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Sent via email

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12 September 2011

Dear [redacted]

Appeal Against Final Appraisal Determination: Dasatinib, high-dose imatinib and nilotinib for the treatment of imatinib-resistant chronic myeloid leukaemia (CML) (part review of NICE technology appraisal guidance 70), and dasatinib and nilotinib for people with CML for whom treatment with imatinib has failed because of intolerance

Thank you for lodging BMS's appeal against the above Final Appraisal Determination.

Introduction

The Institute's appeal procedures provide for an initial scrutiny of points that an appellant wishes to raise, to confirm that they are at least arguably within the permitted grounds of appeal ("valid"). The permitted grounds of appeal are:

- Ground 1: The Institute has failed to act fairly
- Ground 2: The Institute has formulated guidance which cannot reasonably be justified in the light of the evidence submitted.
- Ground 3: The Institute has exceeded its powers.

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 and arguably 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 make my final decision as to whether each appeal point should be referred on to the Appeal Panel.

I can confirm that there will be an oral hearing of the appeal.

Initial View

Ground 1

1.1 The splitting and subsequent combining of the appraisals of dasatinib and nilotinib for CML lacks transparency and has deprived consultees of their procedural and administrative rights.

A valid ground one appeal

1.2 The Institute' choice of comparator is inconsistent with the Methods Guide

A valid ground one appeal, though please note that inconsistency with the methods guide is no longer per se a ground of appeal. I am assuming you will argue that the inconsistency has caused procedural unfairness.

1.3 Considering Dasatinib as Combination Therapy in the Blast Phase of CML is unfair

I could not see any evidence from the FAD that the Committee had considered Dasatinib as combination therapy. FAD 4.3.27 appears to eschew any such consideration and to discuss monotherapy only. No recommendations relating to combination therapy are made in section 1 of the FAD, which further suggests it was not considered.

I look forward to your further comment but I am not presently minded to refer this point to an appeal panel.

1.4 The Review and Approval of Novartis' Patient Access Scheme During an On-Going Multiple Technology Appraisal Is Procedurally Unfair

I am unclear why you say this has caused unfairness to you specifically. It appears to me you could have submitted a patient access scheme of your own had you wished to do so. This possibility was appreciated by your competitor.

As you are aware it is the Department of Health, and not NICE, which considers whether to accept or reject patient access schemes. The PPRS is a DoH document and not a NICE document. If the DoH accepts a scheme in mid appraisal then

presumably it, as the owner of the PPRS, must be taken to be satisfied that the scheme complied with the PPRS. I am not sure how NICE, an outsider to the PPRS, can be expected to go behind this? And surely NICE must seek to incorporate an approved scheme into an appraisal where possible, as otherwise it will be appraising on a false basis.?

I would be grateful for your further comment on this point, as I am presently not minded to refer it to an appeal panel.

1.5 The Decision Not to Apply The End-of-Life Criteria is Unfair

Paragraph 2.3 of the End of Life ("EoL") policy states that "The Appraisal Committee will need to be satisfied that the estimates of the extension to life are robust... and the assumptions used in the reference case economic modelling are plausible objective and robust." I am afraid I do not agree that these are "further considerations" going to the exercise of a discretion. It seems to me the clear meaning of the policy is that unless the Committee is satisfied on these matters the policy does not apply.

The Committee may or may not have been correct not to have been so satisfied in this case, an issue which you raise under ground two, but I cannot see any argument that they have unfairly failed to consider the EoL policy.

I look forward to your further comment but I am not presently minded to refer this point to an appeal panel.

1.6 The failure to provide BMS with a fully executable version of PenTAG/SHTAC model lacks transparency

A valid ground one appeal point.

Ground 2

2.1 Relying on outputs of the SHTAC Model and utilising these to form the basis of guidance to the NHS is Perverse

A valid ground two appeal point.

The appeal panel must be put in a position to be able to consider this point properly. The points which you raise appear to be complex, and to a greater or lesser extent to raise questions of expert judgement. The panel members will not be experts in this area, or have access to expert advice. If this point is merely explored orally at the hearing in the usual way, I feel the panel may struggle to process all of the arguments.

Accordingly, I would like to ensure that the arguments are presented in sufficient detail in advance in writing, and in terms that an informed but non-expert panel can understand. Your appendix is a helpful start in this regard, but the panel will need further assistance. I am therefore asking you to set out the full argument on which

you wish to rely in writing by the end of Monday 3 October. This will be provided to the Appraisal Committee, and I will ask them to provide a full argument in reply, in writing, by the end of Monday 17 October. This in turn will be provided to you with an opportunity to respond to the points made by the committee only, by the end of Monday 24 October. Your argument, the committee's response, and your reply will then all be put before the appeal panel to read and consider before the hearing.

It will still be possible to explore these issues orally at the hearing on 4 November, but the oral hearing should be used mainly for clarification of points raised rather than the presentation of new material.

2.2 The choice of hydroxycarbamide as the most appropriate comparator is perverse

A valid ground two appeal point.

2.3 The Decision Not to Apply The End-of-Life Criteria to Blast Crisis Patients is Perverse

A valid ground two appeal point.

2.4 The Conclusion That Dasatinib Is Not Innovative Is Perverse

A valid ground two appeal point.

2.5 Ultra-orphan

You have cited two documents in support of your appeal point. The first is the Social Values Judgment publication, and your appeal letter cites the relevant passage. It is correct that the document states that NICE does not expect to be asked to evaluate "ultra orphan" drugs, but I do not understand how that expectation supports the proposition that, if such drugs are referred, they must be approached differently.

The second document relied on is a draft opinion on orphan and ultra orphan drugs. The effect of that document was considered by an appeal panel during an appeal against an FAD appraising "Azacitidine for the treatment of myelodysplastic syndromes, chronic myelomonocytic leukaemia and acute myeloid leukaemia" which is available on the Institute's website. The panel in that case set out its understanding of the lack of effect of that document, which as your appeal notes is over five years old, and was only ever a draft not intended for public exposure. At present I cannot see on what basis an appeal panel would depart from those views.

I look forward to your further comment but I am not presently minded to refer this point to an appeal panel.

Ground 3

3.1 The FAD Recommendations are in Breach of the Human Rights Act 1998

A valid ground three appeal point.

The appeal panel must be put in a position to be able to consider this point properly. The panel members are not legally qualified. Whilst their legal advisor will be present at the hearing, if this point is merely explored orally at the hearing in the usual way, I feel the panel may struggle to process all of the arguments.

I therefore propose to proceed in a similar way to point 2.1 above. I am asking you to set out the full argument on which you wish to rely in writing by the end of Monday 3 October. This will be provided to the Appraisal Committee, and I will ask them to provide any argument in reply, in writing, by the end of Monday 17 October. Both arguments will be provided to the panel's legal advisor, who will provide the panel with written advice, which will be shared with you and with the Committee, by the end of Monday 24 October. The panel will also be provided with your argument and the Committee's reply, if any.

I would also draw your attention to the panel's decision in "Azacitidine for the treatment of myelodysplastic syndromes, chronic myelomonocytic leukaemia and acute myeloid leukaemia", where these issues were discussed.

It will still be possible to explore these issues orally at the hearing on 4 November.

3.2 The Acceptance of the Novartis Patient Access Scheme is in Breach of the PPRS

Compliance with the PPRS would be a matter for the Department of Health, which accepted the patient access scheme.

I look forward to your further comment but I am not presently minded to refer this point to an appeal panel.

Conclusion

As I am minded to agree some of your appeal points are valid I will pass them to an appeal panel for consideration.

If you wish to make any further comment on the point I believe is not valid, together with the clarification requested above, please provide to me by **Monday 26 September 2011.**

Yours sincerely

[redacted]
Appeals Committee Chair
National Institute for Health and Clinical Excellence