

National Institute for Health and Care Excellence

Health Technology Evaluation

Betula verrucosa (Itulazax 12 SQ-Bet) for treating moderate to severe allergic rhinitis, conjunctivitis, or both, caused by tree pollen in people 5 to 17 years [ID6537]**Response to stakeholder organisation comments on the draft remit and draft scope**

Please note: Comments received in the course of consultations carried out by NICE are published in the interests of openness and transparency, and to promote understanding of how recommendations are developed. The comments are published as a record of the submissions that NICE has received, and are not endorsed by NICE, its officers or advisory committees.

Comment 1: the draft remit and proposed process

Section	Stakeholder	Comments [sic]	Action
Appropriateness of an evaluation and proposed evaluation route	ALK Abello (Company)	The company agrees that NICE should consider this topic for appraisal. The single technology appraisal route is the most appropriate route for ITULAZAX®.	Comments noted. No action needed.
	Neonatal and Paediatric Pharmacy Group (NPPG)	Supportive of a TA on this topic. Technology has been on some formularies for the same indication and age group for many years.	Comments noted. No action needed.
Wording	ALK Abello (Company)	The wording of the remit is accurate, and the company suggests no further changes.	Comment noted. No action needed.
Timing issues	ALK Abello (Company)	Despite appropriate administration and compliance with existing treatments, a subset of moderate-to-severe allergic rhinitis (AR) and/or conjunctivitis patients have uncontrolled disease and as such their treatment satisfaction is low (1). Currently, there are no oral allergy immunotherapies (AITs) licensed	Comments noted. NICE has scheduled this topic into its work programme. For further

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		<p>for 5- to 17-year-olds with tree pollen allergy in the UK, with current disease-modifying treatments limited to subcutaneous immunotherapy and unlicensed treatments, leaving treatment with antihistamines and avoidance practices as the main treatment strategies for birch pollen-induced AR.</p> <p>ITULAZAX® is an AIT in the form of a sublingual immunotherapy (SLIT) lyophilisate tablet, providing an alternative treatment option for patients with moderate-to-severe AR and/or conjunctivitis induced by pollen from the birch homologous group whose symptoms are inadequately controlled despite compliant use of existing treatments (2, 3). With a lack of treatment options available for this population, AIT offers a novel and innovative treatment option, being the only treatment available to target the underlying mechanisms of the disease, and change its course, inducing immune tolerance, and preventing disease progression (4, 5). It is, therefore, of high importance that NICE consider this intervention for approval for the paediatric population.</p> <p>Early treatment of AR improves long term outcomes for patients particularly preventing asthma development. In a 2024 study, Hamelmann, et al. (6), used a Markov model to quantify the long-term benefits of early initiation of SLIT in childhood for the treatment of AR. They found that over a 20-year period, 24% of children who began SLIT at age 7 and 29% at age 12 developed allergic asthma (AA), whereas only 19% developed AA when treatment was initiated at age 5. This analysis demonstrates the importance of wider access to SLIT for paediatric patients to improve their long-term outcomes.</p> <p>Clinical experts in an advisory board conducted in September 2025 have highlighted several important considerations in terms of early intervention in the treatment of moderate-to-severe AR. Without early treatment, children can develop issues such as facial development problems and speech difficulties due to chronic nasal obstruction. Furthermore, the impact of</p>	<p>details, see the NICE website: https://www.nice.org.uk/guidance/indevelopment/gid-ta11636. No action needed.</p>

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		<p>symptoms on sleep can result in impaired growth in children, as well as impaired performance at school. Early management of the disease can also improve quality of life not just for the child, but for the whole family and caregivers who may be impacted by the child's symptoms (7).</p> <p>References</p> <ol style="list-style-type: none"> 1. Data on file: modified Delphi advisory panel. Hørsholm, Denmark: ALK-Abelló A/S Ltd; 2023. 2. Akdis CA, Barlan IB, Bahceciler N, Akdis M. Immunological mechanisms of sublingual immunotherapy. <i>Allergy</i> 2006;61:11-4. 3. Bousquet J, Khaltaev N, Cruz AA, Denburg J, Fokkens WJ, Togias A, et al. Allergic Rhinitis and its Impact on Asthma (ARIA) 2008 update (in collaboration with the World Health Organization, GA(2)LEN and AllerGen). <i>Allergy</i>. 2008;63 Suppl 86:8-160. 4. Jutel M, Agache I, Bonini S, others. International consensus on allergy immunotherapy. <i>J Allergy Clin Immunol</i>. 2015;136(3):556-68. 5. Bonertz A, Roberts GC, Hoefnagel M, others. Challenges in the implementation of EAACI guidelines on allergen immunotherapy: a global perspective on the regulation of allergen products. <i>Allergy</i>. 2018;73(1):64-76. 6. Hamelmann E, Hammerby E, Scharling KS, Pedersen M, Okkels A, Schmitt J. Quantifying the benefits of early sublingual allergen immunotherapy tablet initiation in children. <i>Allergy</i>. 2024;79(4):1018-27. 7. Data on file: Scottish Allergic Rhinitis Meeting Report_2025.09.19. Hørsholm, Denmark: ALK-Abelló A/S Ltd; 2025. 	
Additional comments on the draft remit	ALK Abello (Company)	No further comments	Comment noted. No action needed.

Comment 2: the draft scope

Section	Consultee/ Commentator	Comments [sic]	Action
Background information	ALK Abello (Company)	The background is defined appropriately.	Comment noted. No action needed.
Population	ALK Abello (Company)	The population is defined appropriately.	Comment noted. No action needed.
Subgroups	ALK Abello (Company)	There are no subgroups that should be considered separately.	Comment noted. No action needed.
Comparators	ALK Abello (Company)	<p>The comparator for this appraisal should be established clinical management without ITULAZAX 12 SQ-Bet SLIT, which consists of symptomatic pharmacotherapy. Pollinex Quattro Birch is not considered part of established clinical management (8), and the treatment is used very infrequently in clinical practice, as was the consensus from clinicians during the scoping stage of the completed ITULAZAX 12 SQ-Bet SLIT adult appraisal (TA1087). Additionally, Pollinex has recently failed to meet its primary endpoint in Phase 3 trials, likely further restricting its use in clinical practice (9).</p> <p>References</p> <p>8. National Institute for Health and Care Excellence. NICE health technology evaluations: the manual. 31 January 2022 [updated 14 July 2025]. Available from: https://www.nice.org.uk/process/pmg36/resources/nice-health-technology-evaluations-the-manual-pdf-72286779244741.</p> <p>9. Phase III failure for Pollinex Quattro Birch puts Allergy Therapeutics in a precarious position for long-awaited US expansion [press release]. GlobalData, 19 March 2019.</p>	Comments noted. The scope has been updated, removing “such as Pollinex Trees”.
Outcomes	ALK Abello (Company)	The outcomes are defined appropriately.	Comment noted. No action needed.

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Equality	ALK Abello (Company)	<p>Tree pollen allergy affects children from lower socioeconomic groups disproportionately because of frequently increased exposure to environmental pollutants, resulting in an increased risk of AR and AA coupled with inability to implement avoidance measures, such as home air filtration (10, 11). In addition, their parents may have less ability to take time off work to travel to appointments in secondary care, resulting in suboptimal management of the condition.</p> <p>Furthermore, the symptoms of the condition impact school performance and, thus, future employment prospects for children who are already disadvantaged.</p> <p>We believe that SLIT offers a treatment option that will address these issues by allowing patients to be managed closer to home (potential for repeat prescriptions in primary care following initiation by a specialist) and provide long-term disease modification, reducing patient symptoms and improving QoL.</p> <p>References</p> <p>10. Wallbanks S, Griffiths B, Thomas M, Price OJ, Sylvester KP. Impact of environmental air pollution on respiratory health and function. <i>Physiol Rep</i>. 2024;12(16):e70006.</p> <p>11. Bergmann KC, Berger M, Klimek L, Pfaar O, Werchan B, Werchan M, et al. Nonpharmacological measures to prevent allergic symptoms in pollen allergy: a critical review. <i>Allergol Select</i>. 2021;5:349-60.</p>	Comments noted. In line with other evaluations in allergic rhinitis and conjunctivitis, these equality issues will be considered by the committee during the evaluation. No action needed.
Other considerations	ALK Abello (Company)	The company believes no other issues need to be considered.	Comment noted. No action needed.
	Neonatal and Paediatric	Current model noted in one centre is to supply all doses via specialist allergy team, with some patients supplied via Homecare.	Comments noted. No action needed.

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	Pharmacy Group (NPPG)	However, no strong objections to patients being managed in primary care following initiation at a specialist centre. Medication is relatively well tolerated and dosing is simple.	
Questions for consultation	ALK Abello (Company)	<p>Where do you consider itulazax 12 SQ-Bet SLIT will fit into the existing care pathway for moderate-to-severe allergic rhinitis, conjunctivitis, or rhinoconjunctivitis?</p> <p>ITULAZAX® is expected to be used as an add-on therapy to established clinical management.</p> <p>ITULAZAX® is indicated in adults and children (5 years or older) for the treatment of moderate-to-severe allergic rhinitis and/or conjunctivitis induced by pollen from the birch homologous group. Eligible patients are required to have a positive test of sensitisation to a member of the birch homologous group (skin prick test and/or specific IgE).</p> <p>AR patients are typically treated in UK clinical practice with a range of symptomatic therapies, in line with NICE guidelines in primary care and BSACI and ARIA guidelines in secondary care (12-14). The overall treatment pathway for AR in the UK is based on the BSACI rhinitis treatment algorithm (12). Notably, the BSACI guidelines recommend allergy immunotherapy (AIT) for the treatment of AR in patients with a seasonal allergy to pollen whose symptoms persist despite maximal drug therapy, combinations of intranasal corticosteroid and antihistamine taken regularly (12). The current ARIA guidelines recommend the consideration of AIT for patients with AR and AA comorbidity caused predominantly by allergen exposure, with poor symptom reduction despite adequate pharmacotherapy during the allergy season and/or change in natural allergy history (14).</p>	Comments noted. No action needed.

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		<p>In line with these guidelines ITULAZAX® is expected to be used as an add-on therapy for paediatric patients with a clinical history of symptoms despite the use of symptom-relieving medication (15).</p> <p>Please select from the following, will 12 SQ-Bet SLIT be:</p> <p>A. Prescribed in primary care with routine follow-up in primary care</p> <p>B. Prescribed in secondary care with routine follow-up in primary care</p> <p>C. Prescribed in secondary care with routine follow-up in secondary care</p> <p>D. Other (please give details):</p> <p>Option B – Initiation in secondary care with repeat prescriptions in primary care, as concluded in the previous NICE recommendation for ACARIZAX® SLIT (TA1045) and consistent with clinical opinion in both the TA1045 (ACARIZAX) and TA1087 (ITULAZAX) (16, 17).</p> <p>For comparators and subsequent treatments, please detail if the setting for prescribing and routine follow-up differs from the intervention. Comparator treatments for 12 SQ-Bet include symptomatic pharmacotherapy which can be prescribed in both primary and secondary care.</p> <p>Would 12 SQ-Bet SLIT be a candidate for managed access?</p> <p>No</p> <p>Do you consider that the use of 12 SQ-Bet SLIT can result in any potential substantial health-related benefits that are unlikely to be included in the QALY calculation?</p>	<p>Comments noted. No action needed.</p> <p>Comments noted. No action needed.</p> <p>Comments noted. No action needed.</p>

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		<p>Paediatric quality of life (QoL) measures are often completed by proxy, which may not accurately reflect the child's own experience, especially since some children are too young to complete such questionnaires themselves due to cognitive and emotional factors (18), as supported by Section 4.3.14 of the NICE manual (8).</p> <p>Additionally, aspects such as school performance, future attainment, and the ability to engage in play and other childhood activities are often overlooked or inadequately captured by existing QoL tools. The burden of frequent medical appointments, combined with the variability in access to allergy services across the UK can significantly extend the journey to receiving appropriate care and the burden of the patient's condition. Furthermore, the mental wellbeing and quality of life of carers are also affected and not captured in the tools, as well as the fact that they may need to take time off work and face financial burden associated with management of their child's AR.</p> <p>Please identify the nature of the data which you understand to be available to enable the committee to take account of these benefits.</p> <p>Clinical expert opinion and published literature on the impact of AR on paediatric patient quality of life.</p> <p>NICE is committed to promoting equality of opportunity, eliminating unlawful discrimination and fostering good relations between people with particular protected characteristics and others. Please let us know if you think that the proposed remit and scope may need changing in order to meet these aims. In particular, please tell us if the proposed remit and scope:</p>	<p>Comments noted. No action needed.</p> <p>Comments noted. No action needed.</p> <p>Comments noted. No action needed.</p>

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		<ul style="list-style-type: none"> • could exclude from full consideration any people protected by the equality legislation who fall within the patient population for which 12 SQ-Bet SLIT is licensed; • could lead to recommendations that have a different impact on people protected by the equality legislation than on the wider population, e.g. by making it more difficult in practice for a specific group to access the technology; • could have any adverse impact on people with a particular disability or disabilities. <p>Please tell us what evidence should be obtained to enable the committee to identify and consider such impacts.</p> <p>NA</p> <p>References</p> <p>8. National Institute for Health and Care Excellence. NICE health technology evaluations: the manual. 31 January 2022 [updated 14 July 2025]. Available from: https://www.nice.org.uk/process/pmg36/resources/nice-health-technology-evaluations-the-manual-pdf-72286779244741.</p> <p>12. Scadding GK, Kariyawasam HH, Scadding G, Mirakian R, Buckley RJ, Dixon T, et al. BSACI guideline for the diagnosis and management of allergic and non-allergic rhinitis (Revised Edition 2017; First edition 2007). Clin Exp Allergy. 2017;47(7):856-89.</p> <p>13. National Institute for Health and Care Excellence. Clinical Knowledge Summaries: Allergic Rhinitis. 2023.</p> <p>14. Bousquet J, Hellings PW, Agache I, Amat F, Annesi-Maesano I, Ansotegui IJ, et al. Allergic Rhinitis and its Impact on Asthma (ARIA) Phase 4</p>	

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		<p>(2018): Change management in allergic rhinitis and asthma multimorbidity using mobile technology. J Allergy Clin Immunol. 2019;143(3):864-79.</p> <p>15. ALK-Abelló A/S Ltd. ITULAZAX® 12 SQ-Bet oral lyophilisate. Summary of product characteristics. Leatherhead, UK: Electronic Medicines Compendium, Datapharm; 2023 [updated 10 July 2025]. Available from: https://www.medicines.org.uk/emc/product/12906/smpc.</p> <p>16. National Institute for Health and Care Excellence. 12 SQ-HDM SLIT for treating allergic rhinitis and allergic asthma caused by house dust mites. 5 March 2025 [Available from: https://www.nice.org.uk/guidance/ta1045].</p> <p>17. National Institute for Health and Care Excellence. Betula verrucosa for treating moderate to severe allergic rhinitis or conjunctivitis caused by tree pollen 6 August 2025 [Available from: https://www.nice.org.uk/guidance/ta1087].</p> <p>18. Jiang M, Ma Y, Li M, Meng R, Ma A, Chen P. A comparison of self-reported and proxy-reported health utilities in children: a systematic review and meta-analysis. Health Qual Life Outcomes. 2021;19(1):45.</p>	
Additional comments on the draft scope	ALK Abello (Company)	NA	Comment noted. No action needed.