HAUTE AUTORITÉ DE SANTÉ

TRANSPARENCY COMMITTEE
SUMMARY
3 NOVEMBER 2021

The legally binding text is the original French opinion version

Standardised ragweed (Ambrosia artemisiifolia) allergen extract)
RAGWIZAX 12 SQ-Amb oral lyophilisate

New indication

Key points

Favourable opinion **in children (from 5 years)**, for the treatment of allergic rhinitis, with or without conjunctivitis, triggered by ragweed pollen, insufficiently controlled by symptomatic treatments.

What therapeutic improvement?

Therapeutic improvement in the management of the condition.

Role in the care pathway?

The care pathway for allergic rhinitis was specified in the context of an expert consensus grouping together various French learned societies (French Allergology Society, French ENT and Face and Neck Surgery Society, French Society for Documentation and Research in General Medicine and French Paediatric Society).

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

For medicinal treatment:
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).
Glucocorticoids:
- 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 glucocorticoids (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 glucocorticoids 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, allergen 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 glucocorticoids + 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 glucocorticoids may be prescribed. In severe rhinitis not responding to glucocorticoids therapy, allergen immunotherapy may be envisaged.

Two types of allergen extracts are available: named-patient preparations (NPPs) and standardised allergen extracts in the form of a proprietary medicinal product with a marketing authorisation.
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 ragweed allergy, only NPPs can be used.

Role of the medicinal product in the care pathway:
In children from 5 years, RAGWIZAX 12 SQ-Amb (standardised ragweed allergen extract) is a second-line treatment for moderate to severe allergic rhinitis, with or without conjunctivitis, triggered by ragweed pollen, insufficiently controlled by symptomatic treatments.

COMMITTEE'S CONCLUSIONS

Considering all of this information and further to debate and voting, the Committee considers:

Clinical benefit

◗ Allergic rhinitis is a common condition that can impair quality of life as a result of the disturbances it causes. In children, allergic rhinitis triggered by ragweed is very frequently associated with asthma and is itself a factor for poor control of asthma, irrespective of severity.

◗ RAGWIZAX 12 SQ-Amb (standardised ragweed allergen extract) is a preventive treatment.

◗ In children, considering the demonstration, in a high number of children, of a modest effect on the total combined score of symptoms and medicines and the absence of quality of life data, the efficacy/adverse effects ratio of RAGWIZAX 12 SQ-Amb (standardised ragweed allergen extract) is moderate.

◗ There are therapeutic alternatives (see section 5 Clinically relevant comparators).

◗ This proprietary medicinal product is a second-line treatment for moderate to severe allergic rhinitis, with or without conjunctivitis, triggered by ragweed pollen, insufficiently controlled by symptomatic treatments.

◗ Public health impact:
Considering:
- the impairment of quality of life as a result of the symptoms of allergic rhinoconjunctivitis triggered by ragweed and the risk of development or exacerbation of asthma,
- its high prevalence, particularly in the Auvergne-Rhône-Alpes region,
- the partially met medical need in the event of poor symptom control using symptomatic treatments,
- the additional partial response that may be provided to the identified medical need, with a modest additional impact demonstrated in terms of morbidity in view of the effect size versus placebo, and the absence of a demonstrated impact in terms of quality of life due to a lack of data,
- the absence of any demonstrated impact on the organisation of care,

RAGWIZAX 12 SQ-Amb (standardised ragweed allergen extract) is unlikely to have an additional impact on public health.

Considering all these elements, the Committee deems that the clinical benefit of RAGWIZAX 12 SQ-Amb oral lyophilisate (standardised ragweed extract) is moderate in the MA indication.

The Committee issues a favourable opinion for inclusion of RAGWIZAX 12 SQ-Amb oral lyophilisate (standardised ragweed extract) in both the hospital formulary list and the retail formulary list of reimbursed proprietary medicinal products approved for use in the indication and at the MA dosages.

◗ **Recommended reimbursement rate: 30%**

Clinical Added Value

Considering:

- the quality of research evidence concerning the efficacy of RAGWIZAX (randomised, double-blind, placebo-controlled comparative study) since it was conducted on a large number (more than 1,000 patients) of children aged from 5 years and adolescents;
- the medical need to have access to medicinal products having demonstrated their efficacy in children in the treatment of allergic rhinitis (with or without conjunctivitis) triggered by this pollen and insufficiently controlled by symptomatic treatments;

but in view of:

- the inclusion of patients in whom symptomatic treatments had not necessarily failed;
- the modest effect size of RAGWIZAX 12 SQ-Amb demonstrated compared to placebo on a composite score (primary endpoint) taking into account the severity of symptoms and the use of symptomatic treatments (difference of -2.73 points between the two groups, on a score ranging from 0 to 38 points);
- the risk of severe anaphylactic reactions;
- the absence of efficacy data in terms of quality of life;

the Transparency Committee considers that **RAGWIZAX 12 SQ-Amb (standardised ragweed extract) provides a minor clinical added value, (CAV IV) in children from 5 years, in the treatment of allergic rhinitis, with or without conjunctivitis, triggered by ragweed pollen, insufficiently controlled by symptomatic treatments.**