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Vice chair
National Institute for Health and Care Excellence
10 Spring Gardens
London SW1A 2BU

17th September 2015

Dear ,

Re. Final Appraisal Determination (FAD) for the Multiple Technology Appraisal for 'Adalimumab, etanercept, infliximab, certolizumab pegol, golimumab, tocilizumab and abatacept for rheumatoid arthritis not previously treated with DMARDs or after conventional DMARDs only have failed' (ID537)

MSD would like to appeal the above mentioned FAD on the basis that NICE has failed to act fairly in making the recommendations. Our detailed arguments are set out below.

Ground 1(a) NICE has Failed to Act Fairly

1.1(a) The FAD unfairly discriminates against Remicade

We are very concerned that the FAD recommendation in paragraph 1.5 (as it applies to infliximab) effectively is a recommendation always to use biosimilar infliximab (to the exclusion of Remicade). This is the clear inference when paragraph 1.5 is read in conjunction with paragraphs 4.88 and 4.99 of the FAD. The relevant sections are as follows (emphasis added):

> *1.5 Start treatment with the least expensive drug (taking into account administration costs, dose needed **and product price per dose**). This may need to be varied for some people because of differences in the mode of administration and treatment schedules.*
>
> *[...]*
>
> *4.88 The Assessment Group also **explored the effect of using the NHS contract prices of the infliximab biosimilars**. Using the highest NHS contract price, the ICER for infliximab was reduced to £30,445 per QALY gained for the severe active subgroup, and to £37,658 per QALY gained in the moderate active subgroup. For the group of patients with the fastest HAQ progression the ICERs were £18,130 per QALY gained for the severe active subgroup and £20,462 per QALY gained for the moderate active subgroup.*
>
> *[...]*
>
> *4.99 The Committee understood that biosimilar versions of infliximab were now available in the NHS and that the scope of the appraisal had been updated to include these. It heard from the clinical experts that policies differ, but in their trusts people starting treatment may have a biosimilar.*

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However, if a person is already on a treatment and their disease is responding, they would not be switched to a biosimilar. The clinical experts noted that few people start treatment with infliximab because it is given by infusion rather than subcutaneous injection and is associated with greater administration costs than other TNF-alpha inhibitors. The Committee discussed comments from consultation that biosimilar products should not be considered interchangeable with the originator products. It understood that the approach adopted by NICE in this appraisal was consistent with the NICE position statement on biosimilars and that the regulatory authorities had concluded that the biosimilar infliximab products were sufficiently similar to the originator product to be granted marketing authorisation. ***The Committee noted that the NHS contract price for biosimilar infliximab was lower than the list price because of tendering by the NHS Commercial Medicines Unit. It noted that the prices from the NHS Commercial Medicines Unit had been included in sensitivity analyses completed by the Assessment Group (see sections 4.86 and 4.89). The Committee concluded that the ICERs for the infliximab biosimilars were a relevant consideration.***

The inclusion of the ICERs for biosimilar infliximab unfairly prejudices Remicade, as it implies that the biosimilars are the only cost effective infliximab. To ensure transparency over the FAD Recommendation in paragraph 1.5, we submit that paragraphs 4.88 and 4.99 need to be removed or at a minimum modified to ensure that readers are not left with the impression that biosimilar infliximab is the only recommended infliximab product.

Ground 1.2(a)The FAD Lacks Transparency

The FAD (specifically sections 4.88 and 4.99 referred to above) describes analyses performed by the Assessment Group using "contract prices" for biosimilar infliximab, which generated an incremental cost-effectiveness ratio. However, the analyses presented draw an unfair comparison and are inconsistent with NICE's own methods guide for the following reasons:

- Contract prices for biosimilar infliximab were considered in isolation; contract prices for Remicade, and for other biologics, were not considered in any analyses This approach is inconsistent and does not allow for a fair and transparent comparison.

- Contract prices do not represent nationally available price reductions as they are negotiated on a regional basis.

- Contract prices are subject to cyclical tender arrangements with the NHS Commercial Medicines Unit and therefore they cannot be guaranteed to remain in place for the duration of NICE guidance.

- There is no clarity or transparency on how the "*highest NHS contract price*" for biosimilar infliximab was determined.

The incorporation of contract prices in this way conflicts with the NICE Guide to the methods of technology appraisal (2013): "*When there are nationally available price reductions, for example for medicines procured for use in secondary care through contracts negotiated by the NHS Commercial Medicines Unit, then the reduced price should be used in the reference-case analysis to best reflect the price relevant to the NHS...Analysis based on price reductions for the NHS will only be considered when the reduced prices are transparent, and consistently available across the NHS, and if the period for which the specified price is available is guaranteed*" (Section 5.2.2).

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Moreover, the biosimilars were introduced into the scope of this appraisal in April 2015, at a very late stage of the appraisal process (the Final Scope was published in November 2012). We note that NICE has based its decision to incorporate these two biosimilars on NICE's biosimilar policy, but that policy was adopted several months after the deadline for submitting evidence in this appraisal had passed. It is not obvious from the policy that it allows NICE to automatically incorporate new technologies. The late addition of biosimilars to an existing process after evidence submissions had already been made compounds the unfairness described above.

Next Steps

We kindly ask for an oral hearing to consider this appeal.

Yours sincerely,

, Managing Director of MSD in UK