09-J3000-69

Original Effective Date: 06/15/20

Reviewed: 06/12/24

Revised: 07/15/24

Subject: Peanut (Arachis hypogaea) Allergen Powder-dnfd (Palforzia)

THIS MEDICAL COVERAGE GUIDELINE IS NOT AN AUTHORIZATION, CERTIFICATION, EXPLANATION OF BENEFITS, OR A GUARANTEE OF PAYMENT, NOR DOES IT SUBSTITUTE FOR OR CONSTITUTE MEDICAL ADVICE. ALL MEDICAL DECISIONS ARE SOLELY THE RESPONSIBILITY OF THE PATIENT AND PHYSICIAN. BENEFITS ARE DETERMINED BY THE GROUP CONTRACT, MEMBER BENEFIT BOOKLET, AND/OR INDIVIDUAL SUBSCRIBER CERTIFICATE IN EFFECT AT THE TIME SERVICES WERE RENDERED. THIS MEDICAL COVERAGE GUIDELINE APPLIES TO ALL LINES OF BUSINESS UNLESS OTHERWISE NOTED IN THE PROGRAM EXCEPTIONS SECTION.

DESCRIPTION:

Peanut allergy is one of the most serious food allergies due to the potential for severe allergic reactions which can be life threatening. Food allergies arise from a failure of the immune system to generate or maintain a tolerance to specific food proteins. The body's immune system reacts to even small amounts of the food as a harmful substance. IgE-mediated food allergy reactions, such as peanut allergy, are characterized by quick onset of symptoms, sometimes within seconds, after ingestion of or exposure to the protein.

Palforzia is an oral immunotherapy (OIT). OIT is a desensitization process in which small doses are initially given, followed by gradual, incremental increases, resulting in the ability of the body to mitigate allergic reactions to peanuts over time. Palforzia was approved by the FDA in January 2020 for use in patients with a confirmed diagnosis of peanut allergy. Initial dose escalation may be administered to patients aged 4 through 17 years while dosing and maintenance may be continued in patients 4 years of age and older.

In a phase 3 trial, participants 4 to 55 years of age with peanut allergy were screened for allergic dose-limiting symptoms at a challenge dose of 100 mg or less of peanut protein (approximately one third of a peanut kernel) in a double-blind, placebo-controlled food challenge. Participants with an allergic response were randomly assigned, in a 3:1 ratio, to receive AR101 (a peanut-derived investigational biologic oral immunotherapy drug) or placebo in an escalating-dose program. Participants who completed the regimen (i.e., received 300 mg per day of the maintenance regimen for approximately 24 weeks) underwent a double-blind, placebo-controlled food challenge at trial exit. The primary efficacy end point was the proportion of participants 4 to 17 years of age who could ingest a challenge dose of 600 mg or more, without dose-limiting symptoms.

Of the 551 participants who received AR101 or placebo, 496 were 4 to 17 years of age; of these, 250 of 372 participants (67.2%) who received active treatment, as compared with 5 of 124 participants (4.0%) who received placebo, were able to ingest a dose of 600 mg or more of peanut protein, without dose-limiting symptoms, at the exit food challenge (difference, 63.2 percentage points; 95% confidence interval, 53.0 to 73.3; P<0.001). During the exit food challenge, the maximum severity of symptoms was moderate in 25% of the participants in the active-drug group and 59% of those in the placebo group and severe in 5% and 11%, respectively. Adverse events during the intervention period affected more than 95% of the participants 4 to 17 years of age. A total of 34.7% of the participants in the active-drug group had mild events, as compared with 50.0% of those in the placebo group; 59.7% and 44.4% of the participants, respectively, had events that were graded as moderate, and 4.3% and 0.8%, respectively, had events that were graded as severe. Efficacy was not shown in the participants 18 years of age or older.

POSITION STATEMENT:

Initiation of peanut (Arachis hypogaea) allergen powder-dnfd (Palforzia) **meets the definition of medical necessity** when **ALL** of the following criteria are met:

1. Member is diagnosed with peanut allergy as evidenced by either of the following:
    a. Positive skin prick test response to a peanut with a wheal diameter greater than or equal to 3 mm larger than negative control – documentation from the medical record must be provided
    b. Peanut serum IgE level greater than or equal to 0.35 kUA/L – laboratory documentation must be provided
2. Member has a history of allergic reaction to peanut – documentation from the medical record must be provided
3. Member adheres to a peanut-avoidant diet
4. Member is 4 to 17 years of age
5. Palforzia is prescribed by or in consultation with an allergist or immunologist
6. Dosing does not exceed 300 mg daily

Approval duration: 6 months

Continuation of peanut (Arachis hypogaea) allergen powder-dnfd (Palforzia) **meets the definition of medical necessity** when **ALL** of the following criteria are met:

1. Authorization/reauthorization has been previously approved by Florida Blue or another health plan in the past two years for management of peanut allergy, **OR** the member has previously met all indication-specific criteria.
2. Member adheres to a peanut-avoidant diet
3. Palforzia is prescribed by or in consultation with an allergist or immunologist
4. Dosing does not exceed 300 mg daily

Approval duration: 12 months

DOSAGE/ADMINISTRATION:

THIS INFORMATION IS PROVIDED FOR INFORMATIONAL PURPOSES ONLY AND SHOULD NOT BE USED AS A SOURCE FOR MAKING PRESCRIBING OR OTHER MEDICAL DETERMINATIONS. PROVIDERS SHOULD REFER TO THE MANUFACTURER'S FULL PRESCRIBING INFORMATION FOR DOSAGE GUIDELINES AND OTHER INFORMATION RELATED TO THIS MEDICATION BEFORE MAKING ANY CLINICAL DECISIONS REGARDING ITS USAGE.

FDA-approved

- Oral administration in 3 sequential phases: Initial Dose Escalation, Up-Dosing, and Maintenance.

Initial Dose Escalation

- Initial Dose Escalation is administered on a single day under the supervision of a health care professional in a health care setting with the ability to manage potentially severe allergic reactions, including anaphylaxis.
- Initial Dose Escalation is administered in sequential order on a single day beginning at Level A (5 Levels A-E, 0.5-6 mg; Table 1).
- Each dose should be separated by an observation period of 20 to 30 minutes.
- No dose level should be omitted.
- Observe patients after the last dose for at least 60 minutes until suitable for discharge.
- Discontinue PALFORZIA if symptoms requiring medical intervention (e.g., use of epinephrine) occur with any dose during Initial Dose Escalation
- Patients who tolerate at least the 3 mg single dose (Level D) of PALFORZIA during Initial Dose Escalation must return to the health care setting for initiation of Up-Dosing.
- If possible, begin Up-Dosing the day after Initial Dose Escalation.
- Repeat Initial Dose Escalation in a health care setting if the patient is unable to begin Up-Dosing within 4 days.

Up-Dosing

- Complete Initial Dose Escalation before starting Up-Dosing.
- Up-Dosing consists of 11 dose levels and is initiated at a 3 mg dose (Level 1).
- The first dose of each new Up-Dosing level is administered 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. Each dose should be consumed daily with a meal at approximately the same time each day, preferably in the evening.
- Administer all the dose levels in Table 2 in sequential order at 2-week intervals if tolerated.
- No dose level should be omitted.

- Do not progress through Up-Dosing more rapidly than shown in Table 2.
- No more than 1 dose should be consumed per day. Instruct patients not to consume a dose at home on the same day as a dose consumed in the clinic.
- Consider dose modification or discontinuation for patients who do not tolerate Up-Dosing as described in Table 2.

Maintenance

- Complete all dose levels of Up-Dosing before starting Maintenance.
- The Maintenance dose of PALFORZIA is 300 mg daily.
- Daily Maintenance is required to maintain the effect of PALFORZIA.
- During Maintenance, contact patient at regular intervals to assess for adverse reactions to PALFORZIA.

The dose configurations for each phase of dosing are provided in Table 1 through Table 3.

Table 1: Dosing Configuration for Initial Dose Escalation (Single Day Dose Escalation)

Dose Level	Total Dose	Dose Configuration
A	0.5 mg	One 0.5 mg capsule
B	1 mg	One 1 mg capsule
C	1.5 mg	One 0.5 mg capsule; One 1 mg capsule
D	3 mg	Three 1 mg capsules
E	6 mg	Six 1 mg capsules

Table 2: Daily Dosing Configuration for Up-Dosing

Dose Level	Total Daily Dose	Daily Dose Configuration	Dose Duration (weeks)
1	3 mg	Three 1 mg capsules	2
2	6 mg	Six 1 mg capsules	2
3	12 mg	Two 1 mg capsules; One 10 mg capsule	2
4	20 mg	One 20 mg capsule	2
5	40 mg	Two 20 mg capsules	2
6	80 mg	Four 20 mg capsules	2
7	120 mg	One 20 mg capsule; One 100 mg capsule	2
8	160 mg	Three 20 mg capsules; One 100 mg capsule	2
9	200 mg	Two 100 mg capsules	2
10	240 mg	Two 20 mg capsules; Two 100 mg capsules	2
11	300 mg	One 300 mg sachet	2

Table 3: Daily Dosing Configuration for Maintenance

Dose Level	Total Daily Dose	Daily Dose Configuration
11	300 mg	One 300 mg sachet

Dose Adjustments

- Dose modifications are not appropriate during Initial Dose Escalation.
- 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.
- Following 1 to 2 consecutive days of missed doses, patients may resume PALFORZIA at the same dose level. Data are insufficient to inform resumption of PALFORZIA following 3 or more consecutive days of missed doses. Patients who miss 3 or more consecutive days of PALFORZIA should consult their healthcare providers; resumption of PALFORZIA should be done under medical supervision.
- Discontinue treatment with PALFORZIA for:
    - Patients who are unable to tolerate doses up to and including the 3 mg dose during Initial Dose Escalation
    - Patients with suspected eosinophilic esophagitis
    - Patients unable to comply with the daily dosing requirements

Drug Availability

- Powder for oral administration supplied in 0.5 mg 1 mg, 10 mg, 20 mg and 100 mg Capsules or 300 mg Sachets

PRECAUTIONS:

Boxed Warning

- 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

- Because of the risk of anaphylaxis, PALFORZIA is available only through a restricted program under a Risk Evaluation and Mitigation Strategy (REMS) called the PALFORZIA REMS

Contraindications

- Uncontrolled asthma
- History of eosinophilic esophagitis or other eosinophilic gastrointestinal disease

Precautions/Warnings

- Anaphylaxis
- Asthma
- Eosinophilic esophagitis
- Gastrointestinal reactions

BILLING/CODING INFORMATION:

HCPCS Coding

J8499	Prescription drug, oral, nonchemotherapeutic, not otherwise specified

ICD-10 Diagnosis Codes That Support Medical Necessity

Z91.010	Allergy to peanuts

REIMBURSEMENT INFORMATION:

Refer to section entitled **POSITION STATEMENT**.

PROGRAM EXCEPTIONS:

Federal Employee Program (FEP): Follow FEP guidelines.

State Account Organization (SAO): Follow SAO guidelines.

Medicare Part D: Florida Blue has delegated to Prime Therapeutics authority to make coverage determinations for the Medicare Part D services referenced in this guideline.

Medicare Advantage: No National Coverage Determination (NCD) and/or Local Coverage Determination (LCD) were found at the time of the last guideline review date.

DEFINITIONS:

None

RELATED GUIDELINES:

None

OTHER:

None

REFERENCES:

1. Clinical Pharmacology [Internet]. Tampa (FL): Gold Standard, Inc.; 2024 [cited 5/20/24]. Available from: http://www.clinicalpharmacology.com/.
2. ClinicalTrials.gov [Internet]. Bethesda (MD): National Library of Medicine; 2000 Feb 29 - [cited 6/2/24]. Available from: http://clinicaltrials.gov/.
3. DRUGDEX® System [Internet]. Greenwood Village (CO): Thomson Micromedex; Updated periodically .
4. Orphan Drug Designations and Approval [Internet]. Silver Spring (MD): US Food and Drug Administration; 2024 [cited 6/2/24]. Available from: http://www.accessdata.fda.gov/scripts/opdlisting/oopd/index.cfm/.
5. PALFORZIA oral powder, peanut (Arachis hypogaea) allergen powder-dnfp oral powder. Aimmune Therapeutics Inc (per manufacturer), Brisbane, CA, 2020.
6. Vickery BP, Vereda A, Casale TB, et al: AR101 oral immunotherapy for peanut allergy. N Engl J Med 2018; 379(21):1991-2001.

COMMITTEE APPROVAL:

This Medical Coverage Guideline (MCG) was approved by the Florida Blue Pharmacy Policy Committee on 06/12/24.

GUIDELINE UPDATE INFORMATION:

06/15/20	New Medical Coverage Guideline.
01/15/21	Updated position statement.
07/15/21	Review and revision to guideline; updated references.
07/15/22	Review and revision to guideline; updated references.
07/15/23	Review and revision to guideline; updated references.
07/15/24	Review and revision to guideline; updated references.