National Institute for
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Mr Ali Azough
Market Access Manager
Celgene Ltd
Morgan House
Madeira Walk
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Berkshire
SL4 1PE

9 September 2009

Dear Mr Azough,

**Azacitidine for the treatment of myelodysplastic syndromes, chronic
myelomonocytic leukaemia, and acute myeloid leukaemia**

The Appraisal Committee met on 3 September 2009 to discuss the comments
received on the ACD for azacitidine for the treatment of myelodysplastic
syndromes, chronic myelomonocytic leukaemia, and acute myeloid
leukaemia.

The Appraisal Committee has concluded that an independent review of the
additional modelling submitted as part of your response to the ACD is
required. However, before this independent review can take place, the
Appraisal Committee requests that you respond to the following matters of
clarification.

We request you to provide a written response to this letter to the Institute by
17:00, **30 September 2009.**

Two versions of this written response should be submitted; one with
academic/commercial in confidence information clearly marked and one from
which this information is removed.

If you present data that are not already referenced in the main body of your submission and that data are seen to be academic/commercial in confidence information, please complete the attached checklist for in confidence information.

If you have further queries on the technical issues raised in this letter, please contact Whitney Miller (Whitney.Miller@nice.org.uk). Procedural questions should be addressed to Jeremy Powell (Jeremy.Powell@nice.org.uk) in the first instance.

Regards

Dr Elisabeth George
Associate Director - Appraisals
Attached: checklist for in confidence information

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Clarification Points

1. Your response to the ACD states that the exponential function for the survival curve provides the best fit to the majority of the treatment arm data (azacitidine (pre-selected for BSC) and azacitidine (pre-selected for SDC)) and the lognormal function provides the best fit to the majority of the comparative care regimen data (BSC and SDC). *Please provide the following analyses (all of which are to include the adjustment for age-dependent mortality) and the concomitant range of ICERs:*

> *i. Estimating overall survival by using the Weibull function to model the survival of both patients receiving azacitidine and those receiving the comparative care regimens.*
>
> *ii. Estimating overall survival by using the exponential function to model the survival of both patients receiving azacitidine and those receiving the comparative care regimens.*
>
> *iii. Estimating overall survival by using the lognormal function to model the survival of both patients receiving azacitidine and those receiving the comparative care regimens.*
>
> *iv. Estimating overall survival by using the exponential function to model the survival of patients receiving azacitidine and the lognormal function to model patients receiving the comparative care regimens.*
>
> *v. Estimating overall survival by modelling baseline survival from the registry data, and then applying the respective hazard ratios associated with azacitidine or active chemotherapy (LDC and SDC) treatment. Please explore through sensitivity analysis the impact of changing the assumption that the hazard ratios will remain constant over time.*

2. In your response to the ACD, you present data obtained from the Düsseldorf MDS registry for patients treated with best supportive care alone. *Please describe the search strategy (including inclusion and exclusion criteria) used to identify these data, and the rationale for choosing these data if other sources were also identified through your searching.*

3. Table A1 in your response to the ACD presents a limited set of patient characteristics from the Düsseldorf MDS registry. *Please provide a more complete description of patient characteristics as they relate to the types of BSC received (such as the percentage receiving GSF, etc.), with full details of the treatments and how these compare with current practice in the UK.*

4. As stated in your response to the ACD, the costs of preparation and administration are assumed to be two-fold greater for the two days of weekend administration per cycle. *Please provide justification as to why a*

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two-fold increase appropriately represents the expected increase in costs associated with weekend administration.

5. *Please clarify component costs and the assumptions which underpin the calculation of the costs of blood transfusion.*

6. The Committee has noted that the use of the NHS 2009/10 tariff was expected to increase to the ICER, while in your response to the ACD, even with the use of the tariff in the base case, and a survival analysis that lead to shorter overall survival in the model, the ICERs are significantly lower than originally estimated. *Please describe what changes in the model have driven these change in the ICERs.*

7. A number of arithmetic errors are noted in your response to the ACD (including, but not limited to, Table C3). *Please correct these.*

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