



# **National Institute for Health and Clinical Excellence**

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Celgene Ltd  
Morgan House, Madeira Walk  
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31 March 2010

Dear ██████████

## **Final Appraisal Determination: Azacitidine for the treatment of Myelodysplastic syndromes, chronic myelomonocytic leukaemia and acute myeloid leukaemia**

Thank you for lodging Celgene'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 and in accordance with its published procedures as set out in the Institute's Guide to the Technology Appraisal Process.
- Ground 2: The Institute has prepared guidance which is perverse 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 Celgene's appeal.

### **Initial View**

Ordinarily, the Institute prefers to receive appeal notices structured by reference to the ground of appeal relied on, so all ground one points grouped together, followed by all ground two points, and so on. Your letter groups the points thematically and to avoid confusion I will do the same in this reply. You should be aware though that at the appeal hearing the panel is likely to want to deal with the points in the usual order, is ground one followed by ground two followed by ground three.

## **A Comparators**

### **Ground one**

#### **1.1.1 Final scope**

I cannot see that there is a procedure/fairness point here. The committee is required to turn its mind to all of the issues within scope, but it is not required to base its final analysis on every issue referred to in the scope. It may decide, for example, that on some issues the data are too uncertain, or the overall impact of an issue to marginal, to need a final conclusion. I would agree that both the scope and the methods guide would require the committee to consider taking chemotherapy as a comparator. However it appears to me from the FAD that they did consider that question, and decided not to carry forward the chemotherapy comparator ICERs into the final analyses.

They may or may not have been perverse in reaching that decision (see below) but I cannot see that they have arguably gone wrong as a matter of process?

My preliminary view is that this is not a valid ground one appeal point

### 1.1.2 Guidelines

For a similar reason, the concerns raised here seem to me to be issues of perversity: that guideline suggest that chemotherapy would indeed have been a valid comparator, and the committee wrongly decided it was not. The committee would not be bound per se by these guidelines, other than in the sense that they may be evidence for what clinical practice is or ought to be. If evidence has been ignored that can and should be considered within the framework of an appeal under ground two, and, at best, it seems to me to add nothing to consider it as a process point under ground one.

My preliminary view is that this is not a valid ground one appeal point

### 1.1.3 Failure to assess fully data from the Celgene survey.

An allegation of failure to give due consideration does not amount to an allegation of unfairness contrary to ground one of the Institute's appeal grounds. The weight to give to a piece of evidence is a matter for the Appraisal Committee's judgement. I note the judgment of Mr Justice Simon in the case of *Douglas Fraser and Kevin Short v the National Institute for Health and Clinical Excellence*. In his judgment Simon J stated (at paragraph 64), when considering a challenge to the weight NICE had given to evidence:

*"On the clearest and highest authority it was for the GDG [ie, NICE] to decide what weight to attach to evidence, and it cannot be said that the decision to make the recommendations on the basis of what was available to the GDG was irrational. Decisions of fact are for those entrusted to make those decisions."*

He added at paragraph 47(iii)

*There is an important distinction to be drawn between the question of whether something is a material consideration and the weight which should be given. The latter is a matter for the decision maker, subject to questions of Wednesbury irrationality; and, providing the decision-maker has taken [it] into account, **the fact that it has given it no weight is not a ground for review**, Emphasis supplied*

I regard the same principle as applying to the appeal panel. Therefore, it seems to me that the argument you make about the weight placed on the evidence is not a valid ground of appeal under this ground.

## Ground two

### 1.2.1, 1.2.2 Survey data, clinical opinion

I read these paragraphs, together with paragraphs 1.1.1-1.1.3 above, as all aspects of or evidence towards the same basic perversity appeal point, that it was perverse not to use an ICER derived from a comparison with chemotherapy as the basis for a final recommendation. I agree that that essential

complaint, as elaborated on under these five headings and as summarised in your paragraph 1.2.5, is a valid ground two appeal point.

### **1.2.3 Standards to identify chemotherapy eligible patients**

I agree this is a valid ground two appeal point.

### **1.2.4 Interpretation of clinical evidence**

I agree this is a valid ground two appeal point

## **Ground 3**

### **1.3**

For the reason give in relation to your para 1.1.1 above, I do not think it is arguable that the scope has been departed from. My preliminary view is there is no valid ground three appeal point here.

## **B End of life treatment**

Ground 1

### **2.1.1 Chemotherapy comparator**

I do not see that these paragraphs add anything in addition to your essential point summarised by me under paras 1.2.1 and 1.2.2 above, and I doubt they can be considered by the appeal panel. If you were correct in your essential argument that the wrong comparator was used, then it must follow that this technology would have to be re-considered under the EoL guidance, but with an ICER derived from the comparison with chemotherapy treatment. That exercise has not been carried out by the committee at all, because it considered (perversely or not) that the right ICER to use was one based on comparison with BSC.

If an appeal panel agrees that the only ICER that could reasonably be used is one based on a comparison with chemotherapy, then it would have to ask the committee to reconsider its recommendations in the light of that ICER and the EoL guidance. I do not think there can be a stand alone criticism of the committee that it has not yet turned its mind to the question, nor do I think the Panel could itself express a view on the correct answer were such an exercise to be called for. First the matter would have to be considered by the committee and then, possibly, reviewed by a panel on appeal, but no appeal panel could take a de novo decision under EoL.

Therefore it seems to me this point falls outside the scope of an appeal altogether.

### **2.1.2/2.2 Wrong even with BSC comparator (ground 1/2)**

In contrast to my concern at 2.1.1 above, this point does relate to a decision already taken by the committee. However I cannot see any process argument here? The point seems to be very plainly that in view of the benefits of treatment the only possible conclusion is that an ICER of £63,000 is acceptable. That goes directly to the committee's judgement and has to be a perversity challenge, I think.

I am minded to conclude this is a valid appeal point under ground two, but not ground one.

In case it assists in preparing for the appeal hearing, may I draw your attention to the panel's recent decision letter relating to sorafenib which briefly touches on the question of multipliers and thresholds in this context.

## **C Ultra orphan indication**

### **Ground 1/3**

#### **3.1-social value judgements and draft guidance**

I am afraid I cannot quite understand how it is that you say the SVJ document makes it clear that ultra-orphan drugs must be appraised in a different way or to different thresholds? It seems to say that it is not expected they will be appraised at all, and is silent on what if anything should be done differently if they are?

The citizen's council is an advisory body, and for its reports to become part of NICE's processes they must be adopted by NICE's board. I am not aware that the Board has adopted guidance on ultra orphan drugs, and if that is correct, it would not be open to the Committee to depart from normal processes and thresholds. I note the draft guidance to which you refer, but unless that has been adopted, I do not agree that a draft document from 2006 would be relevant to a decision taken in 2010. Lapatinib was rather a different case as the draft guidance was current, and indeed came into force before the appraisal was concluded. In any event you overstate the appeal panel's position. They remarked that "*It might have been reasonable for the Institute not to apply the new policy to lapatinib at all, on the basis that the Final Appraisal Determination had been finalised before the policy was adopted.*" The actual basis on which the appeal was allowed was that, having decided to apply the policy, the manufacturer was not then allowed to make a submission on the effect of the policy in that case and that was unfair.

I am minded to conclude this is not a valid ground of appeal under either ground one or ground three.

## **D Human Rights**

Ground 3

### **Para 4**

This is a valid appeal point. As it is almost entirely a legal point, and as neither the appeal panel nor the appraisal committee are legally qualified, I am concerned that merely referring the point as put to an appeal hearing may not generate the most robust scrutiny of the issue. I therefore suggest we proceed as follows. I will request the appraisal committee to make whatever observations they wish on the issue (if any) in writing some time in advance of the hearing. I will then ask the appeal panel's legal advisor to prepare a written note of provisional advice for the appeal panel. The appraisal committee's observations (if any) and the note of provisional advice will be shared with all appellants in advance of the hearing. In this way all sides will be aware in advance of the various positions being advanced, and the hearing will, I hope, run more smoothly.

### **Conclusion**

As I am minded to rule that at least some of your appeal points are valid, I will pass your appeal to the Appeal Panel for consideration.

If you wish to make any further comment on the points that I have indicated that I do not, at this preliminary stage, view as valid, or that I have re-cast, please provide to me this within 10 working days from the date of this letter, no later than **Friday 16 April**. I will then reach a final decision on the validity of those points.

Yours sincerely



**Appeals Committee Chair**  
**National Institute for Health and Clinical Excellence**