DOSING OVERVIEW

PALFORZIA dosing begins with Initial Dose Escalation, followed by Up-Dosing, and continued with Maintenance dosing.

INDICATION

PALFORZIA is an oral immunotherapy indicated for the mitigation of allergic reactions, including anaphylaxis, that may occur with accidental exposure to peanut. PALFORZIA is approved for use in patients with a confirmed diagnosis of peanut allergy. Initial Dose Escalation may be administered to patients aged 4 through 17 years. Up-Dosing and Maintenance may be continued in patients 4 years of age and older.

PALFORZIA is to be used in conjunction with a peanut-avoidant diet.

Limitation of Use: Not indicated for the emergency treatment of allergic reactions, including anaphylaxis.

IMPORTANT SAFETY INFORMATION

WARNING: ANAPHYLAXIS

- **PALFORZIA can cause anaphylaxis, which may be life threatening and can occur at any time during PALFORZIA therapy.**
- **Prescribe injectable epinephrine, instruct and train patients on its appropriate use, and instruct patients to seek immediate medical care upon its use.**
- **Do not administer PALFORZIA to patients with uncontrolled asthma.**
- **Dose modifications may be necessary following an anaphylactic reaction.**
- **Observe patients during and after administration of the Initial Dose Escalation and the first dose of each Up-Dosing level, for at least 60 minutes.**
- **PALFORZIA is available only through a restricted program called the PALFORZIA REMS.**

Please see additional Important Safety Information on pages 2 and 8.

Please see full Prescribing Information, including Boxed WARNING, and Medication Guide at PALFORZIAPro.com.

Palforzia®
Peanut (*Arachis hypogaea*) Allergen Powder-dnfp

BEFORE TREATMENT BEGINS

Follow these steps before initiating treatment[1]

1. **ENROLL IN PALFORZIA REMS** and train staff on PALFORZIA use.
2. **PRESCRIBE EPINEPHRINE AUTO-INJECTOR,** train patients on its use, and instruct them to seek immediate medical care after its use.
3. **TEACH PATIENTS TO RECOGNIZE** the signs and symptoms of anaphylaxis.
4. **ADVISE PATIENTS** to continue to follow a strict peanut-avoidant diet.
5. **INSTRUCT PATIENTS TO CONTACT** your office before taking the next dose of PALFORZIA if symptoms of an escalating or persistent allergic reaction occur as dose modification may be necessary.
6. **ADVISE PATIENTS WITH ASTHMA** to stop taking PALFORZIA and contact your office immediately if they have difficulty breathing or if their asthma becomes difficult to control.

To receive a dose of PALFORZIA in the phase 3 PALISADE trial, study participants had to be free of[2]

- Active wheezing or a flare of atopic disease (e.g., atopic dermatitis)
- Suspected intercurrent illness

Patients may be more likely to experience allergic reactions following PALFORZIA administration in the presence of the following cofactors[1]:

- Exercise
- Hot water exposure
- Intercurrent illness (such as viral infection)
- Fasting
- Menstruation
- Sleep deprivation
- Nonsteroidal anti-inflammatory drug use
- Uncontrolled asthma

Patients should be proactively counseled about the potential for increased risk of anaphylaxis in the presence of these cofactors. If possible, adjust the time of dosing to avoid these cofactors. If it is not possible to avoid these cofactors, consider withholding PALFORZIA temporarily.

IMPORTANT SAFETY INFORMATION (CONTINUED)

CONTRAINDICATIONS

PALFORZIA is contraindicated in patients with uncontrolled asthma, or with a history of eosinophilic esophagitis and other eosinophilic gastrointestinal disease.

TREATMENT REMINDERS

Patients should take PALFORZIA at the same time each day. During Up-Dosing, patients should not take PALFORZIA at home on the day of an Up-Dosing office visit.[1]

Patients should avoid exercise and hot showers or baths immediately prior to or within 3 hours after dosing.[1]

Patients should consume PALFORZIA with a meal, preferably in the evening.[1]

Healthcare providers should observe patients for at least 60 minutes after the last dose of the Initial Dose Escalation and after the first dose of each Up-Dosing level. Parents/caregivers should observe patients for at least 60 minutes after administering PALFORZIA at home.[1]

TIP: In the PALISADE trial, patients continued their usual medications, including those taken for asthma, allergic rhinitis, and atopic dermatitis.[2]

Please see Important Safety Information on pages 1-2 and 8.

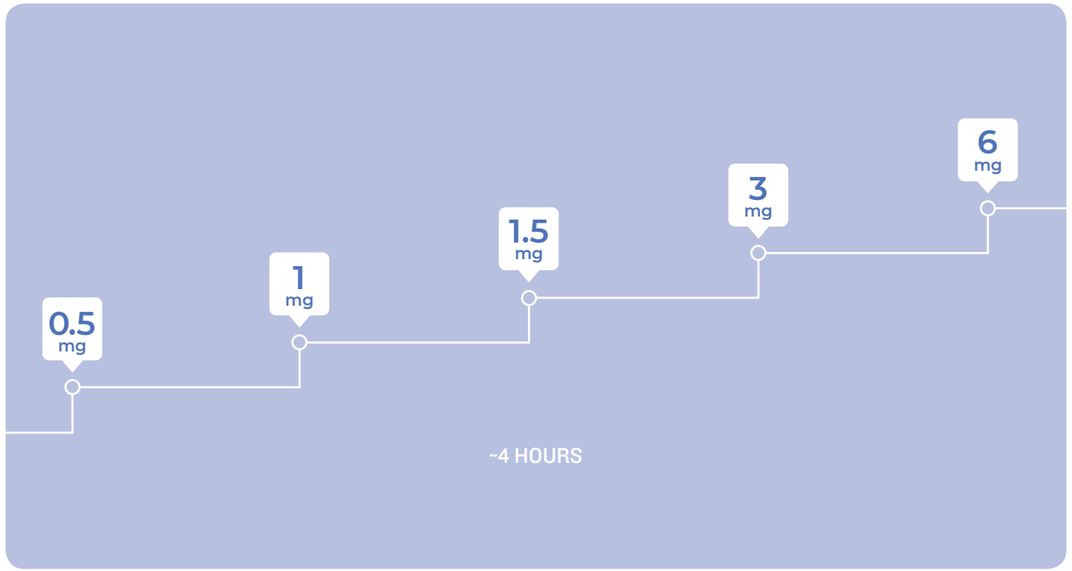
Please see full Prescribing Information, including Boxed WARNING, and Medication Guide at PALFORZIAPro.com.

Palforzia®
Peanut (*Arachis hypogaea*) Allergen Powder-dnfp

INITIAL DOSE ESCALATION

Basic information[1]

- Takes place at the clinic
- Typically lasts ~4 hours
- Consists of 5 sequential dose escalations (no dose level should be omitted)
- Observe patients after final dose for at least 60 minutes



Doses administered during Initial Dose Escalation[1]

Administer all 5 doses sequentially, separated by an observation period of **20 to 30 minutes.** Observe patients after the last dose for at least **60 minutes** until suitable for discharge.

DOSE LEVEL	TOTAL DOSE
A	0.5 mg
B	1 mg
C	1.5 mg
D	3 mg
E	6 mg

Discontinue treatment with PALFORZIA for[1]

- Patients who are unable to tolerate doses up to and including the 3-mg dose during Initial Dose Escalation

TIP: Advise patients to bring refrigerated or room-temperature, semi-solid food to which they are not allergic. Examples: applesauce, yogurt, pudding.

TIP: (Optional) Encourage patients to bring books, tablets, or other devices for entertainment purposes during this visit.

Please see Important Safety Information on pages 1-2 and 8.

Please see full Prescribing Information, including Boxed WARNING, and Medication Guide at PALFORZIAPro.com.

Palforzia®
Peanut (*Arachis hypogaea*)
Allergen Powder-dnfp

INITIAL DOSE ESCALATION (CONTINUED)

Assessing tolerability[1]

Each dose during Initial Dose Escalation should be separated by an observation period of 20 to 30 minutes. Observe patients after last dose for at least 60 minutes until suitable for discharge.

DISCONTINUE PALFORZIA IF:

Symptoms requiring medical intervention (e.g., use of epinephrine) occur

Patients who tolerate at least the 3-mg single dose of PALFORZIA during Initial Dose Escalation must return to the healthcare setting for initiation of Up-Dosing. Begin Up-Dosing the day after Initial Dose Escalation if possible, and within 4 days of Initial Dose Escalation at the latest.

Repeat Initial Dose Escalation in a healthcare setting if the patient is unable to begin Up-Dosing within 4 days.

Dose modifications are not appropriate during Initial Dose Escalation.

Please see next page for additional information on how dose tolerability was assessed, based on clinical trial experience, and refer to the **Assessing Allergic Reactions** brochure.

The following protocol was used to assess dose tolerability and next steps during the Initial Dose Escalation phase in the PALISADE trial[2]:

PALISADE TRIAL ALGORITHM BASED ON SEVERITY OF ALLERGIC REACTIONS FOLLOWING DOSE ADMINISTRATION

NO SYMPTOMS OR ORAL/ PHARYNGEAL PRURITUS SYMPTOMS ONLY	OTHER MILD SYMPTOMS	MODERATE SYMPTOMS	SEVERE SYMPTOMS
Time to next dose: 30 minutes **Next dose:** Advanced to next level	**Time to next dose:** Advanced to next level within 30 to 60 minutes; or treated with antihistamine and then resumed dose escalation within 60 minutes of last dose provided that the patient had no or only minimal residual signs or symptoms If, however, the subject required a second medication (e.g., epinephrine or a beta-agonist) to treat the symptoms, or more than 2 doses of an antihistamine, Initial Dose Escalation was discontinued	**Occurring at ≤3 mg:** Treated as indicated for moderate reactions; stopped Up-Dosing and discontinued PALFORZIA **Occurring at 6 mg:** Treated as indicated for moderate reactions; patient could continue with Up-Dosing the next day	Treated as indicated for severe reactions; discontinued PALFORZIA

Please see **Assessing Allergic Reactions** brochure for full criteria to assess the severity of allergic reactions.

Please see Important Safety Information on pages 1-2 and 8.

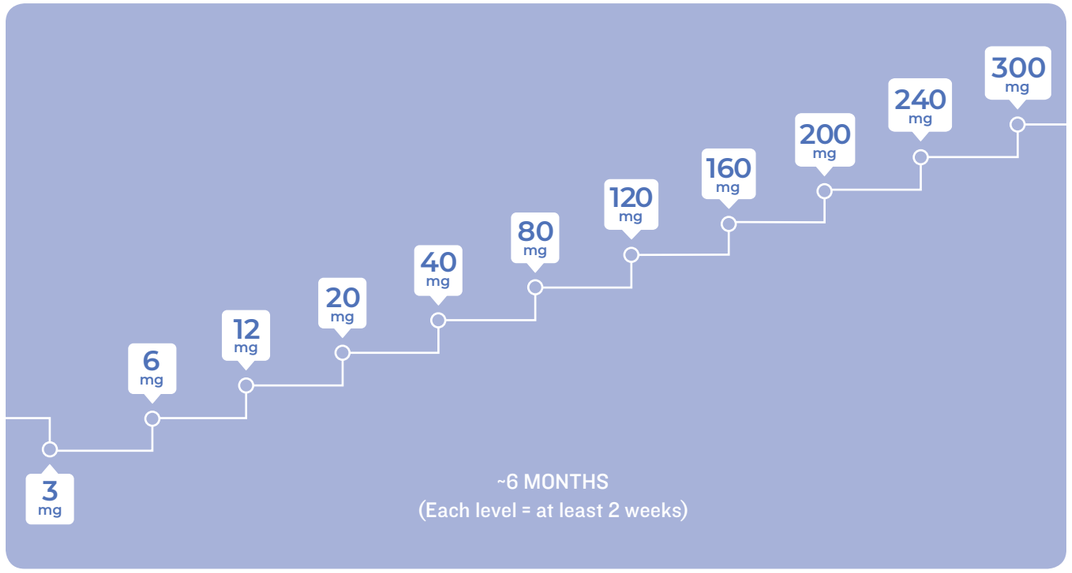
Please see full Prescribing Information, including Boxed WARNING, and Medication Guide at PALFORZIAPro.com.

Palforzia®
Peanut (*Arachis hypogaea*) Allergen Powder-dnfp

UP-DOSING

Basic information[1]

- Takes place in office and at home
- Consists of 11 dose levels and is initiated at a 3-mg dose
- Each dose level is administered daily and increased sequentially in 2-week intervals, if tolerated
- Observe patients for at least 60 minutes after each dose



Instruct patient to return to the healthcare setting every 2 weeks for each subsequent assessment for a new Up-Dosing level. Patients must complete all levels (1-11) of dose escalation prior to initiation of Maintenance dosing.

No more than 1 dose should be consumed per day. Instruct patients not to take a dose at home on the day of a scheduled Up-Dosing office visit.

Discontinue treatment with PALFORZIA for[1]

- Patients with suspected eosinophilic esophagitis
- Patients unable to comply with the daily dosing requirements
- Patients with recurrent asthma exacerbations or persistent loss of asthma control

DO NOT omit a dose level from the dose escalation schedule.
DO NOT escalate dosing faster than every 2 weeks.

Dosing configuration[1]

DOSE LEVEL	TOTAL DAILY DOSE
1	3 mg
2	6 mg
3	12 mg
4	20 mg
5	40 mg
6	80 mg
7	120 mg
8	160 mg
9	200 mg
10	240 mg
11	300 mg

Consider dose modification or discontinuation for patients who do not tolerate Up-Dosing.

Temporary dose modification of PALFORZIA may be required for patients who experience allergic reactions during Up-Dosing or Maintenance, for patients who miss doses, or for practical reasons of patient management. Allergic reactions, including gastrointestinal reactions, that are severe, recurrent, bothersome, or last longer than 90 minutes during Up-Dosing or Maintenance should be actively managed with dose modifications. **Use clinical judgment to determine the best course of action, which can include maintaining the dose level for longer than 2 weeks, reducing, withholding, or discontinuing PALFORZIA doses.**

Please see **Assessing Allergic Reactions** brochure for full criteria to assess the severity of allergic reactions.

Please see Important Safety Information on pages 1-2 and 8.

Please see full Prescribing Information, including Boxed WARNING, and Medication Guide at PALFORZIAPro.com.

Palforzia®
Peanut (*Arachis hypogaea*)
Allergen Powder-dnfp

UP-DOSING (CONTINUED)

Assessing tolerability[1]

The first dose of each new Up-Dosing level is administered under the supervision of a healthcare professional in a healthcare setting with the ability to manage potentially severe allergic reactions, including anaphylaxis.

IF THE FIRST DOSE IS TOLERATED:

The patient may continue that dose level at home

IF THE FIRST DOSE IS NOT TOLERATED:

Consider dose modification or discontinuation*

The following protocol was used during the Up-Dosing phase of the Phase 3 PALISADE trial and is provided for information purposes only.

***Use clinical judgment to determine the best course of action, which can include maintaining the dose level for longer than 2 weeks, or reducing, withholding, or discontinuing PALFORZIA doses.**

Key steps used in the PALISADE trial[2]

TOLERATED

NO SYMPTOMS OR ORAL/ PHARYNGEAL PRURITUS SYMPTOMS ONLY

Next dose could be taken at home

- Continued dose level

MILD SYMPTOMS with minimal/ no intervention

Next dose at home or in clinic per clinical judgment

- Continued dose level

UNCERTAIN

MILD SYMPTOMS

Next dose at home or in clinic per clinical judgment

- Continued dose level under medical supervision to determine tolerability; or
- Continued dose level for an additional 1 to 2 weeks; or
- Reduced dose by 1 to 2 levels for at least 2 to 4 weeks before attempting re-escalation

NOT TOLERATED

MILD SYMPTOMS

Next dose in clinic

- Reduced dose by 1 to 2 levels
- Continued reduced dose for at least 2 to 4 weeks before attempting re-escalation
- When a patient was unable to return to the clinic, the dose was reduced by 1 level and continued at least 2 to 4 weeks

MODERATE SYMPTOMS

Next dose in clinic

- Reduced dose by 1 to 2 levels until dose was tolerated with no or only mild symptoms
- If mild symptoms occurred, continued per “mild symptoms”

SEVERE SYMPTOMS (0 to 1 doses epinephrine)

Next dose in clinic

- Reduced dose by 2 dose levels; if no or mild symptoms resulted (and dose was assessed as tolerated), proceeded with dosing at reduced level for at least 2 to 4 weeks
- If dose reduction still resulted in moderate or severe symptoms, discontinued dosing

SEVERE SYMPTOMS (2 doses of epinephrine)

Next dose in clinic

- Reduced dose by 2 dose levels; if no or mild symptoms resulted (and dose was assessed as tolerated), proceeded with dosing at reduced level for 6 to 8 weeks
- If dose reduction still resulted in moderate or severe symptoms, discontinued dosing

Please see **Assessing Allergic Reactions** brochure for full criteria to assess the severity of allergic reactions.

Please see Important Safety Information on pages 1-2 and 8.

Please see full Prescribing Information, including Boxed WARNING, and Medication Guide at PALFORZIAPro.com.

Palforzia®
Peanut (*Arachis hypogaea*) Allergen Powder-dnfp

MAINTENANCE DOSING

Daily Maintenance dosing at home[1]

If the patient tolerates the last level of Up-Dosing (300 mg), they can transition to Maintenance dosing at home. They will return to the office for periodic follow-up visits at the treating physician's discretion.

TIP: Daily Maintenance dosing is required to maintain the treatment effect of PALFORZIA.

DOSING AT EACH STEP[1]

INITIAL DOSE ESCALATION

Patients are given 5 sequentially increasing doses of PALFORZIA separated by 20 to 30 minutes.

UP-DOSING

Patients take the first dose of each new Up-Dosing level in office every 2 weeks if tolerated, with daily dosing at home in between visits.

MAINTENANCE DOSING

Patients continue daily home dosing at 300 mg, with periodic office visits at the treating physician's discretion.

Please see Important Safety Information on pages 1-2 and 8.

Please see full Prescribing Information, including Boxed WARNING, and Medication Guide at PALFORZIAPro.com.

Palforzia®
Peanut (*Arachis hypogaea*)
Allergen Powder-dnfp

IMPORTANT SAFETY INFORMATION (CONTINUED)

WARNINGS AND PRECAUTIONS

Anaphylaxis

PALFORZIA can cause anaphylaxis, which may be life threatening. PALFORZIA is available only through a restricted program under a Risk Evaluation and Mitigation Strategy (REMS) called the PALFORZIA REMS because of the risk of anaphylaxis. Only prescribers, healthcare settings, pharmacies, and patients certified and enrolled in the REMS Program can prescribe, receive, dispense or administer PALFORZIA.

Anaphylaxis has been reported during all phases of PALFORZIA dosing, including Maintenance and in subjects who have undergone recommended Up-Dosing and dose modification procedures.

Do not initiate PALFORZIA treatment in a patient who has had severe or life-threatening anaphylaxis within the previous 60 days. PALFORZIA may not be suitable for patients with certain medical conditions that may reduce the ability to survive anaphylaxis, including but not limited to markedly compromised lung function, severe mast cell disorder, or cardiovascular disease. In addition, PALFORZIA may not be suitable for patients taking medications that can inhibit or potentiate the effects of epinephrine.

All Initial Dose Escalation doses and the first dose of each Up-Dosing level must be administered under observation in a certified health care setting.

Patients may be more likely to experience allergic reactions following PALFORZIA administration in the presence of cofactors such as exercise, hot water exposure, intercurrent illness (e.g., viral infection), or fasting. Other potential cofactors may include menstruation, sleep deprivation, nonsteroidal anti-inflammatory drug use, or uncontrolled asthma. Patients should be proactively counseled about the potential for the increased risk of anaphylaxis in the presence of these cofactors. If possible, adjust the time of dosing to avoid these cofactors. If it is not possible to avoid these cofactors, consider withholding PALFORZIA temporarily.

Asthma

Uncontrolled asthma is a risk factor for a serious outcome, including death, in anaphylaxis. Ensure patients with asthma have their asthma under control prior to initiation of PALFORZIA.

PALFORZIA should be temporarily withheld if the patient is experiencing an acute asthma exacerbation. Following resolution of the exacerbation, resumption of PALFORZIA should be undertaken cautiously. Re-evaluate patients who have recurrent asthma exacerbations and consider discontinuation of PALFORZIA.

Eosinophilic Gastrointestinal Disease

Discontinue PALFORZIA and consider a diagnosis of eosinophilic esophagitis in patients who experience severe or persistent gastrointestinal symptoms, including dysphagia, vomiting, nausea, gastroesophageal reflux, chest pain, or abdominal pain.

Gastrointestinal Adverse Reactions

Gastrointestinal adverse reactions were commonly reported in PALFORZIA-treated subjects, and dose modification should be considered for patients who report these reactions. For severe or persistent gastrointestinal symptoms consider a diagnosis of eosinophilic esophagitis.

ADVERSE REACTIONS

The most common adverse events reported in subjects treated with PALFORZIA (incidence ≥ 5% and at least 5% greater than placebo) are abdominal pain, vomiting, nausea, oral pruritus, oral paresthesia, throat irritation, cough, rhinorrhea, sneezing, throat tightness, wheezing, dyspnea, pruritus, urticaria, anaphylactic reaction, and ear pruritus.

Please see full Prescribing Information, including Boxed WARNING, and Medication Guide at PALFORZIAPro.com.

References: 1. PALFORZIA [package insert]. Brisbane, CA: Aimmune Therapeutics, Inc.
2. Protocol for: The PALISADE Group of Clinical Investigators: Vickery BP, Vereda A, Casale TB, et al. AR101 oral immunotherapy for peanut allergy. *N Engl J Med*. 2018;379(21): 1991-2001. doi:10.1056/NEJMoa1812856.

Palforzia®
Peanut (*Arachis hypogaea*) Allergen Powder-dnfp