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Administration of Sublingual Immunotherapy (SLIT)

Allergic rhinitis is an IgE-mediated hypersensitivity inflammatory disorder characterised by watery nasal discharge, itchy nose, sneezing, nasal congestion and associated eye symptoms[1-3]. Allergic rhinitis is a significant cause of morbidity, negatively impacting on sleep, home, work and social performance and can result in a substantially reduced quality of life (QOL)[3,4, 5].

Allergen immunotherapy is recommended for patients who, despite allergen avoidance and a supervised trial of optimised pharmacotherapy, still have uncontrolled symptoms of seasonal allergic rhinitis[3,4,6] Immunotherapy has been shown to be clinically effective, and is the only disease-modifying treatment option that can both modify the IgE-mediated allergic response and induce long-term remission [6, 7].

Sublingual immunotherapy (SLIT) has been shown to be effective in reducing the symptoms and medications required in patients with grass-pollen related seasonal allergic rhinitis [3,5-7]. The BSACI has produced guidelines for the use of immunotherapy in patients with allergic rhinoconjunctivitis (**https://www.bsaci.org/guidelines/allergic-rhinitis**)[3]. Sublingual immunotherapy is a treatment that should be prescribed in a specialist allergy service and initiated pre-seasonally, after which the treatment may be self-administered and continued at home.

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How to administer SLIT

- Sublingual immunotherapy should be initiated in a clinical area that has resuscitation facilities and where clinical staff are equipped to manage anaphylaxis.
- Informed consent should be obtained by patient or in the case of a child, a carer with parental responsibility and assent given by the child.
- Patients should be advised that they must be well on the day of administration and if they have asthma this should be well controlled.
- Wash hands prior to procedure and adhere to local Trust's Infection Control and PPE (personal protective equipment) Policy.

PROCEDURE	**RATIONALE**
1.) Check patients' name and DOB against the prescription to confirm that SLIT is being administered to the correct patient.	To ensure the patient receives the correct treatment
2.) Obtain baseline observations prior to commencing SLIT. A visual assessment of skin condition should be made for those patients with eczema. Complete a visual inspection of the mouth, observing for oral lesions or loose teeth. If oral lesions are present, do not proceed with SLIT until the lesions have healed. Ensure patient is not unwell, ensure patient apyrexial. If the patient has inhalers prescribed, ensure their asthma is well controlled. The chest should be clear on auscultation. Lung function testing, peak flow measurements can be used to assess asthma control if available. Ideally the patient should not have required use of reliever inhaler to treat wheeze in the weeks prior to commencing	To have a baseline against which future observations can be compared To reduce the risk of a severe or systemic reaction. To ensure patient is able to safely commence on administration of SLIT.

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treatment.	
3.) Confirm that the patient is not pregnant.	SLIT should not be initiated in patients who are pregnant, due to the possible risk to the foetus if anaphylaxis occurs.
4.) The patient should refrain from eating and drinking for five minutes prior to and following administration of SLIT.	Food or drink in the oral cavity could affect the absorption of the SLIT.
5.) Administer SLIT by placing the treatment in the sublingual pocket under the base of the tongue. Please see individual SPC for product specific advice.	SLIT is absorbed via the sublingual route
6.) SLIT should remain under the tongue for between 1–2 minutes before swallowing.	To ensure SLIT is absorbed by the sublingual glands
7.) Monitor patient for any sign of an allergic reaction for 30–60 minutes following administration of SLIT.	An allergic reaction could occur following administration of SLIT
8.) If commencing two separate SLIT products on the same visit, there should be 30-60 minutes between giving the first product and the second. A further 30-60 mins observation should occur after the second product is given.	An allergic reaction could occur following administration of SLIT
9.) Reassure patient if they experience symptoms such as oral tingling, pruritus, mild tongue swelling, itchy throat or ears that these are common side effects in the early phase of treatment	These are common side effects and should resolve 1 – 2 weeks after beginning SLIT.
10.) Promptly treat any allergic reaction or side effects of SLIT	To ease discomfort and prevent the development of moderate symptoms

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11.) Advise patient that if side effects are unpleasant that they can take an oral non-sedating antihistamine 30-60 minutes prior to taking their SLIT medication.	Pre-dosing with an oral antihistamine in the first 1-2 weeks may help reduce unpleasant side effects in the early stage of treatment.
12.) Advise the patient to stop taking SLIT in the following situations: • For 7 days following oral surgery, including dental extraction • For 7 days after shedding a deciduous tooth • If patient has an oral ulcer or open wound in the mouth or oral mucosa – to temporarily discontinue SLIT until area has healed. If patient is unwell with a fever, or unwell enough to be absent from school or work, they should temporarily discontinue their SLIT until their illness has resolved. If patient receives a vaccine which causes side effects such as fever or joint pain, they should stop their treatment until side effects resolve. Patients with concomitant asthma and experiencing an acute upper respiratory tract infection – to temporarily discontinue until infection has resolved.	To reduce the risk of SLIT being absorbed systemically through an open lesion rather than through the sublingual mucosa. To reduce the risk of systemic allergic reaction to SLIT if immune system pre-activated due to infection/illness/vaccine To reduce the risk of patient experiencing exacerbation of asthma and/or respiratory symptoms.
12.) Document administration of SLIT, any side effects and treatment given.	To record administration and treatments for governance.
13.) Reassess the patient prior to discharge.	To ensure the patient has not had an allergic reaction and is fit for discharge.
14.) Ensure the patient and/or family have the following information on discharge; • How to recognise and manage an allergic reaction	To ensure the patient and family are supported and aware of how to overcome

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• Advise the patient to ensure they have immediate access to a non-sedating antihistamine. • Revision and reinforcement of the importance of compliance with medication • Have a supply of initial treatment and are aware of how to collect ongoing supply • Written information relating to the product they are using • Contact details should they require ongoing support • An expected schedule for how and when they will be followed up, how they will receive supply of SLIT medication	any problems with their treatment. To treat side effects of SLIT.
15.) Advise patient to continue taking SLIT daily as prescribed (typically for the next 3 years).	In order to gain persisting benefit from SLIT treatment.
16.) Follow up patient as appropriate. Perform a retrospective seasonal global assessment of the effectiveness of immunotherapy following each season. For example the Paediatric Allergic Disease Quality of Life Questionnaire (PADQLQ)[9] or for adults the Allergic Rhinitis Control Test (ARCT) [10] .	To monitor effects of immunotherapy.

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References & Bibliography:

1. Min Y. (2010) The pathophysiology, diagnosis and treatment of allergic rhinitis. Allergy Asthma Immunol Res;2(2):65-76.

2. Wallace D, Dykewicz M, Bernstein DI, Blessing-Moore J, Cox L, Khan D, et al. (2008) The diagnosis and management of rhinitis: An updated practice parameter. J Allergy Clin Immunol;122(2):S1-84.

3. Scadding GK, Kariyawasam H, Scadding G, Mirakian R, Buckley RJ, Dixon T, Durham SR, Farooque S, Jones N, Leech S, Nasser SM, Powell R, Roberts G, Rotiroti G, Simpson A., Smith H., & Clark AT. (2017) BSACI guideline for the diagnosis and management of allergic and non-allergic rhinitis (Revised Edition 2017; First edition 2007) Clinical and Experimental Allergy, 38, 19–42.

4. Brożek J, Bousquet J, Baena-Cagnani CE, Bonini S, Canonica GW, Casale TB, Gerth van Wijk R, Ohta K, Zuberbier T, & Schünemann HJ. (2010) Allergic Rhinitis and its Impact on Asthma (ARIA) guidelines: 2010 Revision. Journal of Allergy and Clinical Immunology; 126, (3), 466-476.

5. Roberts G, Xatzipsalti M, Borrego LM, Custovic A, Halken S, Hellings PW, Papadopoulos NG, Rotiroti G, Scadding G, Timmermans F, & Valovirta E. (2013) Paediatric rhinitis: position paper of the European Academy of Allergy and Clinical Immunology; 68: 1102–1116.

6. Calderon M, Alves B, Jacobson M, Sheikh A, & Durham S. (2009) Allergen injection immunotherapy for seasonal allergic rhinitis (Review). Cochrane Database Syst Rev;1:1-98.

7. Walker, S. M., Durham, S. R., Till, S. J., Roberts, G., Corrigan, C. J., Leech, S. C., Krishna, M. T., Rajakulasingham, R. K., Williams, A., Chantrell, J., Dixon, L., Frew, A. J. & Nasser, S. M. (2011), Immunotherapy for allergic rhinitis. Clinical & Experimental Allergy, 41: 1177–1200.

8. Canonica GW, Cox L, Pawankar R, et al. (2014) Sublingual immunotherapy: World Allergy Organization position paper 2013 update. *World Allergy Organ J*.;**7**:6.

9. Durham S, Yang W, Pedersen M, Johansen N, & Rak S. (2006) Sublingual immunotherapy with once-daily grass allergen tablets. A randomised controlled trial in seasonal allergic rhinoconjunctivitis. J Allerg Clin Immunol.; 117(4): 802-9.

10. Roberts G, Hurley C, & Lack G. (2003) Development of a quality-of-life assessment for the allergic child or teenager with multisystem allergic disease. Journal of Allergy and Clinical Immunology;111 (3).

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Manufacturer name	Product name	Allergen	Dose	Considerations
Allergy Therapeutics	Oralvac Compact	Tree pollen (Birch, Alder, Hazel, Olive, Cypress, Plane- available individually) Grass mix (12 Grass pollens) Weed pollen (mugwort, ragweed, plantain, parietaria) Mould (alternaria, cladosporium) House dust mite (Dermatophagoides pteronyssinus, Dermatophagoides farina) Cat dander Dog dander Horse dander	Sublingual drops, One pump delivers 0.07 mL solution. Red bottle (maintenance dosing), orange botte 1:10 dilution of red bottle, and green bottle 1:100 dilution of red bottle. Maintenance dose is 3 pumps of red vial daily for 8 - 12 months per year.	First dose usually administered in hospital. Rush up-dosing in 1 day: 1 drop red vial, 30 mins observation, 3 drops red vial, 30 mins observation. Slow up-dosing (for highly sensitized patients or for patients commencing treatment at home): increasing number of pumps/day, and moving from green bottle to yellow and finally to red over 10 days. **Not licensed in UK.**
ALK Abello	Grazax	Grass (Phleum pratense- Timothy Grass)	Sublingual tablets 75,000 SQT* standardised allergen extract of grass pollen from Timothy grass. *SQT= standardised quality units tablet	First dose needs to be administered in hospital, initiation should be at least 4 months prior to the expected start of the grass pollen season.

				Licensed for use in the UK- for Patients aged 5 years and above. One tablet taken daily throughout the year. Shared care agreement can be put in place if GP to agree to fund treatment for three years following initiation in secondary care.
ALK Abello	Acarizax	House dust mite	Sublingual tablets 12 SQT*-HDM standardised allergen extract from the house dust mites dermatophagoides pteronyssinus and dermatophagoides farina *SQT= standardised quality units tablet	First dose needs to be administered in Hospital One tablet taken daily throughout the year. **Not licensed in the UK.**

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ALK Abello	Itulazax	White birch pollen (Betula verrucosa)	Sublingual tablets 12 SQT*-Bet standardised allergen extract from white birch per tablet. *SQT= standardised quality units tablet	First dose needs to be administered in hospital. Initiation should be at least 4 months prior to the expected start of the Tree Pollen season. One tablet taken daily throughout the year. **Not licensed in the UK.**
Diagenics	SLIM$_{TDC}$	House dust mite (*Dermatophagoides pteronyssinus* and *Dermatophagoides farina mix)*	Each mL of solution contains 3,000 mTU (mannan-Therapeutic Units)	Daily dosage is 2 spray pulsations daily sublingually. Three year treatment course. **Not licensed in the UK.** For adults and children aged over 5 years.

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Inmunotek	Oraltek spray	House dust mite Grass pollen Birch pollen Cat/Dog dander Allergens typically administered in mixes e.g. Birch + HDM. Mixes can be made bespoke for patient.	Concentration of 30,000 TU*/mL. Each spray application is 0.1mL.Therefore each daily dose is 0.2 mL, equivalent to 6,000 TU. *TU= therapeutic units	Administered perlingually (sublingual/ perioral) with a spray application. Daily dosage is 2 sprays, with no up-dosing required. **Not licensed in the UK**
Stallergenes Greer	Staloral Oralair	House dust mite (DP 50% + DF 50%) Birch extract 3 Tree mix containing Alder, Hazel and Birch pollens in equal parts 5-Grass mix containing Cocksfoot pollen, Sweet vernal grass pollen, Rye-grass pollen, Meadow-grass pollen and Timothy pollen.	Maintenance dose 300IR* sublingual drops via pump. Various allergenic concentrations available to facilitate up dosing on initiation. Maintenance dose of one tablet contains 300IR	For use in adults and children over the age of 5 years. Initiate 4 months pre-season and continue co-seasonally for pollens. Perennial dosing for house dust mite. **Not licenced in the UK**

			Initiation pack contains 3x100IR tablets for up dosing over 2 days. *IR= Index of reactivity	
Lofarma	Lais allergoid tablets Lais allergoid drops	Grass mix (33% Yorkshire Fog, 33% Timothy, 33% Meadow Grass) Tree mix (Grey Alder 50% + White Birch 50%) House dust mite (DP 50% + DF 50%) Cat Parietaria (Pellitory Weeds 50%/50%) Cypress Olive Alternaria Mugwort Ragweed	Maintenance with 1000 AU (allergenic units) sublingual tablets: - For seasonal treatment (e.g. pollens) take 1 tablet/day for 5 days a week or alternatively take 1 tablet/day, before and during the pollen season. - For perennial treatment (e.g. house dust mites) take 1 tablet/day for 2 days a week, throughout the year.	Pre and co seasonal: Start Tree dosing in December through February. Start Grass dosing in February through April. Up dosing over 4 days is optional. **Not licensed in the UK.**

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