

Issue date: November 2007

Review date: August 2010

Omalizumab for severe persistent allergic asthma

**This guidance was developed using the
single technology appraisal process**

NICE technology appraisal guidance 133 Omalizumab for severe persistent allergic asthma

Ordering information

You can download the following documents from www.nice.org.uk/TA133

- The full guidance (this document).
- A quick reference guide for healthcare professionals.
- Information for people with severe persistent allergic asthma and their carers ('Understanding NICE guidance').
- Details of all the evidence that was looked at and other background information.

For printed copies of the quick reference guide or 'Understanding NICE guidance', phone the NHS Response Line on 0870 1555 455 and quote:

- N1404 (quick reference guide)
- N1405 ('Understanding NICE guidance').

This guidance is written in the following context

This guidance represents the view of the Institute, which was arrived at after careful consideration of the evidence available. Healthcare professionals are expected to take it fully into account when exercising their clinical judgement. The guidance does not, however, override the individual responsibility of healthcare professionals to make decisions appropriate to the circumstances of the individual patient, in consultation with the patient and/or guardian or carer.

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1 Guidance

- 1.1 Omalizumab is recommended, within its licensed indication, as an option for the treatment of severe persistent allergic (IgE mediated) asthma as add-on therapy to optimised standard therapy, only in adults and adolescents (12 years and older) who have been identified as having severe unstable disease.
- 1.2 For the purposes of this guidance, optimised standard therapy is defined as a full trial of, and documented compliance with, inhaled high-dose corticosteroids and long-acting beta-2 agonists in addition to leukotriene receptor antagonists, theophyllines, oral corticosteroids and beta-2 agonist tablets and smoking cessation where clinically appropriate.
- 1.3 Omalizumab add-on therapy should only be initiated if the patient fulfils the following criteria of severe unstable allergic asthma.
- Confirmation of IgE mediated allergy to a perennial allergen by clinical history and allergy skin testing.
 - Either two or more severe exacerbations of asthma requiring hospital admission within the previous year, or three or more severe exacerbations of asthma within the previous year, at least one of which required admission to hospital, and a further two which required treatment or monitoring in excess of the patient's usual regimen, in an accident and emergency unit.
- 1.4 Omalizumab add-on therapy should be initiated and monitored by a physician experienced in both allergy and respiratory medicine in a specialist centre.

- 1.5 Omalizumab add-on therapy should be discontinued at 16 weeks in patients who have not shown an adequate response to therapy. Response to treatment should be defined on the basis of a full clinical assessment comprising: degree of asthma control, quality of life, control of exacerbations, avoidance of unscheduled healthcare utilisation; spirometry and peak expiratory flow measures and a global evaluation of treatment effectiveness, as assessed by the physician.

2 The technology

- 2.1 Omalizumab (Xolair, Novartis Pharmaceuticals UK) is a recombinant humanised monoclonal antibody that inhibits the binding of IgE to high affinity receptors (FcεRI) on the surface of mast cells and basophils. It prevents the release of pro-inflammatory mediators and reduces allergen-induced airway reactions. Omalizumab is licensed as add-on therapy to improve asthma control in adult and adolescent patients (12 years and older) with severe persistent allergic asthma who have a positive skin test or in vitro reactivity to a perennial aeroallergen and who have reduced lung function (forced expiratory volume in 1 second, FEV1 < 80%) as well as frequent daytime symptoms or night-time awakenings and who have had multiple documented severe asthma exacerbations despite daily high-dose inhaled corticosteroids, plus a long-acting inhaled beta-2 agonist. The licensed indication states that omalizumab treatment should only be considered for patients with convincing IgE mediated asthma.
- 2.2 The most common side effects of omalizumab treatment are bruising, erythema and pain at the site of injection. Rare side effects include increased risk of parasitic infections, anaphylaxis, usually within 2 hours of the first injection and possible drug-

induced malignancies. The prescribing information has been revised based on post marketing surveillance data and indicates that allergic reactions, including anaphylaxis and anaphylactic shock, may occur beyond 2 hours and sometimes beyond 24 hours of first injection. Patients should be informed that such reactions are possible and prompt medical attention should be sought if allergic reactions occur. For full details of side effects and contraindications, see the summary of product characteristics (SPC).

- 2.3 Omalizumab is administered subcutaneously every 2–4 weeks. The dosage is determined by baseline IgE before the start of treatment (measured in international units per millilitre, IU/ml) and body weight (in kg; see the SPC). Omalizumab is available as a powder for reconstitution with solvent; the net price of a 150 mg vial is £256.15 (excluding VAT; British National Formulary [BNF] edition 53). The cost of a 375 mg dose of omalizumab (the maximum recommended dose in the SPC) administered every 2 weeks is approximately £15,400 per patient per annum (excluding VAT). Alternatively, if a 150 mg dose of omalizumab is administered every 4 weeks the cost would be approximately £3,100 per patient per annum (excluding VAT). Costs may vary in different settings because of negotiated procurement discounts.

3 The manufacturer's submission

The Appraisal Committee (appendix A) considered evidence submitted by the manufacturer of omalizumab and a review of this submission by the Evidence Review Group (ERG; appendix B).

- 3.1 The manufacturer approached the decision problem by looking at adults and adolescents (12 years and older) with severe persistent

(IgE mediated) allergic asthma in accordance with the marketing authorisation. Omalizumab as add-on therapy to standard therapy was compared with standard therapy alone, which included inhaled corticosteroids, long-acting beta-2 agonists, short-acting beta-2 agonists, oral corticosteroids, leukotriene antagonists and where appropriate, theophylline. Health outcome measures included the rate of clinically significant asthma exacerbations, the rate of clinically significant severe exacerbations and the rate of emergency visits for asthma. In the manufacturer's submission, clinically significant exacerbations were defined as a worsening of asthma symptoms requiring treatment with systemic corticosteroids. Clinically significant severe exacerbations were defined as a peak expiratory flow rate or FEV₁ < 60% of personal best, requiring treatment with systemic corticosteroids.

- 3.2 The manufacturer's submission presented evidence on the clinical effectiveness of omalizumab add-on therapy based on the results of the pivotal INNOVATE randomised controlled trial (RCT). Following amendments to the INNOVATE trial protocol, partly to reflect revisions of the Global Initiative on Asthma (GINA) guidelines, the manufacturer presented results on a primary intention-to-treat (PITT) population that excluded 13% of randomised patients prior to the implementation of the protocol amendments. The patient population in the INNOVATE RCT underwent a 7-day screening period for evaluating eligibility, followed by an 8-week run-in phase during which asthma management was reviewed and optimised to include advice on allergen avoidance, theophylline monitoring (if applicable) and inhaler technique in order to achieve best control. Efficacy analyses of the PITT population showed that the rate of clinically significant exacerbations in the omalizumab arm (0.74) was lower than in the

standard therapy (placebo) arm (0.92) but this difference was not statistically significant (rate ratio 0.806; 95% confidence interval [CI] 0.600 to 1.083, $p = 0.153$). When post hoc statistical adjustments for baseline asthma exacerbations were made, clinically significant exacerbations were less frequent in the omalizumab arm (0.68) compared with the standard therapy (placebo) arm (0.91). This difference was statistically significant (rate ratio 0.738; 95% CI 0.552 to 0.988, $p = 0.042$). Clinically significant severe exacerbations were also lower in the omalizumab arm of the trial (0.24) than in the placebo arm (0.48) and this was statistically significant (rate ratio 0.499; 95% CI 0.321 to 0.777, $p = 0.002$). Omalizumab-treated patients showed statistically significant improvements from baseline in their asthma quality of life questionnaire (AQLQ) scores: 91% versus 46% in the placebo arm ($p < 0.001$).

- 3.3 The manufacturer's submission also presented post hoc efficacy analyses of a high-risk subgroup, consisting of 39% of patients in the INNOVATE RCT, who had asthma exacerbations requiring hospital admission in the year prior to enrolling in the trial. There was a lower rate of clinically significant exacerbations in the omalizumab arm (0.78) compared to the standard therapy (placebo) arm (1.19; rate ratio 0.656; 95% CI 0.427 to 1.009, $p = 0.153$). Post hoc statistical adjustments to reflect differences in baseline asthma exacerbations which the manufacturer described as clinically relevant, but which were not statistically significant, resulted in a rate ratio of 0.714 (95% CI 0.481 to 1.062, $p = 0.096$). Clinically significant severe exacerbations were also lower in the omalizumab arm of the trial (0.361) versus 0.658 in the placebo arm (rate ratio 0.55; 95% CI not reported, $p = 0.155$). Omalizumab-treated patients showed statistically significant improvements from

baseline in their AQLQ scores (94% versus 36% in the placebo arm, $p = 0.002$). The manufacturer's submission also referred to a study which suggested a correlation between hospitalisation and asthma-related mortality.

- 3.4 The manufacturer's submission presented another post hoc subgroup analysis versus standard therapy, identifying omalizumab responders in both the PITT population and the high risk hospitalisation subgroup according to a rating of excellent or good on the physician global evaluation of treatment effectiveness (GETE) scale at the end of the study. The results were presented to indicate greater treatment effect experienced by patients continuing omalizumab therapy beyond 16 weeks. No p values were given.
- 3.5 The manufacturer specifically presented additional clinical evidence from an open label trial, ETOPA (IA-04), to support the clinical efficacy and safety results from the INNOVATE study. However, patients recruited to ETOPA (IA-04) had moderate to severe asthma and only 52.6% of randomised patients met the inclusion criteria for the INNOVATE study. The rationale for including ETOPA (IA-04) was that it represented 'real life' clinical practice because randomised patients in both arms of the trial did not receive optimised standard therapy. The clinical results from the ETOPA (IA-04) subpopulation who met the INNOVATE inclusion criteria were used to inform the economic analysis as an alternative base-case.
- 3.6 The manufacturer's submission presented an economic analysis comparing omalizumab add-on therapy to standard therapy with standard therapy alone using a Markov transition model with a lifetime horizon of 40 years. The economic model had five health

states: day-to-day symptoms, clinically significant non-severe exacerbations, clinically significant severe exacerbations, asthma death and non-asthma death. In the manufacturer's model it was assumed that the population cohort are assessed at 16 weeks for response to omalizumab treatment, after which omalizumab non-responders switch back to standard therapy and have similar responses and exacerbation rates as the standard therapy group in the model.

- 3.7 The economic analysis was performed for the INNOVATE PITT population and the high-risk hospitalisation subgroup. Base-case analysis for the INNOVATE PITT population produced an incremental cost effectiveness ratio (ICER) of £30,600 per QALY gained and an ICER of £26,500 per QALY gained for the high-risk hospitalisation subgroup. The manufacturer also presented an alternative base-case analysis using subpopulation data from the ETOPA (IA-04) trial that gave an ICER of £21,700 per QALY gained.
- 3.8 One-way sensitivity analyses presented in the manufacturer's submission suggested that the key drivers of the economic model were asthma mortality rate from clinically significant severe exacerbations, omalizumab treatment duration and time horizon. Notably, assuming an asthma mortality rate of 0% from clinically significant severe exacerbations, the base-case ICER increases to £73,200 per QALY gained. Assuming the asthma-related mortality rate is 2.478% gives an ICER of £33,500 per QALY gained. The manufacturer's submission presented a probabilistic sensitivity analysis that showed a mean ICER of £31,700 per QALY gained (95% CI, £23,200 to £48,200 per QALY). No probabilistic sensitivity analysis was performed for the high-risk hospitalisation subgroup.

- 3.9 The ERG identified a number of issues with the parameters used in the economic model and uncertainties relating to the economic analyses presented in the manufacturer's submission. The ERG commented that the one-way sensitivity analysis in the manufacturer's submission was performed on a limited number of parameters and that the ranges of parameter values investigated were inappropriate. The ERG carried out an amended one-way sensitivity analysis that showed that the key drivers of the economic model were utility values assigned to omalizumab responders, the costs of omalizumab and asthma mortality rate.
- 3.10 The ERG in particular noted uncertainties surrounding the following parameter assumptions: costing of omalizumab on a per mg basis, utility values assigned to non-severe clinically significant exacerbations, clinically significant severe exacerbations and asthma mortality rate. The ERG therefore explored a number of scenario analyses on alternative assumptions for these parameters. The scenario analyses for the INNOVATE PITT population ranged from £33,300 to £40,900 per QALY gained while the scenario analyses for the high-risk hospitalisation subgroup ranged from £29,800 to £34,300 per QALY gained. The ERG performed an amended probabilistic sensitivity analysis that showed greater uncertainty around the ICERs for the INNOVATE PITT population than suggested in the manufacturer's economic analyses. The ERG's amended probabilistic sensitivity analysis showed a mean ICER of £38,900 per QALY gained. At a threshold willingness to pay of £30,000 per QALY, omalizumab add-on therapy was estimated to have a 23.6% probability of being cost effective. No probabilistic sensitivity analysis was performed for the high-risk hospitalisation subgroup.

- 3.11 Full details of all the evidence are in the manufacturer's submission and the ERG report, which are available from www.nice.org.uk/TA133

4 Consideration of the evidence

- 4.1 The Appraisal Committee (appendix A) reviewed the data available on the clinical and cost effectiveness of omalizumab, having considered evidence (appendix B) on the nature of the condition and the value placed on the benefits of omalizumab by people with severe persistent allergic asthma, those who represent them, and clinical specialists. It was also mindful of the need to take account of the effective use of NHS resources.
- 4.2 The Committee discussed the decision problem in the context of the NHS in England and Wales and the evidence submitted. It heard from clinical specialists that in clinical practice the population for whom omalizumab treatment is suitable requires careful identification, and that in practice is more narrowly defined than in the marketing authorisation and the pivotal INNOVATE RCT. The Committee considered the appropriate comparator for omalizumab to be fully optimised treatment with existing therapies, noting that clinicians would always wish to establish optimised therapy in an individual patient before commencing omalizumab. It understood that the optimised standard therapy that patients received in the INNOVATE RCT, at baseline, would broadly correspond to patients having had a full trial of and documented compliance with all steps of the 'British Guideline on the Management of Asthma' 2005 (British Thoracic Society [BTS] /Scottish Intercollegiate Guidelines Network [SIGN]).

4.3 The Committee noted that omalizumab as an add-on to standard therapy has been shown to reduce the rate of clinically significant severe exacerbations and emergency visits, and was associated with improvements in quality of life. The Committee however noted a degree of uncertainty surrounding the improvements observed for the primary efficacy outcome of the INNOVATE RCT because statistical significance was only reached after an adjustment for an imbalance in baseline asthma exacerbations. The Committee agreed with the ERG that there were aspects of the INNOVATE RCT that led to uncertainty, including lack of detail on concealment of treatment allocation, the possibility of inadequate double blinding, selection bias, and exclusion of randomised patients from the intention-to-treat (ITT) population. However, the Committee heard from clinical specialists that the blinding of the INNOVATE RCT had been carried out rigorously in centres where they had been involved. Further, the Committee noted that results of several other omalizumab clinical trials offered support to the conclusions from the INNOVATE trial. The Committee heard from patient experts and clinical specialists that omalizumab has resulted in life-changing improvements in quality of life for some patients with severe unstable IgE mediated asthma. The Committee concluded that omalizumab as an add-on to optimised standard therapy is more clinically effective in particular groups of patients than optimised standard therapy alone.

4.4 The Committee discussed the identification of patients for whom omalizumab add-on therapy is suitable and most clinically effective. It heard from clinical experts that, in practice, patients deemed eligible for omalizumab treatment would have had their existing standard treatments optimised as well as having behavioural and psychosocial issues addressed. The Committee noted that the

INNOVATE trial protocol excluded smokers and patients with a smoking history of equal to or greater than 10 pack years. The Committee further heard from the clinical specialists that omalizumab should only be considered in non-smokers and that adherence to a smoking cessation regime was part of the optimisation of care for all asthmatics. The clinical experts stressed that omalizumab treatment should only be initiated after a comprehensive and exhaustive assessment including establishment of correct diagnosis and compliance with standard treatments. The Committee understood that asthmatic patients who are known to be refractory to high-dose oral corticosteroids may be less likely to respond to omalizumab treatment, whereas omalizumab may provide steroid-sparing benefits for patients on lower doses of oral steroids. The Committee appreciated that there was no definitive RCT evidence in this respect. The Committee concluded that it would only be clinically appropriate to consider the use of omalizumab add-on therapy once standard therapy has been optimised and that for the purposes of this guidance, optimised standard therapy is defined as a full trial of, and documented compliance with, inhaled high-dose corticosteroids and long-acting beta-2 agonists in addition to leukotriene receptor antagonists, theophyllines, oral corticosteroids and beta-2 agonist tablets and smoking cessation where clinically appropriate. It noted that despite uncertainty in the post hoc analysis in the high-risk subgroup of the INNOVATE RCT, evidence suggested greater effectiveness in this group, particularly on quality of life.

- 4.5 The Committee initially understood that most adverse events associated with omalizumab were mild and manageable and that serious potential adverse effects such as anaphylaxis were rare and usually occur within 2 hours of injection. The Committee,

however, noted the revised prescribing information in the SPC, based on post-marketing surveillance data. This indicated that allergic reactions, including anaphylaxis and anaphylactic shock, may occur beyond 2 hours, sometimes beyond 24 hours of first injection, and that patients should be informed that such reactions are possible and prompt medical attention should be sought if allergic reactions occur. The Committee also noted that in 35 completed trials of omalizumab, malignancies were reported in 25 of 5015 (0.50%) omalizumab-treated patients compared with 5 of 2854 (0.18%) standard therapy-treated patients. The Committee, however, understood that there was considerable uncertainty as to whether these malignancies were attributable to omalizumab treatment.

4.6 The Committee discussed the following parameters which it considered to be key in determining the cost effectiveness of omalizumab in the INNOVATE trial population and the high-risk hospitalisation subgroup specified by the manufacturer:

- asthma-related mortality risk from clinically significant severe exacerbations
- utility values assigned to omalizumab non-responders and standard therapy
- the time horizon of the model and assumptions made over the long term, such as treatment duration
- the basis for estimating drug costs.

4.7 The Committee considered the mortality rate associated with clinically significant severe exacerbations and noted that this was one of the key drivers of the model. In the manufacturer's base-case, cost per QALY gained for the INNOVATE trial population was

£30,600 assuming a 3.1% mortality rate, but this increased to £36,400 with an assumption of 2% mortality (ERG sensitivity analysis), and £73,200 assuming no effect on mortality. The Committee heard from the clinical specialists that asthma-related mortality is rare and tends to occur in patients with poorly controlled asthma and low adherence to treatment. Such patients would not usually be considered appropriate for omalizumab therapy on the basis of the marketing authorisation, because they could not fulfil the requirement for full optimisation of therapy. Additionally, the Committee considered that the assumption of a 2% mortality rate for this group of severe asthmatics may be an overestimate. Therefore the Committee considered the ICER of £30,500 (corresponding to a 2% asthma mortality rate) for the high-risk hospitalisation subgroup to be an underestimate of the true cost per QALY gained unless a subgroup of patients at a higher risk was defined. The Committee considered that the cost effectiveness evidence relating to the economic analysis of the high-risk hospitalisation subgroup from the INNOVATE trial was the most appropriate of those presented by the manufacturer. It discussed whether there is correlation between frequency of recent hospital admissions and risk of asthma mortality. It was of the opinion that patients who needed more frequent emergency medical attention and hospital admissions than the high risk hospitalisation subgroup would plausibly have a higher risk of asthma mortality. The Committee concluded that the use of omalizumab was likely to be cost effective in such a subset of patients within the high-risk hospitalisation subgroup. These patients were identified as those who have had either two or more severe exacerbations of asthma requiring hospital admission within the previous year, or three or more severe exacerbations of asthma within the previous year, at least one of which required admission to hospital, and a further two

which required treatment or monitoring in excess of the patient's usual regimen, in an accident and emergency unit.

- 4.8 The Committee discussed the utility values used for the health states in the manufacturer's model. In particular, the Committee discussed a scenario analysis explored by the ERG, in which utility values for standard therapy and omalizumab non-responders were estimated from baseline response to AQLQ for all patients rather than from the standard care patients at 28 weeks in the INNOVATE RCT. The Committee thought that this scenario was not a reasonable basis for estimating cost effectiveness as it reflects uneven treatment of placebo effect and optimisation of care in the treatment and control arms. The Committee concluded that the ICER of £34,300 per QALY gained given by the ERG scenario analyses for the high-risk hospitalisation subgroup was more appropriate without the use of utility values estimated from baseline AQLQ scores for omalizumab non-responders and standard therapy.
- 4.9 The Committee discussed the time horizon over which ICERs were estimated in the manufacturer's model. It considered, in principle, that a lifetime horizon was appropriate, but was aware of the uncertainties introduced by extrapolating the results of the 28 week INNOVATE trial. The Committee concluded that it would be acceptable to consider ICERs estimated over a 20 year time horizon.
- 4.10 The Committee discussed the assumption made about treatment duration in the manufacturer's model. It heard from clinical specialists that asthma severity (and therefore the treatments required by patients) can vary during a patient's lifetime. The Committee understood that omalizumab treatment is not curative

and that long-term therapy would be required to control symptoms, therefore the base-case assumption that omalizumab treatment would discontinue after 5 years may not be appropriate. The Committee however noted that the economic results from the manufacturer's model were not very sensitive to changes in the assumption for omalizumab treatment duration. The Committee concluded that it would be acceptable to consider ICERs based on assuming 5 years omalizumab treatment duration.

- 4.11 The Committee understood that in clinical practice omalizumab is discontinued if there is no adequate response to treatment after 16 weeks. Careful assessment of the response to omalizumab treatment is made using all available criteria including: assessment of daily symptoms, quality of life assessment (mini-AQLQ), frequency of exacerbations (an asthma worsening episode requiring additional oral corticosteroids), spirometric and peak expiratory flow measurements and unplanned consultations for asthma. The Committee noted that the manufacturer had developed and presented an assessment protocol for evaluating treatment response that included the criteria listed above and a global evaluation of treatment effectiveness scale (GETE), to be completed by a physician. The Committee was of the opinion that all the available assessments and achieving excellent or good in the GETE would be essential to continue treatment beyond 16 weeks.
- 4.12 The Committee considered the basis for estimating omalizumab drug costs in the manufacturer's model. It noted that this had been done on a per-mg basis (assuming no wastage and reuse of unused vial portions) and that in scenarios in which omalizumab drug costs were estimated on a per-vial basis, the ICERs for

omalizumab were higher. It was mindful that vial sharing might not be feasible in primary care settings. However, the Committee heard from patient experts and clinical specialists that vial wastage could be avoided reasonably easily in regional specialist centres where larger numbers of patients are treated. The Committee therefore concluded that the ICERs for omalizumab in comparison with standard therapy may be lower when omalizumab is administered in a dedicated session in a specialist day care setting where vial wastage can be minimised.

4.13 The Committee further considered that the costs and health impact of long-term adverse effects had not been modelled, including the potentially increased rate of omalizumab-induced malignancies. However, it accepted that this adverse effect has an uncertain and unproven relationship with omalizumab therapy. The Committee noted that failure to account for the costs and health impact of adverse events may however have underestimated the ICERs for omalizumab treatment when compared to standard therapy.

4.14 Overall, therefore, the Committee concluded that there were a number of considerations which meant the ICER was higher than acceptable for patients with severe persistent allergic asthma. However, the Committee was persuaded that for a narrowly defined severely affected group of asthma patients, at an elevated risk of asthma-related mortality, cost-effective treatment with omalizumab was possible, if therapy was discontinued in non-responders at 16 weeks and if vial wastage could be minimised to reduce costs. The Committee concluded that omalizumab add-on therapy is recommended as an option for the treatment of asthma in patients with severe unstable disease (that is, those who have had either two or more severe exacerbations of asthma requiring hospital admission within the previous year, or three or more severe

exacerbations of asthma within the previous year, at least one of which required admission to hospital, and a further two which required treatment or monitoring in excess of the patient's usual regimen, in an accident and emergency unit), who have clinical confirmation of IgE mediation of asthma exacerbations and have had a full trial of, and documented compliance with all standard asthma medication (see 4.4). It also concluded that omalizumab treatment should only be initiated and monitored by physicians experienced in both allergy and chest medicine in a specialist centre.

5 Implementation

- 5.1 The Healthcare Commission assesses the performance of NHS organisations in meeting core and developmental standards set by the Department of Health in 'Standards for better health' issued in July 2004. The Secretary of State has directed that the NHS provides funding and resources for medicines and treatments that have been recommended by NICE technology appraisals normally within 3 months from the date that NICE publishes the guidance. Core standard C5 states that healthcare organisations should ensure they conform to NICE technology appraisals.
- 5.2 'Healthcare Standards for Wales' was issued by the Welsh Assembly Government in May 2005 and provides a framework both for self-assessment by healthcare organisations and for external review and investigation by Healthcare Inspectorate Wales. Standard 12a requires healthcare organisations to ensure that patients and service users are provided with effective treatment and care that conforms to NICE technology appraisal guidance. The Assembly Minister for Health and Social Services issued a Direction in October 2003 which requires Local Health Boards and

NHS Trusts to make funding available to enable the implementation of NICE technology appraisal guidance, normally within 3 months.

5.3 NICE has developed tools to help organisations implement this guidance (listed below). These are available on our website (www.nice.org.uk/TA133).

- Costing report and costing template to estimate the savings and costs associated with implementation.
- Audit criteria to monitor local practice.

6 Related NICE guidance

- Inhaled corticosteroids for the treatment of chronic asthma in children under the age of 12 years. NICE technology appraisal guidance 131 (2007). Available from: www.nice.org.uk/TA131
- Inhaler devices for routine treatment of chronic asthma in older children (aged 5–15 years). NICE technology appraisal guidance 38 (2002). Available from: www.nice.org.uk/TA038
- Guidance on the use of inhaler systems (devices) in children under the age of 5 years with chronic asthma. NICE technology appraisal guidance 10 (2000). Available from: www.nice.org.uk/TA010

NICE is developing the following guidance (details available from www.nice.org.uk).

- Inhaled corticosteroids for the treatment of chronic asthma in adults and children aged 12 years and over. NICE technology appraisal guidance (publication date to be confirmed).

7 Review of guidance

- 7.1 The review date for a technology appraisal refers to the month and year in which the Guidance Executive will consider whether the technology should be reviewed. This decision will be taken in the light of information gathered by the Institute, and in consultation with consultees and commentators.
- 7.2 The guidance on this technology will be considered for review in August 2010.

Andrew Dillon
Chief Executive
November 2007

Appendix A: Appraisal Committee members and NICE project team

A *Appraisal Committee members*

The Appraisal Committee is a standing advisory committee of the Institute. Its members are appointed for a 3-year term. A list of the Committee members who took part in the discussions for this appraisal appears below. The Appraisal Committee meets three times a month except in December, when there are no meetings. The Committee membership is split into three branches, each with a chair and vice chair. Each branch considers its own list of technologies, and ongoing topics are not moved between the branches.

Committee members are asked to declare any interests in the technology to be appraised. If it is considered there is a conflict of interest, the member is excluded from participating further in that appraisal.

The minutes of each Appraisal Committee meeting, which include the names of the members who attended and their declarations of interests, are posted on the NICE website.

Professor David Barnett

Professor of Clinical Pharmacology, University of Leicester

Dr David W Black

Director of Public Health, Chesterfield PCT

Professor Mike Campbell

Professor of Medical Statistics, University of Sheffield

Dr Carol Campbell

Senior Lecturer, University of Teesside

Mr Peter Clarke

Consultant Medical Oncologist, Clatterbridge Centre for Oncology,
Merseyside

Ms Jude Cohen

Chief Executive, Womens Nationwide Cancer Control Campaign

Dr Christine Davey

Senior Researcher, North Yorkshire Alliance R&D Unit

Dr Mike Davies

Consultant Physician, Manchester Royal Infirmary

Mr Richard Devereaux-Phillips

Public Affairs Manager, Medtronic Ltd

Dr Rachel A Elliott

Clinical Senior Lecturer, The University of Manchester

Mrs Eleanor Grey

Lay member

Dr Dyfrig Hughes

Senior Research Fellow in Pharmacoeconomics, Centre for the Economics of
Health and Policy in Health, University of Wales

Dr Catherine Jackson

Clinical Lecturer in Primary Care Medicine, Alyth Health Centre

Dr Peter Jackson

Clinical Pharmacologist, the University of Sheffield

Professor Peter Jones

Professor of Statistics & Dean Faculty of Natural Sciences, Keele University

Ms Rachel Lewis

Nurse Adviser to the Department of Health

Dr Damien Longson

Consultant in Liaison Psychiatry, Manchester Mental Health and Social Care Trust

Professor Jonathan Michaels

Professor of Vascular Surgery, University of Sheffield

Dr Eugene Milne

Deputy Medical Director, North East Strategic Health Authority

Dr Simon Mitchell

Consultant Neonatal Paediatrician, St Mary's Hospital, Manchester

Dr Richard Alexander Nakielny

Consultant Radiologist, Royal Hallamshire Hospital, Sheffield

Dr Katherine Payne

Health Economics Research Fellow, The University of Manchester

Dr Martin J Price

Head of Outcomes Research, Janssen-Cilag Ltd

Mr Miles Scott

Chief Executive, Bradford Teaching Hospitals NHS Foundation Trust

Professor Mark Sculpher

Professor of Health Economics, University of York

Professor Andrew Stevens (Chair)

Professor of Public Health, University of Birmingham

B NICE project team

Each technology appraisal is assigned to a team consisting of one or more health technology analysts (who act as technical leads for the appraisal), a technical adviser and a project manager.

Ebenezer Tetteh

Technical Lead

Helen Chung

Technical Adviser

Chris Feinmann

Project Manager

Appendix B: Sources of evidence considered by the Committee

A The Evidence Review Group (ERG) report for this appraisal was prepared by Southampton Health Technology Assessment Centre (SHTAC):

- Jones J et al. Omalizumab for severe persistent allergic asthma, March 2007.

B The following organisations accepted the invitation to participate in this appraisal. They were invited to comment on the draft scope, the ERG report and the appraisal consultation document (ACD). Organisations listed in I were also invited to make written submissions. Organisations listed in II gave their expert views on omalizumab by providing a written statement to the Committee. Organisations listed in I and II have the opportunity to appeal against the final appraisal determination.

I Manufacturer/sponsor:

- Novartis Pharmaceuticals Ltd

II Professional/specialist and patient/carer groups:

- Asthma UK
- British Paediatric Respiratory Society
- British Society for Allergy & Clinical Immunology (BSCAI)
- British Thoracic Society
- Cochrane Airways Group
- Department of Health
- General Practice Airways Group (GPIAG)
- Royal College of General Practitioners
- Royal College of Nursing
- Royal College of Paediatrics and Child Health
- Royal College of Physicians
- Royal Pharmaceutical Society of Great Britain
- UK Clinical Pharmacy Association (UKCPA)

- Welsh Assembly Government
- III Commentator organisations (did not provide written evidence and without the right of appeal):
- British National Formulary
 - Department of Health, Social Services and Public Safety for Northern Ireland
 - Education for Health
 - NHS Quality Improvement Scotland
- C The following individuals were selected from clinical specialist and patient advocate nominations from the non-manufacturer/sponsor consultees and commentators. They gave their expert personal view on omalizumab by attending the initial Committee discussion and providing written evidence to the Committee. They were invited to comment on the ACD.
- Dr Huw Thomas, Consultant Respiratory Paediatrician, nominated by the Royal College of Paediatrics and Child Health – clinical specialist
 - Dr Dermot Ryan, General Practitioner, nominated by General Practice Airways Group – clinical specialist
 - Professor Edwin Chilvers, Professor of Respiratory Medicine, nominated by Asthma UK – clinical specialist
 - Ms Trish Martin, nominated by Asthma UK – patient expert
 - Samantha O'Reilly, nominated by Asthma UK – patient expert