

NDA 212122/S-009

## **SUPPLEMENT APPROVAL**

AstraZeneca AB  
c/o AstraZeneca Pharmaceuticals LP  
Attention: Adé Fujamade  
Regulatory Affairs Director  
One MedImmune Way  
Gaithersburg, MD 20878

Dear Adé Fujamade:

Please refer to your supplemental new drug application (sNDA) dated and received June 27, 2025, and your amendments, submitted pursuant to section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Breztri Aerosphere inhalation aerosol.

This Prior Approval supplemental new drug application provides for the addition of the indication of the maintenance treatment of asthma in adult and pediatric patients 12 years of age and older and introduces a new strength of Breztri Aerosphere 160/18/4.8 µg.

### **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 the content of labeling [21 CFR 314.50(l)] in structured product labeling (SPL) format using the FDA automated drug registration and listing system (eLIST), as described at FDA.gov.<sup>1</sup> Content of labeling must be identical to the enclosed labeling (text for the Prescribing Information, Patient Package Insert, and Instructions for Use), with the addition of any labeling changes in pending “Changes Being Effected” (CBE) supplements, as well as annual reportable changes not included in the enclosed labeling.

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<sup>1</sup> <http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm>

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*.<sup>2</sup>

The SPL will be accessible from publicly available labeling repositories.

Also within 14 days, amend all pending supplemental applications that include labeling changes for this NDA, including CBE supplements for which FDA has not yet issued an action letter, with the content of labeling [21 CFR 314.50(l)(1)(i)] 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(s), 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 enclosed carton and container labeling, but no more than 30 days after they are printed. We also refer to the communication dated April 27, 2026, wherein you agreed to submit the actuator labeling for the Breztri Aerosphere 160 mcg/9 mcg/4.8 mcg. 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 NDA 212122/S-009.**” 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 in pediatric patients unless this requirement is waived, deferred, or inapplicable.

We are waiving the pediatric study requirement for birth to less than 4 years of age because necessary studies are impossible or highly impracticable.

We are deferring submission of your pediatric studies for ages 4 to less than 12 years for this application because this product is ready for approval for use in adults, but the

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<sup>2</sup> 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>.

pediatric studies in pediatric patients 4 to less than 12 years of age have not been completed.

Your deferred pediatric studies required by section 505B(a) of the FDCA are required postmarketing studies. The status of these postmarketing studies must be reported annually according to 21 CFR 314.81 and section 505B(a)(4)(C) of the FDCA. These required studies are listed below.

- 4983-1 Conduct a randomized, double-blind, placebo-controlled, 3-way cross-over, 3-week treatment period, dose-ranging study of at least two doses of glycopyrrolate in children 4 to 11 years of age with asthma receiving background therapy of budesonide/formoterol fumarate inhalation aerosol (BFF Aerosphere MDI).

Final Protocol Submission: 01/2026 (submitted)  
Study Completion: 12/2029  
Final Report Submission: 03/2030

- 4983-2 Conduct an open-label, single dose, single-period pharmacokinetic study of budesonide/ glycopyrrolate/ formoterol fumarate inhalation aerosol (BGF Aerosphere MDI) in children 4 to 11 years of age with asthma.

Final Protocol Submission: 03/2031  
Study Completion: 03/2033  
Final Report Submission: 06/2033

- 4983-3 Conduct a 52-week, randomized, double-blind, parallel-group, active-controlled, efficacy and safety study of budesonide/ glycopyrrolate/ formoterol fumarate inhalation aerosol (BGF Aerosphere MDI) in children 4 to 11 years of age with asthma.

Final Protocol Submission: 03/2031  
Study Completion: 03/2035  
Final Report Submission: 06/2035

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.<sup>3</sup>

Submit the protocol(s) to your IND 118313, with a cross-reference letter to this NDA. Reports of these required pediatric postmarketing studies must be submitted as an NDA or as a supplement to your approved NDA with the proposed labeling changes you

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<sup>3</sup> 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>.

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.

This product is appropriately labeled for use in ages 12 to <18 years for this indication. Therefore, no additional studies are needed in this pediatric group.

### **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*.<sup>4</sup>

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

### **PATENT LISTING REQUIREMENTS**

Pursuant to 21 CFR 314.53(d)(2) and 314.70(f), certain changes to an approved NDA submitted in a supplement require you to submit patent information for listing in the Orange Book upon approval of the supplement. You must submit the patent information required by 21 CFR 314.53(d)(2)(i)(A) through (C) and 314.53(d)(2)(ii)(A) and (C), as applicable, to FDA on Form FDA 3542 within 30 days after the date of approval of the supplement for the patent information to be timely filed (see 21 CFR 314.53(c)(2)(ii)). You also must ensure that any changes to your approved NDA that require the submission of a request to remove patent information from the Orange Book are submitted to FDA at the time of approval of the supplement pursuant to 21 CFR 314.53(d)(2)(ii)(B) and 314.53(f)(2)(iv).

### **REPORTING REQUIREMENTS**

We remind you that you must comply with reporting requirements for an approved NDA (21 CFR 314.80 and 314.81).

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<sup>4</sup> For the most recent version of a guidance, check the FDA guidance web page at <https://www.fda.gov/media/128163/download>.

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

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

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](https://www.fda.gov).<sup>7</sup>

If you have any questions, contact Linda Ebonine, Senior Regulatory Health Project Manager, at [Linda.Ebonine@fda.hhs.gov](mailto:Linda.Ebonine@fda.hhs.gov).

Sincerely,

*{See appended electronic signature page}*

Kelly Stone, MD, PhD  
Associate Director of Therapeutic Review  
Division of Pulmonology, Allergy, and Critical Care  
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
  - Instructions for Use
- Carton and Container Labeling

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<sup>7</sup> <https://www.fda.gov/combination-products/guidance-regulatory-information/postmarketing-safety-reporting-combination-products>

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**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.**  
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/s/  
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KELLY D STONE  
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