CONFIDENTIAL

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Re: Adalimumab, etanercept, infliximab, certolizumab pegol, golimumab, abatacept and tocilizumab for the treatment of rheumatoid arthritis (review of TA guidance 130, 186, 224, 234 and part review of TA guidance 225 and 247) [ID537]

Dear Meindert

Thank you for your invitation to comment on i) the Appraisal Consultation Document (ACD) and ii) the updated final scope of the ongoing NICE MTA for Rheumatoid Arthritis.

Comments on the ACD
We welcome the draft guidance recommending biologic DMARDs in combination with methotrexate as an option for the treatment of patients with severe rheumatoid arthritis (RA).

We acknowledge that the majority of patients with RA currently receiving a biologic DMARD to manage their condition (severe disease DAS 28 >5.1) will be able to continue to receive appropriate treatment. We also welcome the further clarity of the continuation and stopping rules based on EULAR response, which we believe is consistent with clinical practice in England and Wales.

Although the ACD recommends that treatment should be started with the least expensive drug (taking into account administration costs, dose needed and product price per dose),.we would emphasise that the choice of drug should be based on a comprehensive assessment of the patient's disease severity, clinical course as well as other clinical and individual needs.

With respect to the analysis of patients with the fastest Health Assessment Questionnaire (HAQ) progression, we are unclear about the Committee's rationale

that this dataset is not as applicable to the moderate active group as to the severe active group. ERAS, the dataset on which this analysis was based, contains data on both moderate and severe patients; indeed the mean DAS score at baseline is 4.501 (DSU report, Section 4.1.1). The DSU report does not suggest that patients with moderate and severe RA have different probabilities of belonging to the latent dropout classes, so we believe that the analysis is equally as applicable to patients with moderate RA. Furthermore, the clinical experts who attended the second Committee meeting on 21st May 2015 stated that the initial DAS score does not define patients who progress fastest, and that the Committee did not feel sufficient evidence was presented regarding the characteristics of these patients (ACD, 4.3.18).

On the basis of this evidence, we believe there is insufficient evidence to define patients with the fastest HAQ progression by a DAS score >5.1. The Committee noted the clinical interest in the use of biological DMARDs in people with moderate active disease (ACD section 4.3.5); plus guidelines from the British Society of Rheumatology (BSR)[1] make this recommendation. Access to biologic DMARDs for patients with moderate disease could prevent the joint damage and impairment resulting from RA[2,3,4] and increase patients' productivity[5,6].

We would encourage the Committee to consult further on its proposed recommendation not to recommend the biologic DMARDs in fast progressing patients with moderate disease, and to reconsider the ERAS analysis as well as explore additional data sources in this patient subgroup. Specifically, we believe participants in the appraisal should be invited to submit additional data for fast progressing patients with moderate disease, as, ultimately, we believe the evidence could lead to NICE recommending the use of biologics in patients with moderate RA.

Comments on the updated final scope

We were surprised that the decision was taken to include biosimilars in the scope of the MTA without any consultation. In addition, we were notified of the change to the scope on 13th April 2015, which we believe was an inappropriately late stage in the process. Adding new technologies mid-way through an appraisal is a substantial deviation from NICE's standard process for MTAs, and this change to the Final Scope had implications for all manufacturers involved. We acknowledge that the Committee 'concluded that the availability of biosimilar treatments was not currently a key driver of cost-effectiveness' in this specific appraisal (ACD section 4.3.10); however we are concerned that this sets a precedent, which could be followed by similar 'late inclusion' of biosimilars into subsequent MTAs with limited (or no) timely consultation. This could lead to biosimilar medicines being appraised by NICE without the full and balanced consideration of all available evidence, which is not in line with NICEs Methods of Technology Appraisal.

Finally we confirm that we have not identified any factual inaccuracies in the ACD or the economic model.

We would be grateful if you would consider the points that we make in this response prior to the meeting of the Appraisal Committee on Wednesday 22nd July 2015.

If you have any questions please do not hesitate to contact me.

Yours sincerely,

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References

1 Deighton C, Hyrich K, Ding T et al. BSR and BHPR rheumatoid arthritis guidelines on eligibility criteria for the first biological therapy.2010. Rheumatology 49: 1197
2 Conaghan PG, Hensor EM, Keenan AM, et al. Persistently moderate DAS-28 is not benign: loss of function occurs in early RA despite step-up DMARD therapy. Rheumatology (Oxford) 2010;49:1894–9.
3 Kiely P, Walsh D, Williams R, et al. Outcome in rheumatoid arthritis patients with continued conventional therapy for moderate disease activity—the early RA network (ERAN). Rheumatology (Oxford) 2011;50:926–31.
4 Macedo A, Oakley S, Gullick N, et al. An examination of work instability, functional impairment, and disease activity in employed patients with rheumatoid arthritis. J Rheumatol 2009;36:225–30.
5 Augustsson J, Neovius M, Cullinane-Carli C, et al. Patients with rheumatoid arthritis treated with tumour necrosis factor antagonists increase their participation in the workforce: potential for significant long-term indirect cost gains (data from a population-based registry). Ann Rheum Dis 2010;69:126–31.
6 Radner H, Aletaha D, Smolen JS. Work Productivity, Quality of Life, and Health States of Different Disease Activity States in Patients with Rheumatoid Arthritis (RA). Ann Rheum Dis 2009 2009;68(Suppl 3):396.