HAUTE AUTORITÉ DE SANTÉ

ALLERGY
New medicinal product
November 2019

TRANSPARENCY COMMITTEE OPINION SUMMARY

RAGWIZAX (standard ragweed allergen extract), allergen immunotherapy

Low clinical benefit, in adults, in the treatment of allergic rhinitis, with or without conjunctivitis, triggered by ragweed pollen but no clinical benefit demonstrated in the care pathway

Key points

- RAGWIZAX in adults, in the treatment of allergic rhinitis, with or without conjunctivitis, triggered by ragweed pollen, insufficiently controlled by symptomatic treatments.
- This sublingual immunotherapy treatment has demonstrated low efficacy compared to the placebo for reducing the symptoms of ragweed allergy.
- It is a second line treatment after failure of symptomatic treatments.
- Sublingual standard allergen extracts must be preferred to named-patient preparations (NPPs).

Care pathway

- Desensitisation is indicated where allergic rhinitis is severe and/or prolonged and insufficiently controlled by symptomatic treatments (antihistamines, corticosteroids), in particular where there is related mild or moderate asthma.
  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. It is necessary to follow stringent safety rules if the subcutaneous route is used.
  The subcutaneous route is effective, but is not without risk (anaphylaxis, exacerbation of asthma). The sublingual route is effective and substantially safer. Standard allergen extracts administered by sublingual route, where they are available, must be preferred to named-patient preparations (NPPs).
- **Role of the medicinal product in the care pathway**

  RAGWIZAX is a 2nd line treatment for moderate to severe allergic rhinitis, with or without conjunctivitis, triggered by ragweed pollen, insufficiently controlled by symptomatic treatments.

Clinical data

- RAGWIZAX was assessed in 2 phase II/III superiority, placebo-controlled (P05233 and P05234), randomised, double-blind, parallel group, multicentric studies in adults age 18 to 50 years, with allergic rhino-conjunctivitis caused by ragweed, confirmed by a positive skin test and specific IgE test result of > 0.70 KU/L, with an FEV_1 value at ≥ 70% of the theoretical value. The patients were treated for 52 weeks.
  The primary endpoint of these studies was the total combined score (TCS – score of 0 to 54 points) assessed at the height of the ragweed pollen season, corresponding to the total daily score for rhino-conjunctivitis symptoms (score of 0 to 18 points) and to the score for daily use of symptomatic rhino-conjunctivitis treatments (score of 0 to 36 points), divided by the number of days over the period studied.
  In the two studies, after 52 weeks, the symptoms were less severe in the RAGWIZAX group than in the placebo group. The TCS at the height of the pollen season was 6.22 points versus 8.46 points in study P05233 and 6.41 versus 8.46 in study (p= 0.0002 in the 2 studies) in the RAGWIZAX and placebo groups respectively.
- The adverse effects the most frequently observed (10 to 25%) were oropharyngeal, ear, ocular, respiratory and cutaneous allergic reactions. We also note nervous system disorders (headache, migraine, paresthesia, dizzy sensation) among the common adverse effects. These mild to moderate reactions generally occurred at the start

of treatment, were temporary, and went away of their own accord. As with all allergen immunotherapy treatments, including oral treatments, severe anaphylactic reactions can occur, meaning the treatment should be initiated under medical supervision.

Benefit of the medicinal product

- The clinical benefit* of RAGWIZAX is low.
- RAGWIZAX does not provide clinical added value** (CAV V) in the treatment of allergic rhinitis, with or without conjunctivitis, triggered by ragweed pollen in adults, insufficiently controlled by symptomatic treatments.
- Positive opinion issued for retail pharmacy reimbursement and for hospital treatment.

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This document was drafted on the basis of the Transparency Committee opinion dated 23 October 2019 (CT-17703) available at **www.has-sante.fr**

* The clinical benefit of a medicinal product describes its benefit primarily in terms of its clinical efficacy and the seriousness of the condition being treated. The HAS Transparency Committee assesses the clinical benefit, which may be substantial, moderate, low, or insufficient for the medicinal product to be covered by public funding.

** The clinical added value (CAV) corresponds to the clinical improvement offered by a medicinal product compared to existing treatments. The HAS Transparency Committee assesses the CAV level from I, major, to IV, minor. A level V CAV (equivalent to "no clinical added value") denotes a "lack of clinical improvement"