BLA 761458/Original 1

BLA APPROVAL

GlaxoSmithKline LLC
Attention: David Colton
Director, Global Regulatory Affairs
200 Cambridge Park Drive
Cambridge, Massachusetts 02140

Dear David Colton:

Please refer to your biologics license application (BLA) dated December 13, 2024, received December 16, 2024, and your amendments, under section 351(a) of the Public Health Service Act for Exdensur (depemokimab-ulaa) injection.

BLA 761458 provides for the use of Exdensur (depemokimab-ulaa) injection for the following indications which, for administrative purposes, we have designated as follows:

BLA 761458/Original 1 - Add-on maintenance treatment of severe asthma characterized by an eosinophilic phenotype in adult and pediatric patients aged 12 years and older

(b) (4)

The subject of this action letter is BLA 761458/Original 1. (b) (4)

All future submissions to BLA 761458/Original 1 should specify the BLA number and the Original number to which each submission pertains.

LICENSING

We have approved your BLA for Exdensur (depemokimab-ulaa) effective this date. You are hereby authorized to introduce or deliver for introduction into interstate commerce, Exdensur under your existing Department of Health and Human Services U.S. License No. 1727. Exdensur is indicated for add-on maintenance treatment of severe asthma characterized by an eosinophilic phenotype in adult and pediatric patients aged 12 years and older.

MANUFACTURING LOCATIONS

Under this license, you are approved to manufacture Exdensur drug substance at GlaxoSmithKline LLC, in Conshohocken, PA. The final formulated drug product will be manufactured, filled, labeled, and packaged at Glaxo Operations UK Ltd, Barnard Castle, UK. You may label your product with the proprietary name, Exdensur (depemokimab-ulaa), and market it in 100 mg/mL in a pre-filled syringe (PFS) in an autoinjector (AI) or safety syringe device (SSD) that deliver 100 mg of depemokimab for subcutaneous injection.

DATING PERIOD

The dating period for Exdensur shall be 24 months from the date of manufacture when stored at 2 to 8°C, with an allowance for one week at room temperature not to exceed 30°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 Exdensur 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 Exdensur, or in the manufacturing facilities, will require the submission of information to your biologics license application for our review and written approval, consistent with 21 CFR 601.12.

APPROVAL AND 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, as described at

FDA.gov.[1] Content of labeling must be identical to the enclosed labeling (text for the Prescribing Information and Patient Package Insert). 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.

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 *Providing Regulatory Submissions in Electronic Format — Certain Human Pharmaceutical Product Applications and Related Submissions Using the eCTD Specifications*. For administrative purposes, designate this submission "**Final Printed Carton and Container Labeling for approved BLA 761458**." Approval of this submission by FDA is not required before the labeling is used.

ADVISORY COMMITTEE

Your application for Exdensur (depemokimab-ulaa) was not referred to an FDA advisory committee because the application did not raise significant safety or efficacy issues in the intended population and outside expertise was not necessary; there were no controversial issues that would benefit from advisory committee discussion.

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.

We are waiving the pediatric study requirement for pediatric patients ages birth to less than 6 years of age because necessary studies are impossible or highly impracticable. Severe asthma with an eosinophilic phenotype is unlikely to exist in sufficient numbers for a study to be conducted.

We are deferring submission of your pediatric study for ages 6 to 11 years for this application because this product is ready for approval for use in adult and pediatric

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

patients aged 12 years and older and the pediatric study for 6 to 11 years of age has not been completed.

Your deferred pediatric study required by section 505B(a) of the Federal Food, Drug, and Cosmetic Act is a required postmarketing study. The status of this postmarketing study 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.

4920-1	Conduct a 52-week, open-label, pharmacokinetic, pharmacodynamic, and safety study of depemokimab in pediatric patients 6 years to 11 years of age with severe asthma characterized by an eosinophilic phenotype.	
	Final Protocol Submission:	06/2025 (Submitted)
	Study Completion:	06/2029
	Final Report Submission:	12/2029

FDA considers the term *final* to mean that the applicant has submitted a protocol, the FDA review team has sent comments to the applicant, and the protocol has been revised as needed to meet the goal of the study or clinical trial.[3]

Submit the protocol to your IND 146742, with a cross-reference letter to this BLA. Reports of this required pediatric postmarketing study 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 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.

This product is appropriately labeled for use in ages 12 to 17 years for this indication. Therefore, no additional studies are needed in this pediatric group.

POSTMARKETING REQUIREMENTS UNDER 505(o)

Section 505(o)(3) of the Federal Food, Drug, and Cosmetic Act (FDCA) authorizes FDA to require holders of approved drug and biological product applications to conduct postmarketing studies and clinical trials for certain purposes, if FDA makes certain findings required by the statute.

We have determined that an analysis of spontaneous postmarketing adverse events reported under subsection 505(k)(1) of the FDCA will not be sufficient to identify an unexpected serious risk of pregnancy and maternal complications and adverse effects

[3] See the guidance for Industry *Postmarketing Studies and Clinical Trials—Implementation of Section 505(o)(3) of the Federal Food, Drug, and Cosmetic Act (October 2019).* https://www.fda.gov/RegulatoryInformation/Guidances/default.htm.

on the developing fetus, neonate, and infant from the use of depemokimab during pregnancy or to identify an unexpected serious risk of the potential presence of depemokimab in human breast milk resulting in effects on the breastfed infant.

Furthermore, the active postmarket risk identification and analysis system as available under section 505(k)(3) of the FDCA will not be sufficient to assess these serious risks.

Therefore, based on appropriate scientific data, FDA has determined that you are required to conduct the following studies:

4920-2 Conduct a worldwide descriptive study that collects prospective and retrospective data in women exposed to depemokimab during pregnancy to assess risk of pregnancy and maternal complications, and adverse effects on the developing fetus, neonate, and infant. Assess infant outcomes through at least the first year of life. The minimum number of patients will be specified in the protocol.

The timetable you submitted on November 26, 2025, states that you will conduct this study according to the following schedule:

Draft Protocol Submission:	06/2026
Final Protocol Submission:	12/2026
Interim study report:	12/2028
Interim study report:	12/2030
Interim study report:	12/2032
Interim study report:	12/2034
Interim study report:	12/2036
Study Completion:	12/2036
Final Report Submission:	06/2037

4920-3 Perform a lactation study (milk-only or mother-infant pair study) in lactating women who have received depemokimab to measure concentrations of depemokimab and its major metabolites in breast milk using a validated assay. Assess the effects on the breastfed infant, if available, based on study population.

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

Draft protocol submission:	09/2026
Final protocol:	03/2027
Study completion:	12/2028
Final report submission:	06/2029

FDA considers the term *final* to mean that the applicant has submitted a protocol, the FDA review team has sent comments to the applicant, and the protocol has been revised as needed to meet the goal of the study or clinical trial.[4]

Submit clinical protocols to your IND 146742 with a cross-reference letter to this BLA. Submit nonclinical and chemistry, manufacturing, and controls protocols and all final report(s) to your BLA. Prominently identify the submission with the following wording in bold capital letters at the top of the first page of the submission, as appropriate: **REQUIRED POSTMARKETING PROTOCOL UNDER 505(o) , REQUIRED POSTMARKETING FINAL REPORT UNDER 505(o), REQUIRED POSTMARKETING CORRESPONDENCE UNDER 505(o).**

Section 505(o)(3)(E)(ii) of the FDCA requires you to report periodically on the status of any study or clinical trial required under this section. This section also requires you to periodically report to FDA on the status of any study or clinical trial otherwise undertaken to investigate a safety issue. Section 506B(a)(1) of the FDCA, as well as 21 CFR 601.70 requires you to report annually on the status of any postmarketing commitments or required studies or clinical trials.

FDA will consider the submission of your annual report under section 506B(a)(1) and 21 CFR 601.70 to satisfy the periodic reporting requirement under section 505(o)(3)(E)(ii) provided that you include the elements listed in 505(o) and 21 CFR 601.70. We remind you that to comply with 505(o), your annual report must also include a report on the status of any study or clinical trial otherwise undertaken to investigate a safety issue. Failure to submit an annual report for studies or clinical trials required under 505(o) on the date required will be considered a violation of FDCA section 505(o)(3)(E)(ii) and could result in enforcement action.

[4] See the guidance for Industry *Postmarketing Studies and Clinical Trials—Implementation of Section 505(o)(3) of the Federal Food, Drug, and Cosmetic Act (October 2019).* https://www.fda.gov/RegulatoryInformation/Guidances/default.htm.

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

We remind you of your postmarketing commitments:

4920-4 Qualification of a new Working Reference Standard

The timetable you submitted on July 31, 2025, states that you will conduct this study according to the following schedule:

Final Report Submission: 12/2026

4920-5 Conduct an additional bacterial retention study, including differential pressure monitoring and submit the final report in a CBE-30 supplement

The timetable you submitted on October 31, 2025, states that you will conduct this study according to the following schedule:

Final Report Submission: 02/2026

4920-6 Repeat the CCIT validation for AI and SSD by dye ingress, revise the acceptance criteria (b) (4) as expected and submit the final report in a CBE-0 supplement.

The timetable you submitted on October 31, 2025, states that you will conduct this study according to the following schedule:

Final Report Submission: 01/2026

Submit clinical protocols to your IND 146742 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*.[5]

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.[6] Information and Instructions for completing the form can be found at FDA.gov.[7]

REPORTING REQUIREMENTS

You must submit adverse experience reports under the adverse experience reporting requirements for licensed biological products (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 for licensed biological products (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

[5] For the most recent version of a guidance, check the FDA guidance web page at https://www.fda.gov/media/128163/download.
[6] http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM083570.pdf
[7] http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM375154.pdf

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

POST APPROVAL FEEDBACK MEETING

New molecular entities and new biologics qualify for a post approval feedback meeting. Such meetings are used to discuss the quality of the application and to evaluate the communication process during drug development and marketing application review. The purpose is to learn from successful aspects of the review process and to identify areas that could benefit from improvement. If you would like to have such a meeting with us, call the Regulatory Project Manager for this application.

If you have any questions, contact Julianne Lee, Senior Regulatory Project Manager, at 240-402-5130 or Julianne.Lee@fda.hhs.gov.

Sincerely,

{See appended electronic signature page}

Kathleen Donohue, MD
Deputy Director
Office of Immunology and Inflammation
Office of New Drugs
Center for Drug Evaluation and Research

ENCLOSURE(S):

- Content of Labeling
  - Prescribing Information
  - Patient Package Insert
- 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/

KATHLEEN M DONOHUE
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