HAUTE AUTORITÉ DE SANTÉ

TRANSPARENCY COMMITTEE

SUMMARY

07 OCTOBER 2020

The legally binding text is the original French opinion version

Standardised birch pollen allergen extract

ITULAZAX 12 SQ-Bet oral lyophilisate

First assessment

Key points

Favourable opinion for reimbursement in the treatment of moderate to severe allergic rhinitis, with or without conjunctivitis, triggered by pollens belonging to the birch homologous group in patients with a suggestive clinical history despite the use of symptomatic medicines and a positive sensitisation test to one of the members of the birch homologous group (skin prick test and/or presence of specific IgEs).

What therapeutic improvement?

Therapeutic improvement in management.

Role in the care pathway?

Wherever possible, it is recommended to implement targeted allergen avoidance for a given patient, particularly in children (professional consensus).

- Antihistamines:

The efficacy of antihistamines has been demonstrated on all nasal symptoms, including nasal obstruction, although to a lesser degree (grade A). It is impossible to differentiate between these medicinal products in terms of efficacy on rhinitis symptoms (grade C). First-generation antihistamines are sedative (grade A). Only second-generation H1 antihistamines should be prescribed in allergic rhinitis (professional consensus).

- Corticosteroids:

The efficacy of local glucocorticoids has been demonstrated on all allergic rhinitis symptoms (grade A). Overall, their efficacy is greater than that of H1 antihistamines on nasal symptoms (grade A). There is no conclusive evidence of a difference in clinical efficacy between local corticosteroids (grade C). Local and systemic safety is excellent at the dosages recommended in rhinitis (grade A). Local glucocorticoids are indicated as first-line therapy in severe AR and as second-line therapy in the event of failure of H1 antihistamines (professional consensus). In all cases, and particularly in children, the lowest effective dose of nasal corticosteroids must be sought (professional consensus). IM systemic glucocorticoids must not be used (grade C). Oral glucocorticoids should be avoided. They should only be prescribed for short periods due to their adverse effects (professional consensus).

- Allergen immunotherapy:

Allergen immunotherapy reduces inflammation triggered by the allergen via an aetiological action on the immune system (professional consensus). The subcutaneous route is effective, but is not without risk (anaphylaxis, exacerbation of asthma) (grade A). The sublingual route is effective and much safer (grade A). Only certain allergens have been the subject of studies enabling recommendations to be issued (professional consensus). For these allergens, specific immunotherapy is effective (grade A). No immunotherapy can be started without an accurate diagnosis of allergic sensitisation and determination of the burden of this sensitisation in the patient's symptoms (professional consensus). It is necessary to follow strict safety rules if the subcutaneous route is used (professional consensus). In perennial rhinitis, immunotherapy is indicated when the rhinitis is severe and/or prolonged, especially when there is mild or moderate associated asthma. The main allergens are house dust mites, for which allergen extracts are of good quality.

According to the 2016 ARIA recommendations, inhaled corticosteroid + oral or intranasal antihistamine combinations are proposed in patients with moderate to severe forms. However, the level of evidence for these recommendations is low. If these treatments fail, a short course of oral corticosteroids may be prescribed. In severe rhinitis not responding to corticosteroid therapy, allergen immunotherapy may be envisaged.

According to the HAS Board recommendations dated 21 February 2018, the role of NPPs is either as second-line therapy, following symptomatic medicinal treatments, or as third-line therapy when allergen immunotherapy treatments in the form of a proprietary medicinal product can be used. The data assessing NPPs in the context of these recommendations have shown a low and inadequately demonstrated efficacy.

At present, in the context of allergy to tree pollens belonging to the birch homologous group, only NPPs can be used.

Role of the medicinal product in the care pathway

ITULAZAX (standardised birch pollen allergen extract) is a second-line treatment for adults with allergic rhinitis, with or without conjunctivitis, triggered by tree pollen belonging to the birch homologous group, when symptomatic medicinal products are insufficient. It should be highlighted that there is an absence of long-term data, for periods of over 10 months, despite the fact that immunotherapy requires long-term treatment (at least 3 years).

The Committee reiterates that treatment with ITULAZAX (standardised birch pollen allergen extract) should be initiated by physicians experienced in the treatment of allergies. The first dose must be administered under medical supervision, for at least 30 minutes, in order to assess and treat any immediate-onset adverse reactions, in particular the risk of severe anaphylactic reaction.

COMMITTEE'S CONCLUSIONS

Clinical benefit

◗ Allergic rhinitis is a common condition that can impair quality of life as a result of the disturbances it causes. Allergic rhinitis triggered by tree pollen belonging to the birch homologous group is frequently associated with asthma and is itself a factor for poor control of asthma, irrespective of severity.
◗ ITULAZAX (standardised birch pollen allergen extract) is a preventive treatment.
◗ Its efficacy/adverse effects ratio is low.
◗ There are therapeutic alternatives (NPPs).
◗ This proprietary medicinal product is a second-line treatment for allergic rhinitis, with or without conjunctivitis, triggered by tree pollen belonging to the birch homologous group, insufficiently controlled by symptomatic treatments.

◗ Public health impact:
Considering:
- the severity of symptoms of allergic rhinoconjunctivitis triggered by tree pollen belonging to the birch homologous group and the risk of development or exacerbation of asthma,
- its high prevalence in the northern half of France,
- the partially met medical need in the event of poor symptom control using symptomatic treatments,
- the absence of response to the identified medical need in view of the low efficacy demonstrated compared to placebo in a population in which the transposability is not guaranteed and a safety profile including a risk of severe anaphylactic reactions,
- the absence of robust quality of life data,
- the absence of any demonstrated impact on the organisation of care,

ITULAZAX (standardised birch pollen allergen extract) is unlikely to have an impact on public health.

Given all these elements, the Committee deems that the clinical benefit of ITULAZAX (standardised birch pollen allergen extract) is low in the MA indication.

The Committee issues a favourable opinion for inclusion in both the hospital formulary list and the retail formulary list of reimbursed proprietary medicinal products approved for use in the marketing authorisation indication and dosages.

Clinical Added Value

Considering:
- **demonstration in a phase III comparative, randomised, double-blind study of the superiority of ITULAZAX (standardised birch pollen allergen extract) compared to placebo for a composite score taking into account the severity of the symptoms and the use of symptomatic treatments (primary endpoint);**
- **with an effect size that is modest but deemed to be clinically relevant of (difference of 3 points [-4; -2] on a scale of 0 to 38);**
- **the safety profile of ITULAZAX (standardised birch pollen allergen extract), which is mainly characterised by mild to moderate and transient allergic reactions with, however, a risk of severe anaphylactic reaction (which is actually an allergen immunotherapy class effect),**

but the absence of:
- **robust data in terms of quality of life in a condition that significantly impacts this,**

- **long-term data, for periods of over 10 months, despite the fact that immunotherapy requires long-term treatment (at least 3 years),**

the Committee considers that ITULAZAX (standardised birch pollen allergen extract) provides a minor clinical added value (CAV IV) in the treatment of adults with moderate to severe allergic rhinitis, with or without conjunctivitis, triggered by pollens belonging to the birch homologous group.