

Risk Evaluation and Mitigation Strategy (REMS) Document

PALFORZIA [Peanut (*Arachis hypogaea*) Allergen Powder-dnfp]

REMS Program

I. Administrative Information

Application Number: BLA 125696
Application Holder: Aimmune Therapeutics, Inc.
Initial REMS Approval: 01/2020

II. REMS Goal

The goal of the PALFORZIA REMS Program is to mitigate the risk of anaphylaxis associated with PALFORZIA by:

1. Ensuring that healthcare providers who prescribe and healthcare settings that dispense and administer PALFORZIA are educated on the following:
 - a. the risk of anaphylaxis associated with the use of PALFORZIA
 - b. the Initial Dose Escalation and first dose of each Up-Dosing level must only be administered to patients in a healthcare setting equipped to monitor patients, and to identify and manage anaphylaxis.
2. Ensuring that the Initial Dose Escalation and the first dose of each Up-Dosing level of PALFORZIA are only dispensed and distributed to certified healthcare settings and only administered to patients in certified healthcare settings.
3. Ensuring that PALFORZIA is only dispensed and administered to patients who are informed, by enrolling in the PALFORZIA REMS Program, of the need to have injectable epinephrine available for immediate use at all times, the need for monitoring with the Initial Dose Escalation and first dose of each Up-Dosing level, the need for continued dietary peanut avoidance, and how to recognize the signs and symptoms of anaphylaxis.

III. REMS Requirements

Aimmune Therapeutics, Inc. must ensure that healthcare providers, patients, healthcare settings, pharmacies, and wholesalers-distributors comply with the following requirements:

1. Healthcare providers who prescribe PALFORZIA must:	
To become certified to prescribe	<ol style="list-style-type: none">1. Review the PALFORZIA Prescribing Information.2. Enroll in the REMS by completing the Prescriber Enrollment Form and submitting it to the REMS Program.
Before treatment initiation (first dose)	<ol style="list-style-type: none">3. Enroll the patient by completing and submitting the Patient Enrollment Form to the REMS Program. Provide a completed copy of the form to the patient.4. Counsel the patient on the need to have injectable epinephrine available for immediate use at all times, the need for monitoring with the Initial Dose Escalation and first dose of each Up-Dosing level, the need for continued peanut avoidance in the diet, and how to recognize the signs and symptoms of anaphylaxis.5. Assess the patient's supply of injectable epinephrine and provide prescription if necessary.

During treatment; before dispensing the first dose of each Up-Dosing level	6. Assess the patient’s tolerability of the previous dosing level and appropriateness of continuing the Up-Dosing.
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At all times	7. Report treatment discontinuation or transfer of care to the REMS Program.
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2. Patients who are prescribed PALFORZIA:

Before treatment initiation	1. Enroll in the REMS Program by completing the Patient Enrollment Form with the prescriber. Enrollment information will be provided to the REMS Program. 2. Receive counseling from the prescriber on the need to have injectable epinephrine available for immediate use at all times, the need for monitoring with the Initial Dose Escalation and the first dose of each Up-Dosing level, the need for continued peanut avoidance in the diet, and how to recognize the signs and symptoms of anaphylaxis.
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During treatment, before the first dose of each Up-Dosing level	3. Receive counseling from a healthcare provider on the need for monitoring for anaphylaxis.
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During treatment, during and after administration of the Initial Dose Escalation and the first dose of each Up-Dosing level, for at least 60 minutes	4. Be monitored for anaphylaxis at the healthcare setting.
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At all times	5. Report anaphylaxis to your healthcare provider. 6. Inform your healthcare provider if you need more injectable epinephrine. 7. Have injectable epinephrine available for immediate use. 8. Adhere to the safe use conditions: avoid peanuts and foods that contain peanuts.
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3. Healthcare settings that dispense PALFORZIA must:

To become certified to dispense	1. Have healthcare provider(s) on-site to monitor for and manage anaphylaxis. 2. Have a certified prescriber on-site. 3. Be able to manage anaphylaxis on-site. 4. Designate an authorized representative to carry out the certification process and oversee implementation and compliance with the REMS Program on behalf of the healthcare setting. 5. Have the authorized representative review the Education Program for Healthcare Settings . 6. Have the authorized representative enroll in the REMS Program by completing the Healthcare Setting Enrollment Form and submitting it to the REMS Program. 7. Train all relevant staff involved in dispensing and administering PALFORZIA using the Education Program for Healthcare Settings . 8. Establish processes and procedures to verify the Initial Dose Escalation is prescribed to initiate treatment and the dose, as determined by the certified prescriber, from the Office Dose Kit is dispensed to enrolled patients for the first dose of each Up-Dosing level.
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	<ol style="list-style-type: none"> 9. Establish processes and procedures to verify the patient is monitored by a healthcare provider during and after the Initial Dose Escalation and the first dose of each Up-Dosing level. 10. Establish processes and procedures to verify the patient has injectable epinephrine before the first dose of each Up-Dosing level.
Before administering (first dose)	11. Verify the Initial Dose Escalation is for the enrolled patient.
During treatment; before the first dose of each Up-Dosing level	<ol style="list-style-type: none"> 12. Verify that the patient is enrolled in the REMS through the processes and procedures established as a requirement of the REMS Program. 13. Counsel the patient on the need for monitoring for anaphylaxis. 14. Verify that the dose, as determined by the certified prescriber, is dispensed from the Office Dose Kit through the processes and procedures established as a requirement of the REMS Program. 15. Verify that the patient has injectable epinephrine through the processes and procedures established as a requirement of the REMS Program.
During and after administering the Initial Dose Escalation and the first dose of each Up-Dosing level, for at least 60 minutes	16. Assess the patient for anaphylaxis through the processes and procedures established as a requirement of the REMS Program.
To maintain certification to dispense	17. Have a new Authorized Representative enroll in the REMS Program by completing the Healthcare Setting Enrollment Form if the authorized representative changes.
At all times	<ol style="list-style-type: none"> 18. Not distribute, transfer, loan or sell PALFORZIA. 19. Maintain records of dispensing and that all processes and procedures are in place and are being followed. 20. Comply with audits carried out by Aimmune Therapeutics, Inc., or a third party acting on behalf of Aimmune Therapeutics, Inc., to ensure that all processes and procedures are in place and are being followed.

4. Pharmacies that dispense PALFORZIA must:

To become certified to dispense	<ol style="list-style-type: none"> 1. Designate an authorized representative to carry out the certification process and oversee implementation and compliance with the REMS Program on behalf of the pharmacy. 2. Have the authorized representative review the REMS Program Overview for Pharmacies. 3. Have the Authorized Representative enroll in the REMS Program by completing the Pharmacy Enrollment Form and submitting it to the REMS Program. 4. Train all relevant staff involved in dispensing PALFORZIA using the REMS Program Overview for Pharmacies. 5. For the Initial Dose Escalation: Establish processes and procedures to verify that the prescriber is certified, the patient is enrolled, and the Initial Dose Escalation is only dispensed to certified healthcare settings. 6. For Up-Dosing prescriptions: Establish processes and procedures to verify that the patient is enrolled, the prescriber is certified, and only one dose level is dispensed to the patient at a time.
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Before dispensing the Initial Dose Escalation	7. Verify the prescriber is certified, the patient is enrolled, and the Initial Dose Escalation is only dispensed to a certified healthcare setting through the processes and procedures established as a requirement of the REMS Program.
Before dispensing all Up-Dosing prescriptions	8. Verify that the patient is enrolled, the prescriber is certified, and only one dose level is dispensed to the patient at a time through the processes and procedures established as a requirement of the REMS Program.
To maintain certification to dispense	9. Have a new Authorized Representative enroll in the REMS Program by completing the Pharmacy Enrollment Form if the Authorized Representative changes.
At all times	10. Not dispense the Initial Dose Escalation for use outside a certified healthcare setting. 11. Not distribute, transfer, loan or sell PALFORZIA. 12. Maintain records that all processes and procedures are in place and are being followed. 13. Comply with audits carried out by Aimmune Therapeutics, Inc., or a third party acting on behalf of Aimmune Therapeutics, Inc., to ensure that all processes and procedures are in place and are being followed.

5. Wholesalers-distributors that distribute PALFORZIA must:

To be able to distribute	1. Establish processes and procedures to ensure that PALFORZIA is distributed only to certified pharmacies and certified healthcare settings. 2. Train all relevant staff involved in distributing on the REMS Program requirements.
At all times	3. Distribute only to certified pharmacies and healthcare settings. 4. Maintain records of PALFORZIA distribution. 5. Comply with audits carried out by Aimmune Therapeutics, Inc., or a third party acting on behalf of Aimmune Therapeutics, Inc., to ensure that all processes and procedures are in place and are being followed.

Aimmune Therapeutics, Inc. must provide training to healthcare settings that dispense PALFORZIA.

The training includes the following educational material: [Education Program for Healthcare Settings](#). The training must be available online and by hard copy via fax, e-mail and mail.

Aimmune Therapeutics, Inc. must provide training to pharmacies that dispense PALFORZIA.

The training includes the following educational materials: [REMS Program Overview for Pharmacies](#). The training must be available online and by hard copy via fax, e-mail and mail.

To support REMS Program operations, Aimmune Therapeutics, Inc. must:

1. Establish and maintain a REMS Program website, www.PALFORZIAREMS.com. The REMS Program website must include the capability to complete prescriber and healthcare setting certification online, the capability to enroll patients online, verify prescriber, healthcare setting certification and patient enrollment online, the option to print the Prescribing Information, Medication Guide, and REMS materials. All product websites for consumers and healthcare providers must include prominent REMS-specific links to the REMS Program website. The REMS program website must not link back to the promotional product website(s).

2. Make the REMS Program website fully operational and all REMS Program materials available through the website and REMS Program Coordinating Center by the date PALFORZIA is first commercially distributed.
3. Establish and maintain a REMS Program Coordinating Center for REMS participants at 1-844-725-3679.
4. Establish and maintain a validated, secure database of all REMS Program participants who are enrolled and/or certified in the PALFORZIA REMS Program.
5. Ensure prescribers and healthcare settings are able to become certified in the REMS Program by fax and online.
6. Ensure pharmacies are able to become certified in the REMS Program by fax.
7. Ensure that prescribers are able to enroll patients in the REMS Program by fax and online.
8. Ensure pharmacies are able to verify patient enrollment, prescriber and healthcare setting certification by phone and online.
9. Provide the [Prescriber Enrollment Form](#), the Prescribing Information, and the [Patient Enrollment Form](#) to healthcare providers who (1) attempt to prescribe PALFORZIA and are not yet certified or (2) inquire about how to become certified.
10. Provide the [Healthcare Setting Enrollment Form](#), the [Education Program for Healthcare Settings](#) and the [Patient Enrollment Form](#) to healthcare settings that (1) attempt to dispense PALFORZIA and are not yet certified or (2) inquire about how to become certified.
11. Provide the [Pharmacy Enrollment Form](#) and the [REMS Program Overview for Pharmacies](#) to pharmacies that (1) attempt to dispense PALFORZIA and are not yet certified or (2) inquire about how to become certified.
12. Notify prescribers, healthcare settings and pharmacies within 2 business days after they become certified in the REMS Program.
13. Provide certified pharmacies access to the database of certified prescribers, healthcare settings and enrolled patients.
14. Provide authorized wholesalers-distributors access to the database of certified pharmacies and healthcare settings.
15. Provide certified prescribers and healthcare settings access to the database of certified pharmacies, authorized wholesalers-distributors and enrolled patients.

To ensure REMS participants' compliance with the REMS Program, Aimmune Therapeutics, Inc. must:

16. Maintain adequate records to demonstrate that REMS Program requirements have been met, including, but not limited to records of: PALFORZIA distribution and dispensing; certification of prescribers, healthcare settings, and pharmacies; enrolled patients; audits of REMS participants. These records must be readily available for FDA inspections.
17. Establish a plan for addressing noncompliance with REMS Program requirements.
18. Monitor prescribers, healthcare settings, and pharmacies on an ongoing basis to ensure the requirements of the REMS are being met. Take corrective action if non-compliance is identified, including decertification.
19. Verify annually that the authorized representative's name and information correspond to the certified healthcare setting.
20. Verify annually that the authorized representative's name and information correspond to the certified pharmacy.
21. Maintain an ongoing annual audit plan of 10% (but no less than 50) certified healthcare settings and 10% (but no less than 50) certified pharmacies.

22. Audit 10% but no less than 50 certified healthcare settings no later than 120 calendar days after the healthcare setting places its first order for PALFORZIA to ensure that REMS Program processes and procedures are in place, functioning, and support the REMS Program requirements.
23. Audit 10% but no less than 50 certified pharmacies no later than 120 calendar days after the pharmacy dispenses its first prescription of PALFORZIA to ensure that REMS Program processes and procedures are in place, functioning, and support the REMS Program requirements.
24. Audit all wholesalers-distributors no later than 120 calendar days after they become authorized to distribute the drug and annually thereafter, to ensure that all REMS processes and procedures are in place, functioning, and support the REMS Program requirements.
25. Take reasonable steps to improve implementation of and compliance with the requirements in the PALFORZIA REMS Program based on monitoring and evaluation of the PALFORZIA REMS Program.

IV. REMS Assessment Timetable

Aimmune Therapeutics, Inc. must submit REMS assessments at 6 months and 12 months and annually thereafter from the date of initial approval of the REMS (01/31/2020). To facilitate inclusion of as much information as possible while allowing reasonable time to prepare the submission, the reporting interval covered by each assessment should conclude no earlier than 60 calendar days before the submission date for that assessment. Aimmune Therapeutics, Inc. must submit each assessment so that it will be received by the FDA on or before the due date.

V. REMS Materials

The following materials are part of the PALFORZIA REMS:

Enrollment Forms

Prescriber:

1. [Prescriber Enrollment Form](#)

Patient:

2. [Patient Enrollment Form](#)

Healthcare Settings:

3. [Healthcare Setting Enrollment Form](#)

Pharmacy:

4. [Pharmacy Enrollment Form](#)

Training and Educational Materials

Healthcare settings:

5. [Education Program for Healthcare Settings](#)

Pharmacy:

6. [REMS Program Overview for Pharmacies](#)

Other Materials

7. [REMS Program Website](#)