Sent by e-mail only: XXXXXXXXXXXXXXXX

XXXXXXXXXXX,

XXXXXXXXXXXXXXX, Myeloma UK

11 August 2023

Dear XXXXXXXXXXXXXXXXX

**Re: Final Draft Guidance (FDG) - belantamab mafodotin for treating relapsed or refractory multiple myeloma after 4 or more prior therapies [ID2701]**

Thank you for your letter of 8 August 2023, lodging an appeal against the above Final Draft Guidance (FDG).

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: NICE has not provided adequate reasons for rejecting plausible evidence that would have enabled it to make a decision as to the cost effectiveness of this treatment**

I am not minded to refer this appeal point to the Appeal Panel under ground 1(a) (procedural unfairness). That is because the Committee discusses the NPP data at para 3.8 where it sets out the views of the company, experts and EAG and explains concerns about that data, namely:

1. The EAG considered that feasibility of a matched adjusted indirect comparison (MAIC) was not improved by using NPP;
2. NPP introduced additional uncertainty as it was less mature and included a smaller sample size than DREAMM-2;
3. the median progression-free survival was much longer in the NPP study than in DREAMM-2, which the Committee considered suggested that the population in NPP may be less likely to have disease progression and that this may favour belantamab in the company’s updated naive unadjusted comparison;
4. the extent and direction of the potential bias was unclear in the company’s naive comparison.

I consider it unarguable that the explanation of the Committee's position in respect of the real-world evidence provided is "insufficient for stakeholders to understand the justification for the preference". I cannot see what more might be required whether by section 6.1.8 of the NICE Manual or as a matter of procedural fairness. I note the company's position on confidentiality necessarily constrains the specificity that the Committee can provide in the FDG.

However, I am minded to refer your appeal point 2.1 (see below) under which you may raise your arguments that the Committee’s conclusion that the company’s updated naive comparison lacked validity was unreasonable in the light of the evidence submitted to NICE.

**Appeal point 1(a).2:** **NICE has not provided adequate reasons for refusing the option of allowing Managed Access**

I do not regard this as a valid appeal point under ground 1(a) (procedural unfairness).

I understand your point to be that the Committee provided inadequate reasoning (particularly by reference to the factors at 5.5.28 of the Manual) as to why it was not convinced additional data would address the uncertainty.

I note the relevant test is set out at para 6.4.6 of the Manual as follows:

*"When a committee is unable to recommend a medicine because there is still significant resolvable uncertainty, it can make a recommendation for further evidence to be gathered subject to managed access. The committee can consider a recommendation with managed access when:*

* *the medicine has not been recommended, it has the plausible potential to be cost effective at the currently agreed price, but the evidence is currently too uncertain, and*
* *new evidence that could sufficiently support the case for recommendation is expected from ongoing or planned clinical trials, or could be collected from patients having the medicine in clinical practice, and*
* *these data could feasibly be collected within a reasonable timeframe (up to a maximum of 5 years) without undue burden."*

The Committee explained its conclusion not to recommend for managed access by reference to both the potential for useful additional data collection that could sufficiently support the case for recommendation and cost-effectiveness potential. In my view it is unarguable that the Committee's reasoning at para 3.19 of the FDG, which as I've noted hinges not only on the Committee's view on data collection but also cost effectiveness, is inadequate when read within the FDG as a whole, which explains the Committee's concerns regarding real-world evidence and preference for trial data.

I am however minded to refer your argument under ground 2 as a separate appeal point 2.2 that the Committee's conclusion that "additional data collection would be unlikely to resolve the uncertainty around the efficacy of belantamab compared with the relevant comparators for this" evaluation was unreasonable in light of the evidence.

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

**Appeal point 2.1: The Appraisal Committee's conclusions:**

1. **that the GSK naive comparison using Named Patient Program (NPP) data (which favoured belantamab compared with pomalidomide plus dexamethasone for all outcomes) "lacked validity and added further uncertainty";**
2. **that the randomised subgroup data from DREAMM-3 was preferable to the non-randomised evidence presented by the company; and**
3. **that it had not been presented with sufficient evidence to confirm that belantamab is more clinically effective than pomalidomide plus dexamethasone at a population level**

**are individually and collectively unreasonable.**

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

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 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 25 August 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 August 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

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Dr Mark Chakravarty

Lead Non-Executive Director for Appeals & Vice Chairman

National Institute for Health and Care Excellence