

Mr Tim Irish

Chair Appeal Committee

The National Institute for Health and Care Excellence (NICE) 10 Spring Gardens

London SW1A 2BU

3 August 2020

Dear Mr Irish

#  Appeal against the Final Appraisal Determination for Abiraterone for High-Risk

 **Hormone-Sensitive Metastatic Prostate Cancer**

Thank you for your letter dated 21 July 2020, in which you expressed your preliminary views regarding the admissibility of the points of appeal advanced by Janssen-Cilag Limited (“Janssen”) and set out in the Notice of Appeal submitted on 10 July 2020. We now respond to your initial view of our appeal, addressing those points where you suggest, following preliminary review, that these may not constitute valid points of appeal. For the avoidance of doubt, we provide no further submissions in relation to those points or subpoints of appeal which you agree should proceed to a hearing.

# Ground 1

* 1. **Ground 1(a).1: The Appraisal Committee has failed to consider whether and, if so, to what extent the change in health-related quality of life associated with use of abiraterone has been adequately captured in this appraisal**

You say, in your letter, that you agree that subpoint (a) is a valid appeal point, but that you are not currently persuaded that subpoint (b) is a valid appeal point. Your reasons are:

1. You do not believe the Committee can be faulted for not taking account of the current pandemic which is, you say, likely to be temporary;
2. You would expect the factors referenced by Janssen (reduced administration cost and greater convenience of an oral at-home treatment and reduced immunosuppression) to be included in modelling in the form of costs of a comparator, improved quality of life or fewer adverse incidents; and
3. You question whether the matters raised by Janssen are non-health objectives of the NHS, as they seem to be health related.



 Janssen’s response:

The reference to non-health objectives of the NHS in our appeal letter was not directed towards the health benefits captured in the assessment of cost effectiveness, but to the broader benefits to the NHS resulting from abiraterone treatment as compared with docetaxel. The benefits to which we referred were not the direct costs of hospital administration or the increased adverse events, but the impact of a treatment which requires hospital administration, and potentially aftercare in NHS efficiency, and the impact of abiraterone versus docetaxel treatment on the ability of the service to treat other patients with other conditions, using its limited facilities and staff resources. The benefits of abiraterone in terms of efficient NHS service delivery and response to capacity constraints have not, so far as Janssen is aware, been taken fully into account in the context of this appraisal.

As to whether the Appraisal Committee should have considered the impact of COVID-19 in the context of this appraisal:

* The potential spread of the virus had been identified by the third meeting of the Committee (the WHO declared the outbreak a Public Health Emergency of

 International Concern on 30 January 2020) and a pandemic was declared on 11 March, over three months before the FAD was issued on 19 June 2020. By this time the impact of COVID-19 in limiting the ability of the NHS to deliver routine hospital treatments such as chemotherapy, including for patients with prostate cancer, was clear

* On 20 March 2020 NICE issued a COVID-19 rapid guideline on delivery of systemic anticancer treatments which recommended consideration of modifications to usual service provision including:

“*Think about how to modify usual care to reduce patient exposure to COVID-*

*19 and make best use of resources (workforce, facilities, intensive care, equipment).*

*Try to deliver systemic anticancer treatment in different and less immuno- suppressive regimens, different locations or via another route of administration where possible. Options include:*

o *Switching intravenous treatments to subcutaneous or oral alternatives where this would be beneficial (subject to agreement with commissioners)…..”*

However, the content of the FAD appears to conflict with these guidelines despite the ongoing COVID-19 situation.

* While you express the view that the pandemic is likely to be temporary, we understand that this is currently uncertain, particularly given the possibility of further waves of infections. Furthermore, it is unclear how long social distancing and other measures to safeguard patients and NHS staff, which also impact the treatments which can be provided in a hospital setting, will need to remain in place.

Your preliminary view is that subpoint (a) is not a valid appeal point because you do not think that the Committee were required to take an NHS England commissioning policy as their starting point and there was accordingly no obligation to give a reason for departing from it.

* Your letter of 21 July 2020 appears to suggest that matters which followed the Appraisal Committee meeting of 15 January 2020 should be disregarded. To the extent that this is your preliminary view, we respectfully disagree. Such an approach would be both procedurally unfair and inconsistent with good administration. NICE’s decisions must be valid at the time they are issued and therefore, if there is a period of delay between a meeting of the Appraisal Committee and the date of issue of the FAD, procedural fairness requires that the previous conclusions of the Committee are reviewed to ensure that they remain current before the FAD is circulated.
* Paragraph 3.5.49 of NICE’s Guide to the Processes of Technology Appraisal provides for further assessment following the meeting of the Appraisal Committee and prior to issue of the FAD in “exceptional circumstances”, a definition plainly satisfied by the current COVID-19 crisis. If, despite the devastating effect of COVID-19 on the ability of cancer patients to receive routine hospital treatments, NICE concluded that there was no requirement to take this into account in the context of the current appraisal, that view should have been stated and explained in the FAD.

The benefits to the NHS of abiraterone treatment relative to docetaxel in terms of improved service efficiency and reduced impact on capacity have been highlighted by the COVID-19 crisis, but are clearly important, irrespective of the current pandemic and should have been taken into account, consistent with paragraph 6.3.3 of NICE’s Guide to the Methods of Technology Appraisal, in any event. However, it is unclear whether such matters were considered by the Committee or, if they were taken into account, how they influenced the Committee’s conclusions regarding abiraterone. That is procedurally unfair.

We apologise if the focus of our appeal was unclear from our original letter and hope that the above explanation has addressed your concerns.

* 1. **Ground 1(a).2: The Appraisal Committee’s conclusion that “*there are no clear- cut clinical criteria to define who can have abiraterone in combination but not docetaxel in combination*” does not: (a) provide adequate reasons for diverging from NHS England’s commissioning policy; (b) justify rejection of the criteria proposed by NHS England for determining access to abiraterone through the Blueteq management system; (c) provide reasons for deviating from its conclusions in the earlier appraisal of Radium-223; and (d) explained why it has adopted a different approach to that followed in the appraisal of lenalidomide**
1. NHS England’s Commissioning Policy on docetaxel which determines the patients for

 whom docetaxel will be commissioned

NHS England is the body which will be required to implement the guidance following this appraisal. In these circumstances, NHS England’s proposal for defining those patients who are not eligible to receive docetaxel is clearly a relevant consideration to be taken into account by the Appraisal Committee and, if such proposals were taken into account, the Committee’s reasons for declining to accept them should have been explained.

 Janssen response

Janssen does not suggest that the commissioning policy issued by NHS England, which determines which patients are clinically ineligible for docetaxel therapy, is binding on NICE. However, an aspect of reaching a rational and evidence-based decision is taking all relevant factors or considerations into account and rigorous decision-making requires that deviation from the positions adopted by other influential bodies are explained transparently.

The requirement for NICE to provide adequate reasons for its decisions was confirmed by the Court of Appeal in R (Servier Laboratories Limited) v National Institute for Health and

 Clinical Excellence [2010] EWCA Civ 346, in which the Court emphasised an enhanced requirement for such reasons where its decisions diverged from those of other similar bodies

The commissioning policy is clearly a relevant factor because it demonstrates that NHS England has considered whether patients ineligible for docetaxel therapy can be defined clinically and applies the criteria it has identified. The fact that the NHS already applies a system for identifying patients who cannot receive docetaxel should therefore, on any view, have been taken into account by the Committee in the context of this appraisal.

There is, however, no indication in the FAD that the Appraisal Committee took NHS England’s commissioning policy (and the way in which eligibility for docetaxel is currently determined in the NHS in England) into account or, if it did consider the policy, no explanation has been given for the Committee’s decision to reject the criteria currently used by NHS England to determine eligibility for docetaxel.

1. NHS England proposed Blueteq criteria to define the patients unable to receive

 docetaxel

Your preliminary view is that subpoint (b) is not a valid appeal point for similar reasons as subpoint (a). In addition, you suggest that the Blueteq criteria did not meet the Committee’s concern about a lack of clear-cut clinical criteria, as they include patients who have made an informed choice not to receive docetaxel.

 Janssen response

The response in relation to subpoint (a) is also applicable here. Again, Janssen does not suggest that NICE was bound to follow the Blueteq criteria proposed by NHS England, but we say that the proposed Blueteq criteria should have been taken into account.

The usual approach at the initial scrutiny stage is that the appellant is advised that they will be required to explain why the same approach is required based on similar characteristics of the two appraisals. Janssen is content to proceed on that basis but believes it would be inappropriate and unfair to exclude this subpoint at the initial scrutiny stage.

However, contrary to these procedural requirements, there is no indication that the Blueteq criteria were considered by the Committee in reaching its conclusion at paragraph 3.2 of the FAD, that *“there are no clear-cut clinical criteria to define who can have abiraterone in combination, but not docetaxel in combination”*. If, despite the absence of any mention in the FAD, these criteria were considered, the Committee’s reasons for rejecting NHS England’s proposals are unexplained.

For the avoidance of doubt, there is no indication in the FAD that the Committee rejected the Blueteq criteria proposed by NHS England in their entirety because these included patients who had made an informed choice not to receive docetaxel as well as those who are clinically ineligible. In these circumstances such reasoning, cannot be assumed, particularly given the fact that it was open to the Committee (had it considered this to be appropriate) to accept some, but not all, of the proposed Blueteq criteria.

(d) T he definition of patients unable to take an alternative treatment was also considered

 by Committee B during the appraisal of lenalidomide

You say that you do not agree that subpoint (d) is a valid appeal point because you are not persuaded that the appraisal of lenalidomide has enough in common with this appraisal to be a meaningful guide.

 Janssen response

Janssen is entitled to expect that the same procedures and standards will be applied to abiraterone in the context of the current appraisal as have been applied to other technologies for other indications. Alternatively, to the extent that different procedures or standards are applied, that these will be appropriately justified.

Subpoint (d) is similar to and provides further support to the issue raised in subpoint (c) .

The appraisal of lenalidomide by Committee B, involved consideration of the patients who were ineligible for thalidomide. It was generally accepted that there were no standard criteria to define such patients and the documents for the appraisal of lenalidomide indicate that definition of the thalidomide ineligible population was far less certain than the definition of the docetaxel ineligible population as proposed by multiple stakeholders (including NHS England) for the purposes of the current appraisal. Nevertheless, Committee B was content to rely upon clinical judgment to define the thalidomide ineligible population for the purposes of the appraisal of lenalidomide.

Fairness requires that Janssen is informed why a similar approach has been rejected by the same Committee in the context of the current appraisal.

1 While NICE provided Janssen with a briefing note listing the Committee’s preferred assumptions for the purposes of negotiation of a commercial agreement with NHS England, no reasons or explanations for preferring such assumptions were provided and only some of them were subsequently included in the FAD

# Ground 1(a).4: The conclusions of the Appraisal Committee in relation to the cost effectiveness of abiraterone in this appraisal are opaque

You say that you are not persuaded that this is a valid appeal point. You say that the Committee’s conclusion is clear, even if an ICER or a range of ICERs is not given. You suggest that a reason why ICERs have not been given may be that these would indicate what level of confidential discounts may be given for other treatments and you suggest that this seems to be a reasonable concern. You refer to the fact that Janssen has developed the economic model and the Committee has set out in the FAD and in the Committee slides, comments on the model, and on their preferred assumptions. You suggest that, based on this material, it is possible to understand the Committee’s conclusion and the reasons for it in adequate detail.

 Janssen’s response

Janssen strongly disagrees with the preliminary view expressed in your letter. The assessment of cost-effectiveness is arguably the most important element of an appraisal and it is inconsistent with basic standards of fairness for the Committee’s conclusions and its reasoning in this respect. to lack transparency. NICE’s guide to the methods of technology appraisal states at paragraph 3.1.1:

“*To ensure that the guidance issued by the Institute is appropriate and robust, it is essential that the evidence and analysis, and their interpretation, are of the highest standard and are transparent”.*

The only document which sets out the Committee’s interpretation of the evidence and its conclusions is the FAD1. While certain matters may be included in Committee slides, these simply reflect a presentation given to the Committee at the beginning of a meeting; they do not necessarily represent the view of the entire Committee or its final considered position. We do not therefore accept that it would be appropriate to require Janssen or any other consultee to refer to Committee slides in order to work out the basis for the Committee’s decision-making.

Transparency of evidence and reasoning is essential for rigorous decision-making. In the absence of these matters, it is impossible to confirm that the Committee’s conclusions are accurate and that they are fair. Simple assertions without explanation are susceptible to error and to concerns that the conclusions are arbitrary rather than being based on robust assessment. Furthermore, in the absence of proper reasons it is impossible for a stakeholder to know what it has to do in order to achieve a positive outcome. This is not in the interests of patients, clinicians, the NHS or of Janssen.

The FAD in this case does not disclose key information including:

* The Committee’s conclusions as to the ICERs for abiraterone, beyond that these were above the range usually viewed by NICE as a cost-effective use of NHS resources;
* Whether such ICERs involved a comparison with ADT alone (recognised by the Committee in the FAD to be a proper comparator) or merely a comparison with docetaxel;
* While the FAD states at paragraph 1, that abiraterone was not cost effective at the commercial price offered by Janssen, there is no explanation of this conclusion or how far above the threshold imposed by NICE the Committee’s calculated ICERs fell, even though the ICERs submitted by Janssen, which we understood were based on the assumptions preferred by the Committee, resulted in values below £20,000 per QALY gained versus ADT alone.

These matters are central to the appraisal and the absence of proper transparency in these respects means that the information contained in the FAD cannot be viewed as “adequate”.

There is extensive case law confirming the requirement for transparency (both in relation to evidence and reasoning) in relation to decisions of public bodies. We have not set out such matters in this letter, although we will be pleased to do so if that would assist either you or the Appeal Panel. Much of the case law was addressed by the Court of Appeal in R

 (on the Application of Eisai Ltd) v National Institute for Health and Clinical Excellence

 (NICE) and Others [2008] EWCA Civ 438, to which we referred in our appeal notice and

also in R (Servier Laboratories Limited) v National Institute for Health and Clinical

 Excellence [2010] EWCA Civ 346, confirming the high level of transparency imposed on NICE in relation to the adequacy of reasons underpinning its decision-making. .

Finally, you suggest that a reason for the lack of transparency in the FAD may be that publication of ICERs would indicate what level of confidential discount had been given for other treatments. Docetaxel is however available generically and has been assessed based on a publicly available price With respect to other products considered in this appraisal, NICE’s guide to the processes of technology appraisal explains at paragraph 3.1.22 how the Committee’s conclusions in relation to cost-effectiveness should be provided to stakeholders in circumstances where another product included in the assessment is supplied under a confidential discount.

*“To allow the committee to explore the impact of using the actual cost of the comparator in the analyses, the ERG will also create a confidential appendix to its report, which will reproduce all analyses from the main ERG report using the exact level of discount for the comparator. A lthough the results of these analyses 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” [*emphasis added*].*

In this appraisal however no ICERs or ICER ranges have been provided. No explanation or justification has been provided by the Committee to justify such an approach and it is clearly inappropriate to exclude a point of appeal at the initial scrutiny stage based on speculation as to the Committee’s reasons for omitting key conclusions and explanations.

We hope that the additional clarification provided in this letter satisfies you that this point of appeal should proceed to a full hearing.

# Ground 1(a).5 The fact that NICE disclosed its preferred ICERs to NHS England for the purposes of negotiation of a commercial agreement, but not to Janssen is unfair

You say, in your letter, that you are not convinced that this issue caused any unfairness in the appraisal process which is what the appeal is concerned with. You also refer to your assumption, noted above in relation to your preliminary assessment of Ground 1(a).4 that the Committee had a valid reason for not disclosing precise ICERs, namely to protect the commercially confidential discounts offered by others.

 Janssen’s response

The issue of concern here is the fact that NICE has treated one party to a negotiation differently to another in relation to a procedural matter in this appraisal. That is unfair.

NICE disclosed to NHS England information about the ICERs it had calculated for abiraterone in the context of negotiation of a commercial offer for abiraterone, even though this information was not provided to Janssen and was not ultimately disclosed in the FAD. NHS England declined to accept any commercial offer proposed by Janssen unless this resulted in a cost-effective ICER based on the information provided to it by NICE. Janssen however had no way of knowing the basis upon which the ICERs disclosed by NICE had been calculated or whether these were correct and the imbalance in information precluded any agreement of a commercial offer.

The issue is clearly relevant to the appraisal as demonstrated by the fact that the FAD refers at multiple places (e.g. paragraphs 1, 2.3 and 3.14,) to the fact that no commercial agreement was reached between NHS England and Janssen.

Please let us know if further information or clarification would assist you. Alternatively, we look forward to receiving your final decision in relation to the admissibility of the appeal points we have raised.

Yours sincerely

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