



Our STN: BL 125696/247

**SUPPLEMENT APPROVAL
PMR FULFILLED**

Aimmune Therapeutics, Inc.
Attention: Vandana Garikipati, Ph.D.
1007 US Hwy 202/206, Bldg JR2
Bridgewater, NJ 08807

July 26, 2024

Dear Dr. Garikipati:

We have approved your request received September 28, 2023, to supplement your Biologics License Application (BLA) submitted under section 351(a) of the Public Health Service Act for Peanut (*Arachis hypogaea*) Allergen Powder-dnfp (PALFORZIA) manufactured at CoreRx Inc., Clearwater, Florida facility to extend the age indication to include patients 1 through 3 years of age with a confirmed diagnosis of peanut allergy.

We have also approved a modification to the approved Risk Evaluation and Mitigation Strategy (REMS) to align the REMS Document and REMS materials with editorial changes in the United States Package Insert (USPI) to improve clarity regarding the first dose of each “new” Up-Dosing level, and to include the different dosing regimen for the younger age group (patients 1 through 3 years of age).

The review of this supplement was associated with the following National Clinical Trial (NCT) number: NCT03736447.

LABELING

We hereby approve the draft content of labeling: Package Insert submitted under amendment 29, dated July 23, 2024, Medication Guide submitted under amendment 28, dated July 18, 2024, and the draft carton and container labels submitted under amendment 13 dated April 19, 2024 and amendment 20 dated June 20, 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 July 23, 2024, and Medication Guide submitted on July 18, 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. We request that the labeling approved today be available on your website within 10 days of receipt of this letter.

CARTON AND CONTAINER LABELS

Please electronically submit final printed carton and container labels identical to the carton and container labels submitted on April 19, 2024 and June 20, 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 125696 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.

FULFILLED POSTMARKETING REQUIREMENT

This submission fulfills your postmarketing requirement PMR# 1 identified in the January 31, 2020, approval letter for BLA STN BL 125696 for Peanut (*Arachis hypogaea*) Allergen Powder-dnfp (PALFORZIA). The requirement addressed in this submission is as follows:

1. Deferred pediatric study under Pediatric Research Equity Act for the mitigation of allergic reactions, including anaphylaxis, that may occur with accidental exposure to peanut in pediatric patients ages 1 through < 4 years.

PEDIATRIC REQUIREMENTS

Under the Pediatric Research Equity Act (PREA) (21 U.S.C. 355c), all applications for new active ingredients, 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 note that you have fulfilled the pediatric study requirement for all relevant pediatric age groups for this application.

POSTMARKETING COMMITMENTS SUBJECT TO REPORTING REQUIREMENTS UNDER SECTION 506B

We remind you that there is a PMC still open. 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 this BLA until all Requirements and Commitments subject to the reporting requirements of section 506B of the Federal Food, Drug, and Cosmetic Act 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 <https://www.fda.gov/drugs/guidance-compliance-regulatory-information/postmarket-requirements-and-commitments>.

RISK EVALUATION AND MITIGATION STRATEGY (REMS) REQUIREMENTS

The REMS for Peanut (*Arachis hypogaea*) Allergen Powder-dnfp (PALFORZIA) was originally approved on January 31, 2020, and the most recent REMS modification was approved on May 26, 2021. The REMS consists of elements to assure safe use, an implementation system, and a timetable for submission of assessments of the REMS.

Your proposed modification to the REMS consists of changes to align the REMS Document and REMS materials with editorial changes in the United States Package Insert (USPI) to improve clarity regarding the first dose of each “new” Up-Dosing level, and to include the different dosing regimen for the younger age group (patients 1 through 3 years of age).

Your proposed modified REMS submitted July 23, 2024, and appended to this letter, is approved.

The timetable for submission of assessments of the REMS remains the same as that approved on January 31, 2020.

There are no changes to the REMS assessment plan described in our letter for the most recent REMS modification approved on May 26, 2021.

We remind you that in addition to the REMS assessments submitted according to the timetable in the approved REMS, you must include an adequate rationale to support any proposed REMS modification for the addition, modification, or removal of any goal or element of the REMS, as described in section 505-1(g)(4) of the FDCA.

We also remind you that you must submit a REMS assessment when you submit a supplemental application for a new indication for use as described in section 505-1(g)(2)(A) of the FDCA. This assessment should include:

- a) An evaluation of how the benefit-risk profile will or will not change with the new indication;
- b) A determination of the implications of a change in the benefit-risk profile for the current REMS;
- c) *If the new indication for use introduces unexpected risks:* A description of those risks and an evaluation of whether those risks can be appropriately managed with the currently approved REMS.
- d) *If a REMS assessment was submitted in the 18 months prior to submission of the supplemental application for a new indication for use:* A statement about whether the REMS was meeting its goals at the time of the last assessment and if any modifications of the REMS have been proposed since that assessment.

- e) *If a REMS assessment has not been submitted in the 18 months prior to submission of the supplemental application for a new indication for use:* Provision of as many of the currently listed assessment plan items as is feasible.
- f) *If you propose a REMS modification based on a change in the benefit-risk profile or because of the new indication of use, submit an adequate rationale to support the modification, including:* Provision of the reason(s) why the proposed REMS modification is necessary, the potential effect on the serious risk(s) for which the REMS was required, on patient access to the drug, and/or on the burden on the health care delivery system; and other appropriate evidence or data to support the proposed change. Additionally, include any changes to the assessment plan necessary to assess the proposed modified REMS.
- g) *If you are not proposing REMS modifications,* provide a rationale for why the REMS does not need to be modified.

If the assessment instruments and methodology for your REMS assessments are not included in the REMS supporting document, or if you propose changes to the submitted assessment instruments or methodology, you should update the REMS supporting document to include specific assessment instrument and methodology information at least 90 days before the assessments will be conducted. Updates to the REMS supporting document may be included in a new document that references previous REMS supporting document submission(s) for unchanged portions. Alternatively, updates may be made by modifying the complete previous REMS supporting document, with all changes marked and highlighted. Prominently identify the submission containing the assessment instruments and methodology with the following wording in bold capital letters at the top of the first page of the submission:

BLA 125696 REMS ASSESSMENT METHODOLOGY

Prominently identify any submission containing the REMS assessments or proposed modifications of the REMS with the following wording in bold capital letters at the top of the first page of the submission as appropriate:

BLA 125696 REMS ASSESSMENT

or

NEW SUPPLEMENT FOR BLA 125696 CHANGES BEING EFFECTED IN 30 DAYS PROPOSED MINOR REMS MODIFICATION

or

NEW SUPPLEMENT FOR BLA 125696

**PRIOR APPROVAL SUPPLEMENT
PROPOSED MAJOR REMS MODIFICATION**

or

**NEW SUPPLEMENT FOR BLA 125696
PRIOR APPROVAL SUPPLEMENT
PROPOSED REMS MODIFICATIONS DUE TO SAFETY LABEL CHANGES
SUBMITTED IN SUPPLEMENT XXX**

or

**NEW SUPPLEMENT (NEW INDICATION FOR USE)
FOR BLA 125696
REMS ASSESSMENT
PROPOSED REMS MODIFICATION (if included)**

Should you choose to submit a REMS revision, prominently identify the submission containing the REMS revisions with the following wording in bold capital letters at the top of the first page of the submission:

REMS REVISIONS FOR BLA 125696

To facilitate review of your submission, we request that you submit your proposed modified REMS and other REMS-related materials in Microsoft Word format. If certain documents, such as enrollment forms, are only in PDF format, they may be submitted as such, but the preference is to include as many as possible in Word format.

SUBMISSION OF REMS DOCUMENT IN SPL FORMAT

As soon as possible, but no later than 14 days from the date of this letter, submit the REMS document in Structured Product Labeling (SPL) format using the FDA automated drug registration and listing system (eLIST). Content of the REMS document must be identical to the approved REMS document. The SPL will be publicly available.

Information on submitting REMS in SPL format may be found in the guidance for industry *Providing Regulatory Submission in Electronic Format – Content of the Risk Evaluation and Mitigation Strategies Document Using Structured Product Labeling*.

For additional information on submitting REMS in SPL format, please email FDAREMSwebsite@fda.hhs.gov.

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).

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

Sincerely,

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

Enclosures:
REMS