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 ID6462

Draft scope

Draft remit/evaluation objective

To appraise the clinical and cost effectiveness of Itulazax 12 standardised quality pollen from white birch (betula verrucosa) sublingual lyophilisate immunotherapy (12 SQ-Bet SLIT) within its marketing authorisation for treating moderate to severe allergic rhinitis or conjunctivitis induced by pollen from the birch homologous group.

Background

Birch pollen allergy is an immunoglobulin E (IgE)-mediated hypersensitive reaction to the pollen of birch trees and related species. When a person with an allergy comes into contact with birch pollen, the immune system recognises it as a threat and produces antibodies. Further contact with the pollen then results in the release of inflammatory substances such as histamine, which leads to the typical allergic symptoms, including rhinitis and conjunctivitis.[1]

Allergic rhinitis is inflammation of the nose that occurs when the nasal mucosa becomes exposed and sensitised to allergens. Depending on the nature of the allergen, allergic rhinitis has traditionally been categorised as either seasonal allergic rhinitis (e.g., induced by pollen) or perennial allergic rhinitis (e.g., induced by animals or dust mites). Rhinitis typically causes symptoms such as sneezing, nasal discharge, itching, and congestion. It may also lead to complications such as sinusitis or middle ear infections as well as the worsening of asthma symptoms.[2]

Allergic conjunctivitis is the inflammation of the conjunctiva, the mucous membranes that lines the inside of the eyelids and the sclera, the white part of the eye. Symptoms can include itchy eyes, reddened eyes; swollen conjunctiva and watery discharge, which may be thickened with mucous. Symptoms of rhinoconjunctivitis (commonly referred to as hay fever) may be intermittent or chronic during the pollen season.[3]

Rhinoconjunctivitis can further be categorised as either ‘mild’, ‘moderate’ or ’severe’. The definition of moderate disease from the European Academy of Allergy and Clinical Immunology is that symptoms are “bothersome”. Severe rhinoconjunctivitis occurs when symptoms become hard to tolerate, disrupting daily activities or sleep. .[4]

Allergic rhinitis and conjunctivitis are common conditions: allergic rhinitis is reported to affect around 26% of adults in the UK.[11] Birch pollen is among the top three most-diagnosed allergens responsible for respiratory allergies.[5]

In 2022-23, there were 2,132 admissions and 2,140 finished consultant episodes for allergic rhinitis due to pollen in England and a further 290 admissions and 278 finished consultant episodes for ‘allergic rhinitis, unspecified’.[6]

There is no NICE guidance for treating allergic rhinoconjunctivitis. In practice, initial treatment may involve allergy avoidance. This can be followed by pharmacotherapy aimed at symptom control, which may include antihistamines, topical nasal corticosteroids, and leukotriene receptor antagonists (if asthma is also present). For adults, with more severe allergic rhinitis, which does not respond to usual pharmacotherapy, specific desensitisation with immunotherapy may be considered.[7] Skin prick or specific IgE tests can be used to establish which allergens trigger the immune response if immunotherapy is being considered.

The technology

Itulazax 12 standardised quality pollen from white birch (betula verrucosa) sublingual lyophilisate immunotherapy (12 SQ-Bet SLIT; Itulazax, ALK-Abello) has a marketing authorisation for the treatment of moderate to severe allergic rhinitis and/or conjunctivitis induced by pollen from the birch homologous group. It is indicated in adults with a clinical history of symptoms despite use of symptom-relieving medication and a positive test of sensitisation to a member of the birch homologous group (skin prick test and/or specific IgE). It has been studied in a clinical trial comparing Itulazax 12 SQ-BET SLIT to placebo in people aged 12 to 65 years with moderate to severe allergic rhinoconjunctivitis.

Intervention(s)	Itulazax 12 SQ-Bet SLIT as an add-on to standard therapy

Population(s)	Adults with moderate to severe allergic rhinitis or allergic conjunctivitis, or both caused by pollen from the birch homologous group despite the use of symptom-relieving medication and a positive test of sensitisation to a member of the birch homologous group (skin prick test and/or specific IgE).

Comparators	Established clinical management without Itulazax 12 SQ-Bet SLIT
Outcomes	The outcome measures to be considered include: • combined symptom and medication score • rhinoconjunctivitis symptom scores • complications of allergic rhinoconjuctivitis • medication usage • adverse effects of treatment • health-related quality of life.

Economic analysis	The reference case stipulates that the cost effectiveness of treatments should be expressed in terms of incremental cost per quality-adjusted life year. The reference case stipulates that the time horizon for estimating clinical and cost effectiveness should be sufficiently long to reflect any differences in costs or outcomes between the technologies being compared. Costs will be considered from an NHS and Personal Social Services perspective. The use of Itulazax 12 SQ-Bet SLIT is conditional on a positive test for birch pollen sensitisation confirmed with a skin prick test and/or specific IgE. The economic modelling should include the costs associated with diagnostic testing for birch pollen sensitisation in people with allergic rhinitis or allergic conjunctivitis who would not otherwise have been tested. A sensitivity analysis should be provided without the cost of the diagnostic test. See section 4.8 of the guidance development manual (available here: https://www.nice.org.uk/process/pmg36/chapter/introduction-to-health-technology-evaluation).
Other considerations	Guidance will only be issued in accordance with the marketing authorisation. Where the wording of the therapeutic indication does not include specific treatment combinations, guidance will be issued only in the context of the evidence that has underpinned the marketing authorisation granted by the regulator.
Related NICE recommendations	**Related technology appraisals in development:** STG320 for treating allergic rhinitis or rhinoconjunctivitis caused by house dust mites. NICE technology appraisal guidance [ID1278]. Publication date to be confirmed. **Related interventional procedures:** Cryotherapy for chronic rhinitis (2023) NICE interventional procedures guidance 771 Intranasal phototherapy for allergic rhinitis (2018) NICE interventional procedures guidance 616 **Related diagnostics guidance:** ImmunoCAP ISAC 112 and Microtest for multiplex allergen testing (2016) NICE diagnostics guidance 24 **Related quality standards:** Asthma (2013, updated 2018) NICE quality standard 25.
Related National Policy	The NHS Long Term Plan, 2019. NHS Long Term Plan

	NHS England (2018/2019) NHS manual for prescribed specialist services (2018/2019). Chapter 4 – Adult highly specialist respiratory services NHS England (2018/2019) NHS manual for prescribed specialist services (2018/2019). Chapter 59 Highly specialist allergy services (adults and children)

Questions for consultation

Is a test for birch pollen sensitisation (for example, skin prick test and/or specific IgE) routinely undertaken for all people with birch pollen induced allergic rhinoconjunctivitis?

- When is the test undertaken in clinical practice?

In routine practice, how would you define moderate to severe allergic rhinitis and/or conjunctivitis?

What is established clinical management for moderate to severe allergic rhinitis or conjunctivitis caused by pollen from the birch homologous group?

Do you consider Itulazax treatment to be innovative in its potential to make a significant and substantial impact on health-related benefits and how it might improve the way that current need is met (is this a 'step-change' in the management of the condition)?

Where do you consider Itulazax will fit into the existing care pathway for moderate to severe allergic rhinitis or conjunctivitis caused by birch pollen?

- Will Itulazax be used in addition to established clinical management as an add-on therapy?

Please select from the following, will Itulazax be:

A. Prescribed in primary care with routine follow-up in primary care
B. Prescribed in secondary care with routine follow-up in primary care
C. Prescribed in secondary care with routine follow-up in secondary care
D. Other (please give details):

For comparators and subsequent treatments, please detail if the setting for prescribing and routine follow-up differs from the intervention.

Would Itulazax be a candidate for managed access?

Do you consider that the use of Itulazax can result in any potential substantial health-related benefits that are unlikely to be included in the QALY calculation?

Please identify the nature of the data which you understand to be available to enable the committee to take account of these benefits.

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:

- could exclude from full consideration any people protected by the equality legislation who fall within the patient population for which the Ituluzax 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.

Please tell us what evidence should be obtained to enable the committee to identify and consider such impacts.

NICE intends to evaluate this technology through its Single Technology Appraisal process. (Information on NICE's health technology evaluation processes is available at https://www.nice.org.uk/about/what-we-do/our-programmes/nice-guidance/nice-technology-appraisal-guidance/changes-to-health-technology-evaluation).

References

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3. University of Worcester. (2020). *Pollen Calendars by area.* Available at: https://www.worcester.ac.uk/about/academic-schools/school-of-science-and-the-environment/science-and-the-environment-research/national-pollen-and-aerobiology-research-unit/pollen-calendar.aspx [Accessed 16 Aug. 2024]

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5. Wahn, U., Bachert, C., Heinrich, J., Richter, H., & Zielen, S. (2018). Real-world benefits of allergen immunotherapy for birch pollen-associated allergic rhinitis and asthma[1]. *Allergy*, 74(3), 594-604. https://doi.org/10.1111/all.13598

6. NHS England (2023). *Hospital Admitted Patient Care Activity, 2022-23*, (*ICD-10 codes J30.1 & J30.4)*. Available at: https://view.officeapps.live.com/op/view.aspx?src=https%3A%2F%2Ffiles.digital.nhs.uk%2F7A%2FDB1B00%2Fhosp-epis-stat-admi-diag-2022-23-tab_V2.xlsx&wd [Accessed: 16 August 2024].

7. Scadding, G.K., Kariyawasam, H.H., Scadding, G., et al. (2017). BSACI guideline for the diagnosis and management of allergic and non-allergic rhinitis (Revised Edition 2017; First edition 2007). *Clinical & Experimental Allergy*, 47(7), pp.856-889. Available at: https://doi.org/10.1111/cea.12953.