Sent by e-mail only: **XXXXXXXXXXXXX**

GSK

GSK House

980 Great West Road,

Brentford, Middlesex,

TW8 9GS

T +44 208 047 5000

1 September 2023

Dear GSK

**Re: Final Draft Guidance (FDG) - belantamab mafodotin for treating relapsed or refractory multiple myeloma after 4 or more prior therapies [ID2701]**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 25 August responding to my initial scrutiny views. This is my final decision on initial scrutiny.

I consider the ground 1(a) points followed by the ground 2 points.

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

**Appeal point 1(a).1: The Committee’s conclusions on the validity of belantamab UK RWE and related analyses lack transparency and are inconsistent with the focus placed on real-world data use in the NICE strategy for 2021 to 2026.**

Having considered the additional arguments made in your letter of 25 August, I will refer a valid appeal point under ground 1(a) (not ground 2 as I suggested in my initial scrutiny letter of 11 August 2023) in respect of your argument (A), namely that the Committee has not explained its conclusion, at paragraph 3.8 of the FDG, that the UK RWE considered in this evaluation and relied upon for the purposes of GSK’s naïve unadjusted comparison is subject to “potential bias”.

I remain of the view that your argument (B) is unarguable and should not proceed to an oral hearing.

I have considered the argument made in your appeal letter, referencing the strategy as follows:

*"The importance of RWE is a key focus in the NICE 2021 - 2026 strategy which states under the 4th pillar of the strategy, “We will be scientific leaders driving the research agenda across health and social care and thought leaders at the forefront of developing innovative approaches to using real-world data and data analytics to inform all aspects of our work”.* 24

*Furthermore, the strategy describes the need to integrate real-world data into evaluation processes to inform rapid but robust decisions aiming to speed up access to new and effective treatments and embrace innovation."*

I have also considered your arguments in response to my initial scrutiny letter, in particular:

*"To the extent that NICE has publicly committed itself to a particular policy (in this case, use of real-world evidence) stakeholders are entitled to expect that such commitment will be reflected in the way in which it approaches appraisals. In this case, the Committee’s refusal to base recommendations on real-world evidence conflicts with NICE’s stated policy and is therefore unfair."*

I remain of the view that it is unarguable that the strategy (which sets out NICE's policy intentions over the period running to 2026) gives rise to any procedural expectation that Technology Appraisal Committees will apply NICE's published appraisal processes (set out in the Manual) in a particular way that is not reflected in the Manual itself. Rather, the strategy has been and will be implemented through formal amendments to NICE's published methods and processes, on which stakeholders may rely as a matter of procedural fairness. I do not consider it arguable that the strategy itself is a published procedure applicable to appraisal committees. I accept that the Committee is bound not only by the Manual but also with broader standards of procedural fairness as a matter of English administrative law, however I see no arguable point that those broader standards combined with NICE's above commitments in the strategy require the Committee as a matter of procedural fairness to base recommendations on real-world evidence.

**Appeal point 1(a).2: The Committee’s decision that belantamab is not suitable for use through the Cancer Drugs Fund (CDF) is procedurally unfair**

Having considered the additional arguments made in your letter of 25 August, I agree that this is a valid appeal point and you may make both your arguments (A) and (B).

**Appeal point 1(a).4: The Committee’s conclusion that it would not recommend belantamab in the 5L+ TCR MM post-POM setting due to the uncertainty in the comparative evidence is unfair, given that these limitations were largely driven by the paucity of evidence for the comparator despite being recommended by NICE and in circumstances where the effect of the decision is that patients will be forced to receive a less effective treatment with less evidence of benefit**

Having considered the additional arguments made in your letter of 25 August, I agree that this is a valid appeal point.

**Appeal point 1(a).5: The Committee has failed to fairly consider belantamab in the original (5L+ TCR) or revised positioning (5L+ TCR post-pomalidomide subpopulation) in which belantamab offers significant benefits to UK patients with a high unmet need**

I remain of the view that this appeal point should not proceed to an oral hearing.

I note your argument in your letter of 25 August that:

*"this point of appeal is limited to whether, contrary to the Committee’s conclusion, a subgroup can be identified. At paragraph 3.10 of the FDG, the Committee expressed the view that it could not, disregarding the evidence from the clinical experts that when there is a disease response to belantamab this happens quickly. No explanation is provided to justify rejecting the views of the clinical experts, a requirement of transparency heightened in view of the level of clinical need of affected patients."*

I further note your explanation in your appeal letter that

*"Whilst there is currently no predictive biomarker for response to belantamab, the clinical experts present at the appraisal Committee meetings explained that when there is disease response to belantamab, it happens quickly (median time to response is 1.5 months [final analysis, 95% CI: 1.0, 2.1]) and has a long duration. This illustrates that the identification of patients who benefit from belantamab is feasible and can be done rapidly after treatment initiation*."

I understand this appeal point relates to the conclusion at 3.10 of the FDG where the Committee stated that *"it was not possible to define this subgroup of people who would be expected to have greater clinical benefit than the broader eligible population."* Your appeal letter (quoted above) accepts that this subgroup cannot be identified a priori, i.e. in advance of starting treatment with belantamab. I understand that the clinical experts explained that disease response happens quickly, enabling identification of the subgroup shortly after commencing treatment. That is not the same as defining the subgroup who would be expected to have greater clinical benefit before treatment. I therefore disagree that the Committee disregarded the views of the experts.

In circumstances where it is possible to model responders and non-responders to a technology – as mentioned in my initial scrutiny letter – it is for the company to conduct that modelling using stopping rules. As the company did not do so, I see no arguable point that the Committee's approach was procedurally unfair.

In light of the above, I still consider it unarguable that it was unreasonable for the committee to conclude that it "*was not possible to define this subgroup of people who would be expected to have greater clinical benefit than the broader eligible population".*

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

**Appeal point 2.1; The Committee’s conclusion in relation to the data from the DREAMM-3 are unreasonable in the light of the evidence submitted**

Having considered the additional arguments made in your letter of 25 August, I agree that this is a valid appeal point and you may make both your arguments (A) and (B).

**Appeal point 2.2: The Committee’s failure to recognise belantamab as an innovative intervention with benefits not captured in the economic modelling is inconsistent with the innovation passport granted by MHRA, the evidence submitted by GSK and stakeholders’ comments in response to the consultation on the draft guidance and is therefore unreasonable.**

Having considered the additional arguments made in your letter of 25 August, I agree that this is a valid appeal point.

Conclusion

Therefore the valid appeal points are:

* 1(a).1: The Committee’s conclusions on the validity of belantamab UK RWE and related analyses lack transparency
* 1(a).2: The Committee’s decision that belantamab is not suitable for use through the Cancer Drugs Fund (CDF) is procedurally unfair
* 1(a).3: The Committee’s conclusion that TA897 should not be taken into account in the context of this evaluation is inconsistent with NICE’s processes and is inadequately explained
* 1(a).4: The Committee’s conclusion that it would not recommend belantamab in the 5L+ TCR MM post-POM setting due to the uncertainty in the comparative evidence is unfair, given that these limitations were largely driven by the paucity of evidence for the comparator despite being recommended by NICE and in circumstances where the effect of the decision is that patients will be forced to receive a less effective treatment with less evidence of benefit
* 2.1: The Committee’s conclusion in relation to the data from the DREAMM-3 are unreasonable in the light of the evidence submitted
* 2.2: The Committee’s failure to recognise belantamab as an innovative intervention with benefits not captured in the economic modelling is inconsistent with the innovation passport granted by MHRA, the evidence submitted by GSK and stakeholders’ comments in response to the consultation on the draft guidance and is therefore unreasonable.
* 2.3 The Committee’s conclusions on the severity modifiers in the 5L+ TCR post-POM subgroup are unreasonable given the evidence indicating the applicability of a 1.7 severity weight.

NICE shares the valid appeal grounds of each appellant with the other appellants to assist with preparation for the hearing.

NICE will be in contact with you regarding the administration of the appeal, which will be held orally.

Yours sincerely

Dr Mark Chakravarty

Lead Non-Executive Director for Appeals & Vice Chairman

National Institute for Health and Care Excellence