

Issue date: October 2010

Omalizumab for the treatment of severe persistent allergic asthma in children aged 6 to 11 years

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

NICE technology appraisal guidance 201
Omalizumab for the treatment of severe persistent allergic asthma in children aged 6 to 11 years

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- The NICE guidance (this document).
- A quick reference guide – the recommendations.
- ‘Understanding NICE guidance’ – a summary for patients and carers.
- Details of all the evidence that was looked at and other background information.

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- N2332 (quick reference guide)
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1 **Guidance**

- 1.1 Omalizumab is not recommended for the treatment of severe persistent allergic asthma in children aged 6 to 11 years.
- 1.2 Children currently receiving omalizumab for the treatment of severe persistent allergic asthma should have the option to continue treatment until it is considered appropriate to stop. This decision should be made jointly by the clinician and the child and/or the child's parents or carers.

2 **The technology**

- 2.1 Omalizumab (Xolair, Novartis) is a monoclonal antibody that binds to immunoglobulin E (IgE). Initially omalizumab had marketing authorisation as an add-on therapy to improve control of asthma in adults and adolescents (12 years and older) with severe persistent allergic asthma. The marketing authorisation was extended in July 2009 to children aged 6 to 11 years who have severe persistent allergic asthma, a positive skin test or in-vitro reactivity to a perennial aeroallergen, frequent daytime symptoms or night-time awakenings, and multiple documented severe exacerbations of asthma despite daily high-dose inhaled corticosteroids plus a long-acting inhaled beta-2 agonist. The marketing authorisation states that omalizumab treatment 'should only be considered for patients with convincing IgE (immunoglobulin E) mediated asthma'. It also recommends that at 16 weeks after the start of therapy physicians should assess patients for the effectiveness of treatment before administering further injections, and that the decision to continue omalizumab should be based on whether a marked improvement in overall asthma control is seen.
- 2.2 The most common adverse events reported with omalizumab treatment in children aged under 12 years include headache,

pyrexia and upper abdominal pain. Rare side effects in children and adults include parasitic infections and anaphylactic reactions. For the full details of adverse events and contraindications, see the summary of product characteristics (SPC).

- 2.3 Omalizumab is administered subcutaneously every 2 or 4 weeks. The dosage is determined by the concentration of serum IgE before the start of treatment (measured in international units per millilitre [IU/ml]) and body weight. The price of omalizumab is £256.15 per 150-mg vial (excluding VAT; 'British national formulary' [BNF] edition 59). The dosage administered is 75–600 mg every 2 or 4 weeks, up to a maximum dosage of 600 mg every 2 weeks. Dose and dosing frequency are determined by baseline serum total IgE (measured before the start of treatment) and body weight, and dosing is restricted to patients with a baseline IgE level of 30–1500 IU/ml and a body weight of 20–150 kg. The cost of omalizumab ranges from approximately £1,665 per patient per year (excluding VAT) for a 75 mg dose administered every 4 weeks to approximately £26,640 per patient per year (excluding VAT) for a 600 mg dose (the maximum recommended dose in the SPC) administered every 2 weeks. 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 children aged 6 to 11 years with severe allergic IgE-mediated asthma in accordance with the marketing authorisation. Omalizumab as add-on therapy to standard care was compared with standard care alone. Standard care included high-dose inhaled corticosteroids, long-acting beta-2 agonists and, where appropriate,

oral corticosteroids. The manufacturer included the following measures as health outcomes: clinically significant asthma exacerbations, clinically significant severe asthma exacerbations, emergency visits for asthma, use of oral corticosteroids, response to treatment as measured by the patients' and investigators' Global Evaluation of Treatment Effectiveness (GETE) 5-point scale, mortality, adverse effects of treatment and health-related quality of life. The outcome 'symptom-free days and nights' listed in the scope for this appraisal was not included; instead the manufacturer provided data relating to changes in morning, day, night-time and total symptom scores as an alternative endpoint.

- 3.2 In the manufacturer's submission, clinically significant exacerbations were defined as a worsening of asthma symptoms, as judged clinically by the investigator, which required doubling of the baseline dose of inhaled corticosteroid and/or treatment with rescue systemic (oral or intravenous) corticosteroids for at least 3 days. Clinically significant severe exacerbations were defined as exacerbations that required treatment with systemic corticosteroids and when the child had a peak expiratory flow rate or forced expiratory volume at 1 second (FEV1) of less than 60% of their personal best.
- 3.3 The manufacturer's submission presented evidence on the clinical effectiveness of add-on therapy with omalizumab based on the results of study IA-05, a randomised controlled trial (RCT). The study was an international, multicentre, double-blind, placebo-controlled trial in children aged 6 to 11 years with allergic (skin test-positive) asthma whose disease was inadequately controlled despite regular treatment with inhaled corticosteroids (fluticasone dry powder inhaler equal to or greater than 200 micrograms per day or equivalent, with or without other controlled asthma medications). Children were randomised at a ratio of 2:1 omalizumab plus standard care:standard care alone

and were treated with omalizumab plus standard care or standard care alone for 52 weeks. The manufacturer presented results from a modified intention-to-treat population (n = 576) that excluded the children from two sites where there was incomplete, inconsistent or missing source documentation.

- 3.4 As the IA-05 study focused on children with moderate to severe asthma, a subpopulation with more severe asthma was specified prospectively to provide efficacy data aligned with the pre-existing European Union marketing authorisation in adults and children aged 12 years and over. The manufacturer referred to this subpopulation of the IA-05 study as the 'European Union Population (EUP)'. Standard care for children in the EUP was inhaled corticosteroids (fluticasone at a dosage of at least 500 micrograms per day) and long-acting beta-2 agonists. They included 159 of the 384 (41%) children randomised to omalizumab plus standard care and 76 of the 192 (40%) children randomised to standard care alone. The primary analyses were conducted in the EUP.
- 3.5 Analyses of the the EUP showed that in children treated with omalizumab plus standard care compared with those treated with standard care alone, a statistically significant reduction in the number of clinically significant exacerbations was observed during the 24-week fixed-corticosteroid phase (when the dose of inhaled corticosteroid was kept constant) (relative risk [RR] 0.662, 95% confidence interval [CI] 0.441 to 0.995). During the 52-week treatment phase with omalizumab plus standard care or standard care alone every 2 or 4 weeks the RR was 0.504 (95% CI 0.350 to 0.725). There was no statistically significant difference in the number of clinically significant severe exacerbations between the omalizumab plus standard care and standard care alone groups either during the 24-week fixed-corticosteroid phase (RR 0.665, 95% CI 0.302 to 1.421) or during the 52-week treatment phase (RR

0.545, 95% CI 0.274 to 1.084). The analyses for hospitalisation and/or emergency medical consultation showed that there were no statistically significant differences between the groups in hospitalisation rates, accident and emergency visits, unscheduled doctor visits or total emergency visits during the 24-week fixed-corticosteroid phase or the 52-week treatment phase.

- 3.6 Symptom-free days and nights were not recorded in the IA-05 study. At the request of the ERG, the manufacturer provided the number and proportion of days that scored zero for daytime and night-time symptoms. At baseline a mean of 18.4% of children in the omalizumab plus standard care group and 17.0% of children in the standard care alone group were without daytime symptoms. During the final 4 weeks of the 52-week treatment phase 54.3% of children in the omalizumab plus standard care group and 53.7% of children in the standard care alone group were without daytime symptoms. At baseline a mean of 32.5% of children in the omalizumab plus standard care group and 29.2% of children in the standard care alone group were without night-time symptoms. During the final 4 weeks of the 52-week treatment phase 66.2% of children in the omalizumab plus standard care group and 61.2% of children in the standard care alone group were without night-time symptoms.
- 3.7 At the request of the ERG, the manufacturer also presented data on the effect of omalizumab on exacerbation rates, stratified by the number of exacerbations experienced in the year before randomisation. The results of this analysis in the EUP showed a statistically significant decrease in the rate of clinically significant exacerbations with omalizumab plus standard care during both the 24-week fixed-corticosteroid phase (RR 0.481, 95% CI 0.305 to 0.758) and the 52-week treatment phase (RR 0.388, 95% CI 0.254 to 0.592) in children who had had three or more exacerbations in the year before randomisation. There was no statistically significant

effect for children who had had fewer than three exacerbations in the year before randomisation.

- 3.8 The manufacturer's submission presented a post-hoc efficacy analysis for a high-risk subgroup, the EUP hospitalisation subgroup, which was defined by a recent (within the previous year) hospitalisation for an asthma exacerbation. Of the 50 children in this subgroup (8.7% of the population in study IA-05) 37 were randomised to omalizumab plus standard care and 13 were randomised to standard care alone. In this EUP hospitalisation subgroup, omalizumab plus standard care reduced the rate of clinically significant exacerbations by 26% during the 52-week treatment phase (RR 0.741, 95% CI 0.331 to 1.663) and 47% (RR 0.525, 95% CI 0.221 to 1.245) during the 28-week adjustable-corticosteroid phase (when corticosteroid doses were reviewed at each visit and could be reduced by 25–50%), both compared with standard care alone. Omalizumab plus standard care was also associated with reductions in the rate of clinically significant severe exacerbations of 8% during the 24-week fixed-corticosteroid phase (RR 0.922, 95% CI 0.298 to 2.857), 34% during the 52-week treatment phase (RR 0.655, 95% CI 0.219 to 1.958) and 53% during the 28-week adjustable-corticosteroid phase (RR 0.465, 95% CI 0.126 to 1.720) respectively, compared with standard care alone. However, the differences between groups for both clinically significant and clinically significant severe exacerbations did not reach statistical significance. The manufacturer had considered presenting a post-hoc efficacy analysis for a second high-risk subgroup, the 'maintenance oral corticosteroid' group, which included only children with more severe asthma symptoms who would be considered to be at step 5 of the 'British guideline on the management of asthma' (British Thoracic Society/Scottish Intercollegiate Guidelines Network 2009). However, the small number (n = 6) of children in this subgroup (all of whom were in the omalizumab plus standard care group of the IA-05 study) precluded

any analysis of the efficacy of omalizumab for this high-risk subgroup.

- 3.9 The manufacturer's submission also included a post-hoc 'responder' subgroup of the EUP population. Responders were defined as children who were rated as excellent or good on the GETE scale after 52 weeks of treatment. Of the children receiving omalizumab plus standard care, 74.2% were identified by physicians as responders, compared with 55.3% of children receiving standard care alone ($p < 0.0001$).
- 3.10 Data on oral corticosteroid use were not collected in the IA-05 study. The manufacturer conducted a small, non-systematic survey of oral corticosteroid use in paediatric patients (aged 6 to 11 years) treated with omalizumab in four centres in the UK. All 18 children surveyed who were having maintenance oral corticosteroid therapy were able to stop or reduce the dose of oral corticosteroid.
- 3.11 Health-related quality of life was assessed using the Paediatric Asthma Quality of Life Questionnaire (PAQLQ) in the IA-05 study. The PAQLQ is a standardised questionnaire containing 23 questions in three domains (symptoms, activity limitation and emotional function). There were no statistically significant differences between the omalizumab plus standard care and standard care alone groups in any of the domains or overall PAQLQ scores in the EUP population during the 24-week fixed-corticosteroid phase or the 52-week treatment phase.
- 3.12 The manufacturer presented the adverse events from the European Public Assessment Report (EPAR) produced by the European Medicines Agency. Approximately 94% of the EUP experienced at least one adverse event. The most frequently reported adverse events were nasopharyngitis, upper respiratory tract infection and sinusitis. There was a 10% higher incidence of pyrexia in children

receiving omalizumab plus standard care compared with children receiving standard care alone.

- 3.13 The manufacturer's submission presented an economic analysis comparing omalizumab add-on therapy with standard care alone using a Markov-based patient-level model with a lifetime horizon of 90 years. The model had five health states: day-to-day asthma symptoms; clinically significant exacerbation, clinically significant severe exacerbation, death from all causes and asthma-related death. Transition between all health states apart from transition to death was based on children observed in the EUP population from the IA-05 study. Mortality rates used in the model were taken from a UK-based study by Watson and colleagues (2007) as there were no deaths during the IA-05 study. The Watson study was based on hospital episodes of all-cause deaths admitted under International Classification of Disease codes for hospital asthma and acute severe asthma. The study found the annual mortality rate was 0.097% for people aged under 12 years, 0.319% for people aged 12 to 16 years, 0.383% for people aged 17 to 44 years and 2.48% for people aged 45 years and over. The model's first cycle lasted for 16 weeks, with subsequent cycles of 3 months, and a half-cycle correction was applied.
- 3.14 In the model the group of children having omalizumab add-on therapy was divided at 16 weeks into responders and non-responders. The children who were classified as responders continued treatment with omalizumab and their exacerbation rate was informed by the rate of exacerbations observed in omalizumab responders in the second part of the trial. The children who were classified as non-responders returned to standard care alone and were assumed to have the same exacerbation rates as children in the standard care alone arm of the trial. The period of 16 weeks reflects the time at which the assessment of response should be made according to the marketing authorisation. The manufacturer

assumed that any response at 16 weeks would be the same as that observed in the IA-05 study at 52 weeks, that is, at this 16-week timepoint, the model used response data from the IA-05 study assessment at 52 weeks.

- 3.15 Data on utility values were not available from the IA-05 study as it did not measure utility directly and no mapping function is available to map from the PAQLQ to the EQ-5D. Therefore, data from other sources were used to inform the utility values applied in the model. The manufacturer used data from the INNOVATE study (which evaluated omalizumab as an add-on therapy for adults with severe persistent allergic asthma) to inform the utility values of the day-to-day symptoms state for each treatment. Separate utility values were estimated for the day-to-day symptoms for patients receiving standard care only and for those receiving omalizumab in addition to standard care, using patients' responses to the Adult Asthma Quality of Life Questionnaire (AQLQ) at week 28 of the INNOVATE study. These data were mapped to EQ-5D values using a published mapping function by Tsuchiya and colleagues (2002). The average utility score of omalizumab responders was estimated to be 0.779 and that of patients on standard care alone was assumed to be 0.669). However, as the PAQLQ administered as part of the IA-05 study did not show a significant difference between treatment groups, the manufacturer's submission assumed the lower value (0.669) for children in both groups until 12 years of age, at which point omalizumab responders were assigned the higher score (0.779).
- 3.16 Neither the IA-05 EUP subpopulation nor the INNOVATE study provided values of utility associated with exacerbations. Instead, the manufacturer used EQ-5D values from a prospective study conducted in the UK at four speciality asthma centres (Lloyd et al. 2007). It provided EQ-5D scores for adults with controlled disease, oral corticocorticosteroids with unscheduled physician visits and

asthma-related hospital admissions. The manufacturer assumed that these groups were equivalent to the following health states in the economic model: no clinically significant exacerbation, clinically significant exacerbation and clinically significant severe exacerbation. The manufacturer assumed that the absolute utility values observed in the study (0.572 and 0.326 respectively) were applicable to the patients in the health states 'clinically significant' and 'clinical significant severe' in the model. Exacerbations were assumed to last for an average of 17.1 days, based on data from the EUP.

- 3.17 Data on resources consumed during clinically significant and clinically significant severe exacerbations were available from the EUP. However, the manufacturer did not differentiate between clinically significant exacerbations and clinically significant severe exacerbations and the average cost was calculated across, and applied to, all exacerbations.
- 3.18 The economic analysis was performed for the EUP and the hospitalisation subgroup. For omalizumab plus standard care the base-case analysis for the EUP produced an incremental cost of £55,623, an incremental quality-adjusted life year (QALY) of 0.61 and an incremental cost-effectiveness ratio (ICER) of £91,188 per QALY gained. The analysis for the EUP hospitalisation subgroup produced an incremental cost of £40,890, an incremental QALY of 0.62 and an ICER of £65,911 per QALY gained, both compared with standard care alone.
- 3.19 In the manufacturer's original submission the model included an age-related regression for the utility associated with exacerbations. Following a request from the ERG the manufacturer provided new results for the base case that excluded the age-related regression applied to the utility values in the model. The ICER was reduced from £91,188 to £91,169 per QALY gained.

3.20 One-way sensitivity analyses presented in the manufacturer's submission suggested that the following scenarios had an impact on the base-case ICER, but none reduced the ICER to below £68,029 per QALY gained: duration of treatment with omalizumab, utility for day-to-day symptoms state; age at start of therapy, rate of mortality due to clinically significant severe exacerbations and cost of omalizumab. The one-way sensitivity analyses undertaken by the manufacturer showed that a shortened treatment duration markedly increases the ICER. For treatment durations of 2, 5 and 20 years the ICERs for the EUP increased to £684,665, £137,902 and £77,589 per QALY gained respectively. Probabilistic sensitivity analyses suggested that if the maximum acceptable cost for an additional QALY gained were either £20,000 or £30,000, omalizumab has a 0.0% probability of being cost effective.

3.21 Data on the cost effectiveness of omalizumab in the subgroup of children receiving maintenance oral corticosteroids were not presented in the manufacturer's submission because the small number of children receiving maintenance oral corticosteroids at baseline, all of whom were in the omalizumab plus standard care group, precluded a comparative analysis.

3.22 In general, the ERG considered the manufacturer's economic evaluation to be of good quality, meeting most of the requirements of the NICE reference case. The ERG considered the structure of the Markov model appropriate for the decision problem. The ERG noted the following concerns about the manufacturer's model.

- The rates of response to treatment used in the model were derived from the IA-05 EUP subgroup at 52 weeks rather than at 16 weeks as specified in the marketing authorisation.
- Exacerbation rates were not determined by the modified intention-to-treat analysis of the clinical trial but by comparing the rates observed in children who responded to omalizumab plus standard care – rather than children who

were randomised to omalizumab plus standard care – with the rates observed in children in the standard care alone group for the last 28 weeks of the trial. No attempt was made to assess whether these two groups were similar and non-responders were omitted entirely from the analysis.

- The manufacturer assumed a duration of treatment with omalizumab of 10 years. The ERG stated that no data had been submitted to support this assumption and suggested that in clinical practice the treatment duration would be shorter.
- The manufacturer assumed that rates of exacerbations remained constant over the entire treatment duration for omalizumab plus standard care and over a lifetime for standard care alone. The ERG stated that during this period people would go through adolescence, which may have an impact on their asthma. It was therefore unclear whether this assumption was reasonable.

3.23 The ERG provided a revised cost-effectiveness result for the EUP hospitalisation subgroup that excluded the regression applied to the utility values in the model. The ICER was reduced from £65,911 to £65,884 per QALY gained. The ERG also carried out a series of sensitivity analyses of cost effectiveness in the EUP hospitalisation subgroup as the manufacturer had not presented a sensitivity analysis for this population. The main findings were similar to those in the base-case population.

3.24 The ERG also undertook exploratory analysis to identify the factors underlying the cost-effectiveness results in the population aged 6 to 11 years using the modelling that was used in NICE technology appraisal guidance 133 (TA133) on omalizumab for severe persistent allergic asthma in the population aged 12 years and older. The exploratory analysis focused on the hospitalisation subgroup. The ERG examined the differences in values for the following parameters in the manufacturer's submission and in

TA133: exacerbation rates, proportion of patients who respond to treatment, rate of mortality due to clinically significant severe exacerbations, utility values for day-to-day symptoms and utility decrement for exacerbations and costs.

- 3.25 The exploratory analysis showed that applying the values from the INNOVATE study for dosing of omalizumab and rates of efficacy (as used in TA133) to patients aged 12 years and older in the hospitalisation subgroup resulted in an increase in the ICER from £65,884 to £73,779 per QALY gained. Applying an improvement in utility associated with omalizumab relative to standard care to the day-to-day symptoms state for patients younger than 12 years decreased the ICER from £65,884 to £53,133 per QALY gained. The exploratory analysis demonstrated that mortality associated with clinically significant severe exacerbations had the greatest impact on the ICER: the higher the assumed mortality rate, the lower the ICER. The manufacturer used mortality rates for children based on data from the study by Watson and colleagues (see section 3.13). In contrast, the mortality rate reported in TA133, which considered a cohort with an average age of 45 years, was 3.109%. Applying the higher mortality rate of 3.109% from TA133 to the model once people reach the age of 12 years reduced the ICER to £31,737 per QALY gained. The ERG expressed the view that the high rate of death was reasonable for people aged over 45 years but not for the younger population, based on the evidence from the Watson study. The ERG noted that quadrupling the mortality rates reported by Watson and colleagues for all ages reduced the ICER to £43,121 per QALY gained.
- 3.26 In response to the consultation on the preliminary guidance, the manufacturer submitted cost-effectiveness analyses for an additional subgroup based on patients who had experienced three or more exacerbations in the previous year. The cost-effectiveness estimates presented for this subgroup were obtained using the

manufacturer's original economic model. The subgroup analysis gave an ICER of £82,571 per QALY gained.

- 3.27 Full details of all the evidence are in the manufacturer's submission and the ERG report, which are available from www.nice.org.uk/guidance/TA201

4 Consideration of the evidence

- 4.1 The Appraisal Committee reviewed the data available on the clinical and cost effectiveness of omalizumab, having considered evidence on the nature of severe persistent allergic asthma in children aged 6 to 11 years and the value placed on the benefits of omalizumab by children with the condition, their families and carers, those who represent them and clinical specialists. It also took into account the effective use of NHS resources.

Management of severe persistent allergic asthma in UK clinical practice

- 4.2 The Committee discussed the clinical need of children with severe persistent allergic asthma. It heard from the clinical specialist and the patient expert that severe exacerbations have a large impact on children and their families. For children, this may include attendance at accident and emergency departments, emergency GP visits, reduced attendance at school, limited social life and inability to undertake exercise. The impact on families may include anxiety, sleep deprivation and emotional and financial pressures. The Committee was aware of the concerns of carers and clinicians regarding the long-term use of oral corticosteroids because of side effects that include osteoporotic fractures and retarded growth. The Committee noted that children and their families and carers value the possibility of a reduction in the number of exacerbations without the use of high-dose corticosteroids and are prepared to accept the inconvenience of attending specialist centres to have injections of omalizumab.

4.3 The Committee discussed the decision problem in the context of the NHS in England and Wales and the evidence submitted. It heard from the clinical specialists that the management of asthma in UK clinical practice is based on the 'British guideline on the management of asthma' and uses a stepped treatment approach, with drugs added or withdrawn depending on symptoms and control. The Committee heard from the clinical specialist and patient expert that in clinical practice the population for whom omalizumab would be considered is more narrowly defined than in the marketing authorisation and the IA-05 study, and would include children at step 5 of the 'British guideline on the management of asthma' requiring frequent or maintenance doses of oral corticosteroids. The Committee considered the appropriate comparator for omalizumab to be fully optimised treatment with existing therapies. The Committee noted that clinicians would wish to optimise therapy in an individual child before commencing omalizumab, which would normally be comparable to step 5 of the 'British guideline on the management of asthma'. It understood that standard care at baseline for the majority of children in the IA-05 study would broadly correspond with step 4 of this guideline, with the use of inhaled rather than oral corticosteroids. The Committee agreed that the trial population was not similar to the population of children who are likely to be considered for treatment with omalizumab, as in UK clinical practice these children would be treated with oral in addition to inhaled corticosteroids, rather than inhaled corticosteroids alone.

Clinical effectiveness

4.4 The Committee considered the evidence on the clinical effectiveness of omalizumab as presented in the manufacturer's submission and the ERG's review. The Committee noted that omalizumab as an add-on to standard care has not been shown to statistically significantly affect hospitalisation rates, accident and emergency visits, unscheduled doctor visits or total emergency

visits, symptom-free days and nights or health related quality of life, although for some of these outcomes there was a trend towards a beneficial effect of omalizumab. The Committee was aware that omalizumab has been shown to reduce the rate of clinically significant and clinically significant severe exacerbations, but that the effect on clinically significant severe exacerbations was not statistically significant. The Committee agreed that there were aspects of the IA-05 study that led to uncertainty, including the possibility that the EUP was not sufficiently powered to detect an effect of omalizumab on clinically significant exacerbations. Furthermore, the Committee noted that analyses suggest a benefit in terms of clinically significant exacerbations only in children who had had three or more exacerbations in the year before the start of the study, and that in UK clinical practice these children would be at step 5 of the 'British guideline on the management of asthma' requiring treatment with oral corticosteroids. The Committee noted that the manufacturer had considered post-hoc subgroup analyses of children receiving maintenance oral corticosteroids at baseline, but that the small number of children in this subgroup precluded any analysis. The Committee then considered whether omalizumab might be an alternative to oral corticosteroids. The Committee noted that the manufacturer had undertaken a survey of UK specialist paediatric respiratory centres to examine changes in the use of oral corticosteroids, since the IA-05 study reported changes in the use of inhaled corticosteroids only. The Committee noted the methodological limitations of the survey identified by both the manufacturer and the ERG. The Committee concluded that there was no robust evidence showing a reduction in use of oral corticosteroids with omalizumab, and that an RCT would be required to determine whether omalizumab decreases the use of oral corticosteroids. The Committee concluded that omalizumab as an add-on to optimised standard care is more clinically effective than optimised standard care alone in terms of reducing clinically significant exacerbations for children with severe persistent allergic

asthma who have experienced three or more clinically significant exacerbations in the previous year.

- 4.5 The Committee discussed whether there was another subgroup of children for whom omalizumab add-on therapy might be particularly clinically effective. The Committee noted that the manufacturer had undertaken a preplanned post-hoc subgroup analysis of children with a recent history of asthma-related hospitalisation. The Committee noted that omalizumab as an add-on to standard care had been shown to reduce the rate of clinically significant exacerbations and clinically significant severe exacerbations relative to standard care alone, but that neither analysis showed a statistically significant difference in this subgroup. The Committee heard from the clinical specialist that as a result of individualised management programmes, children and their carers are able to manage exacerbations at home and therefore it is rare in the UK for children with severe asthma to be admitted to hospital. The Committee accepted that the subgroup analysis suggested a possible reduction in the number of exacerbations for children with a recent asthma-related hospitalisation. However, in view of the testimony of the clinical specialist, the Committee concluded that this subgroup was not clinically relevant in NHS clinical practice.

Cost effectiveness

- 4.6 The Committee considered the manufacturer's economic model and the review and exploratory sensitivity analyses performed by the ERG. The Committee agreed that in general the the manufacturer's economic evaluation was of good quality. The Committee noted that the ICERs presented by the manufacturer for the base case and the post-hoc analysis for the hospitalisation subgroup were much higher than £30,000 per QALY gained. The Committee discussed treatment duration, asthma-related mortality risk from clinically significant severe exacerbations and the basis for estimating omalizumab drug costs, which it considered to be

key factors in determining the cost effectiveness of omalizumab in the EUP and the hospitalisation subgroup specified by the manufacturer.

- 4.7 The Committee discussed the assumption about the duration of treatment in the manufacturer's model. It noted that the manufacturer's justification for the choice of the 10-year treatment duration was based on the assumed duration of treatment that informed the development of TA133. The manufacturer noted that some patients recruited to the INNOVATE study (used in TA133) had received treatment with omalizumab for 7 years. The Committee heard from the clinical specialist that the severity of asthma can vary during a person's lifetime and that the required duration of treatment with omalizumab is unknown. However, the clinical specialist and the patient expert stated that they would expect treatment to last approximately 5 years for most people, and that there may be some people who require it for their lifetime. The Committee also noted a statement provided during consultation that omalizumab was very unlikely to be prescribed for 10 years. The Committee noted that the ICERs from the manufacturer's model were sensitive to changes in the assumptions for omalizumab treatment duration and that a shorter duration of treatment substantially increased the ICER. The Committee understood that this was because, based on the quality of life data from the IA-05 study, a difference in the utility value for day-to-day symptoms between treatment and control groups was only applied from age 12 onwards, so with shorter treatment durations there was less time to accrue health-related quality of life benefits. The Committee concluded that assuming a 10-year duration of treatment overestimates the probable duration of treatment in UK clinical practice and that a treatment duration of 5 years was more appropriate. The Committee noted that using a 5-year treatment duration increased the ICER for omalizumab to £137,900 per QALY gained compared with standard care.

- 4.8 The Committee considered the costs associated with omalizumab which, in the model submitted by the manufacturer, were assumed to be constant over time. As the marketing authorisation specifies weight-based dosing, and because children are expected to grow and gain weight between ages 6 and 11, the Committee concluded that the assumption of constant cost could underestimate the true costs of treatment and therefore underestimate the ICER.
- 4.9 The Committee discussed the utility values used in the manufacturer's economic model. It was aware that the manufacturer had assumed no difference in utility values in day-to-day symptoms between omalizumab and standard care for children aged 6 to 11 years (0.699 for both standard care and omalizumab responders) but had assumed a difference in utility in day-to-day symptoms (0.669 for standard care and 0.779 for omalizumab responders) for those aged 12 years and over. Comments received during consultation suggested that the utility values used in the manufacturer's economic model did not capture adequately the potential benefits of omalizumab in terms of increased attendance at school, improved examination results and reduced time off work for carers. The Committee noted that no empirical evidence relating to these potential benefits had been submitted in the manufacturer's original submission or by consultees or commentators during consultation. However, the Committee heard from the manufacturer that unpublished data from the IA-05 study showed children randomised to omalizumab plus standard care were absent from school on average 2 days less over a 52-week period than children randomised to standard care alone. The Committee concluded that there was insufficient evidence to conclude that omalizumab would have a significant impact on school attendance, educational attainment or employment. The Committee was also mindful that the impact of omalizumab on educational attainment and employment were outside NICE's reference case, which specifies that the costs and benefits of a

technology should be considered from the perspective of the NHS and personal social services. The Committee then considered whether it was appropriate for the manufacturer to use different modelling assumptions regarding the utility values for day-to-day symptoms for children aged 6 to 11 years and people aged 12 years and older. Comments received during consultation suggested that children aged 6 to 11 years would be likely to receive the same benefits from omalizumab as people aged 12 years and older. The Committee noted that a carer for a child with asthma treated with omalizumab had observed significant improvements following treatment. The Committee noted that the ERG had undertaken an exploratory analysis for the hospitalisation subgroup in which a difference in utility between treatments was applied to all patients, including those aged 6 to 11 years, resulting in an ICER of £53,000 per QALY gained. The Committee concluded that the utility value used in the economic model for children aged 6 to 11 years may have underestimated the true benefit, but that an adjustment to the utility value would still lead to an ICER that exceeds the range usually considered a cost-effective use of NHS resources.

4.10 The Committee understood that a comment was provided during consultation noting that the Committee had failed to consider the low impact on the health budget of treating children with omalizumab, since relatively few children would need treatment. The Committee noted that the NICE 'Guide to methods of technology appraisal' specifically states that the potential budget impact of the adoption of a new technology does not determine its decision.

4.11 The Committee considered the effect of the mortality rate associated with clinically significant severe exacerbations on the ICERs generated from the model. In the manufacturer's base case, the ICERs for the EUP and the hospitalisation subgroup were

£91,200 per QALY gained and £65,900 per QALY gained respectively, assuming annual mortality rates in the UK from the study by Watson and colleagues (see section 3.13). The Committee considered the ERG's exploratory analysis of the manufacturer's hospitalisation subgroup, in which the annual mortality rates reported in TA133 were applied in the current appraisal to children in the model as they reach 12 years of age. The Committee noted that the ICERs decreased to £31,700 per QALY gained assuming an annual mortality rate of 3.109% and £34,000 per QALY gained assuming an annual mortality rate of 2.478%. The Committee heard from the clinical specialist that asthma-related mortality is rare and tends to occur in people with less severe but poorly controlled asthma, and that omalizumab therapy would not be considered appropriate for these people based on its marketing authorisation, because they would not fulfil the requirement for optimised therapy. Additionally, the Committee heard that the clinical specialist was not aware of any evidence suggesting an association between the number of exacerbations and mortality. The Committee was aware that using mortality rates fourfold higher than the modelled mortality rates would result in an ICER of £43,100 per QALY gained, and concluded that making such an assumption would be inappropriate in the light of the evidence. The Committee was aware that the mortality rates used in the model represent deaths in inpatients only, but heard from the clinical specialist that out-of-hospital deaths account for only a very small percentage of deaths attributable to asthma. The Committee considered that the mortality rates reported in the study by Watson and colleagues may overestimate deaths caused by asthma because the International Classification of Disease codes were likely to have included children with viral illness and wheezing misclassified as asthma. However, the Committee concluded that for the decision problem in this appraisal it was most appropriate to use the mortality rates from the study by Watson and colleagues, as done in the manufacturer's economic model.

- 4.12 The Committee understood that in current clinical practice physicians stop omalizumab if there is no adequate response to treatment after 16 weeks, in line with the marketing authorisation. The Committee heard from the clinical specialist that physicians judge changes in response to treatment with omalizumab carefully, using all available criteria, including: daily symptoms, quality of life, frequency of exacerbations, spirometric and peak expiratory flow measurements and frequency of unplanned consultations for asthma. However, there is no agreement as to the magnitude of improvement required to define an adequate response to omalizumab. The Committee noted that the manufacturer had modelled response at 16 weeks, but that this was based on data from assessment at 52 weeks in the IA-05 study. The Committee considered whether response at 52 weeks was an acceptable proxy for response at 16 weeks. The Committee heard from the clinical specialist that there was no robust evidence to support the biological plausibility of this assumption, and that instead there may be an increase in response over time with omalizumab treatment. It concluded that the use of the 52-week response assessment as a proxy for response at 16 weeks resulted in uncertainty of the ICERs in the manufacturer's model.
- 4.13 The Committee considered what the most plausible ICER for omalizumab compared with standard care would be. It noted the ICERs of £91,200 and £65,900 per QALY gained for the EUP and for the hospitalisation subgroup respectively, based on a 10-year treatment duration, and that for a more plausible treatment duration of 5 years the ICERs would be higher. The Committee concluded that such ICERs were substantially higher than those normally considered to be an acceptable use of NHS resources and concluded that omalizumab for the treatment of severe persistent allergic asthma in children aged 6 to 11 years could not be recommended as a cost-effective use of NHS resources.

- 4.14 The Committee considered whether there were any other specific subgroups of people for whom the technology would be cost effective. The Committee noted that following consultation the manufacturer had presented cost-effectiveness estimates for patients who had experienced three or more exacerbations in the year before entering the study. It noted that the ICER for this subgroup of £82,600 per QALY gained was outside the range normally to be considered to be a cost-effective use of NHS resources. The Committee therefore concluded that omalizumab could not be recommended for this subgroup.
- 4.15 The Committee received comments during the consultation period about the role of omalizumab in research, including the comment that any future trial comparing oral corticosteroids with omalizumab may be unethical. The Committee appreciated that a design in which omalizumab as an add-on to standard care is compared with placebo in patients who are having frequent courses of oral corticosteroids, with oral corticosteroid use as an endpoint, would be better suited to UK clinical practice and provide information that is not available in the current evidence base.
- 4.16 The Committee considered whether its recommendation were associated with any potential issues related to the equality legislation and the requirement for fairness. The Committee understood that during the scoping period of this appraisal the issue was raised whether adherence to asthma treatment in children may be affected by parents or carers not providing regular medication because of socioeconomic or cultural reasons, rather than because of poor understanding. The Committee concluded that such factors would apply equally to all treatment options and therefore no changes to the recommendation could address this issue.
- 4.17 The Committee further considered comments received during consultation that not recommending omalizumab for children aged

6 to 11 years was unfair because omalizumab was recommended under specific circumstances for children aged 12 years and older in NICE technology appraisal 133. The Committee was aware of NICE's obligations to avoid age discrimination in the performance of its functions, which will apply when the Equality Act 2010 is brought into force. However these obligations are stated in the Act not to apply in relation to people who are younger than 18 years. The Committee was also aware of the principles of 'Social value judgements' related to age, which state that patients should not be denied, or have restricted access to, NHS treatment simply because of their age. However, the Committee agreed that its decision on omalizumab for this age group was not made because of the age of the patients, but rather because omalizumab was not cost effective in this age group. This was because the avoidance of asthma-related death is a key driver for the ICER and children very rarely die from asthma. The Committee was aware that it needs to make a decision in each appraisal based on the evidence before it and this is what it has done in this case. In addition, given the very high ICERs, the Committee considered the decision to be reasonable and rational, and in line with the Committee's role and the application of the cost-effectiveness criteria as described in the NICE methods for technology appraisal. The Committee had not identified any special factors which would require or justify making a positive recommendation despite the very high ICERs. However, the Committee noted that the fact that omalizumab for children aged 6 to 11 years was considered separately from omalizumab for people older than 12 years was a result of the timing of the regulatory process in the younger paediatric indication, which was outside NICE's control. The Committee concluded that it would be preferable to develop a single piece of guidance giving recommendations for all age groups, and that the most appropriate way to proceed would be to review the recommendations for all age groups together at the earliest opportunity.

Summary of the Appraisal Committee's key conclusions

TA201 (STA)	Appraisal title: Omalizumab for the treatment of severe persistent allergic asthma in children aged 6 to 11 years	FAD section
Key conclusion		
Omalizumab is not recommended for the treatment of severe persistent allergic asthma in children aged 6 to 11 years.		1.1
Reasons for key conclusion:		
<ul style="list-style-type: none"> Omalizumab as an add-on to optimised standard care is more clinically effective than optimised standard care alone in terms of reducing clinically significant exacerbations for children aged 6 to 11 years with severe persistent allergic asthma only if they have experienced three or more clinically significant exacerbations in the previous year. 		4.4
<ul style="list-style-type: none"> The most plausible ICER for the subgroup of patients who had experienced three or more clinically significant exacerbations in the year before entering the study was £82,600 per QALY gained. The Committee concluded that this ICER was substantially higher than those normally considered to be a cost-effective use of NHS resources. 		4.14
Current practice		
Clinical need of patients	The main aim of treatment of asthma in children is to reduce the impact of the condition on children and their families, which includes attendance at accident and emergency departments, emergency GP visits, reduced attendance at school, limited social life and inability to undertake exercise. The impact on families may include anxiety, sleep deprivation and emotional and financial pressures.	4.2
including the availability of alternative treatments	The Committee noted that clinicians would wish to optimise therapy in an individual child before commencing omalizumab, which would normally be comparable to step 5 of the 'British guideline on the management of asthma'. The Committee heard that children at step 5 of the 'British guideline on the management of asthma' require frequent or maintenance doses of oral corticosteroids.	4.3
The technology		
Proposed benefits of the technology	The Committee noted that children and their families and carers value the possibility of a reduction in the number of exacerbations without the use of high-dose corticosteroids and are prepared to accept the inconvenience of attending specialist centres to have injections of omalizumab.	4.2
How innovative is the technology in its potential to make a significant and substantial impact on health-related benefits?	Omalizumab is a monoclonal antibody that binds to immunoglobulin E (IgE). Omalizumab has a marketing authorisation as an add-on therapy to improve asthma control in patients with severe persistent allergic asthma.	2.1
What is the position of the treatment in the pathway of care for the condition?	The Committee heard that in clinical practice the population for whom omalizumab would be considered is more narrowly defined than in the marketing authorisation and the IA-05 study, and would include children at step 5 of the 'British guideline on the management of asthma' requiring frequent or	4.3

	maintenance doses of oral corticosteroids.	
Adverse effects	The Committee was aware of the concerns of carers and clinicians regarding the long-term use of oral corticosteroids (the possible comparator at step 5 of the guidelines) because of side effects that include osteoporotic fractures and retarded growth. The Committee considered whether omalizumab might be an alternative to oral corticosteroids, but concluded that there was no robust evidence showing a reduction in use of oral corticosteroids with omalizumab.	4.2, 4.4
Evidence for clinical effectiveness		
Availability, nature and quality of evidence	One randomised controlled trial in children receiving omalizumab plus standard care or standard care alone. The manufacturer presented the results for subpopulations for children with more severe asthma to provide efficacy data aligned with the pre-existing EU marketing authorisation in adults and children aged 12 years and above (EUP). This was evaluated by the Committee. The manufacturer also presented post-hoc efficacy analysis of one high-risk subgroup: the EUP hospitalisation subgroup. Following a request from the ERG, the manufacturer also provided analysis of EUP stratified by the number of exacerbations experienced in the previous year.	3.3, 3.4, 4.4 3.7,3.8, 4.3, 4.5
Relevance to general clinical practice in the NHS	The Committee agreed that the trial population was not similar to the population of children who are likely to be considered for treatment with omalizumab, as in UK clinical practice these children would be treated with oral in addition to inhaled corticosteroids, rather than inhaled corticosteroids alone. Based on the testimony of the clinical specialist, the Committee concluded that the EUP hospitalisation subgroup was not clinically relevant in NHS clinical practice.	4.3 4.5
Uncertainties generated by the evidence	The Committee agreed that there were aspects of the IA-05 study that led to uncertainty, including the possibility that the EUP was not sufficiently powered to detect a difference in clinically significant exacerbations with omalizumab.	4.4
Are there any clinically relevant subgroups for which there is evidence of differential effectiveness?	The Committee concluded that omalizumab as an add-on to optimised standard care is more clinically effective than optimised standard care alone in terms of reducing exacerbations for children with severe persistent allergic asthma who have experienced three or more clinically significant exacerbations in the previous year.	4.4
Estimate of the size of the clinical effectiveness including strength of supporting evidence	The Committee agreed that analyses suggest a benefit in terms of clinically significant exacerbations only in children who had had three or more exacerbations in the year before the start of the study. The Committee concluded that omalizumab as an add-on to optimised standard therapy/standard care is more clinically effective than optimised standard therapy/standard care alone in terms of reducing exacerbations for children with severe persistent allergic asthma who have experienced three or more clinically significant exacerbations in the	4.4

	previous year.	
Evidence for cost effectiveness		
Availability and nature of evidence	<p>The manufacturer's submission presented an economic analysis comparing omalizumab add-on therapy with standard care alone.</p> <p>The Committee agreed that in general the the manufacturer's economic evaluation was of good quality.</p>	<p>3.13–3.20</p> <p>4.3</p>
Uncertainties around and plausibility of assumptions and inputs in the economic model	<p>The Committee accepted that the following factors were key uncertainties in the economic model:</p> <ul style="list-style-type: none"> • treatment duration • asthma related mortality risk from clinically significant severe exacerbations • basis for estimating omalizumab related drug costs. 	4.6 – 4.9, 4.11
<p>Incorporation of health-related quality of life benefits and utility values</p> <p>Have any potential significant and substantial health-related benefits been identified that were not included in the economic model, and how have they been considered?</p>	<p>The Committee discussed the utility values used in the manufacturer's economic mode and the comments received during consultation, which suggested that the utility values used in the manufacturer's economic model did not capture adequately the potential benefits of omalizumab The Committee concluded that the utility value used in the economic model for children aged 6 to 11 years may have underestimated the true benefit, but that an adjustment to the utility value would still lead to an ICER that exceeds the range usually considered a cost-effective use of NHS resources.</p>	<p>3.15</p> <p>4.9</p>
Are there specific groups of people for whom the technology is particularly cost-effective?	<p>The Committee noted that following consultation on the Appraisal Consultation Document, the manufacturer had presented cost-effectiveness estimates for patients who had experienced three or more exacerbations in the year before entering the study. It noted that the ICER for this subgroup of £82,600 per QALY gained was outside the range normally to be considered to represent a cost effective use of NHS resources and therefore concluded that omalizumab could not be recommended for this subgroup.</p>	4.14
What are the key drivers of cost effectiveness?	<p>Assumptions about treatment duration and the mortality rate associated with clinically significant severe exacerbations were the key factor in the economic model.</p> <p>The Committee was aware that using mortality rates fourfold higher than the observed mortality rates would result in an ICER of £43,100 per QALY gained, and concluded that making such assumption would be inappropriate in the light of the evidence.</p>	4.11
Most likely cost-effectiveness estimate (given as an ICER)	<p>The manufacturer's ICERs were £91,200 and £65,900 per QALY gained for the EUP and for the hospitalisation subgroup, respectively, based on a 10-year treatment duration. For a more plausible treatment duration of 5 years the ICERs would be higher. The ERG'S exploratory analysis of the hospitalisation subgroup, in which it was assumed that there was a difference in utility values between treatments for all patients, including those aged 6 to 11 years, resulted in an ICER of £53,000 per QALYgained. The Committee concluded that such ICERs were substantially higher than those normally considered to be an acceptable use of NHS resources and concluded that omalizumab for the treatment of severe persistent allergic asthma in children aged 6 to 11 years could not be recommended as a cost-</p>	<p>4.11 and 4.13</p>

	effective use of NHS resources.	
Additional factors taken into account		
Patient Access Schemes (PPRS)	N/A	-
End of life considerations	N/A	-
Equalities considerations and principles of Social Value Judgements	The Committee further considered comments received during consultation that not recommending omalizumab for children aged 6 to 11 years was unfair because omalizumab was recommended under specific circumstances for children aged 12 years and older as a result of the recommendation in NICE technology appraisal 133. The Committee was aware of NICE's obligations to avoid age discrimination in the performance of its functions, which will apply when the Equality Act 2010 is brought into force. However these obligations are stated in the Act not to apply in relation to people who are younger than 18 years. The Committee was also aware of the principles of 'Social value judgements related to age, which state that patients should not be denied, or have restricted access to NHS treatment simply because of their age. However, the Committee agreed that its decision on omalizumab for this age group was not made because of the age of the patients, but rather because omalizumab was not cost-effective in this age group. The Committee noted that the fact that omalizumab for children aged 6 to 11 years was considered separately from omalizumab for people older than 12 years was a result of the timing of the regulatory process in the younger paediatric indication, which was outside NICE's control. The Committee concluded that it would be preferable to develop a single piece of guidance giving recommendations for all age groups, and that the most appropriate way to proceed would be to review the recommendations for all age groups together at the earliest opportunity.	4.17

5 Implementation

5.1 The Secretary of State and the Welsh Assembly Minister for Health and Social Services have issued directions to the NHS on implementing NICE technology appraisal guidance. When a NICE technology appraisal recommends use of a drug or treatment, or other technology, the NHS must provide funding and resources for it within 3 months of the guidance being published. If the Department of Health issues a variation to the 3-month funding direction, details will be available on the NICE website. The NHS is not required to fund treatments that are not recommended by NICE.

5.2 NICE has developed tools to help organisations put this guidance into practice (listed below). These are available on our website (www.nice.org.uk/guidance/TA201)

- A costing statement explaining the resource impact of this guidance.
- Audit support for monitoring local practice.

6 Recommendation for further research

6.1 An RCT should be conducted to compare omalizumab as add-on therapy to standard care with oral corticosteroids in children aged 6 to 11 years with severe persistent allergic asthma, with oral corticosteroid use as an endpoint. This is because there are no trial data available comparing omalizumab with optimised standard treatment at step 5 of the 'British guideline on the management of asthma', namely oral in addition to inhaled corticosteroids.

7 Related NICE guidance

- Omalizumab for severe persistent allergic asthma. NICE technology appraisal guidance 133 (2007). Review date: August 2010. Available from www.nice.org.uk/guidance/TA133
- 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/guidance/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/TA38

8 Review of guidance

- 8.1 The guidance on this technology will be considered for review together with NICE technology appraisal guidance 133 (October 2010). The Guidance Executive will decide whether the technology should be reviewed based on information gathered by NICE, and in consultation with consultees and commentators.

Andrew Dillon
Chief Executive
October 2010

Appendix A: Appraisal Committee members and NICE project team

A *Appraisal Committee members*

The Appraisal Committee is one of NICE's standing advisory committees. 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.

Dr Amanda Adler (Chair)

Consultant Physician, Addenbrooke's Hospital

Dr Ray Armstrong

Consultant Rheumatologist, Southampton General Hospital

Dr Jeff Aronson

Reader in Clinical Pharmacology, University Department of Primary Health Care, University of Oxford

Dr Peter Barry

Consultant in Paediatric Intensive Care, Leicester Royal Infirmary

Dr Michael Boscoe

Consultant Cardiothoracic Anaesthetist, Royal Brompton and Harefield NHS Foundation Trust

Professor John Cairns

Professor of Health Economics, Public Health and Policy, London School of Hygiene and Tropical Medicine

Dr Mark Chakravarty

External Relations Director – Pharmaceuticals and Personal Health, Oral Care Europe

Ms Sally Gooch

Independent Nursing and Healthcare Consultant

Mrs Eleanor Grey

Lay member

Mr Sanjay Gupta

YPD Service Case Manager, Southwark Health and Social Care, Southwark PCT

Dr Neil Iosson

General Practitioner

Dr Rosa Legood

Lecturer, London School of Hygiene and Tropical Medicine

Dr Rubin Minhas

General Practitioner and Clinical Director, BMJ Evidence Centre

Dr Sanjeev Patel

Consultant Physician and Senior Lecturer in Rheumatology, St Helier University Hospital

Dr John Rodriguez

Assistant Director of Public Health, NHS Eastern and Coastal Kent

Dr Florian Alexander Ruths

Consultant Psychiatrist and Cognitive Therapist at the Maudsley Hospital, London

Mr Navin Sewak

Primary Care Pharmacist, NHS Hammersmith and Fulham

Dr Lindsay Smith

General Practitioner, East Somerset Research Consortium

Mr Roderick Smith

Finance Director, West Kent Primary Care Trust

Mr Cliff Snelling

Lay member

Professor Ken Stein (Vice Chair)

Professor of Public Health, Peninsula Technology Assessment Group (PenTAG), University of Exeter

Professor Andrew Stevens

Professor of Public Health, Department of Public Health and Epidemiology, University of Birmingham

Dr Rod Taylor

Associate Professor in Health Services Research, Peninsula Medical School, Universities of Exeter and Plymouth

Ms Nathalie Verin

Health Economics Manager, Boston Scientific UK and Ireland

Dr Colin Watts

Consultant Neurosurgeon, Addenbrookes Hospital

Mr Tom Wilson

Director of Contracting and Performance, NHS Tameside and Glossop

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.

Helen Tucker

Technical Lead

Nicola Hay

Technical Adviser

Jeremy Powell

Project Manager

Appendix B: Sources of evidence considered by the Committee

A The Evidence Review Group (ERG) report for this appraisal was prepared by the Centre for Reviews and Dissemination and the Centre for Health Economics.

- Walker S, Burch J, McKenna C et al. (2010) Omalizumab for the treatment of severe persistent allergic asthma in children aged 6 to 11 years. A single technology appraisal. York: Centre for Reviews and Dissemination and Centre for Health Economics

B The following organisations accepted the invitation to participate in this appraisal as consultees and commentators. 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 and III had the opportunity to give their expert views. Organisations listed in I and II also have the opportunity to appeal against the final appraisal determination.

I Manufacturer:

- Novartis

II Professional/specialist and patient/carer groups:

- Allergy UK
- Asthma UK
- British Society for Allergy & Clinical Immunology
- British Thoracic Society
- Primary Care Respiratory Society UK (formerly General Practice Airways Group)
- Royal College of Nursing
- Royal College of Paediatrics and Child Health
- Royal College of Pathologists
- Royal College of Physicians
- Royal Pharmaceutical Society

III Other consultees:

- Department of Health

- NHS Gloucestershire
- Welsh Assembly Government

IV Commentator organisations (did not provide written evidence and without the right of appeal):

- AstraZeneca
- Boehringer Ingelheim
- Commissioning Support Appraisals Service
- Department of Health, Social Services and Public Safety for Northern Ireland
- GlaxoSmithKline
- Merck Sharp & Dohme
- Napp Laboratories
- NHS Quality Improvement Scotland

C The following individuals were selected from clinical specialist and patient expert nominations from the non-manufacturer 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 are invited to comment on the ACD.

- Dr Jonathan Grigg, Professor of Paediatric and Respiratory Medicine, nominated by the Royal College of Paediatrics and Child Health – clinical specialist
- Anita Critchlow, Respiratory Nurse Specialist, nominated by Asthma UK – patient expert
- David Squire, New Technologies and Drug Therapies Manager, nominated by Gloucestershire Primary Care Trust – NHS commissioning expert

D Representatives from the following manufacturer attended Committee Meetings. They contributed only when asked by the Committee chair to clarify specific issues and comment on factual accuracy.

- Novartis