

# Health Technology Briefing

## May 2024

### SQ tree sublingual immunotherapy tablet for treating moderate to severe allergic rhinitis and/or conjunctivitis in children and adolescents

Company/Developer

ALK-Abello Ltd

New Active Substance

Significant Licence Extension (SLE)

NIHRIO ID: 33360

NICE ID: Not available

UKPS ID: Not available

#### Licensing and Market Availability Plans

Currently in phase III clinical development

#### Summary

The SQ tree sublingual immunotherapy (SLIT)-tablet is currently in clinical development for the treatment of tree pollen-induced allergic rhinitis (AR) and/or conjunctivitis, a highly prevalent respiratory condition. Globally, it is estimated that more than 10 million children have uncontrolled respiratory allergies. Pollen allergies are a major cause of allergic rhinoconjunctivitis, and birch pollen is one of the most common seasonal allergies. AR can impair quality of life, sleep, and work/school performance amongst those affected. Allergen avoidance, although representing optimal management for allergic diseases, is not often feasible and symptomatic treatment with anti-allergic medication may only be partially effective. The SQ SLIT tablet will offer a long-term treatment option for which there are currently few options.

SQ tree SLIT-tablet is an allergen extract (birch homologous group) that is administered under the tongue. Allergy immunotherapy with SQ tree SLIT-tablet is the repeated administration of allergens to allergic individuals with the purpose of changing the immune response to the allergen. This reduces the symptoms of the allergy and has the potential to modify the natural course of the allergic disease. Immunotherapy also reduces the inflammation that characterises rhinitis. If licensed, the SQ tree SLIT-tablet would provide a treatment solution for children and adolescents with moderate to severe AR and/or conjunctivitis induced by pollen from birch and trees belonging to the birch homologous group.

## Proposed Indication

Treatment of moderate to severe allergic rhinitis (AR) and/or conjunctivitis induced by pollen from birch and trees in children and adolescents.<sup>1</sup>

## Technology

### Description

The SQ tree sublingual immunotherapy (SLIT)-tablet (Itulazax) is an allergen extract for immunotherapy of tree (birch homologous group) pollen-induced AR and/or conjunctivitis. Allergy immunotherapy with allergen products is the repeated administration of allergens to allergic individuals with the purpose of modifying the immunological response to the allergen. The pharmacodynamic effects of allergy immunotherapy are exerted on the immune system, but the exact mechanism of action underlying clinical efficacy is not fully understood. However, several studies have shown that the immunological response to allergy immunotherapy is characterised by an induction of allergen specific immunoglobulin G4 (IgG4). Allergen specific IgG4 competes with Immunoglobulin E (IgE) for the binding to allergens, and thereby reduces activation of immune cells.<sup>2</sup>

The SQ tree SLIT-tablet is currently in Phase III development for children and adolescents (5 to 17 years) with moderate to severe AR and/or conjunctivitis induced by pollen from birch and trees belonging to the birch homologous group. In the phase III clinical trial (TreeTop, NCT04878354), SLIT-tablets were administered daily, sublingually.<sup>1</sup>

### Key Innovation

Although widely given as first-line treatment for AR the first-generation sedating antihistamines lack good evidence of efficacy and are known to have adverse effects such as psychomotor retardation and behaviour disturbance.<sup>3,4</sup> If licensed, the SQ SLIT-tablet will offer an additional treatment option for children and adolescents with moderate to severe allergic rhinitis (AR) and/or conjunctivitis induced by pollen from birch and trees belonging to the birch homologous group.

### Regulatory & Development Status

SQ tree SLIT-tablet currently has Marketing Authorisation in the EU/UK for treatment of adult patients with moderate-to-severe allergic rhinitis and/or conjunctivitis induced by pollen from the birch homologous group.<sup>2</sup>

SQ tree SLIT-tablet is not currently in clinical development for any other indication.

## Patient Group

### Disease Area and Clinical Need

AR is an IgE-mediated inflammatory disorder of the nose that occurs when the nasal mucosa becomes exposed and sensitised to allergens. Rhinitis describes inflammation of the nasal mucosa, which causes typical clinical symptoms of sneezing, nasal discharge (rhinorrhoea), itching, and congestion. When the eyes are also involved, the term rhinoconjunctivitis is used.<sup>5</sup> Symptoms of allergic conjunctivitis include:

red or pink eyes, pain, itchiness and swollen eyelids.<sup>6</sup> AR may be classified according to severity, depending on the impact of the condition on sleep and daily activities. AR is considered moderate to severe when sleep and/or daily living activities are affected. For example sleep disturbance, impairment of school or work, leisure or sport.<sup>5</sup> Grass, tree, and weed pollens are common environmental triggers.<sup>7</sup> Birch pollen is among the top three most-diagnosed allergens responsible for respiratory allergies and birch is considered to be the major pollen-allergen-producing tree in northern Europe.<sup>8</sup> The broad cross-reactivity and sequential pollen seasons of birch-related allergens prolong the period of allergic symptoms for many patients. In addition, cross-reactivity of birch pollen allergens extends to plant food allergens, resulting in the pollen food syndrome. Subsequently, the negative impact on health-related quality of life in patients allergic to birch pollen is substantial.<sup>9</sup>

Globally, it is estimated that more than 10 million children have uncontrolled respiratory allergies, and the number is growing. Tree pollen is a common cause of these uncontrolled allergies.<sup>10</sup> AR can cause an impaired quality of life. AR can lead to impaired school performance – poorly controlled symptoms in children may cause difficulty concentrating, irritability, and sleep disturbance.<sup>11</sup> AR affects between 10-15% of children in the UK.<sup>12</sup> It is unusual for infants to develop AR in the first two years of life. It may be, therefore, that more than one season of allergen exposure is needed for sensitisation to occur.<sup>13</sup> It has been estimated that between the ages of 3 and 12, new cases of seasonal AR increase at a constant rate of around 2% per year.<sup>3,14</sup> In England, 2022-23, there were 2,132 admissions and 2,140 finished consultant episodes (FCE) for AR due to pollen (ICD-10 code J30.1), resulting in 85 FCE bed days and 1,913 day cases.<sup>15</sup>

### Recommended Treatment Options

There is no treatment option recommended by NICE for AR and/or conjunctivitis induced by pollen from birch and trees belonging to the birch homologous group in children and adolescents.

The National Health Service (NHS) currently recommends the use of antihistamines, decongestant nasal sprays/drops for children and adults over the age of 6 and salt water nasal sprays to treat AR. In the case that pharmacy medicines do not help to ease AR symptoms, steroid nasal sprays and antihistamines are available on prescription.<sup>16</sup>

### Clinical Trial Information

<p><b>Trial</b></p>	<p>TreeTop, <a href="#">NCT04878354</a>; <a href="#">2020-004372-17</a>; Efficacy and Safety of the SQ Tree Sublingual Immunotherapy Tablet in Children and Adolescents With Moderate to Severe Allergic Rhinitis and/or Conjunctivitis Induced by Pollen From Birch and Trees Belonging to the Birch Homologous Group  <b>Phase III</b> – Completed  <b>Location(s)</b>: Nine EU countries, Canada, and Russian Federation  <b>Study Completion Date</b>: July 2023</p>
<p><b>Trial Design</b></p>	<p>Randomised, parallel assignment, quadruple masking</p>
<p><b>Population</b></p>	<p>N=915 (actual); aged 5-17 years; participants with a clinically relevant history of moderate to severe AR and/or conjunctivitis induced by birch pollen (with or without asthma) despite having received treatment with symptom-relieving medication during at least 1 previous tree pollen season</p>
<p><b>Intervention(s)</b></p>	<p>SQ tree SLIT-tablet daily, sublingually</p>

Comparator(s)	Matched placebo
Outcome(s)	<p>Primary outcome: average total combined score (rhinoconjunctivitis symptoms and medication use) during the birch pollen season [Time frame: 3 months]. European Academy of Allergy and Clinical Immunology - values 0,1,2.</p> <p>See trial record for full list of other outcomes.</p>
Results (efficacy)	<p>The trial achieved its primary endpoint and confirmed the effect of the tree tablet with an improvement of 22% in the total combined rhinoconjunctivitis score (TCS) during the birch pollen season compared to placebo. Results were highly statistically significant (<math>p=0.0004</math>), with a lower bound of the 95%-confidence interval of 10.6%. The trial also demonstrated improvement in TCS during the entire tree pollen season (key secondary endpoint).<sup>10</sup></p>
Results (safety)	<p>The trial demonstrated that treatment with the tree tablet was well tolerated and had a favourable safety profile.<sup>10</sup></p>

### Estimated Cost

The cost of SQ tree SLIT-tablet is not yet known.

### Relevant Guidance

NICE Guidance

No relevant guidance identified.

NHS England (Policy/Commissioning) Guidance

NHS England. 2013/14 NHS Standard Contract for Specialised Allergy Services (All Ages). B09/S/b.

Other Guidance

British Society of Allergy and Clinical Immunology (BSACI). Guideline for the Diagnosis and Management of Allergic and Non-Allergic Rhinitis. 2017.<sup>12</sup>

### Additional Information

ALK-Abello Ltd did not enter information about this technology onto the UK PharmaScan database; the primary source of information for UK horizon scanning organisations on new medicines in development. As a result, the NIHR Innovation Observatory has had to obtain data from other sources. UK PharmaScan is an essential tool to support effective NHS forward planning; allowing more effective decision making and faster uptake of innovative new medicines for patients who could benefit. We urge pharmaceutical companies to use UK PharmaScan so that we can be assured of up-to-date, accurate and comprehensive information on new medicines.

### References

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