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IMMUNOTHERAPY INFORMATION SHEET

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What is immunotherapy?

The aim of immunotherapy/desensitisation is to switch off the allergic response. By giving doses of commercially prepared extracts of substances that a person is allergic to, the immune response to allergen gradually decreases over time. It is the closest thing to natural therapy since medication only suppresses the symptoms, not the underlying immune response.

What conditions is it used for?

Dangerous insect sting reactions/anaphylaxis – routinely recommended

Large local swellings in response to insect stings – not normally recommended, as these only occasionally ever get worse.

Insect bite reactions – no vaccines are available for treatment of these.

Hay fever and allergic asthma – commonly used when people wish to control their symptoms with less medication.

Eczema/dermatitis – not routinely recommended because the jury is out as to whether this actually works well or not. There are small published trials only showing evidence of benefit. A pooled examination of all trials suggested benefit in 30-50% of patients but it is not routinely recommended at this time.

Food allergy – this is not considered to be a routine treatment for food allergy, but rather one still in the research basket. A high proportion of those doing oral immunotherapy have regular side-effects, and can have unpredictable allergic reactions to food eaten. Food patches have been studied, but none are registered at this time. Currently therefore, food immunotherapy is not recommended in Australia or New Zealand outside of research studies.

Why consider immunotherapy?

The trigger is hard to avoid

Medication – doesn't work, causes side-effects or you dislike the idea of using medication

Cost – in those with severe allergic disease, immunotherapy is less expensive than taking drugs for decades.

Lifestyle or occupation – for example, people who can't avoid pets or don't want to avoid pets or who would like to purchase a pet yet are allergic to them.

Asthma prevention – as well as treating the allergic component of asthma, there are increasing number of studies demonstrating that early treatment of hay fever can reduce the risk of allergic asthma development as well.

More options are available than years ago

1. Traditional immunotherapy injections – these have been around since the 1950s and involve weekly injections for a few months and eventually once per month all year round for 3 to 5 years. A 30 minute wait after each injection is required for safety reasons in case an allergic reaction occurs, such as rash or difficulty breathing or dizziness. Best practice is separating different types of extracts, for example dust mite in one injection and grasses in another so that the enzymes in one extract do not degrade the other allergen. That generates potentially more than one extract and therefore a higher cost. These extracts have the longest history of use other many decades.

2. Allergoid injections – these are treated so that allergic reactions are less likely to occur as side-effects. The risk of serious side-effects is considered to much less likely to occur than routine injections. For this reason, only one undertakes weekly injections for a couple of weeks only and then once per month. Mixing of extracts is also possible as the enzymes in one extract are unlikely to break down other allergen extracts in the same bottle. They can make it cheaper and safer, but there is still a 30 minute wait after each injection.

These are the main injectable extracts I use these days as they are cheaper, safer and more convenient.

BUT_ there are NO trials comparing whether one extract is better than another but the immune responses seen are the same with both extracts and they seem to be of similar effectiveness than the older traditional extracts.

3. Oral liquid – oral liquid extracts have been available in Australia since around 2007. They are taken most days all year round. Many patients benefit but my impression is they are not as effective as new oral allergen tablets and they are just as expensive. I rarely use these unless I have to.

4. Oral tablets – grass tablets have been available on the Australian market since 2013 and dust mite tablets since 2017. Published studies show these to be very effective, although they are more expensive than injections usually. There are also cat and other allergen extracts available as well but these are made by smaller drug companies and clear evidence of benefit is limited.

Note: Oral treatment is clearly more attractive in young children but injections are still possible in children if one uses a numbing EMLA patch applied to the injection site 1 hour before.

Safety aspects

After injections, there is a 30 minute wait period for safety reasons after each and every injection. With oral tablets, there is a 30 minute wait after the first dose in case tongue or throat swelling occurs, but after that, doses are taken at home. Oral liquids are considered to be very safe and therefore only a brief wait period after the first dose is needed with other doses taken at home. Antihistamines can be taken before each and every injection to reduce side-effects, and I routinely recommend those on tablet immunotherapy take antihistamines every day for the first fortnight of treatment for the same reason.

Risks and side-effects of injections

*Common ~ 50%: Everyone gets an itchy lump at the site of injection of variable size. You can take an antihistamine after or before the injection to reduce the discomfort. I recommend this as a routine.

*Uncommon ~ 5-10%: Large local itch and swelling. If you get large local reactions, your doctor may temporarily reduce the dose.

*Rare ~ 1%: More serious side-effects can also occur after an injection. These are most common in the first few months of treatment, but can occur at any time. Most side-effects occur within 30 minutes of an injection. A waiting period is compulsory so that you will be close to your treating doctor if there is a problem. It is also wise to avoid exercise for ~3 hours on either side of your injection (some doctors recommend not exercising the rest of the day). If you play sport, have the injection on another day or if you work in a physical job, have injection at end of day.

Serious side-effects can include:

- Rash (hives) all over, throat/tongue swelling
- Hay fever-like symptoms
- Wheeze/asthma-like symptoms
- Dizziness, drop in blood pressure or shock
- Flu'-like symptoms a day or two later

Improving injection safety

- Take an antihistamine before every injection (preferably a few hours before or the night before if you have morning injections)
- Wait 30 minutes after each injection (this is compulsory)
- Do not exercise or play sport or have hot saunas/baths within 3 hours of an injection

Risk and side-effects of oral treatment

Common: Unpleasant taste with liquids although this varies between brands. Children can suck a lollie at the same time. ~ 20 %: Irritation or itching inside the mouth and throat. These can be helped by temporarily reducing the dose or taking an antihistamine beforehand. E.g. the night before. Tablets have no significant taste at all.

*Uncommon: ~ 3-5% Stomach upset, nausea, chest pain, stomach pain, trouble swallowing

*Rare: The risk of potentially dangerous side-effects such as difficulty breathing or rashes is considered to be very uncommon but the tablets are much more potent products so local side-effects are much more likely.

NOTE: the oral tablets are more potent products and more likely to work, and more likely to cause side-effects.

Licencing and Medicare or private rebates for the costs of immunotherapy

- Medical visits are subsidised but no allergen extract is eligible for a rebate under Medicare Australia.
- There is only one brand of fully registered injectable extract made by Stallergenes called Alustal. It was on the market for several years but disappeared from the Australian market around 2016 due to manufacturing issues. These extracts MAY RETURN to the Australian market in 2023/4 with two allergen extracts at this stage: dust mite and 5 grass mix. As these are fully registered, you MAY be eligible for a partial private health fund rebate if you have the right insurance cover. Unfortunately, these are the traditional injections given weekly for a few months, then less often.
- Allergoid injections are imported and licensed for single patient use and are not fully registered and therefore it is unlikely you will obtain any refund from your health fund.
- Oral liquids like Staloral or Oraltek are unlikely generate any private health refund.
- Fully registered tablets in Australia may be eligible for rebates from private health funds if a person has the right health fund cover. If asking about tablets, would need to ask the health fund whether they give money back grass tablets (like Oralair or Grazax) or dust mite tablets (like Acarizax or Actair) which are fully registered in Australia.

What is better: tablets or injections?

This is a sensible and very good question, but one that is not that easy to answer. Most of the injection trials are older studies but compare active injections vs dummy placebo. The tablet studies are much the same, comparing active to dummy/placebo tablet. There are only a handful of studies comparing tablets and injections in the same research study and these are too small (~ 20-30 subjects) to show any meaningful difference. If I have patients on tablets and they do well, I continue them for another few years. If they do not do well, then most do better if switched to injections. I have also had the opposite observation; people doing very well on tablets but switch to injections to save money and they do worse than on the tablets. So some seem to do better on one treatment than another and it is not possible to predict who. *On the other hand, it is useful to be aware that the BEST evidence of benefit from immunotherapy are from the recent well-designed and large placebo-controlled trials of grass and dust mite tablets, which is why these drugs are fully registered in Australia. Furthermore, dust mite tablets have been shown to be of benefit when specifically studied for the treatment of allergic asthma, as opposed to most trials that examine hay fever benefit first with asthma as an afterthought. As described above, there are no comparative trials comparing the benefit of traditional injections to allergoid injections to demonstrate that one is better. As a rough rule of thumb, if you can afford the tablets, I suggest trying the **tablets first** and move to injections if the tablets do not work.*

Review appointments and duration of treatment

If one undertakes immunotherapy for only 12 months, it often returns fairly quickly. Standard recommendations are for a minimum of three years and published studies show that the vast majority of individuals who do so, remain well for at least three years after stopping, with anecdotal evidence suggesting a much longer duration of benefit. Normally, therefore organises specialist review at an appropriate interval after starting treatment to assess benefit and side effects and plan for the future.

How much does immunotherapy cost?

There are a couple of brands on the Australian market and cost will be determined by the brand used, the number of allergen bottles and their concentration and whether these are mixed in the same bottle (and therefore diluted) and whether one needs to purchase one extract or more than one extract. Assuming regular treatment all year round, rough estimates are:

- Routine injectable extracts – roughly \$500 per year (Alutek) or \$600 per year (Alustal) each.
- Allergoid injectable extracts – between \$400 and 800/year each. Depends on the brand, concentration & mix.
- Grass pollen tablets – around \$700 per year, depending on whether one purchases these in small monthly boxes (more expensive) or three monthly boxes (much less expensive) on prescription.
- Dust mite tablets – \$100 per month or \$1200 per year on prescription.
- Cat tablets – \$1200 per year
- Birch tree tablets – around \$700 per year

Sometimes it can be cheaper, for example in a person who has a relatively short grass pollen hay fever season lasting a few months to do injections. Under those circumstances, so-called pre-seasonal immunotherapy injections taken for 3 to 4 months during winter and stopped in early springtime, can be roughly half the injection cost listed above. When deciding on immunotherapy, cost can be influenced if there are any out-of-pocket costs for medical administration and supervision of injections. You need to check with your GP. While immunotherapy is not cheap, routine blood pressure or cholesterol tablets can cost \$40 per month unsubsidised, and a person with bad hay fever or allergic asthma taking multiple drugs all year round can easily spend \$1000 per year for decades.

Making a decision about starting immunotherapy

1. Yes or no? If no, try to avoid the cause and take medication.
2. If yes, what you want to target? Dust mite only, grasses as well, pets? Don't forget, targeting more triggers may add to the expense and result in more than 1 tablet or injection.
3. Once you have decided that, you then decide on the method – injections, oral liquids or oral tablets

Logistics

Most tablets (there are exceptions): first dose you have a 30 minute wait period, you are supplied with a 1 week starter pack, printed instructions how to take them, and a prescription to take to the chemist if the initial dose is tolerated. The rest are taken at home.

Oral liquids: I supply you with an order form, you order and pay for the allergen directly to the drug company. I call you in to collect and start when it arrives, generally after 2 months.

Injections: I supply you with an order form, you order and pay for the allergen directly to the drug company. I call you in to start when it arrives, generally after 2 months. You have your first dose here with a 30 minute wait, then other injections are given by your GP practice, NOT by you and NOT at home.

Storage

Oral liquids and injections: refrigerator temperature (do not freeze!)

Oral tablets: room temperature

Review appointments

I recommend review 6-7 months after you start. So once you start, put a note in your diary to call us 4 months later to book in for a brief review (country patients will be done by telehealth but Medicare rebates only apply if there is an in date referral (and government subsidies for this might change once the COVID crisis is more stable). The aim is to review benefit and plan for the future. If ineffective, you can still take medicines and can do it longer (it is more effective the longer you go on) OR change method. Eg injections instead of tablet, or vice versa or switch from allergoid to traditional injections.

Repeat order forms (“paperwork”) for injectable allergen

I have given you a prescription for allergen that contains multiple repeats, so you should be able to continue to use this for several years to come. Just photocopy the order form and re-use. But you can also use your original order form, and your GP can contact the drug companies and obtain their order forms and complete these for you too.

TABLETS: Getting more supplies

ANY doctor can write prescriptions for immunotherapy tablets if you run out, lose the script or if I am away or unavailable.