



Proposal Form for a New Drug/Technology or New Use for a Drug/Technology to be Considered by the New Drugs Committee for use in the Belfast HSC Trust

TO BE COMPLETED BY THE REQUESTOR(S)

This form should be completed in full and submitted with references supporting the application to [REDACTED]

The form must be completed by the requestor(s) independently of the pharmaceutical industry.

In order for the drug / technology to be considered for review by the New Drugs Committee, the requestor must have the support and signatures of the Clinical Lead and the Service Group Director for the particular specialty.

Drug/ Preparation/ Technology:

Acarizax 12 SQ-House dust Mite (HDM) oral lyophilisate

Do you consider the drug should become available to:-

- All prescribers
- Names Departments / Specialty
- Consultants only
- Other (please specify)

Reason for request:

Brief summary of perceived advantage(s) over current available therapies and specify criteria for patient selection:

Acarizax is indicated for moderate to severe HDM allergic rhinitis (AR) despite use of symptom relieving medication.

These patients have severe symptoms of AR despite maximal medical therapy. They develop chronic AR, which has a significant impact on QOL and sleep. Poor control of AR can also affect asthma control.

Perceived place of this drug within the present treatment pathway:

The requestor should attach guidance and algorithms, for example from specialty guidelines, showing specifically the perceived place of the drug in the existing treatment pathway and indicate if the drug would represent an addition to, or would replace, existing treatments in the pathway. If guidance does not exist please outline the perceived place in a treatment pathway. Please specify prescribing (primary care, secondary care or if shared care protocol is considered appropriate).

This treatment option is currently not available from the Regional Immunology service (RIS) allergy clinic. It is however, widely used in other specialist allergy centres in UK and Ireland.

The proposed treatment pathway is as follows:

GP referral with symptoms consistent with AR; treatment guidance sheet is issued to GP referrer



For patients with severe perennial AR with confirmed sensitisation (positive allergy test), to HDM who are not responding to maximal medical therapy, we offer an OP appointment to assess suitability for HDM desensitisation.



HDM desensitisation discussed with patient, assessed for suitability



Commencement of first dose in hospital setting.



**RIS contact details given to patients for advice/queries
Ongoing telephone review with specialist allergy nurse to ensure tolerability and for re issue of scripts (3 monthly)**

Declaration of interest:

Has the manufacturer or supplier of the drug / technology provided or is proposing to supply any of the following in relation to support for this application to any physician within the specialty:

- | | |
|--|-----|
| 1. Educational support (in addition to product information)
Pt info leaflet available (attached with application) | Yes |
| 2. Sponsorship to conferences or symposia | No |
| 3. Equipment services or finances | No |
| 4. Have you, or anyone in your specialty, at any time been
involved in any clinical trial involving the proposed drug | No |

If the answer is yes to any of these questions please supply details, where possible, on a separate sheet. Further clarification may be sought to allow full consideration by the New Drugs Committee.

Please SIGN and PRINT name:

Signature of Requestor _____ / Lisa Devlin **Date:** 4th Dec 20

Specialty Clinical Lead: _____ / Lisa Devlin **Date:** 4th Dec 20

Service Group Director: _____ / _____ **Date:** _____



NEW DRUG APPLICATION FORM

<p>Drug Name: (1) Generic Name: House dust Mite (HDM) oral lyophilisate desensitisation</p> <p>(2) Brand Name: Acarizax 12 SQ-House dust Mite (HDM) oral lyophilisate desensitisation</p> <p>(3) Pharmaceutical Co.: ALK-Abello</p>
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1.	<p>Type of Drug</p> <p>Is this a new clinical entity or similar to existing medications? Similar to existing medication. We already offer sublingual (S/L) and subcutaneous (S/C) desensitisation for grass pollen, and subcutaneous desensitisation for tree pollen and venom.</p> <p>If it is a similar medication, what are its advantages over existing therapy? Similar to grazax (S/L) desensitisation. We have considerable experience in the use of grazax which is a well tolerated (with careful patient selection), and efficacious treatment. Acarizax is a similar product for a different allergen (house dust mite as opposed to grass pollen)</p>
2.	<p>Clinical Indications</p> <p>Does the applicant intend to use the new drug for a licensed indication? Acarizax is currently not licensed in the UK but used in many allergy clinics throughout the UK. Licensed in ROI. The Regional Unlicensed medicine application form has been completed. Without access to this medication the Immunology Clinic at BHSCCT are unable to offer patients in Northern Ireland the same treatment as is available in other parts of the UK.</p> <p>NB for drugs without a UK product licence the applicant must complete & submit the Regional Unlicensed Medicines application form with this new drugs application form</p> <p>What are the licensed indications? – As above not currently licensed in UK See SPC for IE: Moderate to severe HDM allergic rhinitis (AR) despite use of Symptom relieving medication.</p>

HDM allergic asthma not well controlled by inhaled corticosteroids and associated mild to severe HDM AR. Note, we would **not** be using it for poorly controlled asthma. We have strict protocols in place to ensure desensitisation therapy is not commenced in patients with poor asthma control.

Are there restrictions on who should initiate treatment or administer the drug?

Yes, Hospital administration for the first dose. Our allergy nurses are trained to commence 1st dose immunotherapy as per SOP
Consultant prescription (Immunology)

If yes, what are these restrictions? As above

3. Efficacy

Please provide copies of key papers relating to clinical efficacy and tolerability:

I have attached the SPC (IE) for the efficacy data presented in the MERIT (RCT) Trial (for AR), and the MITRA Trial for Allergic asthma.
A summary of the findings is presented below:

Allergic rhino conjunctivitis; Merit Trial

992 adults with house dust mite (HDM) allergic rhino conjunctivitis (AR) randomised to approximately 1 year of daily treatment with 12 SQ-HDM, 6 SQ-HDM or placebo and were given free access to standardised rhinitis pharmacotherapy. The 12 SQ-HDM group showed a significant reduction in

- rhinitis symptoms score
- and
- medication use.
- and
- rhino conjunctivitis QOL questionnaire score

Post hoc analysis showed a significant reduction in

- the probability of having a day with a rhinitis exacerbation
- and
- the probability of having a day with a rhinitis exacerbation despite use of rhinitis pharmacotherapy

Also; see supportive evidence in AR in relation to allergen challenge post immunotherapy/placebo group with a statistically significant difference in the mean rhinitis symptoms score in the immunotherapy group

Allergic asthma; The MITRA trial

834 adults with house dust mite allergic asthma not well-controlled by daily use of inhaled corticosteroid (ICS). All subjects randomised to 7-12 months' treatment with 12 SQ-HDM, 6 SQ-HDM or placebo in addition to ICS and short-acting beta-agonist prior to ICS reduction.

The 12 SQ-HDM treatment group showed a significant reduction in asthma exacerbations

Post hoc analysis showed statistically significant difference for the asthma daytime symptoms score in favour of 12 SQ-HDM e symptom score and the odds for no nocturnal awakenings.

see supportive evidence for allergic asthma in a phase II trial which showed a significant reduction in inhaled corticosteroid use in patients being treated with 6 SQ-HDM compared to placebo

See also attached:

J ALLERGY CLIN IMMUNOL 2016;138:1631-1638. RCT 1482 subjects (aged >12 years) with HDM-induced AR with or without asthma were randomized to a daily SQ HDM SLIT-tablet (12 SQ-HDM dose) or placebo for up to approximately 52 weeks. Treatment resulted in a reduction in combined rhinitis symptom score. The product was well tolerated.

See RCT Allergy 2018 73(12) 2352-2363 RCT showed efficacy and safety of HDM desensitisation in Japanese children.

See also commentary in Vitiello et al. Clin Mol Allergy (2020) 18:10 (paper attached)

See summary of evidence presented in Expert Review of Clinical immunology 2016; 12 (4): 369–377 (paper attached)

4. Safety

Provide evidence of safety data especially in comparison to similar therapies

See attached section 4.8 SPC (IE) for contraindications and safety data.

Localised reactions of the oral mucosa are very common at initiation of sublingual immunotherapy. These usually subside with ongoing treatment and can be managed with concurrent administration of antihistamine. More severe/systemic reactions are rare, and mitigated by patient selection (i.e. poorly controlled asthma would be a contraindication to commencement of therapy). In addition, the first dose is always administered in conditions where there is appropriate supervision and facilities for resuscitation.

	<p>The trials listed above also provide evidence of safety/tolerability.</p> <p>The safety data listed compares well to the use of another desensitisation therapy 'Grazax' (grass pollen desensitisation).</p>
	<p>Are there any clinically important drug interactions (if yes please specify)?</p> <p>None known</p>
	<p>Are there any specific monitoring requirements (if yes please specify)</p> <p>Nurse led telephone review for tolerability and efficacy. No specific monitoring required.</p>

5.	Current Clinical Use:
	How many patients have received this drug to date, in the UK/Worldwide? >200000

6.	<p>Future Projected Clinical Use</p> <p>How many patients are likely to receive the drug in the Trust?</p> <p>over the next year 30</p> <p>next five years 100</p>
7.	<p>Contraindications</p> <p>Are there particular groups of patients for whom this drug is contraindicated or should be used with caution?</p> <p>Hypersensitivity to any of the excipients (for a full list of excipients, see section 6.1). Patients with FEV1 < 70% of predicted value (after adequate pharmacological treatment) at initiation of treatment.</p> <ul style="list-style-type: none"> • Patients who have experienced a severe asthma exacerbation within the last 3 months. In patients with asthma and experiencing an acute respiratory tract infection, initiation of ACARIZAX treatment should be postponed until the infection has resolved. • Patients with active or poorly controlled autoimmune diseases, immune defects, immunodeficiencies, immunosuppression or malignant neoplastic diseases with current disease relevance. • Patients with acute severe oral inflammation or oral wounds
8.	<p>Clinical Use</p> <p>What are the advantages of this drug over current therapy?</p> <p>This is an add on therapy (initially) to antihistamines and nasal corticosteroids.</p> <p>As the desensitisation therapy becomes efficacious, the use of antihistamines and nasal corticosteroids can be weaned.</p> <p>Would this drug replace any existing preparation?</p> <p>CATEGORISE NEW PRODUCT – please circle category:</p> <p>(a) New product – this is an additional product to current treatments and there will no reduction of activity in any other drug product</p> <p>(b) New Product – this will replace an existing product partially (provide details)</p> <p>As the desensitisation therapy becomes efficacious, the use of antihistamines and nasal corticosteroids can be weaned.</p> <p>(c) New Product – this will replace an existing product fully (provide details)</p>

9. **Cost Effectiveness**

Provide evidence that this drug is more cost effective than existing treatment

ACTIVITY and COST WITHIN SECONDARY CARE

Please state estimated number of units per year in BHSCT for the new product
Activity Year 1: 30 patients **Activity Year 2:** 60 patients **Activity Year 3:** 80 patients
Price per unit [REDACTED]
Cost Year 1 [REDACTED] **Cost Year 2** £59,040 **Cost Year 3** [REDACTED]

Please state estimated number of units per year in BHSCT for the existing product assuming it will continue to be used as in categorisation above (section 8) – **AS ABOVE** – NO ADDITIONAL COST TO BHSCT AS ANTIHISTAMINES & NASAL CORTICOSTEROID ARE SUPPLIED THROUGH PRIMARY CARE.

Activity Year 1 _____ **Activity Year 2** _____ **Activity Year 3** _____
Price per unit £ _____
Cost Year 1 _____ **Cost Year 2** _____ **Cost Year 3** _____

DIRECTORATE BREAKDOWN OF TOTAL COSTS

AS Year 1 _____ **AS Year 2** _____ **AS Year 3** _____ (Acute Services)

C&SS Year [REDACTED] **&SS Year** [REDACTED] **C&SS Year 3** [REDACTED]
(Cancer & Specialist Services)

SHWH Year 1 _____ **SHWH Year 2** _____ **SHWH Year 3** _____
(Specialist Hospitals & Women's Health)

ASPC Year 1 _____ **ASPC Year 2** _____ **ASPC Year 3** _____
(Adult Social & Primary Care Services)

ACTIVITY and COST WITHIN PRIMARY CARE

Is the product on drug tariff No
Please state estimated number of units per year in Primary Care for the new product as a consequence of use in BHSCT: **Supplied through BHSCT**

Activity Year 1 _____ **Activity Year 2** _____ **Activity Year 3** _____
Price per unit in primary care £ _____

Source of pricing information for new product in primary care

Cost Year 1 _____ **Cost Year 2** _____ **Cost Year 3** _____

Please state estimated number of units per year in Primary Care for the existing product as a consequence of use of the new product in BHSCT, assuming it will continue to be used as per categorisation above (section 8): **Unchanged or reduced depending on what the patient is currently receiving.**

Activity Year 1 _____ **Activity Year 2** _____ **Activity Year 3** _____
Price per unit in primary care £ _____

Cost Year 1 _____ **Cost Year 2** _____ **Cost Year 3** _____

Has this drug been appraised or is due to be appraised by NICE?

No

What was the recommendation?

Has this drug been reviewed or is due to be reviewed by SMC?

No

What was the recommendation?

Has this drug been reviewed or is due to be reviewed by AWMSG?

No

What was the recommendation?

What impact would this drug have on the prescribing budget?

See pharmacy costing

Are there any service implications (e.g. would a Local Enhanced Service be required? etc). Is there a Patient Access Scheme (PAS)? If so explain how costs / resource implications have been considered / addressed.

No, this therapy can be administered as part of our current activities.

Successful desensitisation will allow for patient discharge.

To be completed by Service Group Director and Requestor/Specialist Group Lead Clinician

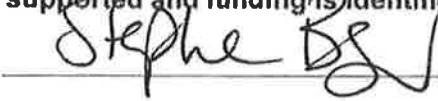
Please SIGN and PRINT name:

I CONFIRM THIS APPLICATION HAS BEEN COMPLETED INDEPENDENTLY OF PHARMACEUTICAL INDUSTRY AND HAS THE SUPPORT OF MAJORITY OF CLINICIANS IN THE SPECIALTY. I UNDERSTAND THAT I WILL BE REQUIRED TO SUBMIT 6 MONTHLY AUDIT DATA TO NDC TO DEMONSTRATE USAGE OF THE DRUG IS COMPLIANT WITH NDC CONDITIONS OF APPROVAL:

Signature of Requestor:  / **SIGN** **PRINT** Lisa Devlin Date: 4/12/20

Specialty Clinical Lead: Lisa Devlin _____ /4th Dec 20

I confirm this application is supported and funding is identified by the Service Group:

Service Group Director:  Date: 29/12/20

APPROVAL DECISION

Name of Medicine	
Requesting Consultant/ Specialty Group	

Following a meeting of the New Drugs Committee on

The following recommendation was made:

- Approved as per submission
- Approved with the following restriction(s):

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- Approval denied due to insufficient evidence/poor safety profile
- Approval denied due to lack of robust economic case
- Approval deferred, request referred back for further information.

Appendix 3 Proposal for New Unlicensed Medicine Form Page 1 of 2

This form is to be used in conjunction with the Trust Policy for Unlicensed Medicines. Before completing this form, you must have read the Trust Unlicensed Medicines Policy which identifies your responsibilities under the policy.

Requester details			
Consultant name:	Dr Lisa Devlin	Hospital site:	Royal Victoria Hospital/
Speciality:	Immunology	Ward/dept:	Immunology Day Centre
Contact details:	<small>lisa.devlin@hcahasth.nhs.uk</small>	Date requested:	4th December 2020
Patient details			
Anticipated usage (please tick)		Apply addressograph if individual patient request	
Single patient/one-off	<input type="checkbox"/>	For your patients only	<input type="checkbox"/>
Fewer than 6 patients per year	<input type="checkbox"/>	For patients within your speciality on a single site	<input type="checkbox"/>
If more than 6 patients per year, please provide estimated numbers	<input type="checkbox"/>	For patients within your speciality on all sites	<input checked="" type="checkbox"/>
<small>We have approximately 30 patients who require HDM desensitisation. Therefore our numbers will be higher than in the first year than subsequent years</small>		Any patient within the Trust	<input checked="" type="checkbox"/>
Unlicensed Medicine Details			
Product name: (International Non Proprietary Name)		Acarizax 12 SQ-House dust Mite (HDM) oral lyophilisate	
Proprietary Name (if known):			
Strength and Pharmaceutical Form:		12SQ-HDM oral lyophilisate	
Manufacturer (if known):		[REDACTED]	
Indication:		<small>Moderate to severe HDM allergic rhinitis (AR) despite use of symptom relieving medication. HDM allergic asthma not well controlled by inhaled corticosteroids and associated mild to severe HDM AR</small>	
Dose / frequency / route:		Acarizax 12 SQ-HDM oral lyophilisate 1 sublingual tab daily for 3 years	
Duration of Treatment:		3 years	
Why is an unlicensed medicine being considered? (Tick as appropriate)			
There is no UK licensed product available to treat or diagnose medical condition. <input checked="" type="checkbox"/>			
The UK licensed product used to treat or diagnose the medical condition is temporarily unavailable <input type="checkbox"/>			
The UK licensed product used to treat or diagnose the medical condition is unsuitable <input type="checkbox"/>			
No therapeutically equivalent UK licensed product available or suitable (provide details): <input type="checkbox"/>			
Patient Safety: <input type="checkbox"/>			
Other (provide details): <input type="checkbox"/>			
<small>This is a widely used product throughout specialist allergy centres in the UK and Ireland. By not offering this treatment, we are not in keeping with a standard of care provided by other allergy centres.</small>			
Was a product licence in the UK withdrawn?			Yes / No / Not known
If yes, contact manufacturer to find out reasons for withdrawal.			

Clinical Evidence	
Is there any evidence to support its use for the proposed indication?	Yes / No
Is there evidence to support its proposed administration schedule? (dose, duration, concentration for parenteral products and route)	Yes / No
Is the active drug currently in a licensed product for use via the same route of administration e.g. tablet, suspension?	Yes / No
Is the product licensed for the specified indication in another EU member state?	Yes / No / Not known
UK product licence applied for?	Yes / No / Not known
If yes, record date of application for licence:	
Are other Trusts using this medicine?	Yes / No / Not known
If so, name:	
Summarise below the supporting evidence, list references and attach copies of references where available.	
Attached is the SPC (IE) which outlines the Clinical efficacy trials. I have also attached a summary to this document	
What are the risks to the patient of not using this drug? Chronic rhinoconjunctivitis with impaired quality of life and impaired sleep quality	
What side effects <u>and</u> significant interactions have been reported? Is any monitoring required? Describe: <small>localised symptoms, itching, tingling, swelling of the oropharynx are relatively common especially in the first few weeks of treatment. Systemic reactions including anaphylaxis is a recognised risk, but in our experience with other sublingual desensitisation, is very rare in our carefully selected patients (i.e. we would not commence therapy in patients with poorly controlled asthma). Dyspepsia, abdominal discomfort, rhinosinusitis, fatigue, oral ulceration have been reported (see attached SPC). No interactions. 1st dose given in the hospital setting. periodic telephone review will be undertaken by our allergy nurse.</small>	
Give details of contraindications and any other risks to the patient. Include precautions in use. hypersensitivity to any of the excipients, poorly controlled asthma, current infection, active/poorly controlled autoimmune disease, immune defects, immunodeficiencies, immunosuppression, or malignant neoplastic disease. Severe oral breakdown.	
Will there be any primary care implications? (e.g. need for a shared care protocol) If so, describe: No monitoring by primary care is required. Patients will receive regular telephone review by our allergy nurse. Our contact details will be provided	

Prescriber (Consultant or SpR – Circle one)			
Print name:	Dr Lisa Devlin/Dr Tanya Coulter	Speciality/ Directorate:	Immunology
Signature:		Date:	4th December 2020
If SpR, state name of patient's consultant:			

Forward completed form to Pharmacy Quality Assurance pharmacist or Pharmacy Services Manager

Authorisation of Application (pharmacy)		
Name	Position	Signature & Date

Documents for Drugs & Therapeutics (D&T) Committee	<i>Tick</i>
Proposal for New Unlicensed Medicine Form	
Unlicensed Medicine Evaluation (UME) Form	
Risk Assessment form for an Unlicensed Medicine (Quality Assurance)	

Outcome of D&T Evaluation	
Approval for use	Yes / No
If no, give reasons	
State restrictions on prescribing / use	
Signature of Chair of D&T:	Date: