Pfizer Response to the Appraisal Consultation Document for:

Adalimumab, etanercept, infliximab, certolizumab pegol, golimumab, tocilizumab and abatacept for rheumatoid arthritis not previously treated with DMARDs of after conventional DMARDs only have failed [ID537]

Pfizer would like to thank NICE for the opportunity to comment on the Appraisal Consultation Document (ACD) for the above appraisal. We welcome the interim recommendation that etanercept in combination with methotrexate continues to be considered a cost effective use of NHS resources for severe rheumatoid arthritis (RA) patients previously treated with methotrexate.

Despite the positive recommendation for combination therapy in severe RA patients previously treated with methotrexate, we are concerned that errors continue to be identified in the Assessment Group (AG) economic model, the most recent of which resulted in a change in cost per quality-adjusted life-years (QALYs) of approximately £20,000. In addition, Pfizer believes that limitations with the AG analyses have led to an underestimation of the cost-effectiveness of biologic disease modifying anti-rheumatic drugs (DMARDs) as outlined in Pfizer's previous consultation responses[1].

Pfizer continues to be confident that etanercept is a cost-effective treatment for all patients included in the scope of this appraisal. Therefore, we are disappointed that the Committee have issued preliminary recommendations that the use of etanercept for patients with moderate-to-severe RA previously treated with methotrexate and as monotherapy are not considered a cost-effective use of NHS resources. The preliminary monotherapy recommendation differs from the current published guidance issued by NICE in the Multiple Technology Appraisal (MTA) of adalimumab, etanercept and infliximab for the treatment of RA (TA130) in 2007, which states:

"TNF-α inhibitors should normally be used in combination with methotrexate. Where a patient is intolerant of methotrexate or where methotrexate treatment is considered to be inappropriate, adalimumab and etanercept may be given as monotherapy."

This change will lead to inequitable access to biologics for patients with severe RA who are intolerant of methotrexate or for whom methotrexate is considered to be inappropriate. Consequently, surgery will become the only treatment option following failure of conventional DMARDs for these patients.

[1] Pfizer submitted consultation responses to the Technology Assessment Report (dated 25/09/2013), the AG economic model (dated 22/01/2014) and the Decision Support Unit analyses (dated 02/04/2015).

More importantly, Pfizer believes that the preliminary recommendation to be unreasonable as important evidence has not been fully considered by the Committee, which has led to an over-estimation of the plausible incremental cost effectiveness ratio (ICER) for biologic DMARD monotherapy in severe RA patients. The main reasons for this over-estimation of the plausible ICER are based on the following three important factors:

i. The efficacy data used by the AG to inform the comparator sequence in the assessment of biologic DMARD monotherapy in severe RA patients previously treated with methotrexate may over-estimate the treatment effect of sulfasalazine. The sequences presented in Table 159 in the Updated Technical Assessment Report (TAR) suggest that the AG compared monotherapy biologic DMARDs to a sulfasalazine and non-biological therapy strategy. However, after review of the AG base case European League Against Rheumatism (EULAR) network (Updated TAR Table 19), it is clear that methotrexate is used in the control arm for each trial (n=8) that informed the efficacy estimates for conventional DMARDs in the economic model. Given that methotrexate has been recognised as potentially the most effective conventional DMARD (Emery 2000, NICE CG79, Pincus 2003, Smolen 2013), it is likely that the effectiveness of sulfasalazine has been overestimated. Consequently, Pfizer believe that the cost-effectiveness of biologic DMARD monotherapy for patients with severe RA previously treated with methotrexate has been underestimated, and will be lower than the current AG base case ICER of £48,300 (Pfizer cannot quantify the impact of this error on ICERs without an updated AG network meta-analysis).

ii. In Section 4.3.20 of the ACD report the Committee states that the most plausible ICER for combination therapy in severe RA patients previously treated with methotrexate was likely to lie between the AGs base case ICER (£41,600) and the ICER for the fastest Stanford Health Assessment Questionnaire (HAQ) progression (£25,300). However, a comparable analysis was not provided for severe RA patients who require monotherapy biologic DMARDs. Pfizer believe that this subset may also experience rapid disease progression. We would suggest that the resulting ICER would lie between those from comparable analyses for severe and moderate RA treated with combination therapy (£25,300 and £28,500 respectively). If calculated this estimate would provide the Committee with an ICER range and more accurate information upon which to consider the most plausible ICER for monotherapy.

iii. Finally, the Committee explain in Section 4.3.23 of the ACD report that ICERs for monotherapy biologic DMARDs were higher than combination biologic DMARD therapy. The Committee clarify that differences in ICERs were primarily driven by the

increased cost of replacing rituximab in combination with methotrexate with a subsequent line of monotherapy biologic. Pfizer is concerned that the decision not to recommend monotherapy biologic DMARDs as a cost-effective use of NHS resources is driven by the inclusion of specific treatments further down the treatment care pathway. This suggests that sensitivity analyses undertaken by the AG (presented in the company papers prepared ahead of the 2nd Committee meeting – dated 21/05/2015) may not have fully addressed this issue. Furthermore, the implausibility of the ICERs is emphasised by the similarity of efficacy estimates presented by the AG for monotherapy and combination therapy in both the European League Against Rheumatism (EULAR) and American College of Rheumatology (ACR) evidence networks.

As a result, Pfizer believes that the ICER considered most plausible by the Committee for etanercept monotherapy in severe RA patients has been over-estimated. Pfizer therefore considers the preliminary recommendation to be unreasonable. The economic estimates provided in our original submission remain the most plausible and demonstrate that etanercept monotherapy continues to be a cost-effective treatment option. Therefore, the Committee should reinstate etanercept monotherapy for this subset of the severe RA patient population to ensure equitable access to appropriate treatment.

References

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