Peanut (*Arachis hypogaea*) Allergen Powder-dnfp: The First FDA-approved Oral Immunotherapy for Desensitization of Peanut Allergy in Children

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Peanut (*Arachis hypogaea*) Allergen Powder-dnfp (Palforzia, Aimmune™ Therapeutics, Inc.; Brisbane, CA) is the first FDA-approved oral immunotherapy indicated for the mitigation of allergic reactions, including anaphylaxis, in patients with peanut allergy. It may be initiated in individuals 4 to 17 years of age and continued for maintenance in those 4 years of age and older. Initiation and dose titration require a stepwise approach and the supervision of a health care professional. Patients taking Peanut (*Arachis hypogaea*) Allergen Powder-dnfp should also follow a peanut-avoidant diet. In addition, patients should have an injectable epinephrine product in case of drug-related anaphylaxis. Commonly reported adverse reactions include gastrointestinal, respiratory, and dermatologic manifestations that are frequently associated with allergic reactions.

ABBREVIATIONS AAP, American Academy of Pediatrics; DBPCFC, double-blind, placebo-controlled food challenge; FDA, US Food and Drug Administration; H2RA, histamine 2 receptor antagonist; IM, intramuscular; PAHAP, Peanut (*Arachis hypogaea*) Allergen Powder-dnfp

KEYWORDS allergy desensitization; allergy mitigation; oral immunotherapy; Peanut (*Arachis hypogaea*) Allergen Powder-dnfp; peanut allergy

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Introduction

Peanut allergy affects about 1.2% of the overall population and approximately 2.5% of the pediatric population in the United States.^{1–3} In children, peanut allergy is the most common food allergy and the main cause of allergy-related death.^{4,5} Over the past 2 decades, recommendations for the introduction of allergenic foods into the infant diet, specifically peanuts, has changed significantly as the incidence of peanut allergy has increased.^{1,5,6} In 2000, the AAP Committee on Nutrition recommended exclusion of allergenic foods from the diets of infants at high risk for allergy.⁶ Pregnant and lactating women were also discouraged from including allergenic foods in their diets. By 2008, it was determined that elimination diets did not prevent the development of IgE antibodies to peanuts. In 2019, the AAP Committee on Nutrition and AAP Section on Allergy and Immunology concluded that the early introduction of peanuts may prevent allergy in high-risk infants.⁶ It is estimated that only 20% of children outgrow their peanut allergy; thus, the number of adults who continue to live with this allergy is expected to increase.⁴

As a result, the federal government has taken certain measures to safeguard individuals in the public arena. The Food Allergen Labeling and Consumer Protection Act requires manufacturers to include the common, or usual, name of high-risk allergens (e.g., peanuts) on pack-

aged food products that contain the allergens. However, the Food Allergen Labeling and Consumer Protection Act does not apply to food produced locally, food from street vendors, festivals, or fast-food restaurants. The American Disabilities Act was also expanded to include food allergies acknowledging the serious consequences of accidental exposure to antigens.⁷ In response to the classification of food allergies as a disability, major industries and public services are encouraged to follow guidelines that limit contact with food allergens. However, these guidelines are discretionary and insufficient to prevent anaphylaxis to ubiquitous allergens like peanuts and related molecules.^{7,8} Interestingly, the prevalence of peanut allergy has increased by 21% since the introduction of the guidelines.⁴

Peanut Allergy

Mechanism of Reaction. Patients who have an allergic reaction to peanut exposure may react rapidly and severely, as in the case of anaphylaxis, the first time they consume a food containing peanuts. Others, however, may develop an allergy after previously tolerating the food. Reactions can also become more severe with subsequent exposures. The most common symptoms exhibited by children include cutaneous manifestations (90%), respiratory issues such as bronchospasm (80%), gastrointestinal issues (45%), and cardiac complications

(41%).^{1,9,10} It has been estimated that medical costs associated with peanut allergy are greater than \$4 billion annually. Nonmedical-related costs (e.g., decreased caregiver productivity, special food preparation) surpass \$20.5 billion annually.⁵ Therefore, the prevention or avoidance of developing a peanut allergy is ideal (if possible) by understanding the complicated interplay and balance between tolerance and allergic responses to the environment.¹¹

Theories as to how sensitization occurs have focused on cutaneous exposure to peanut via household dust or *Arachis* (peanut) oil in lotion.¹² Sensitization is enhanced for children and infants with atopic dermatitis since the epithelial layer is disrupted, and in children with filaggrin loss-of-function gene mutations. Infants with lower gut microbiota diversity experience greater sensitization when compared with age-matched controls. Microbiota diversity is associated with increased production of short-chain fatty acids and their metabolites, which promote the development of tolerance.¹¹

Sensitization occurs as early as the first 4 months of life allowing for a window of time during which the immune system prepares to become tolerant to peanuts. Exclusion of peanuts from the early infant diet has been found to exacerbate the issue. In 2015, a randomized trial examining the early introduction of peanut into the diet of infants supported the early introduction of peanut (by 4 months of age).¹² Results revealed a lower incidence of peanut allergy at 60 months among children who had received peanuts compared with those who had not (3.2% vs 17.2%, respectively).

For children with an elevated risk for peanut allergy, the decision to challenge depends on the immune process that had occurred first: the release of pro-inflammatory cytokines at the skin, or the presentation of peanut antigen to dendritic cells in the gastrointestinal tract. Conditions such as dryness of the skin disrupt the barrier function of the epithelium allowing antigens to provoke a potent T-helper cell 2 response, inducing B cells to produce peanut-antigen specific IgE. Peanut-antigen specific IgE activates basophils and mast cells, which further promote the development of anaphylaxis.⁹

Tolerance develops as a result of an antigen transportation through the intact gastrointestinal epithelium via diffusion or active transport. Antigen presentation promotes naïve T cells to differentiate into T-regulatory cells ultimately stimulating the production of IgG4 and IgA.^{9,12} This prevents the activation of eosinophils, basophils, and mast cells, as well as the corresponding physical symptoms of allergy. Introduction of peanut antigen early and enterally primes the immune system to become tolerant. This is the basis for newest peanut allergy guidelines of the AAP, which recommend that infants with severe eczema and/or egg allergy be introduced to peanut as early as 4 to 6 months of age.¹³

Management of Symptoms. Peanut allergy accounts for 37% of anaphylaxis cases that are due to food allergy. The presentation of anaphylaxis can vary, thus requiring close and careful observation. The National Institute of Allergy and Infectious Diseases asserts the rapid identification of anaphylaxis using internationally developed criteria will identify at least 95% of cases.¹⁴ These criteria represent 3 different groups of symptoms that enable the clinician to quickly identify and treat anaphylaxis. The first group of symptoms includes active hives or angioedema with either respiratory symptoms or hypotension. This group represents the most common symptoms of anaphylaxis, because at least 80% of anaphylaxis cases include skin-mucosal symptoms. The second group of symptoms requires the presence of at least 2 of the following after exposure to the antigen: 1) skin-mucosal tissue involvement; 2) respiratory symptoms; 3) hypotension; 4) gastrointestinal symptoms. This group accounts for cases of anaphylaxis that do not involve skin-mucosal tissues. The third group of symptoms consist of a single symptom that is rare, but urgent—hypotension (after exposure to the allergen).

The aforementioned symptoms require immediate treatment with epinephrine to prevent fatalities.¹⁰ Currently, epinephrine is the only recommended treatment for anaphylaxis. It suppresses airway edema and hypotension through α -1 adrenergic vasoconstrictive action, stabilizes mast cells and subsequent histamine release, and facilitates bronchodilation with β -2 agonism. Auto-injectors have been developed to enable patients to safely administer an IM injection to the anterolateral thigh upon the presentation of anaphylaxis. Patients less than 25 kg should receive 0.15 mg IM, patients weighing 25 kg or more receive 0.3 mg IM. Smaller patients (less than 10 kg) can also receive the 0.15-mg IM dose, as the benefits outweigh the risks. Symptoms should improve within minutes of an injection. Repeat dosing may be necessary as frequently as every 5 minutes.¹⁵

It should be noted that adjunctive therapies such as glucocorticoids and histamine 2 receptor antagonist (H2RA) are unable to stop anaphylactic reactions. At most, these medications are considered supportive. Glucocorticoids have been found potentially beneficial in the setting of airway edema or asthma. H2RAs do not change the underlying pathologic process, but may be used to relieve urticaria.¹⁵

Biphasic anaphylaxis is the recurrence of symptoms after initial symptom resolution without re-exposure to the antigen. The median time to a biphasic event is 18.5 hours, and 50% of patients will require repeated epinephrine administration. Treatments to prevent biphasic reactions are limited. Currently, only rapid administration of epinephrine has been shown to prevent a delayed second reaction. Glucocorticoids and H2RAs do not have a role in the prevention of biphasic reactions.¹⁶

Biphasic reactions occur in up to 14.7% of children affected by anaphylaxis. Risk factors include asthma, protracted anaphylaxis, previous biphasic reaction, repeated doses of epinephrine, wheezing, hypotension, and pharyngeal edema. Patients with these manifestations are considered high risk and should be monitored for 24 hours following the initial epinephrine administration. Patients with medium risk (e.g., mild wheezing, slowly resolving symptoms) should be monitored for 6 to 8 hours after the initial epinephrine administration. Patients responding to epinephrine without risk factors are considered to have a low risk and should be monitored for 3 to 4 hours following the initial epinephrine administration.^{15,16}

Peanut (*Arachis hypogaea*) Allergen Powder-dnfp

In 2020, the FDA approved another medication to help mitigate allergic reactions (including anaphylaxis) that may occur after accidental exposure to peanuts.¹⁷ Peanut (*Arachis hypogaea*) Allergen Powder-dnfp (PAHAP; Palforzia) is the first oral immunotherapy of its kind for the desensitization of peanut allergy in children and should be used along with a peanut-avoidant diet. It is approved for initiation in individuals 4 to 17 years of age with a confirmed diagnosis of peanut allergy and may be continued for maintenance in those 4 years of age and older.^{17,18}

Mechanism of Action. The exact mechanism of PAHAP has not been determined. However, it is a complex biologic drug of peanut protein manufactured from defatted peanut flour with a well-defined allergen profile.¹⁸ Similar to other oral immunotherapies, this allergenic protein is initially ingested in very small quantities and then incrementally increased using a structured 3-phase dosing approach. Over time, the mitigation of allergic reactions to the allergen occurs.^{18,19}

Clinical Experience in Children. The efficacy and safety of PAHAP in children was studied in a phase 3, randomized, double-blind, placebo-controlled trial.¹⁸ This international, multicentered study enrolled patients with peanut allergy between the ages of 4 and 55 years. However, a primary intent-to-treat analysis focused on 496 children and adolescents (ages 4 through 17 years) who received at least 1 dose of study treatment. Three hundred seventy-two of these children and adolescents were randomly assigned (3:1) to receive either PAHAP (n = 372) or placebo (n = 124). An initial dose escalation based on tolerability was introduced on day 1 (from 0.5 mg to 6 mg) and confirmed on day 2 (at 3 mg), followed by an up-titration for 20 to 40 weeks (from 3 mg to 300 mg). Subsequently, there was a maintenance period of 24 to 48 weeks at 300 mg daily. At the end of the study, all participants completed a double-blind, placebo-controlled food challenge (DBPCFC) to mimic an accidental exposure to peanut and assess tolerability.

The primary efficacy endpoint for the study was the

percentage of participants (intent-to-treat population) who tolerated a single dose of 600 mg of peanut protein during the DBPCFC without experiencing more than mild allergic symptoms after 6 months of maintenance treatment. Among patients aged 4 through 17 years, 67.2% of those in the active treatment group met this endpoint as compared with 4% in the placebo group ($p < 0.0001$). More participants in the active treatment group than in the placebo group also tolerated the 300-mg dose and the 1000-mg dose during the end-of-study DBPCFC (76.6% vs 8.1% [$p < 0.0001$] and 50.3% vs 2.4% [$p < 0.0001$], respectively).

It is important to note that 20.4% of patients discontinued treatment during the study, with 12.4% withdrawing due to treatment-related adverse events. The most commonly reported adverse reactions in patients treated with PAHAP ($\geq 5\%$ incidence) were gastrointestinal, respiratory, and dermatologic manifestations frequently associated with allergic reactions.

Dosing and Administration. PAHAP is available as a powder for oral administration.^{17,18} It is available as capsules containing 0.5-, 1-, 10-, 20-, and 100-mg peanut protein, and as a sachet containing 300-mg peanut protein.¹⁵ Capsules should not be swallowed nor should the powder be inhaled. Patients should be instructed to open the capsule(s) or sachet and empty the dose into a few spoonfuls of semisolid food such as applesauce, yogurt, or pudding (refrigerated or at room temperature). It should be mixed well and then promptly consumed in its entirety. Hands should then be washed, and the opened capsule(s) or sachet should be disposed.¹⁸

Each dose of PAHAP should be taken at the same time every day with a meal. Only 1 dose should be administered per day. If a dose is missed, additional doses should not be taken on the same day to make up for the missed doses. Patients should also avoid exercising and hot showers or baths prior to and within 3 hours of taking PAHAP (to allow for the regulation of body temperature and heart rate). It is important to also ensure that patients carry injectable epinephrine and understand its appropriate use prior to initiation and during therapy with PAHAP.¹⁸

Treatment with PAHAP consists of 3 sequential phases: 1) initial dose escalation; 2) up-titration; and 3) maintenance. The initial dose escalation is administered under the supervision of a health care professional in a health care setting in case there is a need to manage potentially severe allergic reactions, including anaphylaxis. The doses are administered in sequential order on a single day beginning at Level A, with each dose separated by 20 to 30 minutes for observation. All dose levels should be completed, and the patient should be observed for at least 60 minutes after the last dose and prior to discharge. PAHAP should be discontinued immediately if any symptoms requiring medical intervention (such as the use of epinephrine)

Table 1. Single Day Dosing Escalation for Initial Dose of Peanut (*Arachis hypogaea*) Allergen

Dose Level*	Total Daily Dose†,‡
A	0.5 mg (one 0.5 mg capsule) administered on a single day§
B	1 mg (one 1 mg capsule) administered on a single day§
C	1.5 mg (one 0.5 mg and one 1 mg capsule) administered on a single day§
D	3 mg (three 1 mg capsule) administered on a single day§
E	6 mg (six 1 mg capsule) administered on a single day¶

* Administered in sequential order on a single day beginning at Level A

† Initial dose escalation supplied as a single card consisting of 5 blisters containing a total of 13 capsules.

‡ Do not swallow capsule whole, but instead open capsule(s) or sachet and empty the entire dose onto a few spoonfuls of refrigerated or room temperature semisolid food (e.g., applesauce, yogurt, pudding). Do not use liquid (e.g., milk, water, juice) to prepare. Mix well. Each dose should be consumed daily with a meal at approximately the same time each day, preferably in the evening.

§ Each dose should be 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.

occur.¹⁸ A summary of all 3 phases, as well as their respective levels and doses, is presented in the Table.

Up-titration should begin the day after initial dose escalation in patients who tolerate at least 3 mg of PAHAP during the initial dose escalation. If up-titration is not initiated within 4 days of the initial dose escalation, a repeat initial dose escalation is warranted. The up-titration phase is initiated at 3 mg and consists of 11 sequential dose levels. The first dose of each new level is administered under the supervision of a health care professional in a health care setting. Patients are observed for at least 60 minutes after receiving the first dose. If the dose is tolerated, the patient continues that dose at home for 2 weeks. All dose levels should be completed sequentially at 2-week intervals, as tolerated. Dose modification or discontinuation may be necessary for patients who do not tolerate up-titration at certain levels.¹⁸

In patients who complete all levels of the up-titration phase, maintenance dosing is initiated at 300 mg daily and should be continued to maintain the effect of PAHAP. It is important that the health care professional communicates with the patient regularly to assess for efficacy and safety. If 1 or 2 doses are missed, the patient may continue the PAHAP at the current dose level. However, data are lacking regarding missed doses for 3 or more consecutive days. In these cases, patients should contact their health care professional and resume treatment under medical supervision.¹⁸

Table 2. Daily Dosing Configuration for Up-Dosing of Peanut (*Arachis hypogaea*) Allergen and Monitoring of Maintenance Therapy

Dose Level	Dosing*
1†	3 mg (three 1 mg capsule) for 2 wks‡,§
2	6 mg (six 1 mg capsules) for 2 wks§
3	12 mg (two 1 mg capsule and one 10 mg capsule) for 2 wks§
4	20 mg (one 20 mg capsule) for 2 wks§
5	40 mg (two 20 mg capsule) for 2 wks§
6	80 mg (four 20 mg capsule) for 2 wks§
7	120 mg (one 20 mg capsule and one 100 mg capsule) for 2 wks§
8	160 mg (three 20 mg capsule and one 100 mg capsule) for 2 wks§
9	200 mg (two 100 mg capsule) for 2 wks§
10	240 mg (two 20 mg capsule and two 100 mg capsule) for 2 wks§
11	300 mg (one 300 mg sachet) for 2 wks§

Begin maintenance therapy: Regular communication and assessment of efficacy and safety required.

* Do not swallow capsule whole, but instead open capsule(s) or sachet and empty the entire dose onto a few spoonfuls of refrigerated or room temperature semisolid food (e.g., applesauce, yogurt, pudding). Do not use liquid (e.g., milk, water, juice) to prepare. Mix well. Each dose should be consumed daily with a meal at approximately the same time each day, preferably in the evening.

† If possible, begin Up-Dosing the day after the final dose of the Initial Dose Escalation. Repeat Initial Dose Escalation in a health care setting if the patient is unable to begin Up-Dosing within 4 days.

‡ Patients who tolerate at least the 3 mg single dose (Table 1: Level D) during Initial Dose Escalation must return to the health care setting for initiation of Up-Dosing.

§ The first dose of each new Up-Dosing level is administered in a sequential order at 2-wk intervals. Each dose should be given under the supervision of a health care professional in a health care setting with the ability to manage potentially severe allergic reactions, including anaphylaxis. Observe patients after administering the first dose of a new Up-Dosing level for at least 60 minutes until suitable for discharge. If the patient tolerates the first dose of the increased dose level, the patient may continue that dose level at home.

Adverse Effects. The most common adverse reactions reported by study participants who received PAHAP were abdominal pain, vomiting, nausea, oral pruritus, oral paresthesia, throat irritation, cough, rhinorrhea, sneezing, throat tightness, wheezing, dyspnea, pruritus, urticaria, ear pruritus, and anaphylactic reaction (which may be life-threatening).¹⁸ Due to the risk for anaphylaxis, PAHAP is available only through a restricted program under a Risk Evaluation and Mitigation Strategy. Under the PAHAP Risk Evaluation and Mitigation Strategy: 1) health care providers must be certified with the program through enrollment; 2) health

care settings must be certified in the program, and have access to equipment and personnel trained to manage anaphylactic reactions; 3) policies and procedures must be in place at the health care settings to ensure that patients are monitored appropriately during the initial dose escalation and first dose of each level of up-titration; 4) patients must be enrolled in the program prior to treatment initiation; 5) patients must be educated on the need for injectable epinephrine for use at all times, the need for monitoring during initial dose escalation and first dose of each level during up-titration, the need to follow a peanut-avoidant diet and how to recognize the signs and symptoms of anaphylaxis; and 6) pharmacies must be certified with the program to dispense to certified health care settings and patients who are enrolled in the program.^{18,20}

Contraindications, Warnings and Precautions. The use of PAHAP is contraindicated in patients with uncontrolled asthma and in those with a history of eosinophilic esophagitis or other eosinophilic gastrointestinal disease. Anaphylaxis, which may be life-threatening, can also occur; therefore, patients should be able to recognize the signs and symptoms of anaphylaxis (e.g., difficulty in swallowing, difficulty in breathing, throat swelling) and understand the need to seek immediate medical care should such a reaction occur. In addition, they should carry and understand how to use injectable epinephrine in such cases.¹⁸

PAHAP should be used with caution in patients with controlled asthma. It should be temporarily withheld when a patient is experiencing an acute exacerbation. In patients who develop signs and symptoms of eosinophilic esophagitis, PAHAP should be discontinued. If patients develop chronic or recurrent local gastrointestinal allergic symptoms, dose modification or discontinuation of treatment may be necessary.¹⁸

Currently, human and animal data are not available to determine whether or not there are any risks related to PAHAP in pregnant women. However, PAHAP can cause anaphylaxis, which may result in significant risk to a fetus. Information regarding PAHAP in lactation is lacking; therefore, it is uncertain whether PAHAP has any effects on a breastfeeding infant or on a mother's milk production.

Summary

PAHAP is the first FDA-approved oral immunotherapy indicated for the mitigation of allergic reactions (including anaphylaxis) in persons with confirmed peanut allergy. It may be initiated in individuals aged 4 years through 17 years and continued for maintenance treatment in patients 4 years and older. PAHAP is not indicated for the emergency treatment of allergic reactions (including anaphylaxis). Therefore, patients should be encouraged to continue a peanut-avoidant diet, recognize the signs and symptoms of an anaphylactic

reaction, and carry and know how to use an injectable epinephrine product in case of emergency.

Article Information

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References

1. American College of Allergy, Asthma and Immunology [ACAAI]. Peanut allergy. Arlington Heights, IL; 2019. Accessed January 7, 2021. <https://acaai.org/allergies/types/food-allergies/types-food-allergy/peanut-allergy>
2. Nicolaou N, Poorafshar M, Murray C, et al. Allergy or tolerance in children sensitized to peanut: prevalence and differentiation using component-resolved diagnostics. *J Allergy Clin Immunol*. 2010;125(1):191–197.e1-13.
3. Gupta R, Warren C, Blumenstock J, et al. The prevalence of childhood food allergy in the United States: an update. Paper presented at: American College of Allergy, Asthma & Immunology Annual Scientific Meeting; October 26–30, 2017; Boston, MA. Abstract OR078.
4. Cannon, HE. The economic impact of peanut allergies. *Am J Manag Care*. 2018;24(suppl 19):S428–S433.
5. Tice JA, Guzauskas GF, Hansen RN, et al. The Effectiveness and Value of Oral Immunotherapy and Viaskin Peanut for Peanut Allergy. *J Manag Care Spec Pharm*. 2020;26(5):620–623.
6. Greer FR, Sicherer SH, Burks AW; Committee on Nutrition; Section on Allergy and Immunology. The effects of early nutritional interventions on the development of atopic disease in infants and children: the role of maternal dietary restriction, breastfeeding, hydrolyzed formulas, and timing of introduction of allergenic complementary foods. *Pediatrics*. 2019;143(4):e20190281. doi:10.1542/peds.2019-0281
7. Rabin RC. Boarding now: parents of children with food allergies. *New York Times*. June 19, 2019. Accessed January 7, 2021. <https://www.nytimes.com/2019/06/19/health/nut-allergies-airlines.html>
8. Centers for Disease Control and Prevention. *Voluntary Guidelines for Managing Food Allergies in Schools and Early Care and Education Programs*. Washington, DC: US Department of Health and Human Services; 2013.

9. Anvari S, Miller J, Yeh CY, Davis CM. IgE-mediated food allergy. *Clin Rev Allergy Immunol*. 2019;57(2):244–260.
10. Food Allergy Research Education (FARE). Food allergy facts and statistics for the U.S. McLean, VA: 2020. Accessed January 7, 2021. <https://www.foodallergy.org/living-food-allergies/food-allergy-essentials/food-allergy-101>
11. Turcanu V, Brough HA, Du Toit G, et al. Immune mechanisms of food allergy and its prevention by early intervention. *Curr Opin Immunol*. 2017;48:92–98.
12. Du Toit G, Tsakok T, Lack S, Lack G. Prevention of food allergy. *J Allergy Clin Immunol*. 2016;137(4):998–1010.
13. Togias A, Cooper SF, Acebal ML, et al. Addendum guidelines for the prevention of peanut allergy in the United States: Report of the National Institute of Allergy and Infectious Diseases-Sponsored Expert Panel. *J Allergy Clin Immunol*. 2017;139(1):29–44.
14. Peavy RD, Metcalfe DD. Understanding the mechanisms of anaphylaxis. *Curr Opin Allergy Clin Immunol*. 2008;8(4):310–315.
15. Farbman KS, Michelson KA. Anaphylaxis in children. *Curr Opin Pediatr*. 2016;28(3):294–297.
16. Lee S, Sadosty AT, Campbell RL. Update on biphasic anaphylaxis. *Curr Opin Allergy Clin Immunol*. 2016;16(4):346–351.
17. US Food and Drug Administration. FDA approves first drug for the treatment of peanut allergy for children. FDA News Release, January 31, 2020. Accessed January 7, 2021. <https://www.fda.gov/news-events/press-announcements/fda-approves-first-drug-treatment-peanut-allergy-children#:~:text=FDA%20approves%20first%20drug%20for%20treatment%20of%20peanut%20allergy%20for%20children,-Share&text=Today%20the%20U.S.%20Food%20and,with%20accidental%20exposure%20to%20peanuts>
18. Palforzia [Peanut (*Arachis hypogaea*) Allergen Powder-dnfp] [prescribing information]. Brisbane, CA: Aimmune Therapeutics, Inc; January 2020. Accessed January 7, 2021. https://www.palforzia.com/static/pi_palforzia.pdf
19. CenterWatch. Peanut (*Arachis hypogaea*) Allergen Powder-dnfp. Published January 2, 2020. Accessed January 7, 2021. <https://www.centerwatch.com/directories/1067-fda-approved-drugs/listing/4583-palforzia-peanut-arachis-hypogaea-allergen-powder-dnfp>
20. US Food and Drug Administration. Approved Risk Evaluation and Mitigation Strategies (REMS): Palforzia [Peanut (*Arachis hypogaea*) Allergen Powder-dnfp. Accessed January 7, 2021. <https://www.accessdata.fda.gov/scripts/cder/remis/index.cfm?event=IndvRemsDetails.page&REMS=398>