



**National Institute for
Health and Clinical Excellence**

04 April 2007

MidCity Place
71 High Holborn
London
WC1V 6NA

Tel: 020 7067 5800
Fax: 020 7067 5801
Email: nice@nice.org.uk
www.nice.org.uk

Dear Dr Price

Health Technology Appraisal
Bortezomib monotherapy for relapsed multiple myeloma

Following the publication of the appeal decision in this appraisal, the Institute has scheduled a further meeting of the Appraisal Committee for 8 May 2007. At this meeting, the Committee will reappraise the evidence for the cost-effectiveness of the licensed indication of bortezomib in the following circumstances:

1. When used only for patients after first relapse;
2. When used only for patients after first relapse, and when treatment ceases after three cycles if a patients fail to respond;
3. When used only for patients after first relapse, and when treatment ceases after three cycles if a patient's disease fails to respond, and when the manufacturer pays for treatment in patients whose disease fails to respond.

In order for the third scenario to be considered, I am writing to request Janssen-Cilag to submit evidence of the cost effectiveness of bortezomib when used in the proposed risk-share scheme as set out Appendix 1 of your letter of appeal dated November 2006.

The Institute is currently liaising with the Department of Health to establish its position on your proposed risk-share scheme. I should be grateful if you would let know whether your proposal for the risk-sharing arrangement is also intended to apply to the NHS in Wales. If so, we will need to have the details of the agreement you have reached with the Welsh Assembly Government.

All assumptions and methodology required to evaluate the cost effectiveness of the three scenarios should be fully documented. If any variation from assumptions and methods made for the economic model already submitted are considered, these should be presented in a separate analysis in order for the Committee to start the

appraisal at the point of their conclusions set out in the current Final Appraisal Determination.

In describing the risk-sharing scheme and its impact on cost-effectiveness we ask you to clarify in particular:

- The scheme proposes that 'response' will be evaluated after '3 – 4 cycles (12 – 16 vials)'.
 - In taking account of the appeal decision, we will need you to provide three separate scenarios; one with a stopping rule after 3 cycles only, the other with a stopping rule after 4 cycles only, and a final scenario in which a '3 to 4 cycle' stopping rule is considered.
 - In all these scenarios, we will need you to detail the proportion of patients that would be assumed to be a responder at the evaluation point, and for the 3 to 4 cycle scenario, the proportion of people assumed to have responded after 3 cycles and after 4 cycles.
- To confirm the definition of response and how you expect this to be evaluated in practice;
- The details of the risk-sharing scheme as agreed with the Department of Health and the Welsh Assembly Government. Specifically, the arrangements for administration and review of the scheme in the NHS in England Wales.

Finally, I would like to draw to your attention that we intend to consider the need to appraise the (unlicensed) use of bortezomib in combination with dexamethasone separately from the consideration of licensed indication. Consideration of this use of bortezomib will require a new referral from the Department of Health. Therefore, in order to not impede the appraisal of the monotherapy (licensed) indication the committee will not consider off-label use of bortezomib at its meeting on 8 May. The Institute is in discussion with the Department of Health on this matter and we would be interested to receive your views on the appropriateness of undertaking a separate appraisal of the use of bortezomib in combination with dexamethasone. Any views that you wish to submit to the Institute will be forwarded to the Department of Health for their consideration of further referrals in relation to bortezomib.

I should be grateful for your response to this letter by end of play **Friday 13 April 2007**.

Please address your response to this letter to Reetan Patel, project manager, on Reetan.patel@nice.org.uk.

Yours sincerely

Carole Longson
Director, Centre for Health Technology Evaluation

cc. Simon Reeve, Andrew Dillon, Meindert Boysen