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Sent by e-mail only Immunocore Ltd.

7 September 2023 Dear Immunocore Ltd.

**Re: Final Appraisal Document — Tebentafusp for treating advanced uveal melanoma [ID1441]**

Thank you for your letter of 31 August 2023, lodging an 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 provide an initial view on whether they are within the permitted grounds of appeal ("valid") and are at least arguable. 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, are arguable, and 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.

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

# Appeal point 1(a).1: 1(a).1 NICE acted unfairly by applying two criteria that it had already confirmed were no-longer appropriate, when it assessed whether tebentafusp should be routed to the Highly Specialised Technology (HST) programme. Consequently, tebentafusp was



**perversely routed through the Single Technology Appraisal (STA) programme, which is not intended for highly specialised health technologies and was unlikely to lead to a positive recommendation.**

I do not regard this as a valid appeal point. That is because NICE's routing decision for a technology appraisal falls outside of the scope of this appeals process. Section 4.2 of NICE's appeals process guide is clear that: "*An appeal can only relate to final draft guidance for a technology appraisal or highly specialised technologies evaluation, or the way that the evaluation was done*."

# Appeal point 1(a).2: NICE acted unfairly and inconsistently by refusing to accept Immunocore’s modelling methods, when they were consistent with what has previously been accepted by NICE in prior technology appraisals and are consistent with best modelling practice.

You make two arguments within this appeal point 1(a).2, namely:

1. The Committee was required as a matter of procedural fairness to accept Immunocore's modelling methods, and failed to do so; and
2. The Committee was required as a matter of procedural fairness to "provide adequate explanations of their decision-making", and failed to do so.

I am minded to refer your second argument to the Appeal Panel as point 1(a).2.

I am not currently minded to refer your first argument. That is because paragraph 3.11 of the FAD demonstrates that the Committee understood the advantages and disadvantages of the different modelling approaches preferred by the company and ERG and considered those options before concluding that using a standard parametric approach to extrapolate the data in both treatment arms was preferred. Assuming your appeal letter is correct that this was inconsistent with the views of clinical experts and previous NICE TAs (including the comparator), I am not persuaded that this in itself creates potential procedural unfairness. Your appeal letter does not point to a specific requirement in NICE TSD 21 or Palmer et al. or otherwise that required the Committee as a matter of procedural fairness to prefer Immunocore's modelling methods. If you wish to pursue this argument I invite you to explain why you consider there is such a requirement in your response to this letter.

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

# Appeal point 2.1: it was unreasonable for NICE to exclude tebentafusp from HST on the basis of two redundant HST criteria.

I do not regard this as a valid appeal point. That is because NICE's routing decision for a technology appraisal falls outside of the scope of this appeals process. Section 4.2 of NICE's appeals process guide is clear that: "*An appeal can only relate to final draft guidance for a technology appraisal or highly specialised technologies evaluation, or the way that the evaluation was done*."

# Appeal point 2.2: The Committee’s decision to apply standard parametric modelling to overall survival cannot reasonably be justified because it led to clinically implausible results, namely, in the EAGs model, the estimate of 5-year survival in the comparator arm is 4-fold higher than published historical data.

I am minded to refer this appeal point to the Appeal Panel. Where you refer to the "EAG" in your appeal points this will be amended to ERG (the evidence review group) as referenced in the FDG.

# Appeal point 2.3: The Committee’s conclusion that overall survival modelling is highly uncertain and standard parametric approaches are the most appropriate to apply to both treatment arms, cannot reasonably be justified.

I am minded to refer this appeal point to the Appeal Panel, save for your argument that:

"*The Committee’s conclusion, in effect, does not add up because it will mean that in order for tebentafusp to be cost-effective using the NICE endorsed EAG modelling approach, it will have to be provided below the cost of providing tebentafusp in England, Wales and Northern Ireland. This is inherently unreasonable and cannot be justified. Details of this calculation are provided in confidential appendix 1 of the appeal*."

I do not consider the above argument to be a valid appeal point. That is because there is no obligation on NICE (as a matter of procedural fairness, reasonableness or otherwise) to recommend a technology as cost effective for use within the NHS solely because that technology is priced at or below cost price. It cannot be right – as you suggest - that NICE is required to recommend any technology provided below cost. Rather, NICE's role is to evaluate clinical and cost effectiveness and make recommendations on that basis.

# Appeal point 2.4: In the context of an appraisal of a medicine for an ultra-rare disease, it is not reasonable for the Committee to reject the Company’s model on the grounds that the decrease in hazards is based on only a limited number of people

I am not minded to refer this appeal point to the Appeal Panel. Section 3.11 of the FAD demonstrates the Committee noted and understood the hazard plot in the tebentafusp group but considered there was still uncertainty in the overall survival modelling. Your appeal letter criticises a statement in the FAD that appears to me to be a factual statement by the Committee rather than a conclusion (“The Committee accepted that the Kaplan–Meier and hazard plots showed the hazards increasing and decreasing. But it noted the decrease in hazards was only based on limited number of people. So it was less certain of the factors that were driving this.”).

Your appeal letter points to no evidence submitted to NICE in light of which it is arguably unreasonable for the Committee to prefer a standard parametric approach "on the grounds that the decrease in hazards is based on only a limited number of people".

If you wish to pursue an argument that the Committee took an unreasonable approach in respect of how rarity was taken into account in its decision-making then I invite you to set this out in detail, with reference to the evidence, in your response to this letter. I refer you to my response to your point 2.7 below, which appears to raise the same or an overlapping issue.

# Appeal point 2.5: The Committee’s conclusion that the Company’s modelling overestimated the proportion of people surviving in the long term, because it generated extrapolations suggesting that people did not appear to die in the period modelled by the parametric section is incorrect. This demonstrates that the Committee misunderstood the modelled survival data, and therefore the Committee’s conclusion cannot reasonably be justified.

I am minded to refer this appeal point to the Appeal Panel.

# Appeal point 2.6: The Committee’s apparent endorsement of a monthly best supportive care costs model, and the Committee’s rejection of an evidence-based expert supported one-off aggregated cost model without justification, cannot reasonably be justified.

I am not minded to refer this appeal point to the Appeal Panel. That is because it is clear from paragraph

3.15 of the FAD that the Committee understood the differences between the approaches proposed by the company and ERG and considered the comments of clinical experts before arriving at its conclusion that the estimated costs of subsequent treatment are uncertain, and, importantly, noting that "it considered this had a limited impact on the cost-effectiveness results." Nothing in your appeal letter persuades me that the Committee endorsed a particular model without justification (as alleged) or that the Committee's conclusion or overall recommendation was unreasonable in light of evidence submitted to NICE.

# Appeal point 2.7: The EAG and the Committee’s preferred scenario is unreasonable because it would require tebentafusp to be provided below-cost in order to be cost-effective. This is inconsistent with NICE’s obligations to support innovation and does not reasonably take into consideration the fact that advanced uveal melanoma is an ultra-rare disease with only 100 patients per year expected to be eligible for tebentafusp.

You make three arguments within this appeal point 2.7, namely the Committee’s decision to apply standard parametric modelling to overall survival is unreasonable because:

1. "the price of tebentafusp required to be cost-effective would be below-cost price";
2. it "is inconsistent with NICE’s obligations to support innovation"; and
3. it "does not reasonably take into consideration the fact that advanced uveal melanoma is an ultra-rare disease with only 100 patients per year expected to be eligible for tebentafusp, and does not recognise the vulnerability of the very small patient group facing terminal disease without other proven treatment options."

I am not currently minded to refer your first argument as to pricing to the Appeal Panel, for the same reasons as set out above in response to your proposed appeal point 2.3.

I am not currently minded to refer your second argument as to innovation, because it is clear the Committee recognised that tebentafusp is an innovative new treatment (para 3.20 of the FAD) and this in itself cannot arguably render the Committee's preferred modelling approach unreasonable. If you wish to pursue this argument I invite you to explain why you consider the approach was unreasonable in your response to this letter.

I am minded to refer your third argument as to rarity to the Appeal Panel as an amended point 2.7. If you wish to do so you may make more detailed submissions in support of this point in your response to this letter.

Conclusion

The above sets out above my initial views on all of your appeal points.

In respect of your points which I am not minded to refer on you are entitled to submit further clarification and/or evidence to me within the next 10 working days, 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 will 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 28 September 2023.

Ordinarily appeals are conducted on the basis of the appellants’ written appeal letters, and the material generated during the appraisal process. Use of additional written material is discouraged, and the panel cannot receive any new evidence. If, exceptionally, you feel there is written material that will not be before the panel that you would wish to rely on you must let the NICE Appeal team know by return of letter, indicating what the material is, why it is desirable to submit it, and when it will be available, by no later than 29 September 2023. Please note that the appeal panel cannot accept papers that are tabled late or ad hoc, as this affects the preparation of the panel and other parties for the appeal.

Yours sincerely

Dr Mark Chakravarty

Lead Non-Executive Director for Appeals & Vice Chairman National Institute for Health and Care Excellence