Cost-effectiveness of omalizumab in patients with severe persistent allergic asthma

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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 study examined the addition of omalizumab to standard care. Omalizumab is an anti-IgE antibody used in addition to standard therapy for the treatment of patients with severe persistent allergic asthma. Omalizumab was assumed to be given for 5 years at an average of 27.7 vials per year. The comparator was standard care alone.

Type of intervention
Treatment.

Economic study type
Cost-utility analysis.

Study population
The study population comprised patients with severe persistent allergic (IgE-mediated) asthma that remained inadequately controlled despite optimal pharmacological treatment. Specifically, only patients who were receiving high-dose inhaled corticosteroid (ICS) plus a long-acting beta agonist (plus additional controller medication if required) were considered.

Setting
The setting was secondary care. The economic study was carried out in Canada.

Dates to which data relate
The effectiveness data were derived from studies published between 1997 and 2005. The resource use data were based on data derived from studies published in 2004 and 2005. The price year was not reported.

Source of effectiveness data
The clinical parameters included in the decision model were severe and non-severe exacerbation rates, omalizumab dosing pattern, exacerbation-related fatality rates and all-cause mortality rates.

Modelling
A Markov model was used to model disease progression. The model was mainly based on one developed elsewhere (Dewilde et al. 2006, see ‘Other Publications of Related Interest’ below for bibliographic details). The model was not represented graphically. The time horizon of the model was lifetime, but the cycle length was not reported. The three health states in the model were reported. No other details were provided.

Sources searched to identify primary studies
Much of the data on exacerbations and dosing pattern were derived from the 1-year, randomised, open-label trial of
omalizumab (the ETOPA study). All these data were obtained from a sub-group of patients in the ETOPA study that better represented the study population analysed. Severe exacerbations that were not specifically recorded in the ETOPA study were assumed to have been similar to the rates observed in the INNOVATE study, a 28-week randomised controlled trial. Exacerbation-related fatality rates came from a community-based study, the design of which was not described. All-cause mortality rates were obtained from Statistics Canada.

**Methods used to judge relevance and validity, and for extracting data**

Overall, the process used to identify the data was not reported. It is possible that the primary studies might have been identified selectively. The authors stated that the ETOPA study was chosen as the main source of effectiveness data because its results could be considered to be more representative of real clinical practice in comparison with a standard randomised controlled trial such as the INNOVATE study.

**Measure of benefits used in the economic analysis**

The summary benefit measure used was the quality-adjusted life-years (QALYs). Quality of life weights were derived from two sources (i.e. the ETOPA trial and a prospective study conducted at four specialty asthma centres in the UK), depending on the Markov disease state. In the prospective study patients had moderate-to-severe asthma. Discounting was not explicitly reported, but it appears that a 5% discount rate has been used for future benefits.

**Direct costs**

The viewpoint of the analysis appears to have been that of the health service payer. The categories of costs included were those related to the treatment of exacerbations, drugs and routine visits. The costs associated with omalizumab administration were not included in the base-case analysis. The unit costs were not presented separately from the resource quantities. Only the average cost per clinically significant severe and non severe exacerbation were reported. The quantities of resources used were derived from the ETOPA trial and the INNOVATE study. The economic analysis relied on the assumption of full compliance. The costs were based on data from the Ontario Schedule of Benefits and fees, as well as data from the Canadian Institute of Health Information. Discounting was relevant, as the long-term costs were measured, and an annual discount rate of 5% was used. The price year was not reported.

**Statistical analysis of costs**

The costs were treated deterministically.

**Indirect Costs**

The productivity costs were not included.

**Currency**

Euros (EUR).

**Sensitivity analysis**

A probabilistic sensitivity analysis was run to define confidence intervals around the incremental cost-utility ratios, and acceptability curves were presented. Parameter distributions were not reported. A univariate sensitivity analysis was also carried out on key variables such as discounting, time horizon, the inclusion of administration costs and the mortality rate. The choice of alternative values was justified, mainly on the basis of alternative published evidence.

**Estimated benefits used in the economic analysis**

The expected QALYs associated with standard therapy were 6.49 and the additional QALYs associated with omalizumab were 1.08.
**Cost results**
The lifetime discounted costs for standard therapy were EUR 27,403, while the additional cost of add-on omalizumab was EUR 33,854.

**Synthesis of costs and benefits**
An incremental cost-utility ratio was calculated in order to combine the costs and benefits.

The incremental cost per QALY gained for omalizumab added to standard therapy in comparison with standard therapy alone was EUR 31,209.

The probabilistic sensitivity analysis showed that the 95% confidence interval around the cost per QALY was EUR 27,739 to EUR 40,840. The probability that omalizumab was cost-effective given a threshold of EUR 35,000 per QALY was 69.7%.

The deterministic sensitivity analysis showed that the incremental cost per QALY ranged from EUR 23,762 (when not discounted) to EUR 66,443 (when asthma-related mortality was excluded). Omalizumab was less attractive when the time horizon was restricted to 5 years (incremental cost per QALY of EUR 52,394). The inclusion of omalizumab administration costs did have a minimal effect on the results of the base case analysis.

**Authors’ conclusions**
Add-on omalizumab was a cost-effective therapy in patients with severe persistent allergic asthma.

**CRD COMMENTARY - Selection of comparators**
The rationale for the choice of the comparator was clear in that it represented the standard care in the authors’ setting. You should decide whether this represents a valid comparator in your own setting.

**Validity of estimate of measure of effectiveness**
The authors combined data from an existing model with data from a clinical trial and other studies. No systematic search for data was reported. It appears that the parameters for the model have mainly been identified selectively. It was stated that the ETOPA study was chosen because it seemed more representative of real-life clinical practice with respect to standard clinical trials, given its design (open-label trial in a naturalistic setting). However, some data also had to be taken from a randomised controlled trial, and the potential heterogeneity between these studies was not investigated. Some assumptions were also made. Since limited information on the primary studies was provided, it is not possible to judge the validity of the data on the basis of the information reported in this paper.

**Validity of estimate of measure of benefit**
The estimation of QALYs was derived appropriately using a Markov model. In the base-case, the QALYs appear to have been discounted in accordance with Canadian guidelines and alternative discount rates were considered in the sensitivity analysis. Some information on the methods used to estimate the utility weights was provided and their sources were explicitly reported. QALYs can be compared with the benefits of other health care interventions.

**Validity of estimate of costs**
The authors did not explicitly state the perspective chosen in the cost analysis, but only the direct medical costs were considered. The unit costs, which were partially reported, and the resource quantities were not presented separately, which limits the possibility of replicating the analysis in other settings. Statistical analyses of the costs were not performed and the cost estimates were specific to the study setting. The sources of the cost and resource consumption data were given for all items. The price year was not reported, which will hamper reflation exercises in other time periods. Discounting was appropriately performed.
Other issues
The authors made some comparisons of their findings with those from other studies, stating that their results were much more favourable than those achieved in the economic evaluation of omalizumab based exclusively on data from the INNOVATE study. It was noted that better results for cost-effectiveness analyses based on naturalistic studies, as opposed to clinical trials, had also been found in a study on etanercept in rheumatoid arthritis. The issue of the generalisability of the study results to other settings was not explicitly addressed, although some sensitivity analyses based on alternative scenarios were considered. The authors noted some limitations of the analysis, such as the use of assumptions and the need to extrapolate 1-year data to a lifetime horizon.

Implications of the study
The study results support the use of omalizumab for the treatment of patients with severe persistent allergic asthma.

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Other publications of related interest
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