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13 August 2021

Dear XXXXXX

**Re: Final Appraisal Document –** **avelumab for maintenance treatment of locally advanced or metastatic urothelial cancer after platinum-based chemotherapy [ID3735]**

Thank you for your letter of 6 August 2021 addressed to Tim Irish, lodging your appeal against the above Final Appraisal Document (FAD). Mr Irish has stepped back from overseeing the NICE appeal process and I am replying as NICE’s lead non executive director for appeals.

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.

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. *The Committee’s conclusion that a stopping rule is inappropriate for avelumab is inconsistent with previous appraisals for immunotherapies (IOs) in metastatic urothelial cancer (mUC).*

As you are aware, past appeal panels have been careful not to set the requirement of consistency unrealistically high. If two appraisals are truly sufficiently similar that an obligation of consistency arises, then the reason for any apparent inconsistency has to be stated.

Here it seems that the committee considered the question of a stopping rule in immunotherapies after platinum-based chemotherapy in urothelial cancer as sufficiently similar to warrant consideration. I will proceed on the basis that that is right. They have identified that in the past a stopping rule was implemented, and have given their reasons for not doing so in this case in a substantial paragraph. I note that the duration of treatment was discussed in the ACD and that consultation comments were received on it.

The committee were clearly aware of past practice and that they were departing from it, and have given their reasons. It seems to me that that has discharged any obligation of consistency that past appeal panels have identified. Your letter appears to take that obligation further, in that you imply that the approach taken in atezolizumab must also be taken here but that goes too far. Committee’s must have room to exercise their own judgement on the facts of each appraisal.

I would not be minded to refer this point to an appeal panel.

* 1. *The Committee has relied upon irrelevant considerations in deciding that it would not implement a stopping rule for avelumab*

I accept that the purpose of a stopping rule in an SmPC and in a NICE recommendation is likely to be different, as past appeal panels have observed. But I cannot accept that the fact that a trial (and hence the SmPC) did not have a stopping rule is irrelevant to whether a stopping rule should be proposed by NICE. For example, if the SmPC did have a stopping rule then, unless NICE was to recommend off label use, its recommendation would also have a stopping rule. It would also be reasonable to suppose that patient-clinician conversations about stopping treatment would be different (and perhaps easier) if treatment beyond the stopping rule was off label. At the least the clinician would have to have a further conversation to obtain informed consent to off label use. And the data generated in a trial with a stopping rule would be more directly relevant to a recommendation with the same stopping rule.

For these reasons I do not think it can be said that the fact that there was no stopping rule in the SmPC or clinical trial is positively something which the committee must not take into account and I would not be minded to refer this point to an appeal panel.

* 1. *The Committee has provided no explanation for its concern that it would be difficult for patients to accept discontinuance of treatment after 2 years and for rejecting the evidence of the clinical and patient experts and patient organisations*

I agree it is important that committees provide adequate reasons for their conclusions. The conclusion here is that a stopping rule should not be included in the preferred model, and the whole of FAD 3.8 gives reasons for that. One reason is that “*It was concerned that it would be difficult for patients to accept that they would no longer be able to have treatment after 2 years if they were free from disease, and they may fear losing treatment benefit*”. Although they do not explicitly say so it is fair to infer that they thought that the evidence to the contrary was optimistic.

I do not accept that an obligation to give reasons extends not only to indicating a disagreement with a certain piece of evidence, but also to giving reasons for that disagreement. Here the committee’s judgement of what was likely was not the same as what the patients and clinicians thought was likely. We can see what the committee thought and why they thought it, and it is hard to see what more can be said.

I would not be minded to refer this point to an appeal panel.

* 1. *In view of the Committee’s view that it would be difficult for patients to accept a stopping rule for avelumab at 2 years, despite substantial evidence to the contrary, the clinical and patient experts should have been invited to attend the second meeting of the Appraisal Committee*

This point can only be on one of two related bases; either there was something that they needed to say that they had not had the chance to say, or the committee had not properly informed itself of some relevant issue and the experts were needed at the meeting so that they could be informed.

Neither of those bases seems to apply here. The stopping rule/duration of treatment topic was in play at the ACD stage and the views of the patients and clinicians were known. Whilst, the committee did not agree with those views, fairness does not require that clinical or patient experts are invited to a second meeting to repeat their views to the committee. The chance to inform and persuade arises in the first meeting and through the ACD consultation. Unless those chances have gone wrong, or some new considerations have arisen, I cannot see that a committee is required to give a further opportunity to repeat the same material at a second meeting. (And, for the avoidance of doubt, my view would be the same even if it would not have been the same material, as any new material could have been shared at the first meeting or in consultation.)

I would not be minded to refer this point to an appeal panel.

* 1. *In questioning whether the evidence of clinical experts regarding life expectancy corresponded to the population eligible for maintenance treatment with avelumab despite evidence to the contrary, the clinical and patient experts should have been invited to attend the second meeting of the Appraisal Committee (17th June 2021)*

My view of this point is the same as my view of point 1.4, save that to the extent that there may be a complaint that the committee did not take the necessary steps properly to acquaint itself with the evidence, that can be considered under your related ground 2 point.

I would not be minded to refer this point to an appeal panel.

* 1. *The Committee’s conclusion that it is not appropriate to pool health-state utilities across treatment arms is inconsistent with previous appraisals for immunotherapies (IOs) in metastatic urothelial cancer (mUC).*

The preference for pooled utilities or those from separate treatment arms is very much an expert judgement for a committee that can only be taken in the light of the data available in each appraisal. There are benefits and disbenefits to each approach and a trade off to be made which will be highly fact specific. I am very sceptical that there can be a meaningful expectation of “consistency” here, even in the same disease, unless perhaps one is dealing with the very same trial data. In any event the committee were clearly aware that a different approach was taken in a previous appraisal. The committee’s reference to patients in the BSC arm possibly having more effective subsequent treatment seems reasonable and is referenced in the committee slides. I note the committee’s preference differed from the ERG but I do not think that is so remarkable in this case as to call for a more detailed explanation.

I would not be minded to refer this point to an appeal panel.

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

*2.1 In considering the application of the end of life criteria, the Committee has misapplied the relevant test and reached a conclusion which does not reflect the balance of the evidence..”*

A valid appeal point. So as to guide preparation for the appeal, but not to restrict the arguments you may wish to make, an appeal panel may particularly wish to consider why what appears to be a similar, but not identical, patient population was held to meet the short life expectancy criterion in TA692, but not in this appraisal.

2.2  *The Committee’s conclusion that it is not appropriate to pool health-state utilities across treatment arms may have been impacted by a misunderstanding of the impact this has on the ICER*

I am not persuaded that this could amount to unreasonableness, although it may be grounds for a factual correction.

I would not be minded to refer this point to an appeal panel.

In respect of your points which I am not minded to refer or you are entitled to submit further clarification and/or evidence to me within the next 10 working days, no later than **5pm on** **Friday 27 August 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 7 September 2021.

Yours sincerely

Dr Mark Chakravarty

Lead Non-executive Director for Appeals

National Institute for Health and Care Excellence