Summary

WHAT IS PEANUT ALLERGY?

Peanut is a common childhood allergen in the United States (US). According to recent estimates approximately 1.4-4.5% of children suffer from peanut allergy. It is more common in males (1.7% versus 0.8%), people with lower income (1.7% versus 1.2%), and there are race/ethnic disparities in the prevalence of peanut allergies (2.8% non-Hispanic blacks, 1.7% Hispanics, and 0.9% non-Hispanic whites). In addition, peanut allergy is the leading cause of death from anaphylaxis due to food, particularly in teenagers, though the rate is low. The national food allergy death registry reports fewer than four deaths per year over the past 10 years in the US.

TREATMENT OPTIONS

Currently, there are no FDA approved treatments for Peanut Allergy, however peanut flour, taken daily in small doses that are gradually increased under the supervision of specialist physicians has been used off-label to attempt to desensitize patients to peanut protein.

AR101 (Aimmune Therapeutics) is defatted, slightly roasted peanut flour that has a characterized allergen profile. The peanut flour is mixed into pudding, applesauce, or other foods. The dose of peanut protein is increased every two weeks to reach a maintenance dose of 300 mg daily. Each dose increase is observed in a physician's office. AR101 is being studied primarily in pediatric patients ages four to 17 years.

Viaskin Peanut (DBV Technologies) is a patch applied daily to the upper back that delivers 250 mcg of peanut antigen for desensitization treatment. The first patch is placed under the supervision of a medical professional, but subsequent patches are applied at home. Viaskin Peanut is being studied primarily in pediatric patients ages four to 11 years.

An FDA approval decision for AR101 is expected in January 2020. The timeline for Viaskin Peanut is currently unknown, but is expected sometime in 2020.

REPORT FINDINGS & RECOMMENDATIONS

- In June 2019, the California Technology Assessment Forum panel voted that the evidence was inadequate to demonstrate a superior net health benefit of either AR101 or Viaskin Peanut compared to strict peanut avoidance.

- While the panel recognized that desensitization as a surrogate outcome was promising, they emphasized the need for improved data to demonstrate that desensitization is linked to improved quality of life and reduced reactions to accidental exposure to peanuts.

Clinical Analyses

ICER EVIDENCE RATINGS

How strong is the evidence that AR101, Viaskin, or OIT improve outcomes in patients with Peanut Allergy?

	AR101	Viaskin Peanut	Peanut OIT	Comparison Between Therapies
Children between the age of 4 to 17 with peanut allergy	Promising but Inconclusive	Promising but Inconclusive	Insufficient	Insufficient

Based on surrogate outcomes (oral food challenges), AR101 appears more efficacious than Viaskin Peanut, but appears to have more adverse effects.

KEY CLINICAL BENEFITS STUDIED IN CLINICAL TRIALS

How effective are AR101, Viaskin, or OIT compared to no treatment?

Key Clinical Outcomes	AR101	Viaskin Peanut	Peanut OIT
Desensitization	Improved	Improved*	Improved
Reduction in Epinephrine Use	No**	No**	No**
Reduction in Systemic Allergic Reaction	No**	No**	No**

*A greater proportion of patients treated with Viaskin achieved desensitization compared to the no treatment arm, however the predefined primary outcome of the trial was not met.

**In studies of AR101, Viaskin Peanut, and OIT, epinephrine use and systemic allergic reactions increased.

Clinical Analyses (continued)

HARMS

AR101: The most common adverse events were gastrointestinal (52% abdominal pain, nausea, vomiting), though most were mild to moderate. Withdrawal rates overall (21.0%) and withdrawals due to adverse events (11.6%) were substantially higher in the AR101 group than those observed in the placebo group. Systemic allergic reactions (14.2% versus 3.2% placebo) and the use of epinephrine (14.0% versus 6.5% placebo) were common.

Viaskin Peanut: The most common adverse events were skin reactions at the site of the patches including itching (34.5%) and redness (28.2%) though most were mild to moderate. Systemic allergic reactions related to the patch were uncommon in the Viaskin Peanut group (3.8%), though epinephrine use was more frequent (9.2% versus 3.4% placebo). Withdrawal due to adverse events was uncommon in the active treatment group (1.7%), but more than 10% withdrew from the study during one year of follow-up.

Peanut OIT: The harms in the OIT studies mirrored those of AR101. The primary adverse events leading to discontinuation were GI, including abdominal pain, nausea, and vomiting. In studies with very high maintenance doses, food aversion also played an important role. No new adverse events were identified. A 2019 meta-analysis concluded that high certainty evidence demonstrates that OIT considerably increases allergic and anaphylactic reactions over avoidance despite effective desensitization.

SOURCES OF UNCERTAINTY

Long-Term Data: There is considerable uncertainty about the long-term outcomes for both AR101 and Viaskin Peanut. There is hope that the rates of systemic allergic reactions, epinephrine use, and reactions to accidental exposure will decrease with continued therapy, but this remains to be demonstrated. The potential need for lifelong therapy raises issues about long-term adherence to treatment, particularly during adolescence and young adulthood.

Standardized Outcomes: Despite the PRACTALL consensus guidelines and the use of the double blind placebo controlled food challenges (DBPCFC) to evaluate the effectiveness of immunotherapy, there is no consensus on what tolerated dose represents a clinically meaningful outcome for desensitization.

Quality of Life: Quality of life outcomes for the Phase 3 trials have not yet been published. It is challenging to fully evaluate the impact of these therapies without placebo-controlled assessments of the change in quality of life.

Economic Analyses

LONG-TERM COST-EFFECTIVENESS

Do these therapies meet established thresholds for long-term cost-effectiveness?

The price for these therapies is not known. Using the analysts' estimated price for AR101 ($4,200/year), the incremental cost-effectiveness ratio was $88,000/QALY. Using the analysts' estimated price for Viaskin Peanut ($6,500/year), the incremental cost-effectiveness ratio was $216,000/QALY.

VALUE-BASED PRICING

What is a fair price for these therapies based on their value to patients and the health care system?

	AR101	Viaskin Peanut
Annual Cost to Achieve $100,000 per QALY	$4,808	$3,010
Annual Cost to Achieve $150,000 per QALY	$7,248	$4,513

No wholesale acquisition costs are currently available for either product. Therefore, no estimates of price discounts are provided.

BUDGET IMPACT ALERT

Using prices from analysts for AR101 ($4,200/year), we estimated that only 41% of eligible patients could be treated in a given year without exceeding ICER's budget impact threshold. Using prices from analysts for Viaskin Peanut ($6,500/year), 71% of eligible patients could be treated in a given year without exceeding ICER's budget impact threshold.

Discussions at the June public meeting suggested that uptake could approach or exceed this level given the unmet need for better management of peanut allergy, and that OIT is generally not covered by payers for this indication. Thus, ICER is issuing an access and affordability alert to make all stakeholders aware of the potential for use of these therapies to result in costs that could have important impacts on existing health care budgets.

Summary of Votes

1. Is the evidence adequate to demonstrate that the net health benefit of AR101 plus strict peanut avoidance is superior to continued avoidance alone?

   Yes: 4 **No: 12**

2. Is the evidence adequate to demonstrate that the net health benefit of Viaskin Peanut plus strict peanut avoidance is superior to continued avoidance alone?

   Yes: 4 **No: 12**

3. Is the evidence adequate to distinguish the net health benefit of AR101 and Viaskin Peanut?

   Yes: 1 **No: 15**

4. Is the evidence adequate to demonstrate that the net health benefit of AR101 is superior to oral immunotherapy as practiced currently?

   Yes: 2 **No: 14**

AR101	Viaskin Peanut	Potential Other Benefits
7/16	9/16	This intervention will reduce important health disparities across racial, ethnic, gender, socio-economic, or regional categories.
11/16	10/16	This intervention will significantly reduce caregiver or broader family burden.
5/16	11/16	This intervention offers a novel mechanism of action or approach that will allow successful treatment of many patients for whom other available treatments have failed.
8/16	9/16	This intervention will have a significant impact on improving return to work and/or overall productivity.
10/16	12/16	Other important benefits or disadvantages that should have an important role in judgments of the value of this intervention.

Summary of Votes (continued)

AR101	Viaskin Peanut	Potential Other Contextual Considerations
8/15	9/15	This intervention is intended for the care of individuals with a condition of particularly high severity in terms of impact on length of life and/or quality of life.
13/15	13/15	Compared to strict avoidance, there is significant uncertainty about the long-term risk of serious side effects of this intervention.
13/15	13/15	Compared to strict avoidance, there is significant uncertainty about the magnitude or durability of the long-term benefits of this intervention.
4/15	4/15	There are additional contextual considerations that should have an important role in judgments of the value of this intervention.

Policy Recommendations

For Manufacturers:

- Manufacturers should pursue further evidence development in order to provide better certainty of long-term safety and effectiveness of desensitization therapies. Evidence should not rely on short-term surrogate outcome measures like desensitization.
- Manufacturers should work with patient groups and the clinical research community to conduct studies that provide evidence on when and how to stop treatment.

For Payers

- Prior authorization criteria should be based on clinical evidence, with input from clinical experts and patient groups.
- Prescribing peanut desensitization therapies should be restricted to specialists (Allergy and Immunology Specialists); or for those patients with inadequate access to allergists, by primary care physicians only in consultation with a specialist.
- Payers may consider limiting coverage for initiation of desensitization treatment to patients between the ages of 4-17 years who represent the population studied to date.
- Payers should not stop coverage at age 18 for patients who have been on continuous desensitization therapy.

Policy Recommendations (continued)

For Researchers

- Longer placebo-controlled, randomized trials are needed to demonstrate that desensitization translates into outcomes that matter to patients.
- Research is needed to develop biomarkers both for initiation of therapy and to support the decision about when it is safe to go off desensitization treatment.

For Specialty Societies & Providers

- Specialty societies should develop a clear, evidence-based definition of desensitization to food allergy.
- Given the remaining uncertainties about the benefits and harms of these novel therapies, specialty societies should take the lead in organizing patient registries to capture treatment effects of desensitization therapies if they enter the market.
- Shared-decision making is essential in the safe and appropriate prescribing of desensitization therapy.

For Regulators

- The FDA should update its guidance for the assessment of outcomes in food allergy therapy to require a common definition of desensitization.
- The FDA should mandate additional randomized clinical trials that demonstrate clinically meaningful benefits for patients (reduction in severe allergic reactions, reduction in epinephrine use, reduction in ER visits/hospitalizations, and improvement in quality of life).

For Patient Organizations

- Patient organizations should help educate families and patients about these therapies, including both potential benefits and potential harms.
- Patient organizations should consider boycotting research sponsored by drug manufacturers that does not measure outcomes of direct relevance to patients.

About ICER

The Institute for Clinical and Economic Review (ICER) is an independent nonprofit research institute that produces reports analyzing the evidence on the effectiveness and value of drugs and other medical services. ICER's reports include evidence-based calculations of prices for new drugs that accurately reflect the degree of improvement expected in long-term patient outcomes, while also highlighting price levels that might contribute to unaffordable short-term cost growth for the overall health care system.

ICER's reports incorporate extensive input from all stakeholders and are the subject of public hearings through three core programs: the California Technology Assessment Forum (CTAF), the Midwest Comparative Effectiveness Public Advisory Council (Midwest CEPAC) and the New England Comparative Effectiveness Public Advisory Council (New England CEPAC). These independent panels review ICER's reports at public meetings to deliberate on the evidence and develop recommendations for how patients, clinicians, insurers, and policymakers can improve the quality and value of health care.

For more information about ICER, please visit ICER's website (www.icer-review.org).