­Sent by email to: [XXXXXXXXXXXXXXXXXXXXXXXXXXXX](mailto:Linda.McNamara@kyowakirin.com)X

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Kyowa Kirin

25 March 2021

Dear XXXXX

**Re: Final Appraisal Document –** **Mogamulizumab for previously treated mycosis fungoides and Sézary syndrome [ID1405]**

Thank you for your letter received on 18 March 2021, lodging Kyowa Kirin’s appeal against the above Final Appraisal Document (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.

You have the opportunity to comment on this letter in order to elaborate on or clarify any of the points raised before I will make my final decision as to whether each appeal point should be referred on to the Appeal Panel.

Initial View

I assess each of your points in turn and then summarise the appeal points that I am presently minded to refer at the end of this letter.

You make fourteen appeal points, nine under ground 1 and five under ground 2. Rather than re-produce the detailed submissions in your appeal letter, which I have considered, I will refer to your appeal points as set out in bullet points at the top of your letter for convenience.

***Ground 1(a): In making the assessment that preceded the recommendation, NICE has failed to act fairly***

1. Your appeal point 1.1: *“The Committee’s decision that allogenic stem cell transplant should not be included in the economic modelling for mogamulizumab because aSCT had not been permitted in the MAVORIC trial is unfair.”*

I understand this point to be in essence that the Committee unfairly failed to take into account that a benefit of mogamulizumab treatment is the possibility that for some patients this may be used as a bridge to aSCT.

This is a valid appeal point.

1. Your appeal point 1.2: *“The Committee’s conclusion that the IPCW-adjusted curve was not clinically plausible for the average person in the modelled population with severe disease is unexplained.”*

I am not persuaded this is a valid appeal point because standards of procedural fairness do not require the Committee to explain the reasons behind every statement or even every issue resolved in the FAD. In my view the FAD and the committee papers as a whole provide intelligible and adequate reasons which enable the appellant to understand why the recommendation was made as it was and what conclusions were reached on the principal issues. I am unwilling at present to refer an appeal point that transparency and procedural fairness require that a Committee must go further. In short, the statement that the IPCW-adjusted curve was not clinically plausible was the reason which the committee was obliged to give, and fairness does not require reasons for reasons.

While I am not minded to refer your point 1.2 separately, it may be that some of your concerns under this point will also sit under your appeal point 2.2, which is valid (see below).

1. Your appeal point 1.3: *“The Committee’s decision not to include carer utilities in the economic model is based on conclusions which are inconsistent with NICE’s Methods Guide and inadequately explained.”*

I am not persuaded this is a valid appeal point under ground 1(a) because:

* I do not think your arguments under this point relating to a failure to give reasons / explain why the Committee rejected the utility gain are arguable for the reasons explained in my response to your point 1.2 above; and
* to the extent your arguments under this point relate to either a misunderstanding of or failure to follow NICE’s Methods Guide, I do not think this is arguable as the Methods Guide does not prescribe whether or how the Committee must incorporate carer utilities in its modelling and the Committee expressly recognised the burden placed on some carers.

That said, I interpret the substance of your point 1.3 to be that it was unreasonable for the Committee to remove carer utility values from the base-case analysis, and on that basis I am minded to refer your point 1.3 to the appeal panel, but under ground 2.

1. Your appeal point 1.4: *“The Committee’s conclusion that mogamulizumab is not a life-extending treatment at the end of life relies on evidence which has not been disclosed and is therefore unfair.”*

This is a valid appeal point.

1. Your appeal point 1.5: *“The Committee’s conclusions regarding the ICER threshold for this appraisal do not take into account the factors identified in NICE’s Methods Guide”*

I am not persuaded this is a valid appeal point. In short, I disagree that it follows from the Committee referring at paragraph 3.14 of the FAD to one factor listed in the Methods Guide that the Committee must not have considered the other factors there listed. I refer to my above comments on the degree of granularity that can be expected of a Committee as a matter of procedural fairness; in my view it is unarguable that the Committee is required to list every one of its considerations in the FAD. In my view it was proper for the Committee to highlight only those factors it considered most important as it is this information that assists the company in understanding the Committee’s concerns. Fundamentally an FAD is guidance to clinicians and it is reasonable that it focuses on matters of most importance to clinicians in a given appraisal rather than, say, treating the list of factors set out in the methods guide as a checklist every element of which must be expressly discussed in a FAD, whether a significant driver of the decision or not.

1. Your appeal point 1.6: *“The Committee’s conclusions regarding the appropriate ICER threshold for this appraisal do not assess uncertainty in accordance with NICE’s Methods Guide.”*

This is a valid appeal point.

1. Your appeal point 1.7: *“The Committee’s conclusions regarding the appropriate ICER threshold for this appraisal lack transparency.”*

This is a valid appeal point.

1. Your appeal point 1.8: *“The Committee’s conclusions regarding the most plausible ICER for this appraisal lack transparency.”*

I am not persuaded this is a valid appeal point. I am not surprised to see a wide most plausible ICER range in an appraisal such as this where the committee found a high degree of uncertainty, and I do not consider it arguable that the width of the range in itself indicates procedural unfairness.

There is no procedural requirement for a Committee to “make a proper determination…as to the most plausible ICER” in any appraisal. Indeed in many cases there will be no single most plausible ICER, as different assumptions etc. may be considered equally plausible. These are points that have been considered by past appeal panels. What is required is for the Committee to give sufficient information for the company to understand the Committee’s concerns around cost efficacy and the issues that would need to be resolved to enable the Committee to make a positive recommendation. In my view it is clear from the FAD as a whole where the issues were in the appraisal, and why the Committee reached its overall conclusion on cost effectiveness.

I therefore disagree with your arguments in your appeal letter that the FAD makes it impossible for the company to “know what the Committee’s conclusions are and… test whether they are reasonable” and that “The effective difference between the upper and lower bounds of the range set out in paragraph 3.15 of the FAD, is however currently so large that it precludes sensible engagement by the company.” If that is so it seems to me it is a consequence of other conclusions in the appraisal rather than an appealable result in its own right. In the circumstances, it is not necessary for the company to be informed of a single most plausible ICER or a narrow range in order for it to engage with the FAD.

1. Your appeal point 1.9: *“The Committee’s statement that the relevant benefits associated with mogamulizumab could be adequately captured in the model disregards its own conclusions, is inconsistent with NICE’s procedures and lacks transparency.”*

I am not persuaded this is a valid appeal point under ground 1(a).

First, it seems to me obvious that the final sentence of paragraph 3.17 of the FAD intends to convey the committee’s view that the “relevant benefits” were in fact adequately captured in the assessment of cost effectiveness, i.e. that the model was in a technical sense fit for purpose.

Secondly, as to your point 1.9(b) regarding failure to reach a conclusion in relation to the impact of including carer utilities in the economic model, I am not persuaded that this is a valid appeal point under ground 1(a). However, I invite you to make these arguments when presenting your point 1.3 above, which I have stated is a valid appeal point under ground 2.

For the avoidance of doubt, I do not consider this a valid point under ground 1(a) as I disagree that procedural fairness requires a Committee to provide this information, but I am happy to refer your points 1.3 and 1.9(b) together as a single appeal point under ground 2.

***Ground 2:******the recommendation is unreasonable in the light of the evidence submitted to NICE***

1. Your appeal point 2.1: *“The Committee’s conclusion that data from the Hospital Episodes Statistics (HES) database was not adequately matched to the data from MAVORIC is incorrect and unreasonable.”*

This is a valid appeal point.

1. Your appeal point 2.2: *“The Committee’s reliance on the TSE method to produce OS estimates for survival in the standard care arm of MAVORIC is inconsistent with the available evidence.”*

This is a valid appeal point. As noted above, your similar arguments (relating to the crossover trial method only) under your point 1.2 may also be made here.

1. Your appeal point 2.3: *“The Committee’s conclusions regarding the disease-modifying effects of mogamulizumab disregard expert evidence and misinterpret the evidence of one patient expert and are therefore unreasonable.”*

I am not persuaded this is a valid appeal point.

As to your arguments under (a), it is possible for reasonable people to reach different conclusions; the fact that the Committee did not adopt the opinions of the experts listed in your appeal letter does not in itself show the Committee was unreasonable.

As to your arguments under (b) regarding time to next treatment, as noted above in my view it is unarguable that the Committee is required to list every one of its considerations in the FAD, and I am therefore not persuaded that the fact the analysis you refer to is not mentioned in the FAD suggests that it was disregarded (as opposed to not being given sufficient weight by the Commission to require express mention). To the extent that your argument is that the results of this analysis render the overall recommendation unreasonable, I do not consider this arguable from the information provided in your appeal letter.

Finally regarding (c), I interpret your argument to be that the evidence (i.e. that when treatment is stopped its benefits do not discontinue immediately but rather symptoms return ‘slowly’) suggests continued clinical benefit whereas the Committee decided from the same evidence that it could not conclude there was continued benefit. It seems to me that as with (a) above, this is an example of the Committee and the company reaching differing but reasonable conclusions.

1. Your appeal point 2.4: *“The Committee’s conclusion that it was not convinced that mogamulizumab provides an OS benefit is unreasonable in light of the evidence available.”*

This is a valid appeal point.

1. Your appeal point 2.5: *“The Committee’s conclusion that mogamulizumab is not considered to be a life-extending treatment at the end of life relies on incorrect and irrelevant data and is therefore unreasonable.”*

This is a valid appeal point.

In summary, I am presently minded to conclude that there are nine valid appeal points, four of which are ground 1 appeal points (namely your points 1.1, 1.4, 1.6 and 1.7) and five of which are ground 2 appeal points (namely:

* your points 1.3 and 1.9(b) (regarding carer utilities) as a single appeal point under ground 2,
* your point 2.1,
* your points 2.2 and 1.2 (to the extent it relates to crossover trial method) as single appeal point,
* your point 2.4, and
* your point 2.5).

In respect of your points which I am not minded to refer or that I am minded to amalgamate or refer only under ground 2, you are entitled to submit further clarification and/or evidence to me within the next 10 working days, no later than **Monday 12 April 2021**, and I will then give a final decision on the points to put before an appeal panel. For the points I am already content to refer on, an oral appeal will be held which under current circumstances is likely to be held remotely.

Once I have made my final decision, and where there is more than one appellant, each appellant will receive the valid appeal points of the other appellants and their redacted appeal letter. This is to enable appellants to avoid duplication at the hearing where there are overlapping appeal points. If the appeal letter and/or responses to scrutiny contain confidential information please ensure you have provided a version with this information redacted by **Tuesday 20 April 2021**.

Yours sincerely

Tim Irish

Vice Chair

National Institute for Health and Care Excellence