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Sent by email: [redacted]

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12 September 2017

Dear [redacted]

Appeal against Final Appraisal Determination (FAD): Inotuzumab ozogamicin for treating relapsed or refractory B cell acute lymphoblastic leukaemia

Thank you for your letter of 4 September 2017 lodging an appeal on behalf of Pfizer Limited against the above FAD.

Introduction

The Institute's appeal procedures provide for an initial scrutiny of points that an appellant wishes to raise, to confirm that they are at least arguably within the permitted grounds of appeal ("valid"). The permitted grounds of appeal are:

- 1(a) NICE has failed to act fairly, or
- 1(b) NICE has exceeded powers
- (2) the recommendation is unreasonable in the light of the evidence submitted to NICE

This letter sets out my initial view of the points of appeal you have raised: principally whether they fall within any of the grounds of appeal, or whether further clarification is required of any point. Only if I am satisfied that your points contain the necessary information and arguably fall within any one of the grounds will your appeal be referred to the Appeal Panel.

Initial View

Ground 1 (a)

Ground 1.1 The appraisal committee has seemingly failed to consider the cost effectiveness of inotuzumab applicable to UK clinical practice when used in accordance with its marketing authorisation

A valid appeal ground.

Ground 1.2 The fact that the clinical experts were not invited to the second meeting of the Appraisal Committee meant that important clinical advice was not available to guide the preparation of the FAD

A valid appeal ground. It may assist you in preparing for the appeal to know that a similar point was raised in a 2011 appeal concerning Ranibizumab for the treatment of diabetic macular oedema (past appeal decisions can be found on NICE's website). NICE's appeal panel does not consider itself bound by previous decisions, but it may have regard to them.

Ground 1.3 The Committee has provided no explanation for its decision to reject the utilities proposed in the revised Pfizer base case for the post HSCT period and submitted in response to consultation

Paragraph 3.20 of the FAD does appear to provide an explanation of this decision, albeit a fairly brief one. It reads as relevant "*The ERG noted that the utility values used in the company's original base case post-cure (0.74 and 0.76) were based on a relevant published study (Kurosawa et al. 2016) and are preferable to the new assumption, which is not supported by evidence*." and "*The committee agreed with the ERG ...The committee concluded that ... utilities from Kurosawa et al. 2016 for disease-free patients are its preferred assumptions*." The reason therefore seems to be that the Kurosawa values are based on a published study and the values proposed post-consultation are not?

I would not presently be minded to allow this appeal point to proceed.

Ground 2

2.1 The Appraisal Committee's reasons for disregarding key assumptions used for the purposes of NICE's appraisal of blinatumomab do not explain the choices that were made in relation to inotuzumab

A valid appeal point. I note that this point is put on grounds of consistency, and that at the very end of the appeal point you state that a lack of consistency is arbitrary and unreasonable. It may assist in preparing for the appeal if I suggest that I agree that in my view that would be the correct approach to take to a requirement of consistency between appraisals (although it will be for the appeal panel to determine what it considers the requirements of consistency are). In other words, the question is whether a lack of consistency leads to a conclusion that the recommendation in this appraisal is arbitrary or unreasonable.

The appeal panel considered the requirement for consistency in a 2014 appeal concerning aflibercept in the treatment of metastatic colorectal cancer. I noted above that NICE's appeal panel does not consider itself bound by previous decisions, but it may have regard to them.

2.2 The Committee has seemingly misunderstood the utilities submitted by Pfizer in response to consultation on the ACD

A valid appeal point.

2.3 The Committee has misinterpreted Pfizer's revised submission on administration costs

In your letter you explain that your response to the ACD modelled one day of inpatient care for inotuzumab and fourteen days for standard of care.

The FAD shows that the committee felt it was likely that there was a difference in the number of inpatient days between inotuzumab and standard care, but that it was not likely to be 1:14. It concluded that your model underestimated the ICER.

Your letter explains that your submission was not that inotuzumab required one day of inpatient care, but that this was the value attributed to the administration of the product. I think that you are saying that additional days of inpatient care were included in your model, but under adverse events. I am not sure from your letter how many such days were included. I think from your letter that you took the same approach to standard care, where you costed fourteen days for administration and a further seven days for adverse events.

I am not sure that I see the alleged misunderstanding. According to FAD 3.22 no new evidence or explanation was presented for why the company was now modelling different numbers of inpatient days from its first submission. I can see that the committee did not accept the figure of one day for inotuzumab, but not that the reason for that was that it felt

you had not included inpatient stays attributable to adverse events at all. It appears from the FAD that they simply did not accept a figure that (according to them) was different from the figure first submitted and was being asserted without evidence or explanation. They then compared that figure to the figure of fourteen days for standard care, which on the explanation contained in your appeal letter seems to have been a correct comparison (i.e. they were comparing like with like in that neither figure included any allowance for adverse events). They concluded that a ratio of 1:14 was not plausible and that the ICER in your revised model was likely to be underestimated.

That seems to be a correct understanding of your submission? Had the committee compared one day's inpatient care with inotuzumab to 21 days for standard care then I would have understood that it might appear that they thought you were arguing that the one days care included care for all reasons, but as it is they seem to have compared inpatient stays for administration only in both cases.

I would welcome any further elaboration on this point, but at present I would not be minded to let it proceed.

As I agree some of your appeal points are valid they will be passed to an appeal panel for consideration. There will be an oral hearing. I would be grateful to receive your comments on the points I am presently not minded to treat as valid within 14 days of this letter, no later than **Tuesday 26 September**, whereupon I will take a final decision.

Yours sincerely

Dr Rosie Benneyworth
Vice Chair
National Institute for Health and Care Excellence