Royal College of Paediatrics and Child Health

Clinical Standards
5-11 Theobalds Road, London WC1X 8SH
Tel: 020 7092 6160/6166 ¦ Fax: 020 7092 6001 ¦ clinical.standards@rcpch.ac.uk

NICE Omalizumab for the treatment of severe persistent allergic asthma in children aged 6 and over and adults

Appraisal Consultation Document (ACD)

Organisation	Royal College of Paediatrics and Child Health (RCPCH)
Title	Submitted by Clinical Standards at RCPCH With thanks to: [redacted] Paediatric Respiratory Society [redacted] response on behalf of the RCPCH Academic CSAC and the RCPCH Allergy Immunology and Infectious Disease CSAC [redacted] on behalf of the Medicines for Children Research Network, British Paediatric Respiratory Society and the RCPCH Academic CSAC
Address	5-11 Theobalds Road, London, WC1X 8SH
Telephone number	020 7092 6160
Email address	Clinical.standards@rcpch.ac.uk

Section number Indicate **section number** If relevant	**Comments** If possible, please provide evidence (citations) to support your statements
General Comment	We strongly disagree with the proposal by NICE not to recommend omalizumab within its marketing authorisation for treating severe persistent allergic asthma. The use of omalizumab in children has been limited to those with severe disease. The majority of paediatric prescribers will be British Paediatrics Respiratory Society (BPRS) members. A recent survey (carried out in November 2012) of BPRS members indicates that at present there are 120 children in England currently using omalizumab. Approximately 50 children per year are started on omalizumab, of which between 50% and 75% will have a good or very good response and continue with treatment. Children with the severest form of asthma frequently require long term oral prednisolone treatment to keep their disease under control. The health consequences of long term oral prednisolone use in children are significant and include adrenal suppression, growth failure, weight gain, behavioural problems, osteoporosis, diabetes and cataracts. Every possible alternative to long term oral steroids for the management of severe asthma in children should be considered. RCPCH would like NICE to consider recommending the continued use of omalizumab in children requiring long-term (more than 3 months daily use) maintenance oral steroids for asthma control who in addition: 1. Fulfil the existing requirements of omalizumab use 2. Have been evaluated in a tertiary level paediatric respiratory clinic 3. Have had all alternative therapies considered 4. Have had their adherence to therapy assessed and confirmed as satisfactory The outcome for continued use should be a significant symptomatic improvement at 16 weeks as per the existing guidance and at least a 50% reduction in maintenance of oral steroid use by 12 months.

Answers to the key questions	"Are the recommendations sound and suitable….?" No "Do aspects to avoid discrimination need particular attention?" Yes
1.1 and 1.2	The 2 recommendations, 1.1 and 1.2 are incompatible. Either, NICE should judge that omalizumab should not be prescribed or even continued for those already receiving it or it should continue to be available for those with nightmare asthma. The 1.2 recommendation is a clear admission that this treatment is highly effective and has revolutionised the lives of a small number of very severe asthmatic patients and it would be unethical to withdraw treatment. However, those individuals who have yet to start the therapy are being discriminated against in being denied this opportunity for a dramatically improved quality of life exclusively on the basis of cost.
2.1	This should state not only that asthma can be severe but it can also be life-threatening.
2.2	This should state that the consequences of asthma in childhood include increased school absences, compromised educational attainment and exam results with an effect on career prospects and therefore the future life of the individual.
2.3	It is sad to say that despite the guidelines, good control is not achieved in a high percentage of cases.
2.4	Step 5 of the guidelines includes considering omalizumab. The list of side effects of oral corticosteroids which are considerable and life crippling are the alternative future on offer for patients who might otherwise benefit from omalizumab.
3.1.1	The evidence is that FEV 1% predicted at baseline has no influence on clinical response to treatment particularly in children.
4.1	NICE have conceded that omalizumab has evidence of efficacy from a large number of relatively high quality trails in adults and young people and less but still equivalent evidence in children down to 6 years of age. It is important to emphasise that conclusions are based on mean responses and conceal the fact that some patients have spectacular improvements while others have none. The recommendation is that response is reviewed at 16 weeks with the opportunity for reimbursement of costs if the response is deemed inadequate.
4.2	The key to the whole evaluation is the model which is used to calculate QALYs. As indicated in this section the range from different studies is very wide. The NICE choice of model has put the costs above their bar for recommendation but this is clearly open to dispute. No QALY has taken fair account of the burdens of severe disease in children. This was admitted by the head of NICE during a meeting with RCPCH.
Conclusions	The summary is that NICE reject the use of omalizumab based exclusively on cost while admitting the following; – It is highly effective in a sub-group of very severe asthmatics – Its side effects are mild by comparison with the alternatives – The alternative of long term oral steroids or other immunosuppressives have extensive, severe and life modifying side effects In the UK omalizumab is used very selectively and less than licensed indications might have suggested. In other words clinicians are acting very responsibly in the use of this product. This is clearly discrimination against a very small patient group who will now be denied an effective and safe treatment which could revolutionise their lives. Many other countries in the Western world have approved its use. Thus the English population is being discriminated against, in comparison to most other EU countries, including Scotland. This is shameful.
Other indications	Trials have recently been completed on the use of omalizumab in chronic urticarial and others are in progress on severe eczema, food allergy and ABPA. All are showing very promising results. On the basis of this assessment it is highly improbable that patients with complex and severe allergic disease will have any chance of receiving this therapy. Furthermore, it is unlikely that Novartis will fund any continuing research into the use of this product in the UK.
Comments on the ACD	Are the clinical and cost effectiveness reasonable? NO Are the provisional recommendations sound and form a good basis? NO Are there discrimination and equity-related issues? YES
1.2	Either NICE recommends usage or not. As it does not recommend omalizumab usage it should state that those receiving it should cease to do so. Otherwise it is sitting on the fence.
2.3	The simplistic statement that control is achieved by stepping up or down treatments according to guideline recommendations is at variance with the experience of those

	involved in the everyday care of asthma. Control of asthma is universally poor in adults and children with little evidence that guidelines have had a major effect on improving that control.
3.1	Lung function is a poor measure of asthma control or response to therapy in children.
4	Not all patients respond in the same way and to the same degree with any medication and clinical assessments of patients starting omalizumab have continued to demonstrate this. All the evidence in this appraisal is based on mean values and ignores those patients in whom significant benefits have been seen. Clinicians are unlikely to continue new medicines which do not work and this is especially true when the financial costs are high. NICE acknowledges that the quality of the studies was 'in general high' with little risk of bias. NICE also acknowledges effectiveness of omalizumab as well as the unpleasant and serious side-effects of prolonged high corticosteroid usage.
Overall views	As the recommendation stands NICE are prepared to prevent the use of the only new technology which has become available for the management of very severe asthma over the last 2 decades. It would be used in a very small number of people, and in children this number would be extremely small. The new evidence which has become available since the outcome of the 2011 recommendation is minimal and it is difficult to understand the scientific reason for the changed decision.

You may add extra rows as needed.

Evaluation report

The evaluation report includes statements from professional and patient groups and manufacturers, and is also available for comment.

Page number Indicate **page number** If relevant	**Comments** If possible, please provide evidence (citations) to support your statements
General	The professionals that were allowed to comment are very small in number and exclude several with much more experience of the use of omalizumab than those actually consulted. The exclusion of those professionals recommended by RCPCH is particularly notable and suggests a pre-existing prejudice in NICE in excluding those who have opinions which would possibly conflict with the final decision.
General	Given that the RCPCH is the recognised and respected UK institution which sets standards of care for the management of children's diseases we believe it is unacceptable that there was no RCPCH representative invited to participate in the Appraisal Committee decisions. We also note there was no representative from the RCP. Three patient experts were invited to participate, but there is no indication that any of them had knowledge of or suffered from very severe problematic asthma. The only other 2 selected individuals were a paediatric and an adult Allergist, both representing the British Society for Allergy and Clinical Immunology. We question whether this very small number of people is sufficient to give specific advice to a committee of 28 persons, none of whom are likely to have had any first-hand knowledge of using the technology. This specific issue was discussed at a meeting between the RCPCH and NICE some 2 or 3 years ago and no progress has been made since.

You may add extra rows as needed.