

New and Emerging Technology Briefing

*National
Horizon
Scanning
Centre*

**Grazax allergy vaccine
for moderate to severe
seasonal allergic
rhinitis (grass pollen
hay fever)**

January 2006

Horizon Scanning Review

Early assessments of new or emerging technologies
contain time-limited information and should be
used with due caution.

Not to be used for commercial purposes

**UNIVERSITY OF
BIRMINGHAM**

Grazax allergy vaccine for moderate to severe seasonal allergic rhinitis (grass pollen hay fever)

Summary

Grazax vaccine is a once daily sublingual tablet for the treatment of moderate to severe grass pollen seasonal allergic rhinitis (hay fever). Treatment is initiated at least eight weeks ahead of the grass pollen season and continued for three years in order to achieve a lasting effect after treatment ends. Randomised trials in over 1,700 patients have shown a 30-40% reduction in symptoms and reduced medication use compared with placebo. The company anticipate that Grazax will be introduced through specialist clinics initially, but could then move into the primary care setting. ALK-Abelló intends to slowly move immunotherapy from a last resort strategy to a baseline therapy.

Developer – ALK-Abelló (Denmark).

Regulatory status – Pre-registration in the EU.

Unit cost – Yet to be determined.

NHS or Government priority – Not a priority area.

Relevant existing UK guidance – PRODIGY guidance–allergic rhinitis (1998), revised July 2005.

Burden of disease – Seasonal allergic rhinitis (hay fever) is estimated to affect around 26% of the population, of whom 52-90% are estimated to be allergic to airborne grass pollens. Those with moderate to severe disease account for approximately 30-62%, equivalent to around 3-9M people in England and Wales.

Potential clinical benefit – Symptom reduction, less dependence on symptom-reducing medications and the potential for long-term remission may be welcomed by many patients, as would a sublingual preparation of immunotherapy. Mainly mild and transient side effects have been reported in clinical trials, even in patients with asthma.

NHS or societal resource impact – If Grazax does enter the market as a baseline therapy, as many as 3-9M patients may be suitable candidates, the vast majority of whom currently control symptoms at their own expense with over-the-counter preparations. If only 50% of these people were to receive this treatment, and Grazax was priced in line with current immunotherapies, the cost to the NHS could be significant.

The technology

Grazax vaccine (*Phleum pratense*) – ALK-Abelló, is a biological grass allergen immunotherapy administered sublingually in the form of a once-daily fast dissolving tablet. The aim of immunotherapy is to desensitise the immune system so that it does not respond when challenged with environmental allergens. The benefits of immunotherapy can include

long-term remission, symptom reduction, reduced need for symptom relieving drugs and the prevention of new sensitisations and allergic asthma.

Grazax tablets contain 75,000 SQ-T units of grass pollen allergen, which is equivalent to about 30 times the amount of pollen to which the average person would be exposed each summer. Treatment is initiated at least eight weeks ahead of the grass pollen season and then continued for three years in order to achieve a lasting effect. It is intended to be self-administered in conjunction with currently available symptom relieving allergy medications, with the potential for patients to decrease their need for symptomatic medication over the course of treatment.

A registration application was filed with Swedish authorities in June 2004. ALK-Abelló state that their strategy is to position Grazax as a baseline therapy against grass allergy and to expand the treatment setting from core allergy specialists, to relevant allergy specialists and possibly primary care.

Burden of disease and patient group

Seasonal allergic rhinitis (hay fever) is estimated to affect around 26% of the population¹; around 15.9M people in England and Wales with an increasing prevalence and severity. People of all ages may be affected but the peak age of onset is adolescence. Risk factors include a personal or family history of atopy, male sex and birth order (first born). In children, poorly controlled symptoms may contribute to learning problems and sleep disturbance. Other allergic problems such as asthma and eczema frequently coexist, adding to the impact. A person with hay fever may be allergic to one, several or many types of different pollen, but approximately 52-90% of people with hay fever are allergic to airborne grass pollens^{1,2}.

People with moderate to severe hay fever are defined as having one or more of the following: abnormal sleep; impairment of daily activities, sport or leisure; problems at work or school. Estimates range from 30-62% of people that are affected by moderate to severe symptoms^{3,4}. On this basis, around 2.5–8.9M people in England and Wales may be eligible for treatment. It is not clear how many patients are currently receiving immunotherapy, although expert opinion puts this figure at around 1%.

Current treatment and alternatives

Treatment for seasonal allergic rhinitis aims to minimise or eliminate symptoms, optimise quality of life and reduce the risk of developing coexistent disease. Often a combination of products is necessary to manage all their symptoms. Most people in the UK rely on over-the-counter medicines to manage the symptoms².

For moderate to severe hay fever, the following management strategies are advised⁵:

Allergy Classification	First-line treatments	Alternative or add-on therapies (if first-line failed or contraindicated)	Comments
Mild persistent or Moderate-severe intermittent	Oral antihistamines, Intranasal corticosteroids/ antihistamines	Intranasal decongestants, Sodium cromoglicate	Sodium cromoglicate is a useful alternative to antihistamines and corticosteroids, especially in children.
Moderate-severe persistent	Intranasal corticosteroids	Oral antihistamines, intranasal antihistamines, sodium cromoglicate, immunotherapy	Ipratropium bromide is useful for persistent runny nose. Leukotriene antagonists may be useful if there is coexisting asthma.

Immunotherapy is, under the current guidelines, an option when other treatments have failed. Pollinex (Allergy) is the only grass pollen extract immunotherapy currently available and is administered by subcutaneous injection. The Committee for the Safety of Medicines (CSM) has concluded that desensitising vaccines should only be used for seasonal allergic hay fever (which has not responded to anti-allergy drugs) caused by pollens. The CSM has also advised that facilities for cardiopulmonary resuscitation must be immediately available and patients must be monitored closely for one hour after each injection. Patients with asthma should not be treated, as they are more likely to develop severe adverse reactions. Immunotherapy should also be avoided in pregnant women and children under five years old.

Cost

There is no information regarding the cost of Gravax at the current time.

A complete pre-seasonal course of Pollinex costs £320.00^a.

Current research evidence

Effectiveness

Trial GT-08

In a multicentre, randomised, double-blind, placebo-controlled, phase III trial, the safety and efficacy of Grazax was assessed in 634 patients with seasonal grass pollen induced rhinoconjunctivitis⁶. Primary outcomes included the recording of rhinoconjunctivitis symptoms and use of rescue medication. Secondary outcomes included quality of life. The results showed that Grazax reduced hay fever symptoms by 30% and reduced the need for symptom-relieving medication by 38% compared with placebo⁷. No other results of the study are currently available.

Trial GT-07

In a multicentre, double-blind study, 114 patients with moderate-to-severe rhinoconjunctivitis and mild-to-moderate asthma induced by grass pollen were randomised 2:1 to receive Grazax or placebo 10-14 weeks prior to and during the grass pollen season⁸. The primary endpoints

^a Costs based on the British National Formulary No. 50 (September 2005)

were average asthma medication and symptom scores during the grass pollen season. Secondary variables were average rhinoconjunctivitis symptom and medication scores during the grass pollen season. The number of well-days was defined *post hoc*. Relative to placebo, the grass pollen allergy tablet reduced rhinoconjunctivitis symptoms by 37% ($p=0.004$) and the need for symptom-relieving medication by 41% ($p=0.036$). Well-days increased by 54% ($p=0.002$). However, differences in asthma medication and symptom scores between treatment groups were negligible. The mean difference in asthma medication score was below 0.1 and 0.3 for asthma symptom score (a single inhalation of salbutamol (200 µg) was scored as 2). No serious adverse events were reported.

Trial GT-02

In a multicentre, randomised, double-blind phase II study, 855 patients with seasonal allergic rhinitis induced by grass pollen received either placebo or Grazax (0.5, 5 or 15 µg/day)^{9,10}. Treatment began eight weeks prior to the allergy season and continued for a mean duration of 18 weeks. Compared to placebo, Grazax, at a dose of 15 µg/day, improved rhinoconjunctivitis symptom scores by 21% and medication scores by 29% ($p\leq 0.01$), and quality of life by 20% ($p<0.05$). The majority of adverse events were minor. They occurred within the first five minutes and resolved within 30 minutes.

Cost-effectiveness

No published cost-effectiveness studies have been identified, although the company state economic studies are ongoing.

Adverse effects

No safety concerns have been identified during the clinical trials, even in patients with mild to moderate asthma.

Ongoing or related research

A double-blind, placebo-controlled extension of GT-08 is ongoing to document the long-term effects of Grazax. In addition, two safety trials in children (GT-09 and GT-11) are planned to start in 2006.

Cost impact and projected diffusion

Until the position of Grazax in the treatment pathway of seasonal allergic rhinitis and its price is confirmed, it is difficult to estimate the potential cost impact. If Grazax does enter the market as a baseline therapy, as many as 3-9M patients may be suitable candidates, the vast majority of whom currently control symptoms at their own expense with over-the-counter preparations. If only 50% of these people were to receive this treatment, and Grazax was priced in line with current immunotherapy, the cost to the NHS could be significant. However, the uptake of Grazax is likely to be moderate in the first instance.

Symptom reduction, less dependence on symptom-reducing medications and improved quality of life that is sustained after stopping treatment may be welcomed by patients, as would a sublingual preparation of immunotherapy. It is anticipated that Grazax will be introduced

through specialist clinics initially, but could then move into the primary care setting if safety over the long-term can be substantiated.

References

- ¹ Bauchau, V, Durham, S.R. Prevalence and rate of diagnosis of allergic rhinitis in Europe. *European Respiratory Journal*. 2004; 24: 758-764.
- ² Mason, P. Management of hay fever in the pharmacy. *The Pharmaceutical Journal*. 2003; 270: 443-445.
- ³ Scadding, G.K., Richards, D.H. and Price, M.J. Patient and physician perspectives on the impact and management of perennial and seasonal allergic rhinitis. *Clinical Otolaryngology & Allied Sciences*. 2000; 25, 551-557.
- ⁴ White, P., Smith, H., Baker N., Davis, W., Frew., A. Symptom control in patients with hay fever in UK general practice: how well are we doing and is there a need for allergen immunotherapy? *Clinical and Experimental Allergy*. 1998; 28: 266-270.
- ⁵ PRODIGY guidance – allergic rhinitis. Available online at <http://www.prodigy.nhs.uk/guidance.asp?gt=Allergic%20rhinitis#8894>. Accessed 22/12/2005.
- ⁶ Controlled-trials. A randomised, parallel-group, double blind, placebo-controlled phase III trials assessing the efficacy and safety of ALK grass tablet in subjects with seasonal grass pollen induced rhinoconjunctivitis. Available online at <http://www.controlled-trials.com/mrct/trial/123185>. Accessed 22/12/2005.
- ⁷ ALK-Abelló Annual Report. Highlights of the year. Available online at <http://ar0405.alk-abello.com/Menu/Summary/Highlights+of+the+year>. Accessed 22/12/2005.
- ⁸ Dahl, R., Stender, A., Rak, S. Specific immunotherapy with SQ standardised grass allergen tablets in asthmatics with rhinoconjunctivitis. *Journal of Allergy and Clinical Immunology*. 2006; 61: 185-190.
- ⁹ Calderon, MA., Rak, S., Durham, SR. Grass pollen tablets for sublingual immunotherapy in seasonal allergic rhinitis. *Journal of Allergy and clinical immunology*. 115 (Suppl.): 65 (plus oral presentation) abstract 261, No. 2 (Feb 2005).
- ¹⁰ ALK-Abello Company presentation. Available online at <http://www.alk-abello-investor.com/DC1088B6-46EB-432D-B9B9-3356511E99E2>. Accessed 22/12/2005.

The National Horizon Scanning Centre is funded by the Research and Development Division of the Department of Health, UK

The National Horizon Scanning Centre,
Department of Public Health and Epidemiology
University of Birmingham, Edgbaston, Birmingham, B15 2TT, England
Tel: +44 (0)121 414 7831 Fax +44 (0)121 414 2269
www.pcpoh.bham.ac.uk/publichealth/horizon