NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE
GUIDANCE EXECUTIVE (GE)

Technology Appraisal Review Proposal paper

Review of TA339; Omalizumab for previously treated chronic spontaneous urticaria

Original publication date:	June 2015
Review date	June 2018
Existing recommendations:	Optimised To see the complete existing recommendations and the original remit for TA339, see Appendix A.

1. Proposal

We propose that TA339 should be transferred to the 'static guidance list.'

2. Rationale

No new evidence was identified that is likely to change the existing recommendations in TA339. The lack of trial data comparing omalizumab with immunosuppressants and long term data on relapse rates were identified as areas of uncertainty in TA339. However, we have found no relevant new trial evidence that addresses these areas of uncertainty.

The company has confirmed that no changes in the marketing authorisation are anticipated and are not aware of any new evidence that would change the existing recommendations.

It is therefore proposed that TA339 is moved to the static list because no evidence has been identified that is likely to alter the conclusions of the guidance (that is, lead to a change in the clinical and cost effectiveness of omalizumab to treat chronic spontaneous urticaria).

3. Summary of new evidence and implications for review

TA339 assessed the use of omalizumab for treating chronic spontaneous urticaria. Because there was a lack of randomised trial evidence comparing omalizumab with immunosuppressants, the model compared omalizumab with 'no further pharmacological treatment'. The committee understood that immunosuppressants such as ciclosporin were used off-label but accepted these were appropriate comparators. However, the evidence was very limited and a robust indirect comparison was not possible. Since its publication in 2015, there have been no new

relevant clinical trials comparing omalizumab with immunosuppressants such as ciclosporin.

In TA339 there was also a lack of robust evidence on long term relapse rates and the committee concluded that linearly extrapolating relapse data from the GLACIAL trial was the most plausible scenario. Since its publication in 2015, no new trial evidence on long term relapse rates in the relevant population has been identified that is likely to change the recommendations.

We identified 4 trials of omalizumab that have been published since TA339 but did not consider these directly relevant because they were not carried out in the population for which the company proposed the use of omalizumab and which was considered clinically appropriate. However, the results from these 4 new trials broadly support the conclusions in TA339 and are unlikely to change the recommendations. A summary of the new evidence is presented in the table below.

Has there been any change to the price of the technology since the guidance was published?
The company has confirmed that no change to the price is anticipated.
Are there any existing or proposed changes to the marketing authorisation that would affect the existing guidance?
There are no proposed changes to the marketing authorisation that would affect the existing guidance.
Were any uncertainties identified in the original guidance? Is there any new evidence that might address this?
In TA339, omalizumab was positioned as a 3rd or 4th line treatment option (that is, after standard treatment with H1-antihistamines [up to 4 times the licensed dose], with leukotriene receptor antagonists [LTRAs] and H2-antihistamines). The committee noted that this was narrower than the population in the marketing authorisation but agreed it was clinically appropriate. The company also positioned omalizumab for this specific subgroup, rather than the wider population in the marketing authorisation. Both the company and committee agreed this was in line with clinical practice. Since 2015, 4 trials of omalizumab have been published but were not carried out in the population for which the company proposed the use of omalizumab and which was considered clinically appropriate in TA339: • XTEND-CIU trial (Maurer et al 2018) compared omalizumab with placebo in people treated with H1 antihistamines with or without H2 antihistamines and LTRAs. The population were not necessarily refractory to combination therapy. • XACT trial (Staubach et al 2016) compared omalizumab with placebo in people with symptoms despite treatment with H1-antihistamine.

- POLARIS study (Hide et al 2017) compared omalizumab with placebo in an East Asian population with symptoms despite treatment with H1-antihistamine.
- Urticaria Research of Tropical Impact and Control Assessment (Sanchez et al 2017) assessed the impact of guideline recommendations for managing chronic spontaneous urticaria. After randomising to alternative H1 antihistamines and increasing the dose, it compared add-on omalizumab or ciclosporin as a 3rd line treatment. The population was not necessarily refractory to combination therapy with LTRAs and H2-antihistamines.

The results from the new trials are not directly relevant but broadly support the conclusions in TA339 and would be unlikely to change the recommendations.

In TA339 there was a lack of direct head-to-head trial evidence comparing omalizumab with immunosuppressants such as ciclosporin. The only trial evidence for immunosuppressants identified in TA339 were for ciclosporin and methotrexate but these trials did not include a comparison with omalizumab. In addition, a robust indirect comparison was not possible due to trial differences. Since TA339 was published, no new direct head-to-head trials have been identified comparing omalizumab with immunosuppressants such as ciclosporin in the relevant population.

In TA339 there was also uncertainty from the lack of robust evidence on long term relapse rates and the committee considered linearly extrapolated data from the GLACIAL trial to be most plausible. Since TA339 was published in 2015, no new trial evidence in the relevant population has been identified to address this area of uncertainty. Post hoc analyses from the GLACIAL and the ASTERIA trials are unlikely to change the recommendations in TA339.

Are there any related pieces of NICE guidance relevant to this appraisal? If so, what implications might this have for the existing guidance?

See Appendix C for a list of related NICE guidance.

Additional comments

None

The search strategy from the original ERG report was adapted and re-run on the Cochrane Library, Medline, Medline In-Process and Embase. References from May 2014 onwards were reviewed. Additional searches of clinical trials registries and other sources were also carried out. The results of the literature search are discussed in the 'Summary of evidence and implications for review' section above. See Appendix C for further details of ongoing and unpublished studies.

4. Equality issues

In TA339 the committee understood that chronic spontaneous urticaria is more prevalent in women and in the 20 to 40 year age group, but did not consider the recommendations would disadvantage either of these groups.

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Appendix A – Information from existing guidance

5. Original remit

To appraise the clinical and cost effectiveness of omalizumab within its licensed indication for previously treated chronic spontaneous urticaria.

6. Current guidance

Omalizumab is recommended as an option as add-on therapy for treating severe chronic spontaneous urticaria in adults and young people aged 12 years and over only if:

- the severity of the condition is assessed objectively, for example, using a weekly urticaria activity score of 28 or more
- the person's condition has not responded to standard treatment with H1-antihistamines and leukotriene receptor antagonists
- omalizumab is stopped at or before the fourth dose if the condition has not responded
- omalizumab is stopped at the end of a course of treatment (6 doses) if the condition has responded, to establish whether the condition has gone into spontaneous remission, and is restarted only if the condition relapses
- omalizumab is administered under the management of a secondary care specialist in dermatology, immunology or allergy
- the company provides omalizumab with the discount agreed in the patient access scheme.

7. Research recommendations from original guidance

N/A

8. Cost information from original guidance

Omalizumab costs £256.15 for a 150 mg prefilled syringe (excluding VAT; 'British national formulary' [BNF] online October 2014). A single dose of 300 mg costs £512.30 and the cost for a 24‑week course of treatment is £3073.80 (excluding VAT).

Appendix B – Explanation of options

When considering whether to review one of its Technology Appraisals NICE must select one of the options in the table below:

Options	Consequence	Selected – 'Yes/No'
A review of the guidance should be planned into the appraisal work programme.	A review of the appraisal will be planned into the NICE's work programme.	No
The decision to review the guidance should be deferred	NICE will reconsider whether a review is necessary at the specified date.	No
A review of the guidance should be combined with a review of a related technology appraisal. The review will be conducted through the MTA process.	A review of the appraisal(s) will be planned into NICE's work programme as a Multiple Technology Appraisal, alongside the specified related technology.	No
A review of the guidance should be combined with a new technology appraisal that has recently been referred to NICE. The review will be conducted through the MTA process.	A review of the appraisal(s) will be planned into NICE's work programme as a Multiple Technology Appraisal, alongside the newly referred technology.	No
The guidance should be incorporated into an on-going clinical guideline.	The on-going guideline will include the recommendations of the technology appraisal. The technology appraisal will remain extant alongside the guideline. Normally it will also be recommended that the technology appraisal guidance is moved to the static list until such time as the clinical guideline is considered for review. This option has the effect of preserving the funding direction associated with a positive recommendation in a NICE technology appraisal.	No

Appendix B

Options	Consequence	Selected – 'Yes/No'
The guidance should be updated in an on-going clinical guideline[1].	Responsibility for the updating the technology appraisal passes to the NICE Clinical Guidelines programme. Once the guideline is published the technology appraisal will be withdrawn. Note that this option does not preserve the funding direction associated with a positive recommendation in a NICE Technology Appraisal. However, if the recommendations are unchanged from the technology appraisal, the technology appraisal can be left in place (effectively the same as incorporation).	No
The guidance should be transferred to the 'static guidance list'.	The guidance will remain in place, in its current form, unless NICE becomes aware of substantive information which would make it reconsider. Literature searches are carried out every 5 years to check whether any of the Appraisals on the static list should be flagged for review.	Yes
The guidance should be withdrawn	The guidance is no longer relevant and an update of the existing recommendations would not add value to the NHS. The guidance will be stood down and any funding direction associated with a positive recommendation will not be preserved.	No

[1] Information on the criteria for NICE allowing a technology appraisal in an ongoing clinical guideline can be found in section 6.20 of the guide to the processes of technology appraisal.

Appendix C – other relevant information

1. Relevant Institute work

Published

Chronic urticaria: off-label doses of cetirizine (2014) NICE evidence summary of unlicensed or off-label medicines 31

Omalizumab for treating severe persistent allergic asthma (2013) NICE technology appraisal guidance 278
"This guidance replaces NICE technology appraisal guidance on omalizumab for the treatment of severe persistent allergic asthma in children aged 6–11 (TA201) and omalizumab for severe persistent asthma (TA133)."

2. Details of changes to the indications of the technology

Indication and price considered in original appraisal	Proposed indication (for this appraisal) and current price
Omalizumab (Xolair, Novartis) is a monoclonal antibody that targets IgE. It has a UK marketing authorisation 'as an add‑on therapy for the treatment of chronic spontaneous urticaria in adult and adolescent (12 years and above) patients with an inadequate response to H1‑antihistamines'. Omalizumab costs £256.15 for a 150 mg prefilled syringe (excluding VAT; 'British national formulary' [BNF] online October 2014). A single dose of 300 mg costs £512.30 and the cost for a 24‑week course of treatment is £3073.80 (excluding VAT).	Indication and price per 150 mg pre-filled syringe is the same, eBNF March 18.

3. Registered and unpublished trials

4. Relevant services covered by NHS England specialised commissioning

NHS England commissions "Highly specialist allergy services (adults and children)", including for treating severe urticaria.

Appendix D – References

Hide, M., Park, H. S., Igarashi, A., et al. (2017). Efficacy and safety of omalizumab in Japanese and Korean patients with refractory chronic spontaneous urticaria. Journal of dermatological science, 87(1), 70-78.

Maurer, M., Kaplan, A., Rosén, K., et al. (2018). The XTEND-CIU study: Long-term use of omalizumab in chronic idiopathic urticaria. Journal of Allergy and Clinical Immunology, 141(3), 1138-1139.

Sánchez, J., Zakzuk, J., & Cardona, R. (2018). Evaluation of a guidelines-based approach to the treatment of chronic spontaneous urticaria. The Journal of Allergy and Clinical Immunology: In Practice, 6(1), 177-182.

Staubach, P., Metz, M., Chapman-Rothe, N., et al. (2016). Effect of omalizumab on angioedema in H1-antihistamine-resistant chronic spontaneous urticaria patients: results from X-ACT, a randomized controlled trial. Allergy, 71(8), 1135-1144.