

NICE guidance on omalizumab for severe asthma



NICE National Institute for Health and Care Excellence

Published Online
April 24, 2013
[http://dx.doi.org/10.1016/S2213-2600\(13\)70066-3](http://dx.doi.org/10.1016/S2213-2600(13)70066-3)

On April 24, 2013, the National Institute for Health and Care Excellence (NICE) published guidance recommending omalizumab as an option for severe, persistent, confirmed allergic (IgE-mediated) asthma. This treatment is recommended as an addition to optimised standard therapy in people aged 6 years and older who need continuous or frequent treatment with oral corticosteroids (defined as four or more courses in the previous year), only if the manufacturer provides omalizumab with the confidential discount agreed in the patient access scheme.¹

Omalizumab was appraised under the Multiple Technology Appraisal process. Both the manufacturer (Novartis, Frimley, UK)² and an independent Assessment Group (the Centre for Reviews and Dissemination/Centre for Health Economics Technology Assessment Group, York, UK) submitted evidence on the clinical effectiveness and cost-effectiveness of omalizumab.³ The Appraisal Committee met three times to develop the guidance and to take evidence from invited experts.

Evidence centred on 11 randomised controlled trials that compared omalizumab with placebo or with no added treatment. Nine trials included adults and adolescents, one included children, and one included both children and adolescents. Three trials (INNOVATE, EXALT, and Chanez and colleagues) had populations that met or closely approximated the UK marketing authorisation for adults and adolescents. Two trials (IA-04 in adults and IA-05 in children) contained subgroups that resembled the marketing authorisation (see appendix for the study references).

Results suggested a benefit for people randomised to omalizumab over the comparator, in terms of number of clinically significant exacerbations and prevention of exacerbations.

The manufacturer developed a model to compare the costs and

health outcomes of omalizumab added to standard care compared with standard care alone in people with severe, persistent, uncontrolled allergic asthma, despite high-dose inhaled corticosteroids plus a long-acting beta₂ agonist. This model structure had been used in NICE technology appraisals 133 and 201 and extrapolated the effects of treatment with omalizumab over the lifetimes of patients. Modelled patients had omalizumab in addition to standard care, or standard care alone. After 16 weeks, people on omalizumab whose asthma improved remained on the treatment for up to 10 years, and were assumed to have exacerbations at the rates observed for responders to treatment in trials. People on omalizumab whose asthma did not improve stopped the treatment, as specified in the marketing authorisation, reverted to standard care, and were assumed to have exacerbations at the rates of patients in trials randomised to standard care.

The manufacturer assumed that asthma-related deaths occurred only during a clinically significant severe exacerbation, and increased with age, as documented by Watson and colleagues⁴ in people admitted to hospital for severe asthma. The manufacturer's estimated base-case deterministic incremental cost-effectiveness ratio (ICER) for omalizumab plus standard care compared with standard care in adults and adolescents was £32 076 per quality-adjusted life year (QALY) gained, and £80 747 per QALY gained for children.

The Assessment Group modelled the effectiveness of omalizumab for adults and adolescents using evidence from INNOVATE and for children from the IA-05 European population. In its base case, it estimated asthma-related mortality from de Vries and colleagues,⁵ which used data from the General Practice Research Database and was constant across all ages. The Assessment Group considered health-

related quality of life associated with day-to-day symptoms of asthma using EQ-5D data from EXALT, whereas the manufacturer had used a regression equation to map scores from the asthma quality-of-life questionnaire from INNOVATE onto EQ-5D.

For children, the Assessment Group assumed that omalizumab improved health-related quality of life equal to that of adults and adolescents, whereas the manufacturer's model assumed that health-related quality of life for children did not improve with omalizumab, based on the trial evidence. For adults and adolescents, adding omalizumab to standard care compared with standard care alone resulted in an estimated ICER of £83 822 per QALY gained, and for children £78 009 per QALY gained.

The Committee considered that the risk of asthma-related mortality associated with severe, persistent asthma was uncertain, probably falling between the estimates from Watson and colleagues⁴ and those from de Vries and colleagues.⁵ For utility, the Committee preferred the Assessment Group's approach, in which the same utility gain was assumed for all age groups and EQ-5D values directly collected in EXALT were used, in line with the NICE reference case.⁶

The Committee considered that omalizumab was innovative in its potential to lead to substantial health-related benefits. It recognised that the model did not capture some benefits associated with omalizumab from the avoidance of adverse effects from oral corticosteroids. The Committee concluded that the potential additional health-related benefits for carers could not currently be quantified.

During the appraisal, the Committee asked the Assessment Group to analyse three populations with very severe persistent allergic asthma in which omalizumab would be considered:⁶ people on maintenance oral corticosteroids who were

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admitted to hospital in the year before treatment with omalizumab; people on maintenance oral corticosteroids not necessarily admitted to hospital in the year before treatment (NICE technology appraisal 133 requires a patient to have been admitted to hospital for a clinically significant severe exacerbation in the year before starting omalizumab; the Committee heard from an expert that admission to hospital as a prerequisite for treatment provides a perverse incentive); and people on maintenance or frequent courses of oral corticosteroids³ who have not necessarily been admitted to hospital in the year before treatment.

The Committee asked the Assessment Group to assume a 10% increase in the efficacy of omalizumab seen in INNOVATE, and a 15% increase in asthma-related mortality to reflect very severe uncontrolled asthma. The Committee requested pooled analyses for children, adolescents, and adults to explore the development of a single recommendation for all populations included in the marketing authorisation.⁷ The Committee appreciated that these assumptions reduced the ICERs for omalizumab, but the ICERs in the combined population exceeded £30 000 per QALY.

Subsequently, the manufacturer agreed a patient access scheme with the Department of Health.⁸ The Committee noted that the manufacturer's revised analyses that incorporated the patient access scheme also varied the proportion of children in the overall population eligible for omalizumab because of Committee concerns that the Assessment Group's original percentage of 2.2% might underestimate the true proportion. The manufacturer's revised ICERs for people on maintenance or frequent courses of oral corticosteroids, but who have not necessarily been hospitalised in the year before treatment were

£23 453, £23 902, and £24 370 per QALY gained when the proportion of children in the overall population was 2.2%, 4.75%, and 7.3%, respectively. Although 7.3% reflected the proportion of children in England and Wales, it did not necessarily reflect the proportion of children in a population eligible for omalizumab, and the Committee preferred a value of 4.75%. However, since the proportion of children did not greatly affect cost-effectiveness, the Committee preferred analyses that pooled adults, adolescents, and children as the basis for a recommendation.

The Committee considered the manufacturer's analyses that incorporated an asthma-related mortality rate midpoint between those of Watson and colleagues⁴ and de Vries and colleagues,⁵ an increase of 15% to reflect very severe uncontrolled asthma, a value of 4.75% to reflect the proportion of children in the population eligible for omalizumab, and the cost of omalizumab with the patient access scheme. This assessment resulted in an ICER of £23 200 per QALY gained when the addition of omalizumab was compared with standard therapy for adults, adolescents, and children on maintenance or frequent courses of oral corticosteroids (four or more courses in the year before receiving omalizumab).

The Committee considered comments on the appraisal consultation document suggesting that omalizumab can have life-changing effects on patients⁹ and reduce dependence on corticosteroids. The Committee concluded that, with the patient access scheme, omalizumab offered a cost-effective use of NHS resources for the treatment of severe, persistent, confirmed allergic (IgE-mediated) asthma in people aged 6 years and older who need continuous or frequent oral corticosteroid treatment, and

recommended it as an option for treatment in this population.¹⁰

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We declare that we have no conflicts of interest.

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Supplementary appendix

This appendix formed part of the original submission. We post it as supplied by the authors.

Supplement to: Diaz RA, Charles Z, George E, Adler AI. NICE guidance on omalizumab for severe asthma. *Lancet Respir Med* 2013; published online April 24. [http://dx.doi.org/10.1016/S2213-2600\(13\)70066-3](http://dx.doi.org/10.1016/S2213-2600(13)70066-3).

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Extra references

INNOVATE

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EXALT

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Chanez

Chanez P, Contin-Bordes C, Garcia G, et al. Omalizumab-induced decrease of FcRI expression in patients with severe allergic asthma. *Respir Med* 2010; **104**: 1608–17.

IA-04 trial

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IA-05 trial

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