peanut (*Arachis hypogaea*) allergen powder-dnfp (Palforzia™)

Policy # 00709
Original Effective Date: 10/12/2020
Current Effective Date: 10/10/2022

Applies to all products administered or underwritten by Blue Cross and Blue Shield of Louisiana and its subsidiary, HMO Louisiana, Inc. (collectively referred to as the "Company"), unless otherwise provided in the applicable contract. Medical technology is constantly evolving, and we reserve the right to review and update Medical Policy periodically.

When Services May Be Eligible for Coverage

Coverage for eligible medical treatments or procedures, drugs, devices or biological products may be provided only if:

- *Benefits are available in the member's contract/certificate, and*
- *Medical necessity criteria and guidelines are met.*

Based on review of available data, the Company may consider peanut (*Arachis hypogaea*) allergen powder-dnfp (Palforzia)™‡ for the mitigation of allergic reactions that may occur with accidental exposure to peanut to be **eligible for coverage.****

Patient Selection Criteria

Coverage eligibility for peanut (*Arachis hypogaea*) allergen powder-dnfp (Palforzia) will be considered when the following criteria are met:

- Patient is 4 to 17 years of age OR patient is 18 years of age or older and has previously started on Palforzia prior to becoming 18 years of age; AND
- Patient has a history of an allergic reaction to peanuts; AND
- Patient has demonstrated signs and symptoms of a significant allergic reaction (hives, swelling, wheezing, hypotension, gastrointestinal symptoms, etc.); AND
- Patient's allergic reaction occurred within a short period of time following a known ingestion of peanut or peanut containing food; AND
- Patient's allergic reaction was significant enough to require a prescription for an epinephrine auto-injector; AND
- Patient had a positive skin prick test (SPT) response to peanut with a wheal diameter greater than or equal to 3 mm larger than the negative control; AND
- Patient had a positive in vitro test (e.g., a blood test) for peanut-specific IgE (psIgE) with a level greater than or equal to 0.35 kUA/L; AND
- Palforzia is used in conjunction with a peanut-avoidant diet; AND
- Patient does NOT have severe or poorly controlled asthma; AND

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- Patient does NOT have a history of eosinophilic esophagitis or other eosinophilic gastrointestinal disease.

When Services Are Considered Investigational

Coverage is not available for investigational medical treatments or procedures, drugs, devices or biological products.

Based on review of available data, the Company considers the use of peanut (*Arachis hypogaea*) allergen powder-dnfp (Palforzia) when the patient selection criteria are not met to be **investigational.***

Background/Overview

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. Palforzia is to be used in conjunction with a peanut-avoidant diet. It should be noted that Palforzia is not indicated for the emergency treatment of allergic reactions, including anaphylaxis. The titration and maintenance dosing of Palforzia can be found in its package insert. Palforzia carries a boxed warning for use in uncontrolled asthma. It also carries warnings in the package insert for eosinophilic esophagitis.

One of the most common foods implicated in food-related allergic reactions in the United States is peanut. It is estimated that peanut allergy affects anywhere from 1.4% to 4.5% of US children. Prior to the approval of Palforzia, there was no FDA approved treatment for peanut allergy. The standard of care has been strictly peanut avoidance with episodes of anaphylaxis managed by injectable epinephrine. Guidelines, to date, have not addressed the availability of Palforzia.

FDA or Other Governmental Regulatory Approval

U.S. Food and Drug Administration (FDA)

Palforzia (approved January 2020) is an oral immunotherapy indicated for the mitigation of allergic reactions, including anaphylaxis, that may occur with accidental exposure to peanut.

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Rationale/Source

This medical policy was developed through consideration of peer-reviewed medical literature generally recognized by the relevant medical community, U.S. Food and Drug Administration approval status, nationally accepted standards of medical practice and accepted standards of medical practice in this community, technology evaluation centers, reference to federal regulations, other plan medical policies, and accredited national guidelines.

The efficacy of Palforzia for the mitigation of allergic reactions, including anaphylaxis, in patients with peanut allergy was investigated in Study 1. Study 1 was a phase 3, randomized, double-blind, placebo-controlled study of the efficacy and safety of Palforzia in patients with peanut allergy aged 4 through 55 years in the United States, Canada, and Europe. To be eligible for the trial, subjects were required to have a diagnosis of peanut allergy supported by either a serum peanut-specific immunoglobulin E (psIgE) level of ≥ 0.35 kUA/L or a mean wheal diameter of at least 3 mm larger than the negative control to a skin-prick test for peanut. The primary analysis population consisted of 496 subjects (Palforzia, N = 372; placebo, N = 124) aged 4 through 17 years in the intent-to-treat (ITT) population who received at least 1 dose of study treatment. After an initial dose escalation ranging from 0.5 mg to 6 mg on day 1 and confirmation of tolerability of the 3 mg dose on day 2, subjects underwent up-dosing for 20-40 weeks starting at 3 mg until the 300 mg dose was reached. The up-dosing period varied for each subject depending on how the dose was tolerated. Subjects then underwent 24-28 weeks of maintenance immunotherapy with 300 mg Palforzia until the end of the study. At the end of the maintenance period, subjects completed an exit double blind placebo-controlled food challenge (DBPCFC) to approximate an accidental exposure to peanut and to assess their ability to tolerate increasing amounts of peanut protein with no more than mild allergic symptoms.

The primary efficacy endpoint was the percentage of subjects tolerating a single dose of 600 mg peanut protein in the exit DBPCFC with no more than mild allergic symptoms after 6 months of maintenance treatment. The primary efficacy endpoint was considered met if the lower bound of the 95% confidence interval (CI) for the difference in response rates between the treatment and the placebo groups was greater than the prespecified margin of 15%. Key secondary endpoints included the comparisons of the response rates after single doses of 300 mg and 1,000 mg peanut protein as well as a comparison of the maximum severity of symptoms at any challenge dose of peanut protein during the exit DBPCFC. When introduced to 600 mg of peanut protein, 67.2% of Palforzia subjects

tolerated the peanut versus 4% in the placebo group. Similar results can be seen when the subjects are introduced to 300 mg and 1,000 mg of peanut protein.

References

1. Palforzia [package insert]. Aimmune Therapeutics, Inc. January 2020.
2. Palforzia Drug Evaluation. Express Scripts. February 2020.
3. Palforzia Prior Authorization Policy. Express Scripts. February 2020.
4. Frequently asked questions about food allergies. U.S. Food and Drug Administration Web site. Available at: https://www.fda.gov/food/food-allergens/frequently-asked-questions-about-food-allergies. Created December 18, 2017. Accessed on January 2, 2020.
5. Gupta RS, Warren CM, Smith BM, et al. The public health impact of parent-reported childhood food allergies in the United States. Pediatrics. 2018;142(6):e20181235.
6. Sicherer SH, Munoz-Furlong A, Godbold JH, et al. US prevalence of self-reported peanut, tree nut, and sesame allergy: 11-year follow-up. J Allergy Clin Immunol. 2010;125:1322-1326.
7. Bunyavanich S, Rifas-Shiman SL, Platts-Mills TA, et al. Peanut allergy prevalence among school-age children in a US cohort not selected for any disease. J Allergy Clin Immunol. 2014;134(3):753-755.
8. Gupta RS, Springston EE, Warrier MR, et al. The prevalence, severity, and distribution of childhood food allergy in the United States. Pediatrics. 2011;128(1):e9-17.

Policy History

Original Effective Date: 10/12/2020
Current Effective Date: 10/10/2022

09/03/2020	Medical Policy Committee review
09/09/2020	Medical Policy Implementation Committee approval. New policy.
09/02/2021	Medical Policy Committee review
09/08/2021	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
09/01/2022	Medical Policy Committee review
09/14/2022	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.

Next Scheduled Review Date: 09/2023

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*Investigational – A medical treatment, procedure, drug, device, or biological product is Investigational if the effectiveness has not been clearly tested and it has not been incorporated into standard medical practice. Any determination we make that a medical treatment, procedure, drug, device, or biological product is Investigational will be based on a consideration of the following:

A. Whether the medical treatment, procedure, drug, device, or biological product can be lawfully marketed without approval of the U.S. Food and Drug Administration (FDA) and whether such approval has been granted at the time the medical treatment, procedure, drug, device, or biological product is sought to be furnished; or
B. Whether the medical treatment, procedure, drug, device, or biological product requires further studies or clinical trials to determine its maximum tolerated dose, toxicity, safety, effectiveness, or effectiveness as compared with the standard means of treatment or diagnosis, must improve health outcomes, according to the consensus of opinion among experts as shown by reliable evidence, including:
    1. Consultation with technology evaluation center(s);
    2. Credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community; or
    3. Reference to federal regulations.

**Medically Necessary (or "Medical Necessity") - Health care services, treatment, procedures, equipment, drugs, devices, items or supplies that a Provider, exercising prudent clinical judgment, would provide to a patient for the purpose of preventing, evaluating, diagnosing or treating an illness, injury, disease or its symptoms, and that are:

A. In accordance with nationally accepted standards of medical practice;
B. Clinically appropriate, in terms of type, frequency, extent, level of care, site and duration, and considered effective for the patient's illness, injury or disease; and
C. Not primarily for the personal comfort or convenience of the patient, physician or other health care provider, and not more costly than an alternative service or sequence of services at least as likely to produce equivalent therapeutic or diagnostic results as to the diagnosis or treatment of that patient's illness, injury or disease.

For these purposes, "nationally accepted standards of medical practice" means standards that are based on credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community, Physician Specialty Society recommendations and the views of Physicians practicing in relevant clinical areas and any other relevant factors.

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‡ Indicated trademarks are the registered trademarks of their respective owners.

NOTICE: If the Patient's health insurance contract contains language that differs from the BCBSLA Medical Policy definition noted above, the definition in the health insurance contract will be relied upon for specific coverage determinations.

NOTICE: Medical Policies are scientific based opinions, provided solely for coverage and informational purposes. Medical Policies should not be construed to suggest that the Company recommends, advocates, requires, encourages, or discourages any particular treatment, procedure, or service, or any particular course of treatment, procedure, or service.