

National Institute for Health and Clinical Excellence

Multiple Technology Appraisal (MTA)

Pharmalgen for the treatment of venom allergy

Response to consultee and commentator comments on the draft remit and draft scope (pre-referral)

Section 1: the draft remit

Section	Consultees	Comments	Action
Appropriateness	British Society for Allergy & Clinical Immunology; Royal College of Physicians & Royal College of Pathologists	yes	Comment noted. No action required.
	British Society of Allergy and Clinical Immunology and Joint Committee of Allergy and Immunology	Yes	Comment noted. No action required.
	Royal College of Paediatrics and child health	Yes, appropriate	Comment noted. No action required.

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	ALK Abelló Ltd	Pharmalgen is a specialist product used in 44 specialist centres in the UK. It's value is in a few high risk individuals with severe venom allergy and other risk factors e.g. Bee keepers. Due to the highly specialised nature of Pharmalgen it may be considered an inappropriate topic for NICE to appraise as it has little bearing on the health of the general population	The extent to which this topic proceeds to the appraisal stage will ultimately depend on whether it receives formal referral from the Department of Health. Ministers' final decisions on referral are based on the advice they receive from NICE on the technical suitability of a topic following the consultation on the remit and scope.
Wording	The Anaphylaxis Campaign	In the 1 st sentence we would suggest that the term "chemicals" instead of "allergens". Our understanding is that the term "allergens" is normally only used if an immune response is triggered. The typically produced symptoms that are present when most people (i.e. not those who are allergic to venom) get stung (2 intense burning pain followed by erythema) are not normally allergic responses so the term "allergen" seems an odd word to use in this context.	The scope has been amended accordingly.
	Royal College of Paediatrics and child health	Yes	Comment noted. No action required.

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Timing Issues	British Society for Allergy & Clinical Immunology; Royal College of Physicians & Royal College of Pathologists	urgent need to provide advice	Comment noted.
	British Society of Allergy and Clinical Immunology and Joint Committee of Allergy and Immunology	There is an urgent need for NICE guidance on Hymenoptera (bee and wasp) immunotherapy	Comment noted.
	Royal College of Paediatrics and child health	Timely, in view of the House of Commons and House of Lords reports on allergy.	Comment noted.
	ALK Abelló Ltd	Pharmalgen has been available in the UK since 1982. It's use is completely stable with around 900 patients treated per year (UK Sales figures) The implication of this is a stable and relatively low budget impact. On this basis, it is our assessment, that the urgency is low.	Comment noted.
Additional comments on the draft remit	British Society of Allergy and Clinical Immunology and Joint Committee of Allergy and Immunology	Total duration of therapy is usually 3 years but in patients with elevated baseline tryptase (and mastocytosis) and a small proportion of patients who have experienced generalised allergic sting reactions despite undergiving desensitisation, treatment may be prolonged for 5 or more years.	The scope has been amended accordingly.

Section 2: the draft scope

Section	Consultees	Comments	Action
Background information	British Society for Allergy & Clinical Immunology; Royal College of Physicians & Royal College of Pathologists	<p>Incidence: the prevalence of systemic reactions to bee or wasp stings is not accurately known, but data from published series in various European countries suggest an estimate of 2%. About half of these are severe or moderately severe.</p> <p>Nothing on the impact on patients who have experienced an anaphylactic reaction. This is frightening; not always well treated acutely; and substantially affects quality of life.</p> <p>Number of deaths are thought to be higher than those reported on death certificates.</p>	<p>Comments noted.</p> <p>The scope has been amended to include text regarding patients' anxiety related to the possibility of future allergic reactions. 'Anxiety related to possibility of future allergic reactions' has also been added as an outcome measure.</p>
	Royal College of Paediatrics and child health	<p>The College notes that anaphylaxis may occur up to one hour after bee or wasp sting.</p> <p>There is a misspelling in 'adrenalin auto-injectors'.</p> <p>We would like clarification on "Bee and wasp venoms (Pharmalgen, ALK-Abello) involve...", as the meaning is not clear.</p>	<p>The scope has been amended accordingly.</p> <p>The scope has been amended accordingly.</p> <p>The text in parentheses refers to the product name (Pharmalgen) and its manufacturer (ALK-Abelló).</p>
	ALK Abelló Ltd	<p>It is difficult to obtain a reliable estimate of the prevalence of anaphylaxis to venom. Estimates of the prevalence of systemic reactions and anaphylaxis in the literature vary widely. (Bilo & Bonifazi. Clin Exp All 2009; 39: 1467-76)</p>	<p>Comment noted.</p>

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The technology/ Intervention	British Society for Allergy & Clinical Immunology; Royal College of Physicians & Royal College of Pathologists	duration is 3 years (not 'up to...')	The scope has been amended accordingly.
	Royal College of Paediatrics and child health	The College notes that the initial phase of treatment is usually referred to as 'updosing'.	The scope has been amended accordingly.
	ALK Abelló Ltd	Maintenance phase lasts 3 to 5 years. The rest of the information is accurate.	The scope has been amended accordingly.
Population	British Society for Allergy & Clinical Immunology; Royal College of Physicians & Royal College of Pathologists	Subgroups where more effective or cost effective: those with severe systemic reactions; those with a raised baseline tryptase - both are risk factors for further reactions to subsequent stings. Beekeepers are at increased risk of re sting. Other occupational risk of re-sting. Venom Immunotherapy is also indicated in moderately severe allergic reactions to stings, as well as anaphylaxis.	The scope now specifies that if the evidence allows, the economic analysis will take account of differences in people's risk of future stings and of severe allergic reactions to subsequent stings. The population has been reworded to additionally include those with a history of mild and moderate allergic reactions.

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	British Society of Allergy and Clinical Immunology and Joint Committee of Allergy and Immunology	Venom immunotherapy should also be considered in patients with history of moderate systemic reaction/s especially where there is a high risk of future stings, e.g. bee keeping or occupational exposure or other factors, e.g. remoteness from medical help, co-morbid conditions predisposing to cardio-respiratory compromise during to allergic reaction and patient preference.	The population has been reworded to additionally include those with a history of mild and moderate allergic reactions. The scope now specifies that if the evidence allows, the economic analysis will take account of differences in people's risk of future stings.
	Royal College of Paediatrics and child health	The College believes that children should be considered separately. The prolonged benefit of immunotherapy in children is greater than that seen in adults and may persist for 20 years after stopping treatment. Children have a lower rate of relapse after stopping immunotherapy than adults.	The scope has been amended to make clear that, if the evidence allows, children will be considered separately.
	ALK Abelló Ltd	Anaphylaxis with demonstrated venom specific IgE	The population has been amended accordingly.
Comparators	British Society for Allergy & Clinical Immunology; Royal College of Physicians & Royal College of Pathologists	there is no equivalent treatment to prevent subsequent allergic reactions. Alternative for moderate to severe allergic reactions is to provide the patient with adrenaline injector for self-injection. Mild systemic reactions may be treated with early high dose antihistamines	The comparators have been amended to include a package of care in the absence of venom immunotherapy (including, advice on avoidance of bee and wasp venom, high-dose antihistamines, and adrenaline auto-injector prescription and training).

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	Royal College of Paediatrics and child health	<p>The comparator of 'no immunotherapy' needs to include the social and economic costs of carrying injectable adrenaline around at all times for the rest of the patient's life.</p> <p>The comparator should not be 'no treatment', but a package of care that includes information on ruling out co-morbidities (e.g. immune disease, ischemic heart disease, hypertension, diabetes, history of stroke, MI), insect venom avoidance and adrenaline injector prescription and training. In the real world we need a comparator that is a complete allergy clinic package of care. The reviewers may need to include small data sets on patients with co morbidities and those aged over 65.</p>	<p>The comparators have been amended to include a package of care in the absence of venom immunotherapy (including, advice on avoidance of bee and wasp venom, high-dose antihistamines, and adrenaline auto-injector prescription and training).</p> <p>The NICE Guide to methods of technology appraisal (section 5.2.7) states that costs borne by patients and their carers that are not reimbursed by the NHS or PSS are not included in the reference case.</p>
Outcomes	<p>British Society for Allergy & Clinical Immunology; Royal College of Physicians & Royal College of Pathologists</p> <p>Royal College of Paediatrics and child health</p>	<p>Emphasis should be on incidence of systemic, rather than local, reactions yes - for other measures</p> <p>Yes. However, the College believes it would be helpful to add the effect of Pharmedgen on the anxiety related to wasp and bee venom anaphylaxis. The proposed QOL score would not measure the consequences of anaphylaxis-related anxiety in respect of activity limitation and environmental limitation. The College suggests adding a scoring system relating to anaphylaxis-related anxiety.</p>	<p>The scope has been amended accordingly.</p> <p>'Anxiety related to possibility of future allergic reactions' has been added as an outcome measure.</p>

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Economic analysis	British Society for Allergy & Clinical Immunology; Royal College of Physicians & Royal College of Pathologists	An interval of several years between stings is common	Comment noted.
	Royal College of Paediatrics and child health	Appropriate	Comment noted. No action required.
	ALK Abelló Ltd	The appropriate time horizon is the remainder of the patients life.	Comment noted.
Equality and Diversity	ALK Abelló Ltd	Use is limited to 44 highly specialized centres with experience in venom immunotherapy	Comment noted. This is not considered to define any group currently protected by the equalities legislation.
Other considerations	British Society of Allergy and Clinical Immunology and Joint Committee of Allergy and Immunology	A more prolonged course of desensitisation in a small proportion of patients as stated above, see comment-1.	The scope has been amended accordingly.

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Questions for consultation	British Society for Allergy & Clinical Immunology; Royal College of Physicians & Royal College of Pathologists	<p>What do you consider to be the relevant clinical outcomes and other potential health related benefits of the technology [X] in the treatment of [Y], particularly when compared with currently used treatment options?</p> <ul style="list-style-type: none"> • reduced mortality due to stings • reduced systemic allergic reactions (both number and severity) to stings • improved quality of life • long term benefit after completion of 3 years venom immunotherapy <p>Please identify the nature of the data, which you understand to be available to enable the Appraisal Committee to take account of these benefits.</p> <p>References included but not reproduced</p>	<p>Comments noted.</p> <p>“Number and severity of type 1 IgE-mediated, systemic allergic reactions” and “anxiety related to possibility of future allergic reactions” have been added to the list of outcome measures.</p>
	British Society of Allergy and Clinical Immunology and Joint Committee of Allergy and Immunology	<p>What do you consider to be the relevant clinical outcomes and other potential health related benefits of the technology [X] in the treatment of [Y], particularly when compared with currently used treatment options?</p> <ul style="list-style-type: none"> • 1. reduction in mortality due to hymenoptera stings 2. reduction in incidence of systemic reactions to hymenoptera stings 3. Improvement in quality of life 4. Long term efficacy <p>Please identify the nature of the data, which you understand to be available to enable the Appraisal Committee to take account of these benefits.</p> <p>References included but not reproduced</p>	<p>Comments noted.</p> <p>“Number and severity of type 1 IgE-mediated, systemic allergic reactions” and “anxiety related to possibility of future allergic reactions” have been added to the list of outcome measures.</p>

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	Royal College of Paediatrics and child health	<p>What do you consider to be the relevant clinical outcomes and other potential health related benefits of the technology [X] in the treatment of [Y], particularly when compared with currently used treatment options?</p> <ul style="list-style-type: none"> The College considers these to be improved quality of life and less anxiety in relation to outdoor play / activity. <p>Please identify the nature of the data, which you understand to be available to enable the Appraisal Committee to take account of these benefits.</p> <ul style="list-style-type: none"> The College identifies the nature of the available data to be quality of life studies, particularly in relation to having to carry an adrenaline autoinjector around at all times. 	<p>Comments noted.</p> <p>“Number and severity of type 1 IgE-mediated, systemic allergic reactions” and “anxiety related to possibility of future allergic reactions” have been added to the list of outcome measures.</p>
Additional comments on the draft scope.		No comments received.	

The following consultees/commentators indicated that they had no comments on the draft remit and/or the draft scope:

Department of Health
National Public Health Service for Wales (now Public Health Wales NHS Trust)
RICE - Research Institute for Care of Older People
Royal College of Nursing
Royal College of Pathologists
Welsh Assembly Government
Medicines and Healthcare products regulatory agency (MHRA)