Our STN: BL 125775/132

SUPPLEMENT APPROVAL
RELEASE FROM POSTMARKETING REQUIREMENT AND COMMITMENT
NEW POSTMARKETING REQUIREMENT AND COMMITMENT

June 7, 2024

GlaxoSmithKline Biologicals
Attention: Nitisha Pyndiah, Ph.D.
14200 Shady Grove Road
Rockville, MD 20850-7464

Dear Dr. Pyndiah:

We have approved your request received December 7, 2023, to supplement your Biologics License Application (BLA) submitted under section 351(a) of the Public Health Service Act for Respiratory Syncytial Virus Vaccine, Adjuvanted (AREXVY) manufactured at your facility in (b) (4) Belgium to include use in individuals 50 through 59 years of age who are at increased risk for Lower Respiratory Tract Disease (LRTD) caused by Respiratory Syncytial Virus (RSV).

The review of this supplement was associated with the following National Clinical Trial (NCT) number: NCT05590403.

LABELING

We hereby approve the draft content of labeling: Package Insert submitted under amendment 19, dated June 7, 2024, and the draft carton label submitted under amendment 11, dated May 14, 2024.

CONTENT OF LABELING

As soon as possible, but no later than 14 days from the date of this letter, please submit the final content of labeling (21 CFR 601.14) in Structured Product Labeling (SPL) format via the FDA automated drug registration and listing system (eLIST), as described at http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm. Content of labeling must be identical to the Package Insert submitted on June 7, 2024. 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* at http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM072392.pdf.

The SPL will be accessible via publicly available labeling repositories.

CARTON AND CONTAINER LABELS

Please electronically submit final printed carton label identical to the carton label submitted on June 7, 2024, according to the guidance for industry *Providing Regulatory Submissions in Electronic Format — Certain Human Pharmaceutical Product Applications and Related Submissions Using the eCTD Specifications* at https://www.fda.gov/regulatory-information/search-fda-guidance-documents/providing-regulatory-submissions-electronic-format-certain-human-pharmaceutical-product-applications.

All final labeling should be submitted as Product Correspondence to this BLA, STN BL 125775, at the time of use and include implementation information on Form FDA 356h.

ADVERTISING AND PROMOTIONAL LABELING

You may submit two draft copies of the proposed introductory advertising and promotional labeling with Form FDA 2253 to the Advertising and Promotional Labeling Branch at the following address:

Food and Drug Administration
Center for Biologics Evaluation and Research
Document Control Center
10903 New Hampshire Ave.
WO71–G112
Silver Spring, MD 20993-0002

You must submit copies of your final advertising and promotional labeling at the time of initial dissemination or publication, accompanied by Form FDA 2253 (21 CFR 601.12(f)(4)).

All promotional claims must be consistent with and not contrary to approved labeling. You should not make a comparative promotional claim or claim of superiority over other products unless you have substantial evidence or substantial clinical experience to support such claims (21 CFR 202.1(e)(6)).

For each pending supplemental application for this BLA that includes proposed revised labeling, please submit an amendment to update the proposed revised labeling with the changes approved today.

RELEASE FROM POSTMARKETING REQUIREMENTS UNDER SECTION 505(o)

Section 505(o) 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 (section 505(o)(3)(A), 21 U.S.C. 355(o)(3)(A)).

We have determined that an analysis of spontaneous postmarketing adverse events reported under section 505(k)(1) of the FDCA will not be sufficient to assess a signal of a serious risk of Guillain-Barré syndrome (GBS) and acute disseminated encephalomyelitis (ADEM).

Furthermore, the pharmacovigilance system that FDA is required to maintain under section 505(k)(3) of the FDCA is not sufficient to assess this serious risk.

We also refer to your submission received September 2, 2022, reporting on the following postmarketing requirement (PMR) identified in the STN 125775/0 approval letter dated May 3, 2023.

PMR #3 EPI-RSV-041 VS US DB (220149), a postmarketing active surveillance study, to evaluate Guillain-Barré syndrome (GBS) and acute disseminated encephalomyelitis (ADEM) in adults 60 years and older vaccinated with AREXVY in the United States. Using a self-controlled risk interval (SCRI) design, the study will be conducted in the Sentinel System, and evaluate 1.9 million individuals vaccinated with AREXVY.

We have completed the review of your submission and conclude that you are released from the above PMR because we are expanding the use to include individuals 50 years of age and older at increased risk for LRTD caused by RSV.

The above PMR is now considered closed and will be replaced by the new PMR described below.

NEW POSTMARKETING REQUIREMENTS UNDER SECTION 505(o)

PMR #1 EPI-RSV-041 VS US DB (220149), to evaluate Guillain-Barré syndrome (GBS) and acute disseminated encephalomyelitis (ADEM) in adults 50 years of age and older vaccinated with AREXVY in the United States. Using a self-controlled risk interval (SCRI) design, the study will be conducted in the Sentinel System, and evaluate 1.9 million individuals vaccinated with AREXVY.

We acknowledge the timetable you submitted on May 3, 2024, which states that you will conduct this study, according to the following schedule:

Final Protocol Submission: June 30, 2024

Study Completion Date: June 30, 2030

Final Report Submission: December 31, 2031

Please submit the protocol to your IND 18540, with a cross-reference letter to BLA STN BL 125775 explaining that this protocol was submitted to the IND. Please refer to the sequential number for each study/clinical trial and the submission number as shown in this letter.

Please submit the final study report to the BLA. If the information in the final study report supports a change in the labeling, the final study report must be submitted as a supplement to BLA STN BL 125775. For administrative purposes, all submissions related to this postmarketing study required under section 505(o) must be submitted to this BLA and be clearly designated as:

- **Required Postmarketing Correspondence under Section 505(o)**
- **Required Postmarketing Final Report under Section 505(o)**
- **Supplement contains Required Postmarketing Final Report under Section 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. In addition, section 506B of the FDCA and 21 CFR 601.70 require you to report annually on the status of any postmarketing commitments or required studies or clinical trials.

You must describe the status in an annual report on postmarketing studies for this product. Label your annual report as an **Annual Status Report of Postmarketing Requirements/Commitments** and submit it to the FDA each year within 60 calendar days of the anniversary date of the approval of BLA STN BL 125775 until all requirements and commitments subject to the reporting requirements of section 506B of the FDCA are fulfilled or released. The status report for each study should include:

- the sequential number for each study as shown in this letter;
- information to identify and describe the postmarketing requirement;
- the original milestone schedule for the requirement;
- the revised milestone schedule for the requirement, if appropriate;
- the current status of the requirement (i.e., pending, ongoing, delayed, terminated, or submitted); and,
- an explanation of the status for the study or clinical trial. The explanation should include how the study is progressing in reference to the original projected schedule, including, the patient accrual rate (i.e., number enrolled to date and the total planned enrollment).

As described in 21 CFR 601.70(e), we may publicly disclose information regarding these postmarketing studies on our website at http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Post-marketingPhaseIVCommitments/default.htm.

We will consider the submission of your annual report under section 506B of the FDCA 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 section 505(o) and 21 CFR 601.70. We remind you that to comply with section 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 periodically report on the status of studies or clinical trials required under section 505(o) may be a violation of FDCA section 505(o)(3)(E)(ii) and could result in regulatory action.

RELEASE FROM POSTMARKETING COMMITMENT

We also refer to your submission received September 2, 2022, reporting on the following postmarketing commitment (PMC) identified in the STN 125775/0 approval letter dated May 3, 2023.

PMC #4 EPI-RSV-041 VS US DB (220149), a postmarketing active surveillance study, to evaluate atrial fibrillation in adults 60 years and older vaccinated with AREXVY in the United States. Using a self-controlled risk interval (SCRI) design, the study will be conducted in the Sentinel System.

We have completed the review of your submission and conclude that you are released from the above PMC because we are expanding the use to include individuals 50 years of age and older at increased risk for LRTD caused by RSV.

The above PMC will be replaced by the new PMC described below.

NEW POSTMARKETING COMMITMENTS SUBJECT TO THE REPORTING REQUIREMENTS UNDER SECTION 506B

PMC #2 EPI-RSV-041 VS US DB (220149), to evaluate atrial fibrillation in adults 50 years of age and older vaccinated with AREXVY in the United States. Using a self-controlled risk interval (SCRI) design, the study will be conducted in the Sentinel System.

Final protocol submission: June 30, 2024

Study/Clinical trial completion: June 30, 2030

Final Report Submission: December 31, 2031

Please submit clinical protocols to your IND 18540, and a cross-reference letter to BLA STN BL 125775 explaining that this protocol was submitted to the IND.

Please submit the final study report to the BLA. If the information in the final study report supports a change in the labeling, the final study report must be submitted as a supplement. Please use the following designators to prominently label all submissions,

including supplements, relating to these postmarketing study commitments as appropriate:

- **Postmarketing Commitment – Correspondence Status Update**
- **Postmarketing Commitment – Final Study Report**
- **Supplement contains Postmarketing Commitment Final Study Report**

For each postmarketing study subject to the reporting requirements of 21 CFR 601.70, you must describe the status in an annual report on postmarketing studies for this product. Label your annual report as an **Annual Status Report of Postmarketing Requirements/Commitments** and submit it to the FDA each year within 60 calendar days of the anniversary date of the approval of BLA STN BL 125775/132 until all requirements and commitments subject to the reporting requirements of section 506B of the Federal Food, Drug, and Cosmetic Act (FDCA) are fulfilled or released. The status report for each study should include:

- the sequential number for each study as shown in this letter;
- information to identify and describe the postmarketing commitment;
- the original schedule for the commitment;
- the status of the commitment (i.e., pending, ongoing, delayed, terminated, or submitted); and,
- an explanation of the status including, for clinical studies, the patient accrual rate (i.e., number enrolled to date and the total planned enrollment).

As described in 21 CFR 601.70(e), we may publicly disclose information regarding these postmarketing studies on our website at http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Post-marketingPhaseIVCommitments/default.htm.

We will include information contained in the above-referenced supplement in your BLA file.

Sincerely,

Rebecca Reindel, M.D.
Division Director
Division of Clinical and Toxicology Review
Office of Vaccines Research and Review
Center for Biologics Evaluation and Research