Appendix G - professional organisation statement template

NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Single Technology Appraisal (STA)

Omalizumab for previously treated chronic spontaneous urticaria [ID707]

Thank you for agreeing to give us a statement on your organisation's view of the technology and the way it should be used in the NHS.

Healthcare professionals can provide a unique perspective on the technology within the context of current clinical practice which is not typically available from the published literature.

To help you in making your statement, we have provided a template. The questions are there as prompts to guide you. It is not essential that you answer all of them.

Please do not exceed the 8-page limit.

About you

Your name: [redacted]

Name of your organisation: Royal College of Pathologists
Are you (tick all that apply):

- a specialist in the treatment of people with the condition for which NICE is considering this technology? ☐
- a specialist in the clinical evidence base that is to support the technology (e.g. involved in clinical trials for the technology)?
- an employee of a healthcare professional organisation that represents clinicians treating the condition for which NICE is considering the technology? If so, what is your position in the organisation where appropriate (e.g. policy officer, trustee, member etc)?
- other? (please specify)

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What is the expected place of the technology in current practice?

How is the condition currently treated in the NHS? Is there significant geographical variation in current practice? Are there differences of opinion between professionals as to what current practice should be? What are the current alternatives (if any) to the technology, and what are their respective advantages and disadvantages?

Are there any subgroups of patients with the condition who have a different prognosis from the typical patient? Are there differences in the capacity of different subgroups to benefit from or to be put at risk by the technology?

In what setting should/could the technology be used – for example, primary or secondary care, specialist clinics? Would there be any requirements for additional professional input (for example, community care, specialist nursing, other healthcare professionals)?

If the technology is already available, is there variation in how it is being used in the NHS? Is it always used within its licensed indications? If not, under what circumstances does this occur?

Please tell us about any relevant **clinical guidelines** and comment on the appropriateness of the methodology used in developing the guideline and the specific evidence that underpinned the various recommendations.

Chronic spontaneous urticaria (CSU) or chronic 'hives' is characterised by red, swollen, itchy and painful wheals on the skin which may resemble nettle- rash. This condition varies greatly in its severity, duration and how it affects patients. In many cases this a self-limiting problem which in 50% of patients will resolve within 6 months of the onset. However there is a significant number of patients who have a prolonged course of illness, sometimes lasting for decades, and causing a significant impact on quality of life.

Many of the CSU sufferers are treated in the primary care. However there are many inadequacies with this. Often patients are not given the correct diagnosis and frequently the treatments are inadequate. Even when the condition is correctly diagnosed and all appropriate treatment steps have been tried (including x4 license dose of non-sedating antihistamines) there is considerable variation in access to specialist care and medicines across the country. Whilst in some areas, people with CSU who need specialist treatment are referred to see a dermatologist or immunologist relatively quickly; there are many areas in the country where the wait is much longer. There is also variation in how CSU is treated within the specialist setting. Although there are various guidelines (please see below), there is sometimes reluctance to prescribe more potent therapies such us immunomodulatory drugs including ciclosporin and methotrexate, for fear of causing potentially serious side-effects, whilst treating a condition which by some is perceived to be essentially benign and self-limiting illness. However the effects of CSU on quality of life can be far-reaching; these include sleep deprivation, depression and social isolation. It has been reported that in comparison to some other dermatological and medical conditions, people with urticaria have a significantly worse quality of life (1).

Therefore there is a need to optimise treatment pathway for CSU. Introduction of omalizumab as a standard treatment option will offer an opportunity to revisit the current referral and treatment guidelines to ensure that recommendations are followed correctly and that appropriate patients are referred to specialist centers. Omalizumab should be provided by specialist centers (dermatology, immunology or allergy), which have extensive experience in assessing and treating large numbers of patients with CSU. This is how omalizumab has currently been provided for a limited number of CSU patients in the UK.

There are currently international and national guidelines on management of CSU. The international guideline is a result of collaboration between a number of stakeholders including: European Academy of Allergy and Clinical Immunology (EAACI), Global Allergy and Asthma European Network (GA²LEN), European Dermatology Forum (EDF), World Allergy Organisation (WAO) (2). In the UK both British association of dermatologists (BAD) and British society of allergy and clinical immunology (BSACI) have previously issued guidelines. These are currently under review and new recommendations are expected later this year. However, it is expected that in both cases the recommendations will be similar to the international ones (Figure 1).

Figure 1 Recommended treatment algorithm for CSU adopted from 2.

According to these guidelines omalizumab should be to used in patients who have failed to respond to updosing of antihistamines and addition of leukotriene antagonist. However, these recommendations do not differentiate between use of omalizumab and other immunomodulatory therapies such as ciclosporin or dapsone.

These recommendations were recently revised (3). The number of treatment steps has been reduced and dapsone or H2 blocker such as ranitidine are no longer recommend due to lack of data to support their efficacy. Omalizumab is recommended for patients who failed updosing of antihistamines within a period of 4 weeks. However in this case, as before, there is no differentiation between

omalizumab and ciclosporin, and to complicate the matter further leukotriene antagonists was also added as an option at the same treatment stage.

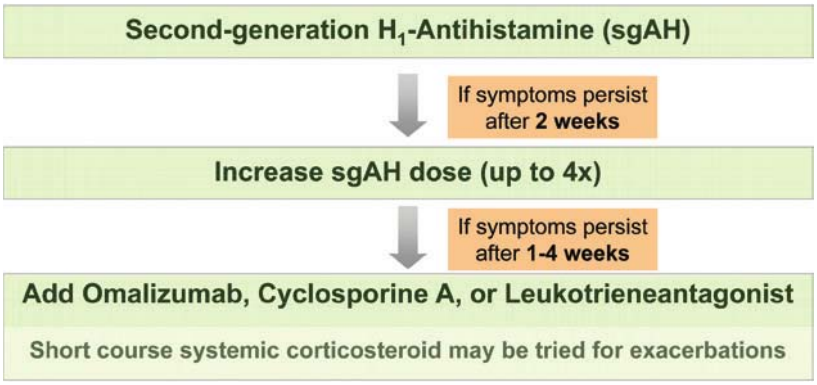

Figure 2 Revised recommendations for treatment of CSU adopted from 3

In summary as far as the guidelines are concerned there is currently no distinction between omalizumab and other immunomodulatory therapies and these treatment options are seen as equal. However, of all available therapies, only omalizumab in addition to the low dose antihistamines is a licenced treatment for CSU. In my opinion and experience it is certainly more effective and superior to leukotriene antagonists. Furthermore the overall body of the evidence for effectiveness of omalizumab in CSU is certainly comparative to other immunodulatory treatments and probably superior. (Please see next paragraph)

1. Weldon DR, Quality of life in patients with urticaria. Allergy Asthma Proceedings: 27(2): 96-00
2. Zuberbier et al, Allergy 2009: 64: 1427-1443
3. Maurer M. JDDG, 2013;1110: 971-978

The advantages and disadvantages of the technology

NICE is particularly interested in your views on how the technology, when it becomes available, will compare with current alternatives used in the UK. Will the technology be easier or more difficult to use, and are there any practical implications (for example, concomitant treatments, other additional clinical requirements, patient acceptability/ease of use or the need for additional tests) surrounding its future use?

If appropriate, please give your view on the nature of any rules, informal or formal, for starting and stopping the use of the technology; this might include any requirements for additional testing to identify appropriate subgroups for treatment or to assess response and the potential for discontinuation.

If you are familiar with the evidence base for the technology, please comment on whether the use of the technology under clinical trial conditions reflects that observed

in clinical practice. Do the circumstances in which the trials were conducted reflect current UK practice, and if not, how could the results be extrapolated to a UK setting? What, in your view, are the most important outcomes, and were they measured in the trials? If surrogate measures of outcome were used, do they adequately predict long-term outcomes?

What is the relative significance of any side effects or adverse reactions? In what ways do these affect the management of the condition and the patient's quality of life? Are there any adverse effects that were not apparent in clinical trials but have come to light subsequently during routine clinical practice?

Omalizumab has been show to be effective for CSU in randomized control trails (RCT) (4,5) and there are also a number of case series published across the world to further support this claim (6,7,8). In particular omalizumab has been effective in cases where all other treatment modalities have failed. In the UK, the use of omalizumab for CSU up till now has been limited. Unlike in RTC where omalizumab was used in patients which might have only failed antihistamines, in the UK omalizumab has predominantly been used in situations when all other treatment modalities including ciclosporin and other immunomodulatory drugs were either ineffective, contraindicated or could not be taken due to side-effects. Generally the rate of complete remission and or very good response to omalizumab ranges between 65-90%. The response to omalizumab is very rapid with the majority of responders to therapy showing improvement and frequently resolution of symptoms even after first injection. However, currently there is insufficient evidence to inform how this treatment should be administered beyond the first few months. The trial data (also from personal experience) suggest that many patients will experience relapse of symptoms within 12 weeks of stopping the treatment. We do not know what is the optimum duration of treatment, what proportion of patients is likely to achieve long-term remission and in whom the treatment can be stopped and what proportion might need on-going therapy. However there is evidence to suggest (also form personal experience) that treatment is as effective when used again in cases who relapsed after initial withdrawal of omalizumab. It is also unlikely that a therapeutic response will be observed in a patient who failed to show any response to the treatment after 3 monthly injections. Generally the treatment has been shown to be safe with no serious side-effects reported.

4. Kaplan A, Ledford D, Ashby M, Canvin J, Zazzali JL, Conner E, Veith J, Kamath N, Staubach P, Jakob T, Stirling RG, Kuna P, Berger W, Maurer M, Rosén K Omalizumab in patients with symptomatic chronic idiopathic/spontaneous urticaria despite standard combination therapyJ Allergy Clin Immunol. 2013 Jul;132(1):101-9.

5. Maurer M, Rosén K, Hsieh HJ, Saini S, Grattan C, Gimenéz-Arnau A, Agarwal S, Doyle R, Canvin J, Kaplan A, Casale T. Omalizumab for the treatment of chronic idiopathic or spontaneous urticaria.N Engl J Med. 2013 Mar 7;368(10):924-35

6. Viswanathan RK, Moss MH, Mathur SK Retrospective analysis of the efficacy of omalizumab in chronic refractory urticaria. Allergy Asthma Proc. 2013 Sep-Oct;34(5):446-52.

7. Metz M, Ohanyan T, Church MK, Maurer M. Omalizumab is an effective and rapidly acting therapy in difficult-to-treat chronic urticaria: a retrospective clinical analysis. J Dermatol Sci. 2014 Jan;73(1):57-62.

8. Labrador-Horrillo M, Valero A, Velasco M, Jáuregui I, Sastre J, Bartra J, Silvestre JF, Ortiz de Frutos J, Gimenez-Arnau A, Ferrer M. Efficacy of omalizumab in chronic spontaneous urticaria refractory to conventional therapy: analysis of 110 patients in real-life practice.Expert Opin Biol Ther. 2013 Sep;13(9):1225

Any additional sources of evidence

Can you provide information about any relevant evidence that might not be found by a technology-focused systematic review of the available trial evidence? This could be information on recent and informal unpublished evidence, or information from registries and other nationally coordinated clinical audits. Any such information must include sufficient detail to allow a judgement to be made as to the quality of the evidence and to allow potential sources of bias to be determined.

A survey of UK wide experience with omalizumab in CSU was recently conducted. This study included 55 patients with CSU from 5 different centres. Most patients had previously failed third-line therapies including ciclosporin. Overall response rate to treatment was about 80%, which means that patients either achieved full remission or significant reduction in their symptoms. This is comparable to most other similar published case series.

Implementation issues

The NHS is required by the Department of Health and the Welsh Assembly Government to provide funding and resources for medicines and treatments that have been recommended by NICE technology appraisal guidance. This provision has to be made within 3 months from the date of publication of the guidance.

If the technology is unlikely to be available in sufficient quantity, or the staff and facilities to fulfil the general nature of the guidance cannot be put in place within 3 months, NICE may advise the Department of Health and the Welsh Assembly Government to vary this direction.

Please note that NICE cannot suggest such a variation on the basis of budgetary constraints alone.

How would possible NICE guidance on this technology affect the delivery of care for patients with this condition? Would NHS staff need extra education and training? Would any additional resources be required (for example, facilities or equipment)?

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I do not think that significant additional resources would be required to deliver this treatment. Additional nursing support will be required to deliver the treatment and monitor patients during the therapy. Some of this could be shared with nurses who have previous experience of providing omalizumab for asthma.

Equality

NICE is committed to promoting equality of opportunity, eliminating unlawful discrimination and fostering good relations between people with particular protected characteristics and others. Please let us know if you think that this appraisal:

- could exclude from full consideration any people protected by the equality legislation who fall within the patient population for which [the treatment(s)] is/are/will be licensed;
- could lead to recommendations that have a different impact on people protected by the equality legislation than on the wider population, e.g. by making it more difficult in practice for a specific group to access the technology;
- could lead to recommendations that have any adverse impact on people with a particular disability or disabilities.

Please tell us what evidence should be obtained to enable the Committee to identify and consider such impacts.

No comment here