Guideline for the Administration of Allergen Immunotherapy: Subcutaneous Immunotherapy (SCIT) and Sublingual Immunotherapy (SLIT) in Paediatrics

Key Document code:	WAHT-TP-053	
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Approved by:	Paediatric Quality Improvement meeting	Medicines Safety Committee
Date of Approval:	18th December 2024	12th February 2025
Date of review: **This is the most current version and should be used until a revised document is in place**	12th February 2028	

Key Amendments

Date	Amendments	Approved by
12th February 2025	NEW document replaces Guideline for the Administration of subcutaneous Immunotherapy (SCIT)	Paediatric Governance Meeting and Medicines Safety Committee

Criteria for staff involved in the prescription and administration of immunotherapy (Subcutaneous Immunotherapy and Sublingual Immunotherapy)

In order to ensure patient safety, the minimum staffing levels required for the administration of SCIT and SLIT in clinic is for one doctor and one nurse, each of whom:

1. Have completed resuscitation training and training in the management of anaphylaxis per Trust Guidelines.
2. Are fully conversant with this policy
3. Understand the indications and contraindications for immunotherapy

Please see the Hereford and Worcestershire Integrated Pathway for Pediatric management of allergic rhinitis, before considering immunotherapy
https://www.hwics.org.uk/application/files/2217/1776/3098/Paediatric_Allergic_Rhinitis_Pathway_v1.0_07062024.pdf

Abbreviations

ASCIA – Australasian Society of Clinical Immunology and Allergy
AIT – Allergen immunotherapy
EAACI – European Academy of Allergy and Clinical Immunology
EoE – Eosinophilic esophagitis
HDM – House Dust Mite
NICE – National Institute for Health and Care Excellence
PADQOL - Paediatric Allergic Diseases Quality of Life
QoL – Quality of Life
SCIT – Subcutaneous Immunotherapy
SLIT – Sublingual Immunotherapy
SOP – Standard Operating Procedure
SpIgE – Specific Immunoglobulin E
SPT – Skin Prick Test

What is Allergen Specific Immunotherapy?

Allergen Immunotherapy (AIT) is sometimes known as, ‘desensitization’ or ‘Allergen Specific Immunotherapy’ or ‘allergy vaccination’. It is a treatment which modulates a person’s allergic response

to an allergen, e.g., insect venom, pollen, house dust mite or animal dander. It is recommended for children and young people with moderate to severe allergic rhinitis.

This is not a food specific immunotherapy guideline. These will be covered in individual guidelines e.g. milk (WAHT-PAE-152) and egg allergy (WAHT- TP-053).

AIT involves giving the patient repeated exposure of a particular allergen at regular intervals to modulate the immune response. This can either be very small doses given every day or by gradually building up the dose over a season. As the AIT starts to work, the body becomes able to tolerate the allergen. AIT only affects the allergen and symptoms to which is being treated, so patients who are multi-allergic and polysensitized will still develop symptoms from other allergens.

The main aims of AIT are:

• Reduce symptom severity and medication use in allergic rhinitis and allergic asthma. This may lead to improvement of QoL, improved functional capacity at school (or at work), reduced absenteeism, and reduced hospital admissions for asthma.
• Improve tolerance to allergen exposure.
• Possibly reduces the risk of new allergic sensitisations in patients.
• Possibly reduces the risk of asthma development in patients with allergic rhino conjunctivitis
(ASCIA, 2019; Roberts et al., 2017)

There are two main types of AIT:

Subcutaneous immunotherapy (SCIT) - the allergen is administered as subcutaneous injections. For pollens this is usually four to five injections given pre-allergen season, for three to five years.

Sublingual immunotherapy (SLIT) – the allergen is given under the tongue as a spray (drops) or a dissolvable tablet, every day, for three years.

The choice of immunotherapy needs to be discussed with the patient with consideration to their clinical presentation.

Who should be offered Immunotherapy?

Immunotherapy should be offered to children and young people, who:

- Despite maximal pharmacotherapy interventions (e.g. antihistamines, eye drops or nasal sprays) and non-pharmacotherapy interventions (such as house dust mite reduction measures, nasal washing or douching), remain symptomatic.
- Have symptoms significantly impacting their quality of life (QoL). Each patient should have QoL assessments completed (e.g. the Juniper Rhino-conjunctivitis Questionnaire or Paediatric Allergic Diseases Quality of Life, PADQOL).
- Have evidence of a relationship between allergen exposure and symptoms and have a specific IgE to the relevant allergic trigger as demonstrated by SPT and/or blood SpIgE (and component resolved diagnostics where possible).
- Can provide consent and a commitment to adhere to the treatment course which will be assessed over the treatment course.

Each patient considered for AIT should be assessed in a dedicated immunotherapy clinic, led by a consultant with a special interest in allergic diseases. Each family will be provided with written information on immunotherapy and be given enough time to consider if this is the right treatment for them.

SCIT should be considered in anyone who has had a severe reaction to a wasp or bee sting, (NICE, 2012). For these people, there is a risk of potentially fatal anaphylaxis if they have a repeat sting. Venom SCIT is a very effective risk reduction strategy for this patient group with 95% effectiveness against severe reactions for wasp venom and 80% effectiveness against severe reactions for bee venom, making it a potentially life-saving treatment.

Contraindications to AIT and other factors to consider

The potential benefits of the treatment are considered against the potential risks for each individual. Some factors, listed below, increase the risk of potentially severe responses to immunotherapy.

Concurrent asthma.

- AIT should not be initiated in severe or uncontrolled asthma (Roberts et al., 2017)
- People with asthma should be considered for insect venom desensitization (Pistsios et al., 2015) where there is a risk of anaphylaxis from a repeat sting, as the risk of unplanned allergy exposure outweighs the risk of treatment. However, the individual's asthma must be well controlled.
- People who have seasonal asthma may be considered for pollen immunotherapy.

Medication. Some medication can potentially increase the risk of an allergic reaction occurring or reduce the individual's response to adrenaline should they experience an allergic reaction. Where people are taking the following medications, the clinician must discuss the risks and benefits of AIT in the light of their underlying medical condition.

- There is some evidence that the use of ACE Inhibitors can increase the risk of allergic reaction.
- The use of beta blockers can interfere with the action of adrenaline.
- Monoamine Oxidase Inhibitors (MOAI's) and tricyclic antidepressants – there is the potential for people to develop hypertensive crisis when adrenaline is administered to those taking MAOI's. Tricyclic antidepressants may also potentiate the risk of reaction.

Hypersensitivity to any of the ingredients as listed in the product specifications

Other:

- Malignancy or systemic diseases affecting the immune system e.g. autoimmune diseases, immunodeficiency
- Inflammatory conditions in the oral cavity (for SLIT)
- Pregnancy - AIT should not be initiated if the patient is pregnant, however it may be continued in pregnancy and breastfeeding if the patient becomes pregnant after treatment initiation (Roberts et al., 2017)
- Non-Adherence **-** those unable to commit or adhere to treatment course
- Eosinophilic Oesophagitis (EoE**) -** for patients with a diagnosis or suspicion of EoE, SLIT is a contraindication, but SCIT may be considered (ASCIA, 2019).

Some reports mention that AIT can **exacerbate** existing asthma, eczema or undiagnosed autoimmune conditions in some patients but definitive research for this is lacking.

Initiating immunotherapy

SCIT

All doses of SCIT must be given in Children's Clinic, Worcester Royal Hospital, where both medical and nursing staff are available, and are familiar with the procedure to ensure patient safety. There must be access to full resuscitation equipment. Emergency allergic reaction medication must be prescribed before treatment is given.

Subsequent injections

Patients should return for future injections in accordance with the dosage schedule recommended by the product manufacturers and paediatric consultant.

The patient should be reviewed prior to each injection and the following recorded:

1. Are they feeling well?
2. Have they started any new medication since last being seen and, if so, what?
3. Have they had any exposure to the allergen (venom) since last being seen and, if so, what?

4. Have they experienced any side effects since following their last dose? If so, record the side effect, including speed of onset following drug administration, site, severity, duration and any treatment taken to manage it.
5. Any other questions or concerns

Following this review, the planned drug dosage must be discussed with the prescriber and the dosage adjusted where:

1. There has been a delay in the recommended treatment interval
2. The patient has experienced systemic side effects with the previous dose
3. The patient has experienced moderate local side effects with the previous dose

The dose should be omitted where:

1. The patient is unwell on the day of treatment
2. The patient has started taking medication listed in the contraindications and factors to consider for SCIT

Additional care of people undergoing SCIT immunotherapy who have a diagnosis of asthma

Where a person undergoing immunotherapy has a diagnosis of asthma (i.e Clenil® or equivalent >/= 400microgram per day or inhalers containing fluticasone>/= 200microgram/day), additional monitoring should include:

1. Lung function prior to first injection
2. Completion of peak flow prior to each subsequent injection. Injections should be delayed and their asthma treatment reviewed, if peak flow reading is not within patient's normal range (>/= 80% usual/predicted).
3. Where there is concern about symptoms or peak flow readings, lung function should be completed in place of peak flow readings with lung function showing an FEV1 less than 80% predicted, then AIT should be delayed and their asthma treatment reviewed.

Please see the SOP for the administration of SCIT (WAHT-TP-053).

SLIT

The first dose of SLIT should be initiated under supervision in Children's Clinic, Worcester Acute Hospitals NHS Trust. Emergency allergic reaction medication must be prescribed before treatment is given. It is recommended that SLIT is commenced a minimum of two months, but ideally, four months prior to the start of the targeted pollen season.

If a patient on established therapy has omitted their treatment for >14 days, then recommencing treatment under supervision should be considered.

Please see the SOP on SLIT administration (WAHT-TP-053). Patients and their families will also be given details on how to take their medication and how to order repeat prescriptions (Patient Information WAHT-PI-2013).

All patients should be given the opportunity to join the National Registry for Immunotherapy (BRIT Registry). Information about this will be given to parents and young people and informed consent/assent will be obtained at their first dose.

Management of Adverse Reactions in Hospital

As with any treatment, AIT has potential side effects. These range from common mild effects, e.g. swelling and redness at the injection site, to rare but severe side effects, e.g. anaphylaxis. Consequently, the treatment must be given in an environment where full resuscitation equipment is available and where staff are trained and experienced in offering this treatment

Mild or moderate local reactions, e.g. localized discomfort, redness or swelling at the injection site (SCIT) or mouth and tongue tingling, throat itch (SLIT):

1. Reassure patient that symptoms are likely to be transient
2. Record the time of onset and monitor for progression of symptoms
3. Look for:
    - SCIT size of the swelling (not the redness). If swelling is not subsiding, give dose of antihistamine as prescribed
    - SLIT ongoing, localized discomfort, give dose of antihistamine as prescribed
4. Monitor observations and local reaction symptoms
5. Inform doctor

Mild systemic reactions, e.g. rhinitis, generalized erythema, and/or urticaria:

1. Check pulse, blood pressure and peak flow and compare with baseline recordings, providing the results are comparable:
2. Give dose of antihistamine as prescribed
3. Inform doctor
4. Monitor for progression of symptoms, with monitoring of pulse, blood pressure, chest auscultation and consider a sitting peak flow.
5. Keep patient resting on the bed. Do not allow patient to walk around.

Moderate systemic reactions, e.g. infrequent cough, mild angioedema, nausea, or sensations of tightness in the throat without respiratory difficulty:

1. Be aware that these symptoms can be the precursors to anaphylaxis. Have a very low threshold for stepping up treatment to “management of severe systemic symptoms”.
2. Check pulse, blood pressure and peak flow and compare with baseline recordings, providing the results are comparable:
3. Inform doctor
4. If asthma symptoms then consider adrenaline and/or inhaled salbutamol and oral antihistamine as advised by the doctor
5. Monitor for progression of symptoms with monitoring of observations as indicated, or minimum every 15 mins

Severe systemic symptoms, e.g. laryngeal oedema, respiratory distress, drop in blood pressure with raised pulse, wheeze drop in peak flow:

1. Treat as for anaphylaxis according to Resuscitation Council Guidelines (2021).

Patients on SLIT should continue to take non-sedating antihistamines prior to treatment doses at home for a period of 4-6 weeks before reassessment. Consider stopping treatment after discussion with the patient’s consultant if there are exacerbations in asthma and/or eczema.

Assessing benefit of treatment

Where a person is being desensitized against an allergen, Patient Reported Outcome Measures (PROMs) e.g. the Juniper RQLQ or PADQOL should be used prior to commencement of the treatment (ideally while their baseline preventative treatment is being maximized) and in the case of pollen allergy, start of pollen season, mid-season, end of season and out of season. Where there is no identified improvement of symptoms or quality of life, treatment should be discontinued, or an alternative product considered.

The timescale of improvement varies with treatment e.g. pollen one to two years, HDM six months
For bee and wasp venom desensitization programs, the patient should receive maintenance treatment for at least 3 years. If they are stung and have a significant reaction while on treatment, then they should discuss the potential benefit of increasing the maintenance, to provide increased protection, with their consultant.

Treatment should be discontinued if the patient and family fail to adhere with treatment dosing.

Treatment will also be discontinued if the patient wishes to and all adherence strategies or additional treatments have been considered.

REFERENCES

ASCIA (2019) Aeroallergen Immunotherapy. A Guide for Clinical Immunology/Allergy Specialist. Accessed online https://www.allergy.org.au/images/stories/pospapers/ASCIA_HP_Aeroallergen_Immunotherapy_Guide_2024.pdf [accessed on 28th October 2024]

Roberts et al (2017) EAACI Guidelines on Allergen Immunotherapy: Allergic rhinoconjunctivitis. Allergy. Vol 73,issue 4 p 765-798

National Institute for Clinical ICE (2012) Pharmalgen for the treatment of bee and wasp venom allergy, TA246. updated August 2017. https://www.nice.org.uk/guidance/ta246/chapter/1-Guidance [accessed on 28th October 2024]

Pitsios, C., Demoly P., Bilò M., et al., (2015) Clinical contraindications to allergen immunotherapy: an EAACI position paper. Allergy Vol 70, Issue 8, p897-909

Resuscitation Council UK (2021) Emergency treatment of anaphylaxis. Guidelines for health care providers. Resuscitation Council UK. London