Xx xxxxx xxxxxxx

Managing Director, UK & Ireland

MSD

Sent by email: xxxxxxxxxxxx[@merck.com](mailto:kalpana.doca@merck.com)

29 April 2020

Dear xx xxxxxxx

**Re: Final Appraisal Document - Pembrolizumab for treating locally advanced or metastatic urothelial carcinoma after platinum - containing chemotherapy [ID1536] (CDF guidance review of TA519)**

Thank you for your letter of 21 April 2020, responding to my initial scrutiny letter. This letter represents my final decision on initial scrutiny.

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

1. **Ground 1a.1 – Fundamental differences with the approach taken in TA525 evidence an inconsistent methodology, in breach of the Methods Guide and the principle of procedural fairness**

Already accepted as a valid appeal point.

Thank you for your further comments on the material from past appraisals to be put before the appeal panel in this case. My objective here is to enable the appeal panel to consider this point fairly, while retaining the focus on this appraisal, and ensuring that any material from other appraisals is kept to a proportionate and manageable length. I consider that a plausible consistency point ought to be able to be demonstrated from a reasonably modest volume of papers.

Therefore I will ask that NICE includes the following documents in the appeal papers:

* The FAD from TA525
* The third set of committee slides from TA525
* A document containing extracts from any other papers in TA525 or TA520, prepared by you, and complying with the specification below.

The extract document referred to above should be no longer than 15 pages in length at 10 point font, and should contain nothing except verbatim extracts from documents that were before or generated by the committee in TA525 or 520, (and for the avoidance of doubt no summary or argument based on those extracts). Any ellipsis should be marked in the usual way and should not change the meaning of any extract. The document should for each extract state precisely where the extract is taken from, and include a hyperlink to the relevant document on the NICE website which is for the convenience of NICE staff in confirming the accuracy and context of the extract only.

It would be helpful if you could provide NICE with the extract document requested within 14 days of receiving this letter, or if that is not possible, to indicate when the document can be expected.

It is possible that the committee will want to draw the appeal panel’s attention to other documents from TA525 or 520. If they do so I would allow them to include a similar volume of material to that which I have allowed you to include, and again without commentary.

This will then form the body of material from earlier appraisals that will be before the panel in this appeal and from which you can make your consistency arguments.

**Ground 1a.2 – It is procedurally unfair to have introduced paragraph 3.19 (“The costs of pembrolizumab are likely underestimated in the model”) in the FAD at a very late stage, without explanation or any opportunity to respond**

Already accepted as a valid appeal point.

***Ground 1b NICE has exceeded its powers***

**Ground 1b.1 – NICE has breached its legal obligations under human rights and equalities laws**

I have considered your further points and now agree these arguments should go forward as points in their own right. I also agree they should be addressed in the same way that they have been addressed in past appraisals, which is as follows:

* The committee will be given an opportunity to make any comments they wish on the points as they stand in your original and most recent letter. For the avoidance of doubt the committee, who are not legally qualified, are not expected or required to make any response and if they do not the panel will not draw inferences. My understanding is that a response is not usually made.
* The panel’s legal advisor will prepare a written note of legal advice on your points, which will be circulated in advance to the panel, the appellants and the committee. I would hope this will be done not less than three weeks before the hearing.
* You (and the committee if it wishes) may prepare a short note in response to the panel’s advice, which should be confined to the law and not introduce any wholly new points, within seven days of receiving that advice.

This will form the material on which the panel will take its decision on these points. It will be for the panel to decide if in light of the written material it wants to hear any additional oral submissions either on the law or on any relevant factual issue.

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

**Ground 2.1 – The Appraisal Committee’s assessment of duration of treatment effect and its effect on cost-effectiveness is illogical and unreasonable**

**Ground 2.2 – The Appraisal Committee’s analysis of evidence from the clinical expert in paragraph 3.15 of the FAD is internally inconsistent and its conclusions are unreasonable**

Agreed as valid points with 2.2 to be taken as an aspect of 2.1, thank you.

**Ground 2.3 – The Appraisal Committee’s decisions that: (i) a range of possible ICERs from £48,518 to £70,520 applies; and (ii) the “most plausible” ICER for pembrolizumab is likely to be above £50,000, are unreasonable in light of the evidence submitted**

I agree this should remain as a standalone point.

**Ground 2.4 – The statement that “the costs of pembrolizumab are likely underestimated in the model” lacks meaningful explanation and evidence and it is unreasonable to have taken it into account for the purposes of assessing cost-effectiveness**

Agreed as a valid appeal point.

**Ground 2.5 – The conclusion that new data from KEYNOTE-045 “shows the 2-stage method may not be appropriate, and the unadjusted method should also be taken into account” results from a flawed and unreasonable interpretation of the evidence**

Agreed as a valid appeal point.

NICE will now contact you to make arrangements for an oral appeal hearing, which subject to the then current requirements and guidance on lockdown is expected to be conducted remotely.

Many thanks

Yours sincerely

Dr Rima Makarem

Interim Vice-Chair, National Institute for Health and Care Excellence