Cost-effectiveness of grass allergen tablet (GRAZAX) for the prevention of seasonal grass pollen induced rhinoconjunctivitis: a Northern European perspective

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Record Status
This is a critical abstract of an economic evaluation that meets the criteria for inclusion on NHS EED. Each abstract contains a brief summary of the methods, the results and conclusions followed by a detailed critical assessment on the reliability of the study and the conclusions drawn.

Health technology
The authors investigated the use of a grass allergen tablet (GRAZAX) for the prevention of grass pollen-induced rhinoconjunctivitis. This intervention was compared with symptomatic medication.

Type of intervention
Primary prevention.

Economic study type
Cost-utility analysis.

Study population
The study population comprised patients allergic to grass pollen.

Setting
The study setting was primary care. The economic analysis was performed in 7 European countries. Specifically, the United Kingdom, Germany, the Netherlands, Sweden, Denmark, Norway and Finland.

Dates to which data relate
The effectiveness and resource use data were derived from a study carried out in the 2005 pollen season. The price year was 2005.

Link between effectiveness and cost data
Some elements of resource use (i.e. use of symptomatic medication, hospitalisation and hours missed from work) were obtained prospectively from a sub-sample of the patients in the effectiveness study. As the authors adopted a Northern European perspective, they only analysed trial data on resource use and quality of life for the 493 study patients from the UK, Germany, the Netherlands, Denmark and Sweden.

Study sample
The authors only provided a summary of the methods used in the effectiveness study as further details were published elsewhere (Dahl et al. 2006, see 'Other Publications of Related Interest' for bibliographic details). In the study, 316 patients were enrolled to a grass allergen tablet arm and 318 patients to a placebo arm.

Study design
The study was a randomised, double-blind, placebo-controlled trial that was carried out as part of a multinational trial in 8 European countries (Austria, Denmark, Germany, Italy, the Netherlands, Spain, Sweden and the UK). The authors did
not report the loss to follow-up or the duration of the trial. The time horizon of the trial appears to have been one pollen season.

**Analysis of effectiveness**
The authors did not report whether the analysis was conducted on an intention to treat basis. The primary health outcomes used were the improvements in rhinoconjunctivitis symptom and medication scores and quality of life scores. Quality of life scores were derived using validated country-specific versions of the EuroQol-5D (EQ-5D) instrument. The authors did not report the time points at which quality of life was assessed. It would appear from the demographic data provided in the present article that both groups were comparable at analysis (see Dahl et al. 2006 for further details).

**Effectiveness results**
Patients receiving the grass allergen tablets showed a 30% reduction in rhinoconjunctivitis symptom score and a 38% reduction in rhinoconjunctivitis medication score, (p<0.0001), compared with placebo. The authors did not specify the time point at which this statistic applied.

The mean quality of life was 0.976 in the grass allergen tablet group (n=212) compared with 0.947 in the symptomatic treatment group (n=208), (p<0.001). The authors did not specify the time point at which this statistic applied.

**Clinical conclusions**
The results from the trial showed that the grass allergen tablets were effective at preventing rhinoconjunctivitis and that they improved the patients' quality of life.

**Modelling**
The authors extrapolated the results from the trial-based economic evaluation to a 9-year time horizon, using linear extrapolation. The duration of the trial was one pollen season. Since the grass allergen tablets would be taken for 3 consecutive years, it was assumed that the effectiveness would be the same for the first 3 years and there would be an additional sustained effect for a further 6 years.

**Measure of benefits used in the economic analysis**
The measure of benefits used was the quality-adjusted life-years (QALYs) gained. To obtain QALYs, the quality of life scores were assigned utility weights based on random preferences of approximately 3,000 members of the UK population. The QALYs were discounted according to country-specific discount rates (between 3% and 5%).

**Direct costs**
The direct costs to the health care system were used in the study. These included physician visits, acute ward hospital stay, symptomatic rescue medication for allergic rhinitis and asthma, and hospitalisation. Patients recorded symptomatic medication and hospitalisation in diaries on a daily basis. The number of standard physician visits was based on evidence from a European survey. The authors reported that protocol-driven resource use, such as monitoring visits, was not included in the analysis as these costs would not be incurred in real life settings. Further, as no patient reported a hospital visit, this resource use was not included in the analysis. The unit costs for each country were derived from a number of sources, including tariffs and retail drug prices. Since the costs were incurred during 9 years, discounting was relevant and was appropriately undertaken. The discount rate ranged from 3 to 5%, depending on country-specific guidelines.

**Statistical analysis of costs**
Resource use and costs were treated as point estimates (i.e. the data were deterministic).
Indirect Costs
The productivity costs included in the analysis were the hours missed from work for each patient. Patients recorded the number of hours missed from work on a daily basis. The unit costs for work hours missed were estimated using average wage rates reported by national statistics bureaus from the 7 countries.

Currency
Euros (EUR).

Sensitivity analysis
The authors undertook a one-way sensitivity analysis by varying the annual costs of the allergen tablets between EUR 1,200 and EUR 4,400.

Estimated benefits used in the economic analysis
When extrapolating the results of the trial, the number of QALYs gained using allergen tablets compared with symptomatic treatment was 0.222, discounted at 4% per annum.

Cost results
The costs associated with each group in the trial were not reported.

Synthesis of costs and benefits
The costs and benefits were combined using an incremental cost-utility analysis (i.e. the additional cost per QALY gained).

Using EUR 1,500 for the annual treatment cost of the grass allergen tablet, the cost per QALY gained ranged from EUR 12,930 in the Netherlands to EUR 18,263 in Germany.

The results also showed that, when the total annual cost of the grass allergen tablets was below EUR 2,300, the tablets would be cost-effective at a threshold of EUR 29,200 per QALY in all 7 countries.

When using a health care system perspective, the annual cost of the allergen tablets should be below EUR 2,200 for them to be cost-effective at the EUR 29,200 per QALY threshold.

Authors’ conclusions
Allergen-specific immunotherapy with the grass allergen tablet was a cost-effective intervention for the prevention of grass pollen-induced rhinoconjunctivitis in Northern European countries, for a tablet price of below EUR 6.00.

CRD COMMENTARY - Selection of comparators
The justification given for using symptomatic treatment as the comparator was that it represented current practice in the authors’ settings. You should decide if the comparator used represents current practice in your own setting.

Validity of estimate of measure of effectiveness
The authors provided only a brief summary of the methods and results of the effectiveness study as these had been published elsewhere. The study would appear to be both internally and externally valid as the results were based on data from a randomised, double-blind, placebo-controlled clinical trial carried out in 8 countries. The long-term effectiveness was derived from published studies on an active ingredient in the tablet. The details of these studies were not reported.

Validity of estimate of measure of benefit
The measure of benefits used was the QALYs. These were derived directly from the trial and then extrapolated over a 9-year time horizon. The EQ-5D was used on a sub-sample of Northern European study participants to derive the utilities used to construct QALYs. These were assigned weights using results from a representative UK population.

Validity of estimate of costs
The analysis of the costs was performed from a societal perspective. It would appear that, given this perspective, no major relevant resource use categories were omitted. The authors reported that protocol-driven costs, such as monitoring visits, were excluded since they would not be incurred in real life settings. Resource use was derived from the study participants and the published literature. The unit costs were derived from a variety of sources including tariffs and drug price lists. The authors did not report the costs for each group. Cost-utility analyses were performed by varying the annual costs of the allergen tablets between EUR 1,200 and EUR 4,400. Since the costs were incurred during 9 years, discounting was relevant and was appropriately performed. The price year was reported, which will aid any future inflation exercises. The costs and the quantities were not reported separately, which will limit the generalisability of the authors' results.

Other issues
The authors reported that, to their knowledge, this was the first study that analysed the cost-effectiveness of sublingual immunotherapy according to pharmacoeconomic evaluation guidelines. The issue of generalisability to other settings was addressed as the results were based on 7 northern European countries. The authors do not appear to have presented their results selectively and their conclusions reflected the scope of the analysis. The authors reported as a limitation to their study the fact that reduced productivity and possible increased efficacy of the intervention were not included, which might have led to an underestimation of the true effect of the intervention.

Implications of the study
The authors reported that allergen-specific immunotherapy with the grass allergen tablet ought to be seen as an important part of the optimal treatment for allergic rhinoconjunctivitis in Northern Europe.

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Other publications of related interest
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