

BLA 761224

BLA APPROVAL

AstraZeneca AB
c/o AstraZeneca Pharmaceuticals, LP
One MedImmune Way
Gaithersburg, MD 20878

Attention: Abir Absar, PhD
Regulatory Affairs Director

Dear Dr. Absar:

Please refer to your biologics license application (BLA) dated and received on May 7, 2021, and your amendments, submitted under section 351(a) of the Public Health Service Act for TEZSPIRE (tezepelumab-ekko) solution for subcutaneous injection.

We have approved your BLA for TEZSPIRE effective this date. You are hereby authorized to introduce or deliver for introduction into interstate commerce, TEZSPIRE under your existing Department of Health and Human Services U.S. License No. 2059. TEZSPIRE is indicated for the add-on maintenance treatment of adult and pediatric patients aged 12 years and older with severe asthma.

MANUFACTURING LOCATIONS

Under this license, you are approved to manufacture tezepelumab-ekko drug substance at Amgen Inc., Thousand Oaks, California. The final formulated drug product will be manufactured, filled, labeled, and packaged at Amgen Manufacturing Limited, Juncos, Puerto Rico. You may label your product with the proprietary name, TEZSPIRE, and market it in 210 mg/1.91 mL (110 mg/mL) solution in single-dose glass vials and 210 mg/1.91 mL (110 mg/mL) solution in a single-dose pre-filled syringe.

DATING PERIOD

The dating period for TEZSPIRE shall be 36 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 (b) (4) months from the date of manufacture when stored at (b) (4). Results of ongoing stability should be submitted throughout the dating period, as they become available, including the results of stability studies from the first three production lots.

FDA LOT RELEASE

You are not currently required to submit samples of future lots of TEZSPIRE 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 TEZSPIRE, 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. 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 and Patient Information). 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 *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 761224.**” Approval of this submission by FDA is not required before the labeling is used.

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>.

ADVISORY COMMITTEE

Your application for TEZSPIRE was not referred to an FDA advisory committee because 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 ages 0 through 2 years because necessary studies are impossible or highly impracticable. This is because studies are impossible or highly impractical due to insufficient numbers of pediatric patients to study in this age group with severe asthma who require add-on treatment.

We are deferring submission of your pediatric studies for ages 2 through 11 years for this application because this product is ready for approval for use in adults and the pediatric studies have not been completed.

Your deferred pediatric studies required by 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)(4)(B) of the Federal Food, Drug, and Cosmetic Act. These required studies are listed below.

4188-1 Conduct a PK/safety study in children 5-11 years of age with asthma requiring daily controller medication.

- Final Protocol Submission: 11/2020 (submitted)
- Study Completion: 12/2023
- Final Report Submission: 05/2024

4188-2 Conduct a 52-week efficacy and safety study in children 5 to < 12 years of age with severe asthma.

- Draft Protocol Submission: 02/2024
- Final Protocol Submission: 06/2024
- Study Completion: 04/2028
- Final Report Submission: 09/2028

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4188-3 Conduct an efficacy, safety, and PK study in children 2 years to < 5 years of age with severe asthma with a continued safety evaluation out to a minimum of 52 weeks.

- Draft Protocol Submission: 06/2029
- Final Protocol Submission: 12/2029
- Study Completion: 03/2036
- Final Report Submission: 09/2036

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 protocols to your IND 103031, 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*.⁴

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.⁵ Information and Instructions for completing the form can be found at FDA.gov.⁶

REPORTING REQUIREMENTS

You must submit adverse experience reports under the adverse experience reporting requirements for licensed biological products (21 CFR 600.80).

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>.

⁴ For the most recent version of a guidance, check the FDA guidance web page at

<https://www.fda.gov/media/128163/download>.

⁵ <http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM083570.pdf>

⁶ <http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM375154.pdf>

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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

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 biological products 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, call Linda Ebonine, Senior Regulatory Health Project Manager, at (240) 402-4483.

Sincerely,

{See appended electronic signature page}

Julie Beitz, MD
Office Director
Office of Immunology and Inflammation
Office of New Drugs
Center for Drug Evaluation and Research

ENCLOSURE(S):

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

JULIE G BEITZ
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