**Incyte Biosciences UK Ltd**

 First Floor, Q1

The Square, Randalls Way, Leatherhead KT22 7TW

 Tel 0800 783 3711

 Web www.incyte.com

Company Registration No. 08247692

Dr Mark Chakravarty

Lead Non-Executive Director for Appeals

National Institute for Health and Care Excellence

2nd Floor

2 Redman Place

London E20 1JQ

10 October 2022

Dear Dr Chakravarty,

# Appeal against the Final Appraisal Document for tafasitamab with lenalidomide for treating relapsed or refractory diffuse large B-cell lymphoma [ID3795]

Thank you for your letter dated 26 September 2022, in which you provide your preliminary view of the admissibility of the points of appeal set out in Incyte’s letter of appeal dated 16 September 2022.

We provide, as you suggested in your letter, additional detail to elaborate, comment on or clarify those points of appeal (listed below) where your preliminary view was that these should not be referred to the appeal panel.

# Ground 1

1.1 The Committee has not taken loss of lenalidomide exclusivity and the associated impact on lenalidomide costs into account in the context of this appraisal

You express the preliminary view that this point of appeal should not proceed to an oral hearing. You provide several reasons for this decision, to which we respond below.

1. You say that the Committee “is required to use public list prices for technologies unless there are nationally available price reductions” and refer to paragraph 5.5.2 of the 2013 Methods Guide.

However paragraph 5.5.1 of the 2013 Methods Guide confirms that “resources should be valued using the prices relevant to the NHS and personal and social services” and NICE’s guidance is purposeless if the recommendations are based on costs which have no relationship with those paid by the NHS.

Incyte repeatedly notified NICE and the Committee of the loss of lenalidomide exclusivity and the likely implications for the price of the product. The NHS national generic tender for lenalidomide was published on 28 June 2022, with a deadline for bids of 18 July 2022. Delivery of product under the tender should have commenced on 1 September 2022. Therefore at the time of the second Committee meeting on 2 August, all bids would have been received by CMU some two weeks previously and by the date of issue of the FAD on 2 September 2022, lenalidomide was being supplied in accordance with nationally agreed prices under the new tender and the conclusions of the Committee on cost-effectiveness were therefore irrelevant. In other words, by the date of issue of the FAD, the guidance did not reflect the nationally agreed prices for lenalidomide as required by the Methods Guide - and at the date of the second Committee meeting, the Committee knew (or should have known) that would be the case.

1. The Committee can only consider evidence submitted to it at the time of the appraisal and there was no nationally available price other than the list price for branded Revlimid at the relevant time.

In the case of confidential prices under tenders, it is a matter for NICE to request such information from CMU. In the context of the current appraisal, Incyte did not have access to the tender prices for generic lenalidomide and could not “submit” these to the Committee. In contrast, NICE was aware of the tender and was in a position to obtain the relevant information for the purposes of this appraisal. The fact that it either did not request such information from CMU or chose not to use it, constitutes a procedural flaw in this appraisal.

For completeness, it is Incyte’s position that details of a national price under the tender would have been available at the time of the second Committee meeting, if this had been requested by NICE. However if that is not the position, NICE should have delayed the Committee meeting so that this information could be taken into account and the guidance issued by NICE had relevance to the NHS.

1. The ERG base case analysis was set on the known list price

There is no reason why the ERG should not have been asked to recalculate the base case analysis using pricing information from the tender.

1. The future price trajectory for generic lenalidomide was unknown at that time and could not have been known

We have explained in our response to point 2) above why this reason is incorrect. The relevant date for the purposes of the Committee’s consideration of the effective price of lenalidomide is 2 August 2022. At that time the tender had been concluded and, NICE could have or did request details of the prices awarded under the resulting nationally applicable framework contracts.

1. It was therefore, in your initial view, neither unfair nor contrary to the Methods Guide for the Committee to base its cost-effectiveness conclusions on the list price of Revlimid, that being the national available price at that time.

As explained above, the Committee was aware on 2 August that generic lenalidomide would be available, as a tender had recently been concluded. In circumstances where the prices under that tender were effective before the FAD for tafasitimab was issued, either the tender price should have been incorporated into the appraisal or the meeting of the Committee should have been delayed. The current situation where the cost effectiveness assessment which formed the basis for the recommendations in the FAD was incorrect and irrelevant by the time the FAD was issued (and the Committee knew that would be the case) does not constitute a fair or credible basis for decision making.

1. There is clear evidence in the papers made available to the committee that they did consider a range of price scenarios around both the company and the ERG cases in attempting to assess the plausible ICER range - with several price scenarios approximating to the putative discount for generic lenalidomide over its branded analogue

Irrespective of the context of the papers made available to the Committee, the FAD includes no indication that the Committee recognised or paid any attention to the loss of lenalidomide exclusivity, despite the material effect on the ICER. In particular, paragraph 3.9 of the FAD states: “The committee concluded that the most plausible ICER was likely between the company’s and ERG’s base-case estimates”, neither of which were based on the tender prices for lenalidomide (because, in Incyte’s case, we do not have access to the data). If the Committee had genuinely considered scenarios involving tender prices for generic lenalidomide it is difficult to see why these would not have been provided the most plausible ICERs,

Furthermore, we are aware of no evidence that any scenarios presented to the Committee reflected the levels of discount provided in the tender for lenalidomide.

In the above circumstances, we are not aware of any basis for concluding that the Committee “considered” prices approximating to any potential discount for lenalidomide.

In summary, the national generic tender (details of which were available to NICE on request) had been concluded before the second meeting of the Committee. In these circumstances the tender price for generic lenalidomide should have been taken into account in the cost effectiveness assessments which formed the basis for the Committee’s recommendations, failing which the guidance is irrelevant before it is even issued. However the wording of the FAD indicates that this did not occur.

## 1.2 The Committee’s conclusions regarding the cost-effectiveness of tafasitamab and lenalidomide lack transparency and are therefore unfair

You express the preliminary view that this point of appeal should not be permitted to proceed to an oral hearing on the basis, in essence that you consider the information provided in the FAD - namely the statement:

“The Committee concluded that the most plausible ICER was likely between the company’s and ERG’s base-case estimates, noting that the ERG’s base case ICER was considerably higher than the company’s and considerably higher than the level usually considered to be cost-effective”.

This is does not meet standards of procedural fairness. In particular, it is a fundamental requirement that a company should be given sufficient information to be able to understand the basis for the decision complained of and to know what it has to do in order to achieve a positive outcome. It is irrelevant that the Committee’s assessment exceeded the range normally considered cost-effective; Incyte is still entitled to be informed how far NICE believes it would have to move on price before a positive recommendation would be given. Further, rigorous and credible decision making requires the Committee to explain its decision so that stakeholders can understand whether the basis for decision making is robust.

In the above circumstances, in the context of confidential discounts offered for comparator products, NICE has defined the way in which its conclusions on cost-effectiveness should be set out, in its Guide to the Processes of Technology Appraisal at paragraph 3.1.22:

“Although the results of these analyses [i.e. those where a confidential discount is available for a comparator] are classed as commercial in confidence, NICE will have to publish an ICER range that informs the recommendation(s), after taking into account the exact level of the discount provided in the commercial arrangement for the comparator”.

In this case however the Committee has not provided an ICER range but simply said that the most plausible ICER was likely to lie between the company’s and the ERG’s base cases, without any further clarification or explanation of its position. You refer in your letter to slides presented to the Committee; these however do not reflect the conclusions of the decision maker (the Committee) or the basis upon which the draft recommendations in the FAD were made.

In summary therefore, the failure to provide a credible ICER range to inform the cost effectiveness assessment set out in the FAD is lacking in transparency and breaches NICE’s procedures. It is therefore unfair.

## 1.3 The Committee’s decision that tafasitamab and lenalidomide should not be recommended for use through the Cancer Drugs Fund in view of the lack of comparative evidence is procedurally unfair

You agree that this point of appeal should proceed to an oral hearing, and expressed the preliminary view that it should proceed under Ground 2. Your position is noted.

# Ground 2

**2.1 The Committee’s conclusion that patients eligible for treatment with tafasitamab and lenalidomide do not meet the end of life criteria does not reflect the balance of the available evidence**

Your position is noted

## 2.2 The Committee’s conclusion that the company’s base case ICERs were not plausible because the model survival outputs were not consistent with TA 649 disregards the evidence generated since that appraisal

You express the preliminary view is that this point of appeal should not proceed to an oral hearing because you say the Committee did not rely solely on TA649 but also recognised at paragraph 3.9 that the ERG’s survival outputs may overestimate survival for polatuzumab vedotin and took into account feedback from the clinical experts. However this appears to misunderstand the FAD.

At paragraph 3.9, the Committee concludes that Incyte’s base case ICERs were not plausible because the model survival outputs were not consistent with TA649, even though it accepted that the ERG’s estimates might overestimate survival for polatuzumab vedotin. While your letter suggests that the evidence from the clinical experts supported the survival estimates for polatuzumab vedotin relied upon in TA649, this is incorrect; the experts in fact supported the survival estimates presented by Incyte (see page 55 Committee papers for second Committee meeting).

Therefore the Committee’s only reason for criticising Incyte’s base case ICERs based on the model survival outputs (which also reflect the evidence of the clinical experts) as stated in the FAD and referenced in your letter, is the lack of consistency with TA649. For the reasons set out in our appeal letter, this conclusion disregards the evidence generated since TA649 and is therefore unreasonable.

2.3 The Committee’s conclusion that the evidence presented did not demonstrate that tafasitamab is innovative is inconsistent with the Promising Innovative Medicine (PIM) designation by MHRA and the Committee’s own conclusions elsewhere in the FAD

You say that this point should not be admitted on the basis of your conclusion that tafasitamab does not satisfy the test at paragraph 6.3.3 of the Methods Guide that, to be considered innovative, a technology should add “demonstrable and distinctive benefits of a substantial nature which may not have been adequately captured in the reference case QALY measure”.

However, tafasitamab has the particular benefit that it may be administered in an outpatient setting and is also associated with a favourable toxicity profile. This situation was accepted by the Committee, who recognised at paragraph 3.1 of the FAD that “any treatment delivered in an outpatient setting would have a significant, positive effect on the quality of life of patients and their families” and also concluded that “people with the condition have a high unmet need for effective treatments with manageable side effects”. Additional points that contribute to the innovative nature of tafasitamab are that it is the first treatment to continue until disease progression (all others are of fixed duration) and the fact that tafasitamab treatment does not involve chemotherapy for patients ineligible for intensive therapy, which benefits older patients with comorbidities

The meaning of the Committee’s observations at paragraph 3.1 of the FAD therefore appear to meet the test for innovation at paragraph 6.3.3 of the Methods Guide and nothing in the FAD explains why, given the content of paragraph 3.1, the Committee concluded at paragraph 3.11 that the test was not met.

With respect to the inconsistency between the Committee’s conclusion that tafasitamab does not meet the test for innovation and the contrary assessments by FDA and MHRA, Incyte does not suggest that NICE is bound to agree with the conclusions of other bodies. However where its conclusion conflicts with authoritative statements by such other bodies, some explanation for a different assessment should be provided.

We hope that the matters set out in this letter have clarified our appeal and that you now agree that all points may proceed to a full hearing.

Yours sincerely

Incyte Biosciences UK Ltd