

## Oral Immunotherapy for Food Allergy

Oral immunotherapy (OIT) is a potential treatment for food allergy. It involves giving gradually increasing amounts of food allergen under medical supervision and continued daily consumption of the food allergen. If the goal of desensitisation is reached, there is a temporary increase in the amount of food allergen that can be consumed before an allergic reaction occurs.

OIT is an emerging treatment, and there are no OIT products for food allergies registered by the Therapeutic Goods Administration (TGA) in Australia or Medsafe in New Zealand. One OIT product for peanut allergy (Palforzia™ developed by the company Aimmune Therapeutics) has received Food and Drug Administration (FDA) approval for use in the USA in 2020.

It is important to note that current OIT methods are not a cure for food allergy. There are concerns about potential harm of OIT for food allergy outweighing the benefits in some people with severe food allergy, as well as considerable cost implications. This applies to OIT products that are registered as well as OIT used in clinical trials.

The benefits and harms of different forms of OIT are still being studied in clinical trials in Australia and globally. More data needs to be collected about safety, tolerability, cost-effectiveness, quality of life and long term outcomes.

### Recent publications provide a comprehensive review of OIT for peanut allergy

Two publications over the last year have provided the most comprehensive and rigorous reviews of OIT for peanut allergy to date.

The first was a meta-analysis (a method to combine data from multiple studies) of 12 peanut OIT (POIT) trials published in the Lancet journal in April 2019. It reviewed the effectiveness and safety of peanut OIT compared with peanut avoidance, combining all the studies where peanut allergic children had been randomly assigned to either take peanut or avoid it. This means that all these studies of peanut OIT included a randomised control group. There were 1,041 children in these studies, with approximately two thirds taking peanut OIT and the remainder acting as controls. Results showed that whilst OIT can achieve the goal of desensitisation for many people, those receiving OIT had more frequent allergic reactions, including severe allergic reactions (anaphylaxis). They also required more frequent treatment with adrenaline (epinephrine) autoinjectors (such as EpiPen®) than patients who avoided peanut and did not receive OIT.

The Lancet publication supports the need for improved food allergy treatment approaches with an enhanced safety profile and trials focused on patient-important outcomes. ASCIA also supports this approach.

Another meta-analysis that was published in Scientific Reports in January 2020 analysed the same 12 controlled and an additional 15 non-controlled studies. These 27 studies involved 1,488 children receiving peanut oral immunotherapy (POIT). This analysis showed that certain aspects of treatment programs could increase the risk of anaphylaxis, while the inclusion of another component (co-treatment) may reduce the risk. This analysis also highlights the lack of data collected to date around patient-important outcomes such as protection from accidental reactions for those who have undergone peanut OIT in the past.

Both publications indicate that more research is required to establish the optimal treatment routine for safe and effective OIT for food allergy.

### Food allergy

Food allergy occurs in around 5-10% of children, and 2-4% of adults in Australia and New Zealand. The most common foods that cause allergic reactions are egg, peanut, cow's milk (dairy), tree nuts, soy, sesame, wheat, fish and other seafood (crustaceans).

Whilst most food allergies result in mild to moderate allergic reactions, some food allergies can be severe, resulting in potentially life-threatening anaphylaxis.

Most food allergies in children are not severe and some may be 'outgrown' with time; studies have shown that 5% of children still have their food allergy at five years of age.

Peanut, tree nut, seed and crustacean allergies are less likely to be 'outgrown' and tend to be lifelong allergies. When food allergy develops for the first time in adults, it usually persists.

### **The possible benefits from OIT are desensitisation and sustained unresponsiveness**

Published trials show that OIT for food allergy can result in desensitisation in many people, but most do not show sustained unresponsiveness:

- **Desensitisation** is a temporary state that allows a person to consume more of the food allergen than they could prior to OIT, but the underlying food allergy is still present. Desensitisation requires the food allergen to be consumed regularly, without stopping.
- **Sustained desensitisation** means that a person has remained desensitised to a larger amount of food than they could tolerate before treatment, after having paused treatment for a period of days or weeks.
- **Sustained unresponsiveness** means that a person can consume standard serves of the food allergen after a long period of avoidance or stopping OIT, without having an allergic reaction. This may sometimes be called ongoing tolerance or remission.

### **Safety and effectiveness of OIT**

It is important that people with food allergy and their families are aware that most OIT methods are not currently standardised or approved for routine treatment of food allergy globally.

There are no OIT products for food allergies registered by the TGA in Australia or Medsafe in New Zealand. One OIT product for peanut allergy (Palforzia™ developed by the company Aimmune Therapeutics) has received FDA approval for use in the USA in 2020. This form of OIT uses standardised amounts of peanut allergen powder contained in capsules.

Recent publications have shown that OIT leads to more allergic and adverse reactions compared with placebo or allergen avoidance (current standard care).

People who are on OIT can still have allergic reactions due to accidental exposure, or due to the OIT itself.

There may also be other complications of OIT, for example, inflammation of the oesophagus, which is the muscular tube that connects the mouth to the stomach.

Currently there are several clinical trials of OIT and other treatments for food allergy underway in Australia and other countries. In some of these trials, OIT is combined with another component (co-treatment) that may help to make allergic reactions less severe, improve safety and encourage tolerance.

The trials aim to develop standardised and proven methods to maximise benefit and reduce the risk of potential harm in people with severe food allergy. These trials are all hospital based due to high rates of allergic reactions.

Until these trials are completed, with methods, safety and effectiveness determined, ASCIA recommends that OIT for food allergy using a treatment that is not approved (by TGA in Australia, Medsafe in New Zealand, or FDA in USA) should not be performed outside of clinical trials.

### **Current ASCIA recommendations for management of food allergy**

Until OIT and other treatments for food allergy are proven and standardised for routine use, and approved by regulatory bodies (such as FDA, TGA or Medsafe), avoidance of confirmed food allergens is recommended for the management of food allergy.

All patients receiving OIT (Palforzia™ or other OIT administered as part of a clinical trial) should be advised of the increased likelihood of allergic reactions (including anaphylaxis) and be prepared for these events.

It is important for people with food allergy and their families to:

- Know the signs and symptoms of mild to moderate and anaphylaxis.
- Know what to do when an allergic reaction occurs.
- Read and understand food labels for food allergy.
- Inform wait staff that they have food allergy when eating out.
- Be aware of cross contamination of food allergens when preparing food.
- Carry their adrenaline autoinjector (if prescribed), and an ASCIA Action Plan for Anaphylaxis.

### Further information and support

Lancet publication: [www.thelancet.com/journals/lancet/article/PIIS0140-6736\(19\)30420-9/fulltext](http://www.thelancet.com/journals/lancet/article/PIIS0140-6736(19)30420-9/fulltext)

Scientific Reports publication: <https://doi.org/10.1038/s41598-019-56961-3>

Information about food allergy: [www.allergy.org.au/patients/food-allergy](http://www.allergy.org.au/patients/food-allergy)

Information about venom or aeroallergen immunotherapy: [www.allergy.org.au/patients/allergy-treatment](http://www.allergy.org.au/patients/allergy-treatment)

Patient support:

Allergy & Anaphylaxis Australia [www.allergyfacts.org.au](http://www.allergyfacts.org.au)

Allergy New Zealand [www.allergy.org.nz](http://www.allergy.org.nz)

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