



BLA 125526/S-012
BLA 761122/S-002
BLA 761122/S-003

**SUPPLEMENT APPROVAL
FULFILLMENT OF
POSTMARKETING REQUIREMENTS**

GlaxoSmithKline
1250 S. Collegeville Road
Collegeville, PA 19426-0989

Attention: Brittany Dustman, PharmD
Manager, Global Regulatory Affairs

Dear Dr. Dustman:

Please refer to your supplemental biologics license applications (sBLA):

1. BLA 125526/S-012: dated November 16, 2018, received November 16, 2018
2. BLA 761122/S-002: dated July 29, 2019, received July 29, 2019
3. BLA 761122/S-003: dated August 28, 2019, received August 28, 2019

and your amendments submitted under section 351(a) of the Public Health Service Act for Nucala (mepolizumab) Lyophilized Powder for Subcutaneous Injection, and Liquid Formulation for Subcutaneous Injection via Autoinjector (AI) or Safety Syringe Device (SSD).

The Prior Approval supplemental biologics applications to BLA 125526/S-012, and BLA 761122/S-003 provide for an extension of indication for add-on maintenance treatment of patients with severe asthma, and with an eosinophilic phenotype to include patients aged 6 to 11 years.

The Prior Approval supplemental biologics application to BLA 761122/S-002 provides for labeling revisions to the USPI, PPI and the IFUs for the Autoinjector and the Safety Syringe Device.

APPROVAL & LABELING

We have completed our review of applications BLA 125526/S-012, BLA 761122/S-002, and BLA 761122/S-003, as amended. They are 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 that is identical to the enclosed labeling (text for the Prescribing Information, Patient Package Insert, and Instructions for Use) and include the labeling changes proposed in any pending “Changes Being Effectuated” (CBE) supplements.

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.

Also within 14 days, amend all pending supplemental applications that include labeling changes for this BLA, including pending “Changes Being Effectuated” (CBE) supplements, for which FDA has not yet issued an action letter, with the content of labeling [21 CFR 601.12(f)] 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 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 125526/S-012.**” 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

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 <https://www.fda.gov/RegulatoryInformation/Guidances/default.htm>.

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 had previously waived the pediatric study requirement for patients less than 6 years of age because necessary studies are impossible or highly impracticable. This is because the disease (severe asthma with an eosinophilic phenotype) is unlikely to exist in sufficient numbers to allow for a study to be conducted (refer to the approval letters dated November 4, 2015) for BLA 125226 and June 6, 2019, for BLA 761122).

FULFILLMENT OF POSTMARKETING REQUIREMENT(S)/COMMITMENT(S)

We refer to your supplemental biologics license applications (sBLA) submitted under section 351 of the Public Health Service Act for Nucala (mepolizumab) Lyophilized Powder for Subcutaneous Injection, and Liquid Formulation for Subcutaneous Injection via Autoinjector (AI) or Safety Syringe Device (SSD).

We have received your submission dated November 16, 2018, to BLA 125526/S-012 and August 28, 2019, to BLA 761122/S-003, containing the final reports for the following postmarketing requirements listed in the:

November 4, 2015, approval for BLA 125526:

- 2979-1 Conduct a 12 week, randomized, open-label, pharmacokinetic and pharmacodynamics study of Nucala (mepolizumab) in pediatric patients with asthma 6 years to 11 years of age (Part A of Study 200363).
- 2979-2 Conduct a 12 month long-term safety and pharmacodynamics extension study of Nucala (mepolizumab) in pediatric patients with asthma 6 years to 11 years of age (Part B of Study 200363).

June 6, 2019, approval for BLA 761122:

- 3620-3 Conduct a 12-week, randomized, open-label, pharmacokinetic and pharmacodynamics study of Nucala (mepolizumab) in pediatric patients with asthma 6 years to 11 years of age (Part A of Study 200363).
- 3620-4 Conduct a 12-month long-term safety and pharmacodynamics extension study of Nucala (mepolizumab) in pediatric patients with asthma 6 years to 11 years of age (Part B of Study 200363).

We have reviewed your submissions and conclude that the above requirements were fulfilled.

We remind you that there are postmarketing commitments listed in the June 6, 2019, approval letter for BLA 761122 that are still open.

PROMOTIONAL MATERIALS

You may request advisory comments on proposed introductory advertising and promotional labeling. To do so, submit, in triplicate, a cover letter requesting advisory comments, the proposed materials in draft or mock-up form with annotated references, and the Prescribing Information to:

OPDP Regulatory Project Manager
Food and Drug Administration
Center for Drug Evaluation and Research
Office of Prescription Drug Promotion
5901-B Ammendale Road
Beltsville, MD 20705-1266

Alternatively, you may submit a request for advisory comments electronically in eCTD format. For more information about submitting promotional materials in eCTD format, see the draft guidance for industry *Providing Regulatory Submissions in Electronic and Non-Electronic Format—Promotional Labeling and Advertising Materials for Human Prescription Drugs*.³

As required under 21 CFR 601.12(f)(4), you must submit final promotional materials, and the Prescribing Information, at the time of initial dissemination or publication, accompanied by a Form FDA 2253. Form FDA 2253 is available at FDA.gov.⁴ Information and Instructions for completing the form can be found at FDA.gov.⁵ For more information about submission of promotional materials to the Office of Prescription Drug Promotion (OPDP), see FDA.gov.⁶

REPORTING REQUIREMENTS

We remind you that you must comply with reporting requirements for an approved BLA (in 21 CFR 600.80 and in 21 CFR 600.81).

³ When final, this guidance will represent the FDA's current thinking on this topic. For the most recent version of a guidance, check the FDA guidance web page at <https://www.fda.gov/RegulatoryInformation/Guidances/default.htm>.

⁴ <http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM083570.pdf>

⁵ <http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM375154.pdf>

⁶ <http://www.fda.gov/AboutFDA/CentersOffices/CDER/ucm090142.htm>

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If you have any questions, call Ji Hyun LaRose, Regulatory Project Manager, at (301) 796-9017.

Sincerely,

{See appended electronic signature page}

Sally Seymour, MD
Director
Division of Pulmonary, Allergy, and
Rheumatology Products
Office of Drug Evaluation II
Center for Drug Evaluation and Research

ENCLOSURE(S):

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

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signing with the delegated authority of Dr. Sally Seymour, Division Director, DPARP