Shared Care Protocol (SCP) for Sublingual Immunotherapy (SLIT) (Grazax®/Acarizax®)

- For adults and children diagnosed with severe allergic rhinitis to grass pollen or house dust mite

Prescribing guideline developed by:
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Specialist responsibilities

- Assess the patient and provide diagnosis; ensure that this diagnosis is within scope of this shared care protocol (section 2) and communicated to primary care.
- Discuss the benefits and risks of the treatment with the patient and/or their carer and provide the appropriate counselling (see section 11) to enable the patient to reach an informed decision. Obtain and document patient consent. Provide an appropriate patient information leaflet.
- Importance of compliance will be discussed with patients and assessed after the first month of treatment and at yearly reviews. If any concern regarding compliance is raised then alternatives (Subcutaneous immunotherapy) will be considered.
- Assess for contraindications and cautions (see section 4) and interactions (see section 7).
- Conduct required baseline investigations and initial monitoring (see section 8).
- Initiate and optimise treatment as outlined in section 5. Prescribe the maintenance treatment for at least 8 weeks and until optimised.
- Once treatment is optimised, complete the shared care documentation (Appendix 1) and send to patient's GP practice detailing the diagnosis, current and ongoing dose, any relevant test results and when the next monitoring is required. Include contact information (section 13).
- Conduct the scheduled reviews and monitoring in section 8 and communicate the results to primary care. After each review, advise primary care whether treatment should be continued, confirm the ongoing dose, and whether the ongoing monitoring outlined in section 9 remains appropriate.
- Provide advice to primary care on the management of adverse effects if required.

Primary care responsibilities

- Respond to the request from the specialist for shared care in writing within 14 days where applicable. Agreement letter Appendix 2; Refusal letter Appendix 3
- If accepted, prescribe ongoing treatment as detailed in the specialists' request and as per section 5, taking into any account potential drug interactions in section 7.
- Manage adverse effects as detailed in section 10 and discuss with specialist team when required.
- Stop Grazax®/Acarizax® and discuss urgently with the specialist if the patient report signs of anaphylaxis (patients will be counselled regarding this)
- Stop treatment as advised by the specialist.
- Prescribe any rescue medication for break-through symptom relief, as advised by the specialist see section 11.
- To consider adding a stop date (of 3 years) to GP computer systems

Patient and/or carer responsibilities

- Take Grazax®/Acarizax® as prescribed and avoid withdrawal unless advised by the primary care prescriber or specialist.
- Attend regularly for monitoring and review (telephone) appointments with specialist and keep contact details up to date with both prescribers. Be aware that medicines may be stopped if they do not attend.
- Report adverse effects to their secondary care prescriber. Seek immediate medical attention if they develop any symptoms as detailed in section 11.
- Report the use of any over the counter medications to their primary care prescriber and be aware they should discuss the use of Grazax®/Acarizax® with their pharmacist before purchasing any OTC medicines.

1. Background

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NICE Clinical Knowledge Summaries (CKS) recommends that patients diagnosed with severe allergic rhinitis confirmed by skin prick test &/or blood tests who remain symptomatic despite maximum medical treatment should be offered Immunotherapy. This is the only type of treatment which has been shown to modulate the immune response to the allergen, achieving tolerance and resolution of symptoms in many individuals.

Grazax® is an oral lyophilisate immunotherapy tablet which contains an extract of Timothy grass pollen allergen. Grazax® modifies the allergic disease by increasing immunological tolerance towards grass pollen.

Acarizax® is an oral lyophilisate immunotherapy tablet which contains an extract from the house dust mites *Dermatophagoides pteronyssinus* and *Dermatophagoides farina*. Acarizax® modifies the allergic disease by increasing immunological tolerance towards house dust mite.

2. Indications (Please state whether licensed or unlicensed)

- Grazax® is licensed to treat rhinitis and conjunctivitis caused by grass pollen in adults and children (5 years or older).
- Acarizax® is licensed to treat persistent moderate to severe house dust mite allergic rhinitis despite use of symptom-relieving medication (12-65 years) and house dust mite allergic asthma not well controlled by inhaled corticosteroids and associated with mild to severe house dust mite allergic rhinitis in adults (18-65 years).

3. Locally agreed off-label use

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- Not applicable

4. Contraindications and cautions

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This information does not replace the Summary of Product Characteristics (SPC) and should be read in conjunction with it. Please see Grazax SPC Acarizax SPC & Grazax BNF Acarizax BNF for comprehensive information.

Contraindications:

- Pregnancy: Treatment with Grazax®/Acarizax® should not be initiated during pregnancy
- Grazax® should be withheld from patients with severe or uncontrolled asthma (FEV1 <70% predicted value despite asthma treatment) outside the grass pollen season (grass pollen season is May to July).Grass pollen-induced (seasonal) wheeze should not exclude a patient from treatment with Grazax®.
- Acarizax® should be withheld from patients with severe or uncontrolled asthma (FEV1 <70% predicted value despite asthma treatment)
- History of allergic (hypersensitivity) reaction to any of the excipients in this medicine.
- Previously have had an allergic reaction in connection with injection of allergen extract of grass pollen/house dust mite - unless further investigations were carried out to exclude allergy to Grazax®/Acarizax®.
- Inflammatory condition in oral cavity with severe symptoms
- Eosinophilic gastrointestinal disorder (including eosinophilic oesophagitis)

Cautions:

- History of severe allergy to fish
- Malignancy
- Severe disease affecting immune system

5. Initiation and ongoing dose regime

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- Transfer of monitoring and prescribing to primary care is normally after the patient has been treated for 8 weeks, the patient's dose has been optimised, and with satisfactory investigation results for at least 4 weeks
- The duration of treatment & frequency of review will be determined by the specialist, based on clinical response and tolerability. Maximum duration of treatment is 3 years unless advised otherwise by Allergy specialist.
- All dose or formulation adjustments will be the responsibility of the initiating specialist unless directions have been discussed and agreed with the primary care clinician
- Termination of treatment will be the responsibility of the specialist.

Initial stabilisation:

The loading period must be prescribed by the initiating specialist.

Following assessment and written consent, first tablet administered in clinical immunology and allergy outpatient department or paediatric day care under supervision. Patient observed for any adverse effects for a minimum of 30 minutes. Once stable transferred to maintenance dose of one tablet each day which is to be self-administered at home.

Maintenance dose (following initial stabilisation):

The initial maintenance dose must be prescribed by the initiating specialist.

Conditions requiring dose adjustment:

None

6. Pharmaceutical aspects

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Route of administration:	Sub-lingual
Formulation:	Oral lyophilisate tablet (Grazax® 75,000 SQ-T/ Acarizax® 12 SQ-HDM)
Administration details:	One tablet daily for 3 years
Other important information:	For best results, Grazax® treatment should ideally be started at least 4 months prior to the expected start of the grass pollen season.

7. Significant medicine interactions

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The following list is not exhaustive. Please see or Grazax SPC Acarizax SPC or Grazax BNF Acarizax BNF for comprehensive information and recommended management.

- No interaction trials have been conducted in humans and no potential drug interactions have been identified from any source.

8. Baseline investigations, initial monitoring and ongoing monitoring to be undertaken by specialist

Monitoring at baseline and during initiation is the responsibility of the specialist; only once the patient is optimised on the chosen medication with no anticipated further changes expected in immediate future will prescribing and monitoring be transferred to primary care.

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Baseline investigations:
Diagnosis is confirmed by an Allergy Specialist (history along with blood test and/or skin prick test confirming sensitisation to grass pollen/house dust mite)

Initial monitoring:
A nurse or consultant telephone consultation should take place 1 month after the first dose to ensure compliance and to discuss any side effects

On-going monitoring:
A nurse or consultant telephone consultation should then take place after the first grass pollen season (Grazax®)/after 6 months (Acarizax®) and then annually (during the 3 years course of treatment) to ensure effectiveness of treatment, adverse effects, and compliance. The desensitisation monitoring form will be completed at each consultation to assess the patient's symptoms.

The specialist will retain the responsibility for monitoring the patient's ongoing response to treatment and advise if a dose change or treatment cessation is appropriate. This should usually be undertaken annually.
When a patient is reviewed, advise primary care whether treatment should be continued, confirm the ongoing dose, and whether the ongoing monitoring outlined in section 9 remains appropriate.

9. Ongoing monitoring requirements to be undertaken by primary care

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See section 10 for further guidance on management of adverse effects/responding to monitoring results.

Monitoring	Frequency
• No monitoring required	

10. Adverse effects and other management

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Any serious adverse reactions should be reported to the MHRA via the Yellow Card scheme. Visit www.mhra.gov.uk/yellowcard

For information on incidence of ADRs see relevant summaries of product characteristics

See section 11 below for more details	

11. Advice to patients and carers

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The specialist will counsel the patient with regard to the benefits and risks of treatment and will provide the patient with any relevant information and advice, including patient information leaflets on individual medicines.

The patient should be advised to report any of the following signs or symptoms to their specialist care prescriber without delay:

1) Mild adverse effects: Patients should be advised to take long-acting non-sedating antihistamines to control mild symptoms (mouth/ ear/ eye/ nose/ throat irritation or itching, sneezing, runny nose) alongside their Grazax®/Acarizax® tablets. This may need to be prescribed by primary care or self-care depending on the antihistamine being taken.

2) Moderate adverse effects: Patient to be advised to take oral high dose antihistamines (these may need to be prescribed by primary care or self-care depending on the antihistamine being taken), stop Grazax®/Acarizax® and contact their specialist care prescriber during working hours if they develop these symptoms:
   a. Generalised urticarial rash
   b. Angioedema involving face or lips

3) Severe adverse effects: Patients should be advised to stop taking Grazax®/Acarizax® and contact the emergency service (call 999) immediately if they develop serious side effects:
   a. Rapid swelling of tongue or throat
   b. Difficulties in swallowing
   c. Difficulties in breathing
   d. Voice changes
   e. Worsening of existing asthma
   f. Severe discomfort

4) Severe mouth inflammation: If patients develop severe mouth inflammation, then they should stop taking Grazax®/Acarizax® and contact their specialist care prescriber during working hours to discuss.

5) Oral surgery: In case of oral surgery, including dental extraction, and shedding of a tooth, treatment with Grazax®/Acarizax® should be stopped for 7 days to allow healing of the oral cavity.

6) Asthma & Infection: If a patient has asthma and is experiencing an acute upper respiratory tract infection, Grazax®/Acarizax® treatment should be temporarily discontinued until the infection has resolved then restarted at home (unless it was stopped for more than 7 days).

7) Symptoms suggestive of eosinophilic oesophagitis: If a patient exhibits treatment-related abdominal pain, dysphagia, nausea or early satiety then the treatment should be stopped, and the patient assessed by the specialist clinical team.

8) Treatment interruption for >7days: Patient should contact their specialist care prescriber if treatment was interrupted for more than 7 days and explain the reason why and for how long treatment has been stopped. Potential outcomes might be:
   a. Patient can continue with treatment at home
   b. Patients need to come to day care to receive their next sublingual tablet
   c. Need to discontinue treatment (e.g., issues of compliance or developing contraindications)

For 2, 4, 7 and 8 and any other queries – the nursing team and junior doctors will review these queries and discuss at MDT/with consultant as needed. Issues raised and outcomes will be documented in the patient's notes.

Telephone number for patients: ***Adult Clinical Immunology & Allergy Unit*** **0114** ***2266583, Children Allergy Department 0114 305 3897***

12. Pregnancy, paternal exposure and breast feeding

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It is the responsibility of the specialist to provide advice on the need for contraception to male and female patients on initiation and at each review, but the ongoing responsibility for providing this advice rests with both the primary care prescriber and the specialist.

Pregnancy:

Treatment with Grazax®/Acarizax® should not be initiated during pregnancy. If pregnancy occurs during treatment, the treatment may continue after evaluation of the general condition (including lung function) of the patient and reactions to previous administration of Grazax. In patients with pre-existing asthma close supervision during pregnancy is recommended.
Patients will be risk assessed before starting the treatment:

- If low risk, then they will be offered first appointment. Pregnancy test will be performed. If positive immunotherapy will not be started. If negative, SLIT will be started with advice to report to specialist if become pregnant. We will assess general condition and reactions to previous Grazax®/Acarizax® and advise accordingly.
- If high risk (e.g., pre-existing asthma) then other options of immunotherapy will be offered. If SLIT is best option, then contraception will be recommended, and we will ask GP to start prescribing contraception before treatment is offered.

Breastfeeding:

No clinical data are available for the use of Grazax®/Acarizax® during lactation. No effects on the breastfed infants are anticipated.

Paternal exposure:

No clinical data available

13. Specialist contact information

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Adults

Name: *Dr Shrimpton, Dr Sargur, Dr Arnold, Dr York, and Dr Boules*

Role and specialty: *Immunology & Allergy Consultants*

Daytime telephone number: *Clinical Immunology & Allergy Unit 0114 2269020*

Email address: *sth.ciauadmins@nhs.net*

Alternative contact: *N/A*

Out of hours contact details: *Attend A & E if severe symptoms*

Paediatrics

Names: Drs Minshall, Jay and Sonmez-Ajtai

Role and speciality: Paediatric Allergy Consultants

Daytime telephone number: 0114 305 3897

Email address: claire.hack@nhs.net or Rachel.dimmock@nhs.net

Out of hours contact details: *Attend Paediatric A & E if severe symptoms*

14. Additional information

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Where patient care is transferred from one specialist service or GP practice to another, a new shared care agreement must be completed. Advise patient to inform both GP and specialist of any changes

15. References

1. Canonica GW, Poulsen PB, Vestenbæk U. Cost-effectiveness of GRAZAXs for prevention of grass pollen induced rhinoconjunctivitis in Southern Europe. Respiratory Medicine 2007; 101:1885–1894
2. Germain N, Gerth van Wijk R, Aballéa S, et al. The Burden of Allergic Rhinitis and Impact of GRAZAX®. Grass Allergy Immunotherapy Treatment on Quality of Life in Germany and The Netherlands: Results from a Qualitative Study. J Aller Medications 2019; 5:038
3. Hébert J, Blaiss M, Waserman S, et al. The efficacy and safety of the Timothy grass allergy sublingual immunotherapy tablet in Canadian adults and children. Allergy, Asthma & Clinical Immunology 2014; 10:53
4. Durham S and Penagos M. Sublingual or subcutaneous immunotherapy for allergic rhinitis? J Allergy Clin Immunol 2016; 137:339-49.
5. Nolte H, Maloney J. The global development and clinical efficacy of sublingual tablet immunotherapy for allergic diseases. Allergology International 67(2018):301-308.

6. Demoly P, Emminger W, Rehm D, et al. Effective treatment of house dust mite–induced allergic rhinitis with 2 doses of the SQ HDM SLIT-tablet: Results from a randomized, double-blind, placebo-controlled phase III trial. J Allergy Clin Immunol 2016; 137:444-51.
7. Compalati E, Passalacqua G, Bonini M, et al. The efficacy of sublingual immunotherapy for house dust mites respiratory allergy: results of a GA ^{2}LEN meta-analysis. Allergy 2009: 64: 1570–1579
8. NICE guideline: https://cks.nice.org.uk/topics/allergic-rhinitis/
9. Walker SM, Durham SR, Till SJ, et al. Immunotherapy for allergic rhinitis. Clinical & Experimental Allergy; 41: 1177
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16. Other relevant national guidance

- Shared Care for Medicines Guidance – A Standard Approach (RMOC). Available from https://www.sps.nhs.uk/articles/rmoc-shared-care-guidance/
- NHSE policy – Responsibility for prescribing between primary & secondary/tertiary care. Available from https://www.england.nhs.uk/publication/responsibility-for-prescribing-between-primary-and-secondary-tertiary-care/
- General Medical Council. Good practice in prescribing and managing medicines and devices. Shared care. Available from https://www.gmc-uk.org/ethical-guidance/ethical-guidance-for-doctors/good-practice-in-prescribing-and-managing-medicines-and-devices/shared-care
- NICE NG197: Shared decision making. Last updated June 2021. https://www.nice.org.uk/guidance/ng197/.

17. Local arrangements for referral

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Define the referral procedure from hospital to primary care prescriber & route of return should the patient's condition change.

Patients will be referred from hospital to primary care on the 'secondary to primary care agreement letter' (Appendix 1) and primary care should respond to the request from the specialist for shared care in writing within 14 days. The patient will not be discharged from secondary care until the end of their treatment. Primary care can contact the secondary care specialist using the contact information in section 13.

Appendix 1: Shared Care Request letter (Specialist to Primary Care Prescriber)

Dear *[insert Primary Care Prescriber's name]*

Patient name: *[insert patient's name]*
Date of birth: *[insert date of birth]*
NHS Number*: [insert NHS Number]*
Diagnosis: *[insert diagnosis]*

As per the agreed Sheffield/Barnsley/Rotherham/Doncaster Bassetlaw APC shared care protocol for *Grazax®/Acarizax®* (*delete as appropriate) for the treatment of *Severe Allergic Rhinitis,* this patient is now suitable for prescribing to move to primary care.

The patient fulfils criteria for shared care, and I am therefore requesting your agreement to participate in shared care. Where baseline investigations are set out in the shared care protocol, I have carried these out.

I can confirm that the following has happened with regard to this treatment:

	Specialist to complete
The patient has been initiated on this therapy and has been on an optimised dose for the following period of time:	
Baseline investigation and monitoring as set out in the shared care documents have been completed and were satisfactory	*Yes / No*
The condition being treated has a predictable course of progression and the patient can be suitably maintained by primary care	*Yes / No*
The risks and benefits of treatment have been explained to the patient	*Yes / No*
The roles of the specialist/specialist team/ Primary Care Prescriber / Patient and pharmacist have been explained and agreed	*Yes / No*
The patient has agreed to this shared care arrangement, understands the need for ongoing monitoring, and has agreed to attend all necessary appointments	*Yes / No*
I have enclosed a copy of the shared care protocol which covers this treatment/the SCP can be found here (insert electronic/ web link)	*Yes / No*
I have included with the letter copies of the information the patient has received	*Yes / No*
I have provided the patient with sufficient medication to last until	
I have arranged a follow up with this patient in the following timescale	

Treatment was started on *[insert date started]* and the current dose is *[insert dose and frequency]*.

If you agree, please undertake treatment from *[insert date]* NB: date must be at least 1 month from initiation of treatment.

Please could you reply to this request for shared care and initiation of the suggested medication to either accept or decline within 14 days.

Appendix 2: Shared Care Agreement Letter (Primary Care Prescriber to Specialist)

Primary Care Prescriber Response

Dear *[insert Doctor's name]*

Patient *[insert Patient's name]*

NHS Number *[insert NHS Number]*

Identifier *[insert patient's date of birth and/oraddress]*

Thank you for your request for me to accept prescribing responsibility for this patient under a shared care agreement and to provide the following treatment

Medicine	Route	Dose & frequency

I can confirm that I am willing to take on this responsibility from *[insert date]* and will complete the monitoring as set out in the shared care protocol for this medicine/condition.

Primary Care Prescriber signature: _____ Date: _____

Primary Care Prescriber address/practice stamp:

Appendix 3: Shared Care Refusal Letter (Primary Care Prescriber to Specialist)

Re*:*
Patient *[insert Patient's name]*

NHS Number *[insert NHS Number]*

Identifier *[insert patient's date of birth and/oraddress]*

Thank you for your request for me to accept prescribing responsibility for this patient.

In the interest of patient safety NHS *[insert CCG name]***,** in conjunction with local acute trusts have classified *Grazax®/Acarizax®* (*delete as appropriate) as a Shared Care drug and requires a number of conditions to be met before transfer can be made to primary care.

I regret to inform you that in this instance I am unable to take on responsibility due to the following:

		Tick which applies
1.	**The prescriber does not feel clinically confident in managing this individual patient's condition, and there is a sound clinical basis for refusing to accept shared care** As the patient's primary care prescriber I do not feel clinically confident to manage this patient's condition because *[insert reason]*. I have consulted with other primary care prescribers in my practice who support my decision. This is not an issue which would be resolved through adequate and appropriate training of prescribers within my practice. **I have discussed my decision with the patient and request that prescribing for this individual remain with you as the specialist, due to the sound clinical basis given above.**	
2.	**The medicine or condition does not fall within the criteria defining suitability for inclusion in a shared care arrangement** As the medicine requested to be prescribed is not included on the national list of shared care drugs as identified by RMOC or is not a locally agreed shared care medicine I am unable to accept clinical responsibility for prescribing this medication at this time. **Until this medicine is identified either nationally or locally as requiring shared care the responsibility for providing this patient with their medication remains with you**	
3.	**A minimum duration of supply by the initiating clinician** As the patient has not had the minimum supply of medication to be provided by the initiating specialist, I am unable to take clinical responsibility for prescribing this medication at this time. Therefore, can you please contact the patient as soon as possible in order to provide them with the medication that you have recommended. ***Until the patient has had the appropriate length of supply the responsibility for providing the patient with their medication remains with you.***	
4.	**Initiation and optimisation by the initiating specialist** As the patient has not been optimised on this medication, I am unable to take clinical responsibility for prescribing this medication at this time. Therefore, can you please contact the patient as soon as possible to provide them with the medication that you have recommended.	

	Until the patient is optimised on this medication the responsibility for providing the patient with their medication remains with you.	
5.	**Shared Care Protocol not received** As legal responsibility for clinical care lies with the clinician who signs the prescription, I need to ensure that I am in possession of sufficient clinical information for me to be confident to prescribe this treatment for my patient and it is clear where each of our responsibilities lie to ensure the patient is safely managed***.*** For this reason, I am unable to take clinical responsibility for prescribing this medication at this time, therefore would you please contact the patient as soon as possible to provide them with the medication that you have recommended. ***Until I receive the appropriate SCP, responsibility for providing the patient with their medication remains with you.***	
6.	**Other (Primary Care Prescriber to complete if there are other reasons why shared care cannot be accepted)**	

I would be willing to consider prescribing for this patient once the above criteria have been met for this treatment.

NHS England 'Responsibility for prescribing between Primary & Secondary/Tertiary care' guidance (2018) states that "when decisions are made to transfer clinical and prescribing responsibility for a patient between care settings, it is of the utmost importance that the GP feels clinically competent to prescribe the necessary medicines. It is therefore essential that a transfer involving medicines with which GPs would not normally be familiar should not take place without full local agreement, and the dissemination of sufficient, up-to-date information to individual GPs." In this case we would also see the term GP being interchangeable with the term Primary Care Prescriber.

Please do not hesitate to contact me if you wish to discuss any aspect of my letter in more detail and I hope to receive more information regarding this shared care agreement as soon as possible

Yours sincerely

Primary Care Prescriber signature: _____ Date: _____

Primary Care Prescriber address/practice stamp: