



➤ DRUG HIGHLIGHT: Emerging Treatments for Peanut Allergies

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Introduction

Several therapeutic approaches to manage peanut allergy are currently being studied. These approaches have focused on mitigating the allergic response to peanuts by using peanut extracts administered in various forms and routes of delivery to gradually desensitize patients to peanut allergen. Monoclonal antibodies targeting the antibody-mediated response to peanut allergens are also being studied as monotherapy and in combination with oral immunotherapy.

Incidence / Prevalence of Peanut Allergy

Results from two studies presented at the American College of Allergy, Asthma, & Immunology Scientific Meeting in October 2018 estimated that 2.2% of children and adolescents (approximately 1.25 million) in the United States have a peanut allergy (an approximate increase of 21% since 2010). The study authors also reported increased annual incidence in newborns from 2001 (a rate of 1.7%, 66,000 babies) to 2017 (5.2%, 210,000 babies).

Current Use of Oral Immunotherapy (OIT) for Food Allergies

Non-FDA approved OIT therapy has been used to treat peanut allergy by a relatively small number of allergists, both in academic and non-academic medical settings. However, due to lack of standardization in OIT treatment and safety concerns, its use has not been widespread. In 2014, the Updated Food Allergy Practice Parameter advised against performing OIT in routine clinical practice, citing inadequate evidence supporting therapeutic benefit over risks of therapy.



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Potential 2019-2020 Approvals

AR-101 (Palforzia)/Aimmune	Oral Immunotherapy (OIT)	BLA filed December 2018	2H 2019/1H 2020
Viaskin Peanut/DBV	Epicutaneous Immunotherapy (EPIT)	BLA filed October 2018 withdrawn in December 2018*	2H 2019/1H 2020

* DBV filed their BLA submission in October 2018, but withdrew the application in December 2018, citing a need to provide more detailed information on manufacturing procedures and quality controls. The company believes it can refile the NDA submission without conducting additional trials. No date for refiling has been announced.

AR-101 (Palforzia)/Aimmune Therapeutics

AR-101 is a peanut-derived OIT drug and is considered to be a biologic (BLA submission pathway). OIT is administered in very small doses with gradual dose increases intended to increase the patient's tolerance to a maintenance dose of the oral therapy that will provide protection from potentially life-threatening exposures to peanut allergens. AR-101, if approved, would be the first FDA-approved standardized peanut-derived oral immunotherapy drug for treatment of peanut allergy.

It was recently announced that Palforzia will be the brand name, replacing AR101 which was used while the drug was being developed and undergoing clinical trials.

If approved, patients will initiate a dose escalation period which lasts six months or longer. The patient then continues to take a daily therapeutic dose to maintain desensitization.

Latest AR-101/Aimmune Therapeutic News

Aimmune Therapeutics' peanut allergy treatment took a step toward approval, as a panel of experts convened by the FDA voted in support of Palforzia's safety and efficacy on **September 13, 2019**. Following presentations from experts, physicians, and the public, the FDA advisory committee voted 7 to 2 in favor of the drug's effectiveness and 8 to 1 on safety. Some panel members raised concerns about higher rates of epinephrine use, as well as systemic allergic reactions, among those treated with drug compared to those on placebo.

Palforzia is an oral immunotherapy consisting of peanut powder taken daily along with food. Clinical trials showed Palforzia was superior to placebo in improving study patients' ability to consume peanuts, and if approved, would be indicated for children aged 4 to 17 years. A trial of 554 patients aged 4-17 produced the following results:

- 67.2% tolerated a 600mg dose of peanut protein in the exit food challenge, compared to 4.0% of placebo patients;
- 50.3% tolerated a 1000mg dose of peanut protein in the exit food challenge, compared to 2.4% of placebo patients;
- Of the 79.6% of those that completed the trial, 96.3% tolerated a 300-mg dose of peanut protein in the exit food challenge, 84.5% tolerated a 600-mg dose, and 63.2% tolerated a 1000-mg dose.



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The review also illustrated challenges for Aimmune's peanut immunotherapy. The panel discussed a Risk Evaluation and Mitigation Strategies (REMS) plan that Aimmune and regulators are finalizing. The FDA said they would require patients to have documentation of an epinephrine prescription, attest to carry epinephrine, and limit dose escalation to certified facilities.

During the trial, 14.5% experienced systemic hypersensitivity reactions compared with 3.2% of placebo patients. Aimmune claims that of those that experienced reactions, 98.2% were classified as "mild" or "moderate" and included nausea, itchiness in the throat, and vomiting. The research showed an almost tripling of the risk of an anaphylactic reaction (9.4%) during the time the patient is building tolerance to reach the maintenance dose compared with placebo (3.8%).

The FDA is not required to follow the advice of the advisory committee, but the committee is seen as having significant influence in the approval decision. Aimmune expects a decision on U.S. approval by late January 2020. Due to the questions raised about efficacy and long-term safety of Palforzia, the initial uptake upon approval may be lower than expected despite the perceived demand.

In related news, Aimmune Therapeutics' has begun enrolling patients for a Phase 2 clinical trial of AR201, a therapeutic candidate for egg allergy, and is working on unnamed therapy for allergy to tree nuts.

Viaskin Peanut / DBV Technologies

Viaskin Peanut is a transdermal patch used to deliver epicutaneous immunotherapy (EPIT) and is also considered as a biologic. Unlike OIT, EPIT is based on providing continuous antigen exposure at the same dose rather than gradual dose escalation. The Viaskin Peanut mechanism of action delivers peanut allergen protein to specific epidermal dendritic cells (Langerhans cells) which allows for drug delivery directly to the lymph nodes without entry to the bloodstream. It is believed that this contributes to a better safety profile for Viaskin Peanut compared with OIT.

Monoclonal Antibody Therapy

Monoclonal antibodies that reduce the antibody-mediated allergic response associated with various food allergies (e.g. tree nuts, peanuts, milk, egg) are an area of current interest. An appealing aspect of monoclonal antibody therapy is that it is non-specific and can potentially reduce the allergic response to multiple food allergies and other associated conditions such as asthma and eczema. OIT is associated with allergic reactions that can cause patients to discontinue therapy, particularly early in the course of treatment. Smaller trials involving omalizumab in combination with OIT have demonstrated improved tolerability of OIT treatment. A phase 2 trial of AR-101 in combination with dupilumab (Dupixent) is currently ongoing.

Xolair (omalizumab) was granted Breakthrough Therapy status in August 2018 for the prevention of severe food allergy reactions based on seven trials over the past decade assessing efficacy and safety versus various food allergens such as peanut, milk, and egg.



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Institute for Clinical and Economic Review (ICER) Guidance

In June 2019, the Institute for Clinical and Economic Review (ICER) met to deliberate and vote on Palforzia and epicutaneous immunotherapy (Viaskin Peanut, DBV Technologies) for the treatment of peanut allergy. ICER assigned a clinical evidence rating of promising, but inconclusive for both Palforzia and Viaskin Peanut versus avoidance and rapid use of epinephrine alone. The rating was based on increased desensitization rates versus placebo in clinical trials balanced by the possibility of net harms in patients receiving Palforzia and Viaskin Peanut due to higher rates of allergic reactions and epinephrine use in patients compared to those that received placebo in clinical trials.

Potential Managed Care Considerations

1. Palforzia and Viaskin Peanut will likely both have appeal based on dosage form preferences, labeling, and efficacy/safety profiles. Palforzia appears to have better efficacy but with a higher incidence of adverse effects. Viaskin Peanut appears to be less effective but safer. Palforzia will be used in patients 4-17 years old while Viaskin Peanut will only be used in patients 4-11 years old.

2. Prior Authorization Considerations

- a. Restriction to Allergist – due to complexity and need for safety monitoring
- b. Age restriction per manufacturer labeling
- c. Clinical trials required screening using an oral food challenge. Plans may want to consider alternative documentation to establish the peanut allergy diagnosis (e.g. clinical history confirmed with IgE levels, skin prick testing) unless clinical history and IgE test results do not clearly indicate an allergy.

3. Maintenance of the desensitization will require a continuation of the maintenance dose of OIT or EPIT for an indefinite period for most patients. Plans will need to consider whether to cover maintenance therapy for an indefinite period and if so, establish reauthorization timepoints with appropriate criteria for confirming the benefit of ongoing therapy for each patient.

4. Include in coverage policies that coadministration of OIT with a monoclonal antibody (e.g. omalizumab, dupilumab) for purposes of improving tolerability of OIT should be considered as investigational until the monoclonal antibody is approved by FDA for this indication. Real world clinical experience with Palforzia and results from ongoing trials will determine the demand for coadministration of a monoclonal antibody with OIT in the future.

Potential Budget Impact

Pricing has not been announced for either Palforzia or Viaskin Peanut making it difficult to assess budget impact at this time. Since these are new treatments with potential for long-term use in any patient between 4-17 years old with peanut allergy (approximately 1.25 million patients), there should be a substantial impact on drug budgets. The potential for concurrent use of monoclonal antibodies in the future would potentially add to this impact. From an overall budget perspective, a potential cost offset may be a decrease in the rate of ED visits/hospitalizations related to severe peanut allergy reactions. Quality of life measures will also be an important consideration in determining the value of these therapies.

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