The Royal College of Pathologists
Pathology: the science behind the cure

Royal College of Pathologists and British Society for Haematology response to the

NICE Appraisal consultation document for Bortezomib and thalidomide for the first-line treatment of multiple myeloma.

The Royal College of Pathologists and the British Society for Haematology welcome the Appraisal Committee's preliminary recommendations and believe that if implemented the guidance would ensure that patients would receive therapy that gives the best chance of prolonged survival and improved quality of life.

Has all the relevant evidence been taken into account?

We agree that relevant evidence has been taken into account and particularly appreciate the fact that the Committee has taken into consideration data from the MRC Myeloma IX trial, which in addition to related evidence from clinical experts, has been used in formulating provisional guidance. One consequence of this is that clinicians are able to select the alkylating agent (either Melphalan or Cyclophosphamide) which most appropriately meets the clinical needs of an individual patient.

It is a matter of regret that because of the design of some otherwise relevant trials it was not possible to include all their data. We therefore welcome initiatives which encourage NICE's closer involvement in trial design in future.

Are the summaries of clinical and cost effectiveness reasonable interpretations of the evidence?

We note the wide variation in the results of economic analyses provided by both the manufacturers and the assessment group and recognise the difficulty this creates in determining the clinical and cost effectiveness of the technologies under consideration, but believe that the committee has taken into account all the variables and produced a fair and reasonable interpretation of the evidence.

We particularly welcome the re-evaluation of the ICER of Bortezomib at £22,500 per QALY gained for VMP compared with MP as a result of accepting that four cycles (31 vials) was more likely to reflect clinical practice than the 40 vials used in initial calculations. We confirm that 31 vials agree more closely with clinical practice than the higher figure of 40.

Are the provisional recommendations sound and a suitable basis for guidance to the NHS?
We agree that the recommendations are sound and a suitable basis for guidance to the NHS and if implemented will permit clinicians to select in the context of the MDT process, the most suitable regimen for an individual patient. We believe that this flexibility in itself will lead to greater cost effectiveness, maximising as it will the chance to improve renal function, to avoid serious thrombotic problems and minimise the costs associated with treating these myeloma or treatment related problems. Furthermore and most importantly the consequence of the recommendations

will also be that patients will have the greatest chance of best response and improved quality of life.

We do however have some reservations about the wording of the guidance and are concerned that the use of the word 'contraindications' in para 1.2 of the guidance 'the person is unable to tolerate or has contraindications to thalidomide' may be open to misinterpretation.

We believe that the intention of the Committee is to recommend that clinicians, whilst using a thalidomide regimen in the majority of patients, should be able to select a bortezomib regimen for those patients who would be disadvantaged by treatment with thalidomide. These patients would include those at high risk of thrombosis, or with impaired renal function. In such patients, the use of 'bortezomib in combination with an alkylating agent and a steroid is likely to be a cost-effective option…' because it is the only option that is as clinically effective in treating the cancer.

We are anxious lest the term 'contraindications' is interpreted in the pharmacological sense to mean the contraindications which are listed in the SPC for thalidomide which are as follows:

- Hypersensitivity to thalidomide or to any of the recipients.
- Pregnant women (see section 4.6).
- Women of childbearing potential unless all the conditions of the Thalidomide Celgene Pregnancy Prevention Programme are met
- Patients unable to follow or comply with the required contraceptive measures

These do not cover the clinical situations in which thalidomide would be considered to be clinically inappropriate, as stated above and in section 4.3.2 of the ACD. We would like to avoid any such opportunities for misinterpretation which may lead to conflict between clinicians and PCT's, resulting in delays to patients receiving effective treatment, and in 'post-code prescribing'.

We would therefore respectfully suggest that the Committee consider replacing the term 'contraindicated' by 'clinically inappropriate' or using the form of words as in para 4.3.2 of the ACD to qualify 'contraindicated' by saying 'such as those with clotting disorders and impaired renal function'.

In summary the provisional recommendations of the Appraisal Committee are welcomed by RCPath and BSH as we believe they will ensure patients will receive effective therapy to have the best chance of prolonged survival and improved quality of life. To avoid misinterpretation of the Committee's intentions we suggest a change of wording of para 1.2 of the provisional recommendations.