NHS England

NHS England Response to NICE ACD – Urticaria (chronic spontaneous, previously treated) - Omalizumab [ID707]

Please find NHS England's response to the ACD – Urticaria (chronic spontaneous, previously treated) - omalizumab [ID707], which has been reviewed by the Specialised Dermatology CRG

Has all of the relevant evidence been taken into account?
Specialists working in tertiary urticaria clinics at St John's Institute of Dermatology, London and elsewhere have reported a high proportion of treatment-refractory CSU patients showing a complete response to omalizumab. This is in line with a recent publication of the real-life experience of treating CSU patients and other subtypes of chronic urticaria with omalizumab which described a complete response in 83% of CSU patients and only a 7% failure rate i.e. better than expected from analysis of the GLACIAL study data and which may indicate higher cost-effectiveness. *Metz M et al. Omalizumab is an effective and rapidly acting therapy in difficult-to-treat chronic urticaria: a retrospective analysis. J Dermatol Sci 2014; 73:57-62.* Experience with Biologics for the treatment of psoriasis suggests that if medication is stopped and then restarted efficacy may be lost. As a result, many patients remain on Biologics long term. Clinical experience at St John's Institute of Dermatology, London suggests that for Omalizumab, subsequent courses are equally effective (section 4.16). The slightly lower frequency of response of patients recruited into the Glacial study (33.7% complete response, 52.4% almost complete response (UAS7, 1-6) than patients with similar baseline characteristics recruited into the Asteria I and II studies (40% and 58.8% responses respectively, pooled data) probably reflects a harder-to treat study population. A more favourable cost-effectiveness analysis of omalizumab in the Asteria I and II population (refractory to the licensed dose of a second generation H1 antihistamine) seems likely at the possible expense of a larger eligible population.
Are the summaries of clinical and cost effectiveness reasonable interpretations of the evidence?
The CRG consider the cost effectiveness summary reasonable. Regarding clinical effectiveness, the committees view is reasonable but in common with other conditions where there has not been a well defined treatment pathway, comparative data will be hard to find. The additional information requested from the company is considered appropriate and relevant.

Are the provisional recommendations sound and a suitable basis for guidance to the NHS?
There is currently no trial data to position omalizumab beyond H1 antihistamines (with or without H2 antihistamine, antileukotrienes or both). Because it has not been compared to single therapies, such as ciclosporin, or a basket of therapies beyond H1 antihistamines, omalizumab is recommended as a third line therapeutic option for patients who have not responded to up-dosed H1 antihistamines in the latest international guidelines on urticaria [ref]. The committee's view that omalizumab could be considered in the same place as immunosuppressive drugs in the treatment pathway (section 4.3) in the population of CSU patients included in the GLACIAL study is considered appropriate (i.e. as a third line agent). *Zuberbier et al. The EAACI/GA(2) LEN/EDF/WAO Guideline for the definition, classification, diagnosis, and management of urticaria: the 2013 revision and update. Allergy 2014; 69:868-87.* The mean baseline UAS7 score of 30 in GLACIAL reflects the severity of CSU in patients treated in that study. In real world practice, limiting eligibility to omalizumab to severe or moderate health states is pragmatic.
Any other comments
Omalizumab represents a significant advance in the management of chronic spontaneous urticaria (CSU), clinical trials and worldwide use to date showing that it is effective, safe and requires few screening investigations or safety monitoring in contrast to existing off-licence therapies that carry important risk profiles (immunosuppressive drugs and oral corticosteroids). In addition, it is also often effective for patients who have not responded to these other agents or in whom they are contraindicated. Like psoriasis, CSU may cause substantial problems with functioning, work, home, social and personal life. The degree of impairment in quality of life can be assessed by the dermatology life quality index (DLQI), a well-characterized patient related outcome measure. A score of 10 is used as a threshold value for defining the need for treating psoriasis patients with biologics when conventional therapies have failed. A comparable threshold score should be used to assess the need of patients with CSU who have failed to respond to second-generation H1 antihistamines at above licensed doses. The mean overall DLQI score of patients recruited into the GLACIAL phase III study was 13.1 showing comparable life quality impairment with other inflammatory disorders affecting skin for which biological drugs have been approved by NICE. Studies suggest that H1 antihistamines will control urticaria symptoms adequately in around 50% of patients and that up-dosing to fourfold may control up to 75% of patients. *Staevska M et al. The effectiveness of levocetirizine and desloratadine in 4-times conventional doses in difficult to treat chronic urticaria. J Allergy Clin*

Immunol 2010; 125:676-82.
The remaining 25% require third line drugs, including immunosuppressive drugs (e.g. ciclosporin, methotrexate) or anti-inflammatories (e.g. dapsone, short or long courses of oral corticosteroids) with varying success, regular hospital and GP monitoring and risk of adverse effects from their medication. In addition, a small number of these patients respond very poorly, or not all, to all available treatments with consequent huge impairment in their quality of life (DLQI scores in excess of 20/30 despite best available treatment). These patients deserve better treatment outcomes and are currently being denied effective and safe treatment.

Although a patient access scheme may provide access for some patients, there is likely to be inequity of access until a final decision is made.

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