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## **OMALIZUMAB**

### **A Position Statement of the NSW Therapeutic Advisory Group Inc.**

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## EXECUTIVE SUMMARY

Omalizumab (rhuMab-E25) is a recombinant humanised murine monoclonal antibody to IgE. Omalizumab recognises the specific F<sub>c</sub> epsilon3 portion of circulating IgE that binds to the high affinity IgE receptor, F<sub>c</sub> epsilonRI, on mast cells and basophils. Omalizumab forms complexes with free IgE, thus blocking the interaction between IgE and effector cells. Current therapies such as inhaled corticosteroids (ICS) and leukotriene modifiers act later in the allergic cascade, after the inflammatory mediators have been released.

Omalizumab (Xolair<sup>®</sup>) was approved by the TGA in April 2002 for the *management of adult and adolescent patients with moderate allergic asthma, who are already being treated with inhaled steroids, and who have raised serum immunoglobulin E levels.*

There are no current published trials that examine the cost-benefit ratio of omalizumab in severe or moderate to severe asthma.

It is uncertain where this new therapy will fit into the current overall armamentarium for treating asthma. Its efficacy and safety has been shown for adult asthmatic patients who are atopic (at least 1 positive skin test and IgE > 30 and < 700 IU/ ml) and also for skin test positive children. It is improbable that omalizumab would be effective in patients with non-atopic asthma and no analyses of its efficacy in studies of highly atopic patients (IgE > 700 IU) have been published.

Omalizumab has to date only been studied as an adjunct to other therapies in clinical trials, and has not been compared to current best practice treatment for asthma or alternative steroid sparing agents such as antileukotriene agents. Current evidence shows that the administration of omalizumab is useful in reducing the dose of inhaled corticosteroids (ICS) in patients with moderate to severe asthma. Since these patients are those in whom long acting beta agonists(LABA) are prescribed to permit the reduction in dosage of inhaled corticosteroids, comparative trials between LABA and omalizumab( yet to be conducted), will be necessary to assess the respective cost-effectiveness of these therapies in allowing reduction of ICS.

One published trial<sup>1</sup> has provided evidence for efficacy of omalizumab in the treatment of allergic rhinitis. Further studies will be necessary to investigate and determine its cost-effectiveness in this patient group.

One published study of children<sup>2</sup> has demonstrated that adding omalizumab to existing therapy with inhaled corticosteroids permits a substantial reduction in inhaled corticosteroids. Its ultimate place in therapy will be determined by the acceptability of fortnightly or monthly injections and cost-effectiveness comparisons with existing therapies.

On current evidence it is likely to be a very expensive treatment with potentially serious side effects (malignancy) and thus it is unlikely that it would become widespread treatment for the majority of adult patients. It may however be useful in patients with poor control already on high dose inhaled corticosteroids, or those using long term or frequent short courses of systemic corticosteroids.

Safety information from subjects exposed to omalizumab details serious adverse events including malignancy-solid organ/ epithelial cancers predominantly- (although a definitive causal link has not been established) and very rarely, anaphylaxis. Although there is no published data which establishes a direct pathophysiological link between anti-IgE therapy and cancer development or progression, the potential for alteration in IgE mediated effector cell function must be considered.

## 1. INTRODUCTION

Immunoglobulin E (IgE) plays a central role in the development of allergic diseases. Exposure to allergen initiates a complex series of events leading to the production of allergen- specific IgE, which binds to high affinity receptors on effector cells such as mast cells and basophils. The cross – linking of these cell-bound IgE molecules by antigen results in the release of pro-inflammatory mediators such as histamine, prostaglandins, leukotrienes, chemokines and cytokines from these cells.

Atopy is a condition characterised by an increased tendency to IgE-based sensitivity due to the production of specific IgE antibody to common environmental allergens eg house dust mite, pollens, moulds or animal danders. About 40% of the population is atopic and about half of this group develop clinical disease ranging from trivial rhinitis to life-threatening asthma. After sensitisation, continuing exposure to allergens leads to a significant increase in the prevalence of asthma <sup>3</sup>. An immunological reaction to allergen is the initiating event of airway inflammation in many cases of asthma <sup>4</sup> and continued exposure results in chronic inflammation-currently treated with inhaled corticosteroids, sodium cromoglycate or nedocromil sodium.

Omalizumab (rhuMab-E25) is a recombinant humanised murine monoclonal antibody to IgE. Omalizumab recognises the specific F<sub>c</sub> epsilon3 portion of circulating IgE that binds to the high affinity IgE receptor, F<sub>c</sub> epsilonRI, on mast cells and basophils. Omalizumab forms complexes with free IgE, thus blocking the interaction between IgE and effector cells. Current therapies such as inhaled corticosteroids (ICS) and leukotriene modifiers act later in the allergic cascade, after the inflammatory mediators have been released.

Omalizumab (Xolair<sup>®</sup>) was approved by the TGA in April 2002 for the *management of adult and adolescent patients with moderate allergic asthma, who are already being treated with inhaled steroids, and who have raised serum immunoglobulin levels*. This was the first marketing licence worldwide. Subsequently, in June 2003, the drug was approved by the FDA<sup>5</sup>, for *adults and adolescents(12 years of age and above) with moderate to severe persistent asthma who have a positive skin test or in-vitro reactivity to perennial aeroallergen and whose symptoms are inadequately controlled with inhaled corticosteroids*.

This document will examine the evidence for the ADEC approved indication as well as evidence for other conditions associated with raised IgE levels.

## 2. CLINICAL TRIALS

### 2.1 Asthma

Milgrom et al<sup>6</sup> studied the efficacy of omalizumab given **intravenously** as treatment for *allergic asthma*<sup>a</sup> in 317 patients taking oral or inhaled steroids or both (aged 11-50 years) in a multicentre, randomised, double-blind placebo controlled trial. Subjects were given either high- dose omalizumab 5.8 micrograms/ kg / nanogram of IgE per ml (n=106), low- dose 2.5 micrograms/ kg/ nanogram of IgE per ml (n=106) or placebo (n=105). Patients continued on the usual regimen of corticosteroids that they had received prior to enrolment for the first 12 weeks of the study. Doses of corticosteroid were then tapered over an 8 week period if possible<sup>b</sup>. Primary outcomes were daytime and nocturnal asthma symptom scores at 12 weeks. Secondary outcomes were use of bronchodilators as rescue medications, doses of corticosteroids, peak expiratory flow rate and asthma specific quality of life. The mean asthma symptom score at enrolment was 4.0. After 12 weeks, the mean score was  $2.8 \pm 0.1$  for subjects in the high-dose group ( $p=0.008$  for comparison with the placebo group) and  $2.8 \pm 0.1$  in the low- dose group ( $p= 0.005$ ) as compared with  $3.1 \pm 0.1$  for those in the placebo group. For the 35 subjects taking oral corticosteroids at baseline, the median reduction in the dose of prednisone over the 8 week tapering phase was 50% in the high-dose group ( $p=0.045$ ) and 65% in the low dose group ( $p=ns$ ) as compared with 0% in the placebo group. Fifty one percent of the subjects in the high-dose group ( $p=ns$ ) and 49% of those in the low-dose group ( $p=ns$ ) had a reduction in their dose of inhaled corticosteroids of at least 50% as compared with 38% of subjects in the placebo group. Eighteen percent of high-dose subjects ( $p=ns$ ) and 23% of those in the low- dose group ( $p=0.048$ ) stopped taking inhaled corticosteroids compared with 12% of those in the placebo group.

There were 17 reports of urticaria (8 high-dose, 6 low-dose and 3 placebo), 10 of which occurred within one hour after the infusion on the first day of treatment (7 high dose, 3 low dose).

In a similar trial, Soler et al<sup>7</sup> studied the effects of omalizumab on exacerbation and steroid requirement in 546 *moderate to severe allergic asthmatics*<sup>c</sup> aged 12-75 years who were symptomatic despite inhaled corticosteroids (beclomethasone dipropionate 500-1200mcg/day). Patients were randomised to receive either placebo (n= 272) or omalizumab (n= 274)  $\geq$  0.016mg/kg of body weight per IU of IgE/ml **subcutaneously** every 4 weeks for 28 weeks. Primary efficacy variable was the number of asthma exacerbations (defined as worsening of symptoms requiring treatment with systemic corticosteroids) experienced per patient during the stable-steroid phase and the steroid reduction phase of the study. Patients taking regular oral corticosteroids were not included. The number of asthma exacerbations per patient demonstrated statistically significant difference ( $p<0.001$ ) between omalizumab and placebo 0.28 (95%CI 0.15-0.41) vs 0.66 (95% CI 0.49-0.83) for steroid-stable phase and 0.36 (95% CI 0.24-0.48) vs 0.75 (95% CI 0.58-0.92). The proportion of patients who were able to reduce the beclomethasone dipropionate dose at the end of the steroid reduction period compared to the steroid stable phase was significantly higher in the

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<sup>a</sup> classified on the basis of a baseline value for mean forced expiratory volume/sec of 71% of the predicted value, mean daily symptom score of 4 on a 7 point scale and the daily use of a beta agonist as a rescue medication

<sup>b</sup> For subjects who required 600 micrograms or more of inhaled triamcinolone, an attempt was made to reduce the dose by 200 micrograms every 2 weeks; for those taking less than 600 micrograms per day the target reduction was 25% of the baseline value every 2 weeks. For subjects taking 20mg or less of oral corticosteroids daily (or 40mg on alternate days) the dose was reduced by no more than 20% at one-week intervals. For subjects who were taking both oral and inhaled steroids, only the dose or the oral agent was tapered.

<sup>c</sup> patients met standard criteria of the American Thoracic Society

omalizumab group than in the placebo group ( $p < 0.001$ ). The prescribed daily dose of beclomethasone dipropionate at the end of the steroid reduction phase was significantly lower on omalizumab (median 100 $\mu$ g, interquartile range: 0-400 $\mu$ g) than on placebo (median 300 $\mu$ g, interquartile range: 100-600 $\mu$ g)  $p < 0.001$ . Nine patients on omalizumab and three on placebo had serious adverse events excluding asthma exacerbations. Local injection site symptoms occurred in 11.8% of omalizumab injections and 7.7% of placebo injections. This study showed that monthly injections of omalizumab in allergic asthmatics, whose asthma was uncontrolled despite regular treatment with inhaled steroids, simultaneously reduced both asthma exacerbations and corticosteroid dosage.

The ability of omalizumab to maintain disease control was investigated in a 24- week double-blind extension to the above trial <sup>8</sup>. The number of asthma exacerbations per patient during the extension phase was significantly lower in the omalizumab group compared with the placebo group (0.48, 95% CI 0.30-0.66 vs 1.14, 95% CI 0.81-1.46;  $p < 0.001$ ). A higher incidence of adverse events affecting the digestive system was detected in omalizumab group (32%) versus placebo group (25%) over the 52- week period.

Busse et al <sup>9</sup> conducted a phase III double-blind, placebo controlled study in 525 allergic asthmatics aged 12-75 years ( $n=268$  omalizumab or  $n=257$  placebo) who were symptomatic despite inhaled corticosteroid (ICS). The aim of the study was to assess the efficacy and tolerability of subcutaneous omalizumab in adolescents and adults with *severe allergic asthma* whose disease was not adequately controlled with ICS. During the 4- week run-in to the study, all subjects were switched from their ICS to beclomethasone dipropionate (BDP), and the BDP dose adjusted upward or downward to maintain previous asthma control. A stable BDP dose was required for 4 weeks prior to randomisation. For the first 16 weeks of the study patients received omalizumab (0.016 mg/kg/ IgE (IU/ml) per 4 weeks) or placebo **subcutaneously**, and a stable dose of BDP; ICS was tapered during a further 12- week period. During the stable steroid phase, treatment with omalizumab resulted in significantly fewer patients experiencing an exacerbation than placebo (14.6% vs 23.3%;  $p=0.009$ ), and in significantly fewer exacerbations per patient (0.28 vs 0.54;  $p=0.006$ ). Significantly, more omalizumab recipients than placebo recipients achieved a greater than 50% reduction in BDP dose (72.4% vs 54.9%;  $p < 0.001$ ) and BDP was able to be discontinued in 39.6% of omalizumab recipients compared with 19.1% of placebo recipients ( $p < 0.001$ ). The incidence of adverse events was the same in both groups, with the most common drug-related events being urticaria and injection site reactions.

Corren<sup>10</sup> investigated the effect of **subcutaneous** omalizumab on the rate of serious exacerbations during long-term therapy from a pooled analysis of 3 multicentre studies. Overall 767 patients were randomised to omalizumab and 638 patients to placebo. The pooled results showed that the rate of unscheduled asthma-related outpatient visits was lower for omalizumab-treated patients than placebo-treated patients (relative risk 0.6, 95% CI 0.44-0.81,  $p < 0.01$ ). Hospitalisations were markedly reduced in patients receiving omalizumab (relative risk 0.08, 95% CI 0.00-0.25,  $p < 0.01$ ). Avoidance of outpatient visits and hospitalisations lessens the likelihood of absenteeism from work or school, allowing patients to spend more time doing normal activities and thus would be expected to confer quality of life benefits. The ability of omalizumab to reduce hospitalizations by up to 92% may have a substantial impact on the cost of care in patients with allergic asthma.

The safety, steroid-sparing effects, and impact on disease exacerbations of omalizumab in the treatment of childhood asthma has been evaluated in a double-blind placebo controlled study over 28 weeks<sup>2</sup> with plans for an open-label extension trial. The ability of omalizumab to replace inhaled corticosteroid was evaluated to assess drug efficacy. Three hundred and thirty four males and premenarchal females ages 6-12 years with *moderate to severe asthma* requiring treatment with inhaled corticosteroids were randomized to receive either **subcutaneous** placebo (n=109) or omalizumab (n=225) at a dose of 0.016mg/kg/IgE per 4 weeks. Steroid dose was kept stable for 16 weeks, reduced over 8 weeks to the minimum effective dose and then maintained constant for 4 weeks. The median reduction in the dose of steroid from baseline was 100% in the omalizumab group compared with 66.7% in the placebo group ( $p = 0.001$ ). Steroid was able to be withdrawn completely in 55% of the omalizumab group versus 39% of placebo treated patients ( $p = 0.004$ ). Urticaria was reported in 9 omalizumab patients (4%) and 1 placebo patient (0.9%).

A Cochrane review of omalizumab in *chronic asthma* (various definitions, including allergic asthma) has recently been published<sup>11</sup>. The reviewers concluded that omalizumab was significantly more effective than placebo at increasing the numbers of patients who were able to reduce or withdraw their inhaled steroids, and was effective in reducing asthma exacerbations. They noted the need for further assessment in the paediatric and severe adult population.

## 2.2 Allergic Rhinitis

Casale et al<sup>1</sup> studied the effects of omalizumab 50mg (n=137), 150mg (n=134) or 300mg (n=129) given subcutaneously, on symptoms of *moderate to severe seasonal allergic rhinitis*<sup>d</sup> (SAR) of at least 2 years duration in 536 patients aged 12-75 years. The trial was a randomised, double-blind, dose ranging placebo controlled trial, and treatments were given at 3-week intervals for a total of 4 treatments. The primary efficacy parameter was average daily nasal symptom score, with secondary efficacy measures including daily ocular symptom severity, rescue medication used and rhinoconjunctivitis quality of life questionnaire scores. Average nasal and ocular symptom severity and duration scores over the entire pollen season were consistently and significantly lower in the omalizumab 300mg group than placebo. Patients in the 300mg (41% vs 18%  $p < 0.001$ ) and 150mg

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<sup>d</sup> At least a 2 year history of SAR to ragweed.

(29% vs 18%  $p < 0.04$ ) omalizumab groups had a significantly greater percentage of days with minimal nasal symptoms than did those in the placebo group. The frequency of adverse events was similar in the active treatment and placebo groups. Most commonly reported were weight gain (all groups  $< 3\%$ ) and headache ( $< 2.2\%$ ). One patient on omalizumab 150mg had urticaria and was withdrawn from treatment. Injection site reactions were mild and infrequent (0.2% per patient). There were no clinically significant alterations in laboratory values in any group, no reactivity for antibodies to the FAB fragment of omalizumab was observed, and there was no evidence of immune complex-mediated disorders. It should be noted that the dosages used in this study were not weight-adjusted and are lower than those proposed for treatment of allergic asthma.

A randomised double-blind trial (unpublished) has been conducted to assess the safety and efficacy of subcutaneously administered omalizumab vs specific immunotherapy (SIT) vs a combination of both, for symptom prevention in 221 children with birch pollen and grass pollen-induced SAR. See study D01<sup>12</sup>. There were 4 treatment arms. Each subject was started on SIT-Birch or SIR-grass (12 weeks), and omalizumab or placebo was added and maintained for 24 weeks. The dose of omalizumab was given subcutaneously, based on body weight and baseline serum IgE. The primary efficacy variable was symptom load, the sum of daily symptom severity score plus rescue medication use. Combination therapy reduced symptom load by 48% ( $p < 0.001$ ) over SIT alone.

No published studies of the use of omalizumab in perennial allergic rhinitis (PAR) could be identified.

Improvements were seen in placebo treated patients in many of the above trials. It is a common finding in asthma trials that participation in the trial, with attendant regular review, improves asthma control and reduces medication use. A meta-analysis of well designed long-term drug therapy studies in stable asthmatics<sup>13</sup> showed that the pooled placebo effect is small but measurable in terms of objective measures of lung function such as FEV<sub>1</sub>. Approximately 6% of placebo treated patients showed a 10% increase in FEV<sub>1</sub>. A very high proportion of patients in the placebo arm of Milgrom's study<sup>6</sup> were able to withdraw corticosteroids (however the trial included asthmatics on oral corticosteroids, many of whom had relatively minor lung function deficits and may not have needed such intensive treatment).

### **3. ADVERSE EVENTS**

Use of a humanised anti IgE antibody raises theoretical concerns about immune complex mediated pathology and abnormal immune responses to parasitic infection.

Adverse reactions with Xolair™ were observed (all studies) at a frequency of 6.6% of patients treated with active drug, during clinical trials. The commonest adverse events observed were headaches, viral infections and upper respiratory tract infections.

A briefing document, available from the FDA site, contains a summary of safety information within the biological licence application submitted to the FDA by Genetech<sup>12</sup>. The safety database consists of detailed information from subjects exposed to omalizumab, for one year or less for any single subject. Adolescents and geriatric subjects account for 9% and 4% of the safety database. Serious adverse events included malignancy (solid organ/ epithelial cancers predominantly) and

anaphylaxis. Other adverse events occurring more frequently in omalizumab- treated patients than placebo- treated patients included rash (6.5% vs 4.9%), and bleeding (epistaxis, menorrhagia and haematoma- 2.5% vs 1.6%).

The observed incidence of malignancy among Xolair-treated patients was numerically higher than among patients in control groups, but was not statistically significant. Malignant neoplasms were observed in 20 of 4127 (0.5%) compared with 5 of 2236 (0.2%) control patients in clinical studies of asthma and other allergic disorders. The observed malignancies were of a variety of types <sup>5</sup>

Anaphylaxis has occurred within 2 hours of the first or subsequent administration of Xolair™ in 3 patients without other identifiable allergic triggers <sup>5</sup>. Overall the data suggest that the drug is very rarely associated with life threatening anaphylactic reactions.

At serum concentrations in excess of maximum human exposure used in pivotal clinical trials, dose-related thrombocytopenia occurred in 2 out of 4 non-human primate species studied. Thrombocytopenia was more pronounced in juvenile animals. No Xolair™-related thrombocytopenia has been observed in clinical trials.<sup>14</sup>

Adverse reactions at injection sites occurred in 7-12% of injections (both placebo and active drug sites) in the study by Soler <sup>7</sup>. This may be an issue when considering compliance in patients who will receive injections every two weeks.

#### **4. ECONOMIC DATA**

Omalizumab (Xolair™) is not listed on the Pharmaceutical Benefits Scheme (PBS). There are no current published Australian trials that examine the cost-benefit ratio of adding omalizumab to standard asthma care in severe or moderate to severe asthma. Cost effectiveness modelling based on the results of ongoing Australian clinical trials has yet to be performed.

The total annual cost to the community associated with asthma management in Australia was estimated in 1989 as \$627 million, or \$769 per asthmatic person <sup>15</sup>. (These costs are likely to have increased because of increases in medication costs and asthma prevalence).

In the study of childhood asthma by Milgrom <sup>2</sup>, over the 28 week trial period, patients in the omalizumab group missed a mean of 0.65 school days, as compared with a mean of 1.21 days in the placebo group (p=0.40). The mean number of unscheduled medical contacts attributable to asthma-related medical problems was significantly smaller (p<0.001) in the omalizumab group than in the placebo group throughout the treatment period (0.15 vs 5.35)

As previously noted, Corren et al <sup>10</sup> showed that the rate of unscheduled asthma-related outpatient visits was lower for omalizumab- treated patients than placebo-treated patients (relative risk 0.6, 95% CI 0.44-0.81, p<0.01), as were asthma- related emergency room visits (relative risk 0.47, 95% CI 0.47-1.01, p=0.05). Hospitalisations were markedly reduced in patients receiving omalizumab (relative risk 0.08, 95% CI 0.00-0.25, p<0.01). Avoidance of these lessens the likelihood of absenteeism from work or school, allowing patients to spend more time doing normal activities and thus would be expected to confer quality of life benefits. The ability of omalizumab to reduce

hospitalizations by up to 92% may have a substantial impact on the cost of care in patients with allergic asthma<sup>16</sup>.

The ex-factory cost of each vial of omalizumab is \$650<sup>e</sup> but overall cost of therapy will depend on the number of vials required to treat the patient. Given the recommended dose is between 1 and 6 vials per month, the annual cost of treating a patient may run into thousands of dollars.

## 5. PLACE IN THERAPY

About 40% of Australians will have respiratory symptoms consistent with asthma in their lives, and allergy is an important cause of asthma in both adults and children<sup>17</sup>

ADEC approved the use of omalizumab in April 2002 for *adult and adolescent patients with moderate allergic asthma, on inhaled steroids, who have raised serum IgE*. Approved Product Information, and a dosage card for health professionals, has been prepared by the manufacturer. The latter includes a nomogram for determining the dose to be given and the frequency, based on patients' weight and baseline IgE. The presentation is vials of 150mg of active ingredient, and the product information recommends a dose of 150-375mg be administered subcutaneously every 2 or 4 weeks.

It is uncertain where this new therapy will fit into the current overall armamentarium for treating asthma. Its efficacy and safety has been shown for adult asthmatic patients who are atopic (at least 1 positive skin test and IgE > 30 and < 700 IU/ml) and also for skin test positive children. It is improbable that omalizumab would be effective in patients with non-atopic asthma and no analyses of its efficacy in studies of highly atopic patients (IgE > 700 IU) have been published

It should be noted that omalizumab has to date only been studied as an adjunct to other therapies in clinical trials so its appropriate position in asthma management guidelines has yet to be established. Its steroid-sparing effects may be important in severe asthmatic patients who are at risk of side effects from daily use of high-dose inhaled steroids. In patients with moderate disease, the steroid sparing effect needs to be balanced against the cost of IgE treatment.

It is thus important to determine whether or not omalizumab is any more clinically beneficial or cost effective than other medications such as long-acting beta agonists (LABA) or antileukotriene agents.

Use in severe asthmatics (asthmatic patients that are intolerant of existing therapy, who are symptomatic, have a poor quality of life and require regular hospitalisation, despite being optimised on other treatments) is a potential use being investigated by Novartis, however no recommendations can be made at this time. In the US, severe asthmatics are already included in the FDA approved indication.

As previously noted, Australia was the first country to approve omalizumab. The approval was based on two pivotal clinical studies<sup>7,9</sup>, which were conceived prior to the routine use of LABA in management of severe asthma, and hence LABA were excluded in these studies. ADEC and the TGA determined, based largely on the concomitant medications used in the two studies, that the

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<sup>e</sup> Information provided March 2004 by Novartis Pharmaceuticals Aust.

patients recruited were predominately moderate asthmatics, at least according to current Australian standards.

In contrast to this interpretation, the US FDA agreed that the patients in these studies had asthma severity ranging from moderate to severe. Also in the US data were submitted from a subsequent trial<sup>18</sup>, in which subsets of patients were also taking an LABA or oral corticosteroids as maintenance therapy, suggesting that they had disease that was more difficult to manage.

On current evidence it is likely to be a very expensive treatment with potentially serious side effects (malignancy) and thus it is unlikely that it would become widespread treatment for the majority of adult patients. It may however be useful in patients with poor control already on high dose inhaled corticosteroids, or those using long term or frequent short courses of systemic corticosteroids.

## 6. RECOMMENDATIONS

- (i) Current evidence shows that the administration of omalizumab is useful in reducing the dose of inhaled corticosteroids (ICS) in patients with moderate to severe asthma. Since these patients are those in whom long- acting beta agonists are prescribed to permit the reduction in dosage of inhaled corticosteroids, comparative trials between LABA and omalizumab, which have yet to be conducted, will be necessary to assess the respective cost-effectiveness of these therapies in allowing reduction of ICS.
- (ii) One published trial <sup>1</sup> has provided evidence for efficacy of omalizumab in the treatment of allergic rhinitis. Further studies will be necessary to investigate determine its cost-effectiveness in this patient group
- (iii) One published study of children <sup>2</sup> has demonstrated that adding omalizumab to existing therapy with inhaled corticosteroids permits a substantial reduction in inhaled corticosteroids. Its ultimate place in therapy will be determined by the acceptability of fortnightly or monthly injections and cost-effectiveness comparisons with existing therapies

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