as interchangeable with US-licensed Xolair injection 75 mg/0.5 mL in a single-dose prefilled syringe for subcutaneous use

- 150 mg/mL injection in a single-dose prefilled syringe for subcutaneous use as interchangeable with US-licensed Xolair injection 150 mg/mL in a single-dose prefilled syringe for subcutaneous use

BLA 761399 provides for the use of Omlyclo (omalizumab-igec) for treatment of:

1. Moderate to severe persistent asthma in adults and pediatric patients 6 years of age and older with a positive skin test or in vitro reactivity to a perennial aeroallergen and symptoms that are inadequately controlled with inhaled corticosteroids.

2. Chronic rhinosinusitis with nasal polyps (CRSwNP) in adult patients 18 years of age and older with inadequate response to nasal corticosteroids, as add-on maintenance treatment.

3. IgE-mediated food allergy in adult and pediatric patients aged 1 year and older for the reduction of allergic reactions (Type I), including anaphylaxis, that may

occur with accidental exposure to one or more foods. To be used in conjunction with food allergen avoidance.

4. Chronic spontaneous urticaria (CSU) in adults and adolescents 12 years of age and older who remain symptomatic despite H1 antihistamine treatment.

This BLA also provides for unbranded biological product labeling.

LICENSING

We have approved your BLA for Omlyclo (omalizumab-igec) effective this date. You are hereby authorized to introduce or deliver for introduction into interstate commerce, Omlyclo under your existing Department of Health and Human Services U.S. License No. 1996. Omlyclo is indicated for the same indications as US-licensed Xolair (Asthma, Chronic rhinosinusitis with nasal polyps (CRSwNP), IgE-Mediated Food Allergy (FA), and Chronic spontaneous urticaria (CSU)).

MANUFACTURING LOCATIONS

Under this license, you are approved to manufacture Omlyclo (omalizumab-igec) drug substance at (b) (4) The final formulated drug product will be manufactured, filled, labeled, and packaged at Celltrion Pharm, Inc., Cheongju-si, Republic of Korea. You may label your product with the proprietary name, Omlyclo (omalizumab-igec), and market it in 75 mg/0.5 mL (150 mg/mL) and 150 mg/1.0 mL (150 mg/mL) prefilled syringes for subcutaneous injection.

DATING PERIOD

The dating period for Omlyclo (omalizumab-igec) shall be 18 months from the date of manufacture when stored at 5°C ±3°C, protected from light. 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)

We have approved the stability protocol(s) 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 Omlyclo (omalizumab-igec) 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 Omlyclo, 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.

FIRST INTERCHANGEABLE EXCLUSIVITY

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

Omlyclo (omazilumab-igec) injection, 75 mg/0.5 mL and 150 mg/mL for subcutaneous 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 products qualify as first interchangeable biosimilar biological products for purposes of section 351(k)(6) of the PHS Act. The expiration date of any first interchangeable exclusivity has yet to be determined.

For each interchangeable biosimilar biological product approved by this letter, submit a general correspondence to this 351(k) BLA 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, please submit a general correspondence to this 351(k) BLA informing the Agency of the date of any final court decision (as defined in section 351(k)(6) of the PHS Act) on all patents in suit in any action implicating this BLA instituted under section 351(l)(6) of the PHS Act, or the date of dismissal with or without prejudice of any action implicating this BLA instituted under section 351(l)(6), within 30 days of such date or within 30 days of this approval if such date occurred prior to approval. If any action implicating this BLA instituted under section 351(l)(6) is still ongoing at the time of this approval, submit a general correspondence informing the Agency of this within 30 days of this approval. Submit a duplicate copy of the correspondence(s) via email to PurpleBook@fda.hhs.gov.

APPROVAL & LABELING

We have completed our review of this application. 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]

[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 761399**." 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 commitments:

4805-1 To perform the stopper movement study of the CT-P39 pre-filled syringe to ensure that sterility of the drug product is not impacted under worst case transportation conditions according to (b) (4) This additional study will be performed using syringes with worst-case plunger insertion depth considering the actual shipping condition of CT-P39.

The timetable you submitted on February 12, 2025, states that you will conduct this study according to the following schedule:

Final Report Submission: 08/25

Submit clinical protocols to your IND 142684 for this product. 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**."

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

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:

[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

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, contact Linda Ebonine, Senior Regulatory Health Project Manager, at Linda.Ebonine@fda.hhs.gov.

Sincerely,

{See appended electronic signature page}

Banu Karimi-Shah, MD
Acting Director
Division of Pulmonology, Allergy, and Critical Care
Office of Immunology and Inflammation
Office of New Drugs
Center for Drug Evaluation and Research

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/

KELLY D STONE
03/07/2025 11:08:49 AM
Signing with the delegated authority of Dr. Banu Karimi-Shah, Acting Director, DPACC