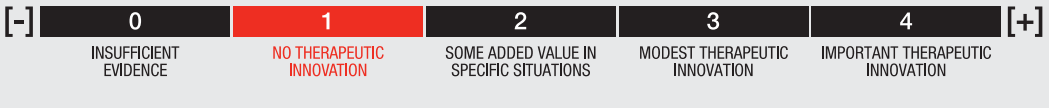
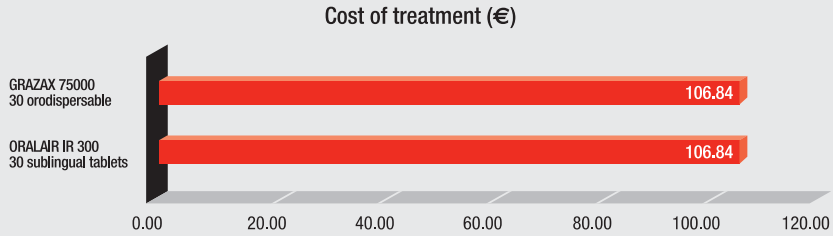
www.dtb.navarra.es

03/2013

Grass pollen extract (▲Oralair®) for allergic rhinitis

An expensive, long-term preventive treatment of modest efficacy





This drug does not offer significant advantages compared to symptomatic management

Indications[1]

This allergen extract of five pollen grasses *(Dactylis glomerata, Anthoxanthum odoratum, Lolium perenne, Poa pratensis and Phleum pratense)* is indicated in the management of allergic rhinitis, with or without conjunctivitis, caused by grass pollen in adults, adolescents and children over 5 years of age that present clinically relevant symptoms. The diagnosis of allergy to grass pollen should be confirmed by a positive skin test and/or a positive specific IgE test for grass pollens.

Management should be initiated by specialists with experience in the management of allergy-related disease.

Mechanism of action and pharmacokinetics[1]

The mechanism of action regarding the clinical effects of specific immunotherapy is not completely known. Treatment with the extract of grass pollen induces a competitive systemic response of antibodies against grass pollen and produces a rise in specific IgG. The clinical relevance of these findings is not established.

Posology and form of adminstration[1]

The approach for initiating treatment is to give one tablet with 100 RI (Reactivity Index) on the first day, then 2 two tablets of 100 RI on the second day and one tablet of 300 RI per day on the third day and continue until the pollen season ends.

The first tablet should be taken under medical supervision and the patient should be kept under observation for 30 minutes. The tablet should be placed under the tongue, until completely dissolved (at least one full minute) and after that should be swallowed. The tablet is recommended in the mornings before breakfast.

- An allergen extract of five grass pollens is indicated for the management of allergic rhinitis caused by grass pollen with clinically relevant symptoms and diagnosed with specific tests.
- The allergenic extract has shown modest efficacy in trials compared to placebo.
- There are no comparative trials with other immunotherapies.
- A high percentage of patients included in the trials suffered local adverse reactions, especially children, of which the most frequent was oral pruritus (32%). Although rare, there is a risk of severe adverse reactions (angioedema, dysphagia, and respiratory problems).

The qualification assigned to the drug was agreed by the Drug Assessment Committees of Andalusia, Basque Country, Catalonia Institute of Health, Aragon and Navarre. The current report is based on the available information and is susceptible to be updated according to the latest evidence. Let us remind the reader about the importance of notifying the Pharmacovigilance Centre when there are suspicions of adverse reactions to drugs.

Treatment should start approximately 4 months before the expected onset of the pollen season. If no important improvement of symptoms is obtained during the first pollen season, then there is no indication to continue treatment.

Clinical efficacy

Three multicenter, randomised, double-blind, placebo-controlled clinical trials have been published. Two of them were carried out in adults[2,3], and one in children over 5 years or adolescents[4] with allergic rhinitis due to grass pollen of at least two years, diagnosed by specific tests. During the trials, treatment was initiated two or four months before the pollen season up to the end of the season. As primary endpoint for efficacy, the total score of six symptoms of rhinoconjunctivitis (sneezing, runny nose, nasal itching, nasal congestion, tearing, and eye itching) was employed on a scale of 0-3 with a maximum score of 18.

In the first trial, therapy started 4 months before the pollen season and continued till the end of the season. The total score of symptoms with pollen extract 300 RI/d was 3.58 compared to 4.94 under placebo (mean difference of -1.39;95%CI:-2.09 to -0.69). [2]

The second study was carried out during three consecutive pollen seasons. Of the groups under 300RI daily of pollen extract therapy, one started treatment 2 months before the onset of the pollen season and the other 4 months before. At the end of the third pollen season the total score of symptoms was as follows: pollen extract 300 RI daily (group starting two months before pollen season), 3.38; group starting 4 months before the pollen season, 3.46; and placebo group, 5.28. The difference between the two groups under the pollen extract compared to placebo was -1.96 (95%CI, -2.76 to -1.16) and -1.81 (95%CI, -2.61 to – 1.02).[3]

In the trial involving children and adolescents, the total score of symptoms was 3.25 in the group under 300RI daily pollen extract and 4.51 in the group under placebo (mean difference of -1.13; 95%CI, -1.80 to – 0.46).[4]

Surrogate endpoints included the use of rescue medication (no medication=0, antihistamine agents =1, nasal corticoids=3). The mean scores of rescue medication under the pollen extract was 0.313 and 0.604 while under placebo the scores were 0.473 and 0.794. Though statistically significant the differences are scarce.

Safety

Adverse reactions

Mild to moderate local allergic reactions can be observed, of which 50% are produced during the first 3 days of treatment.[1] The most frequent reaction is oral cavity pruritus, which lasted an average of 12.5 days and affected 26% of the patients treated with the five-grass pollen extract, followed by throat irritation. The percentage of patients that prematurely interrupted their treatment due to adverse effects was 5.2%.[2,3]

In the study on children and adolescents the most frequently reported adverse reaction was oral pruritus (32% vs 1% under placebo). There were 7 cases of withdrawal due to adverse effects in the treatment group and two in the placebo group.[4]

Other adverse reactions with a frequency between ≥1% and <10% include: headache, paresthesia, conjunctivitis, eye pruritus, ear pruritus, oral oedema, nasal congestion, runny nose, dry throat, sneezing, pain in the upper half of the abdomen, nausea, dyspepsia, glositis, glosodynia, oedema and other alterations in the tongue, dry mouth, pain and discomfort in the oral cavity, facial oedema, pruritus, urticaria, fatigue.[1] In the case of severe adverse reactions (angioedema, dysphagia, changes ni breathing and voice), treatment should be discontinued with immediate consultation of a physician.[1]

Contraindications[1]

Hypersensitivity or intolerance to lactose or galactose; severe or unstable asthma;, treatment with betablockers; severe immunodeficiency or autoinmune disease; malign disease; oral inflammation such as liquen planus, oral ulcers and mycosis.

Warnings and precautions[1]

In case of oral surgery, including dental extraction, treatment with the pollen extract should be suspended for 7 days to allow for scarring.

Use in special situations[1]

Pregancy: treatment should not be initiated. If already under treatment, the patients falls pregnant this can be continued after evaluation. **Breastfeeding:** no data available. Not recommeded. The effects on babies are unknown. **Children under 5:** no experience. **Adults over 45 years:** No experience.

Interactions[1]

No interactions have yet been described with the concurrent use of medications for symptom relief in allergic rhinitis (antihistamine drugs and corticoids). There is no information on the possible risks of simultaneous immunotherapy with other allergens[1].

Place in therapeutics

There are no available clinical trials comparing the five-grass pollen extract to symptom relief agents for allergic rhinitis, or subcutaneous immunotherapy, or sublingual immunotherapy with the pollen allergen extract Phleum pratense. Studies versus placebo have shown that sublingual immunotherapy presents modest efficacy in the reduction of symptoms of allergic rhinitis, the need for symptom relief medication, and improvement in quality of life.

Local adverse effects are frequent especially in children and moreover, the possibility of severe adverse effects should be taken into account. The indication for treatment with the pollen extract should be carried out after specific diagnostic tests are made and evaluation by specialists. Medical supervision is necessary during the administration of the first dose. A high percentage of patients treated with the extract still require symptomatic relief medication.

The five-grass pollen extract does not appear to represent a therapeutical advancement in the management of allergic rhinitis compared to the previously available treatment options.

Presentations

Oralair® (Stallergenes S.A.)
Oralair® Initiation100/300 RI 1 x 3 + 1 x 28 sublingual tablets (106.84 €).
Oralair® 300 RI 30 sublingual tablets comp. (106.84 €).
Requires medical prescription and authorisation

References

A complete report on the five-grass pollen extract can be found at: http://www.dtb.navarra.es

Servicio Navarro de Salud
Osasunbidea

INFORMATION:
Servicio de Prestaciones Farmacéuticas Plaza de la Paz s/n, 4ª planta - 31002 Pamplona **T** 848429047 **F** 848429010