Bortezomib and Thalidomide for the first-line treatment of myeloma
Myeloma UK response to the Technology Assessment Report

Myeloma UK welcomes the opportunity to comment on the Technology Assessment Report for the above Multiple Technology Appraisal. Overall, we consider the Assessment Report to be well-balanced and thorough. However, there are a number of areas of interpretation we would like to comment on. We hope the following will be helpful to the Appraisal Committee alongside our earlier consultee submission.

1. CTDa

Myeloma UK is disappointed that the MRC IX trial data comparing MP with CTDa was determined not to meet the inclusion criteria for the clinical effectiveness systematic review. In particular, we are concerned about the Assessment Group's reason for excluding the data on the basis that research questions were asked in the study that were additional to those required for this MTA.

The MRC IX trial is a robust 2 x 2 study involving large numbers of patients and which is recognised as asking important and relevant questions in a UK context. Our medical advisors are in no doubt that the single arm CTDa (without maintenance) is a powerful arm with regard to the numbers of patients involved, the robustness of the study design and the relevance of the outcomes.

It is very concerning that the important outcomes of this publicly-funded trial may potentially not be allowed to translate into clinical practice in the UK.

We understand that a substantial amount of data has been provided for the purpose of this MTA and that the trial investigators are happy to provide any additional data or clarification required to enable its inclusion in the review.

2. MPT

Myeloma UK agrees that the evidence suggests that MPT represents a clinically and cost-effective use of NHS resources. Although most clinicians in the UK have less experience of using this combination compared to CTDa, clinicians have told us that it offers them a welcome further option to treat patients according to their individual circumstances.

3. VMP

Myeloma UK agrees with the findings of the Assessment Group that the evidence supports the superior clinical effectiveness of VMP compared to MP alone. However, we are concerned that the incremental cost per QALY as determined by the Assessment Group suggests a comparatively less cost-effective use of resources than MPT. In its conclusion the ERG notes that:

> The cost effectiveness estimates for MPT, VMP and CTDa versus MP were £9,174, £29,837 and £33,216 per QALY gained respectively. However MPT dominated VMP as it was cheaper and more effective.

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We agree that MPT has a preferable cost-effectiveness ratio to MP than the ratio of VMP to MP, but we hope that the Appraisal Committee will recognise that VMP is both a proven and cost-effective treatment option for which there is a clinical need alongside MPT.

Clinicians in the UK view VMP as having an important role to play in this setting. As set out in more detail in our stakeholder submission, the complex nature of myeloma means that clinicians require different treatment options to hand to ensure the best outcomes for individual patients.

While thalidomide-based treatment regimens such as MPT and CTDa are appropriate for many patients, clinicians have told us that VMP offers a more appropriate option for some patients and they would therefore highly value its availability as an alternative.

The increased use of VMP on the NHS in this setting will increase our understanding of the roles it has to play. Myeloma UK therefore considers there would be merit in collecting data in the NHS clinic subsequent to it being recommended for use in order to establish this understanding.

We also observe that the economic assessment assumes that patients would receive the same dosing schedule and full number of (nine) cycles as in the RCT protocol and the Summary of Product Characteristics (SPC). However, Myeloma UK understands that the use of VMP in clinical practice for this group of patients does not reflect the trial circumstances or the SPC.

Clinicians tell us that in practice patients usually have substantially fewer than nine cycles of bortezomib and that they often follow a once-weekly dosing schedule rather than twice-weekly. We note that dosing modifications were accounted for in the evaluation of MPT on the recommendation of clinical experts. Similarly, the actual cost to the NHS of VMP is also likely to be lower in practice.

4. Adverse events

Myeloma UK is aware that in the clinical practice setting most of the commonly-experienced adverse events associated with thalidomide and bortezomib can be well-managed; for example, with dose reduction. This suggests that the actual adverse events therefore may be significantly less significant than those used in the economic assessment.

5. Head-to-head comparisons

Myeloma UK agrees with the ERG's conclusion that:

> Head to head trials of bortezomib containing, and thalidomide containing combination regimens are desirable. These trials should include assessments of patient HRQoL in response to treatment.

Myeloma UK considers that such trials would be very valuable and clinicians tell us that they share this view.

From a commercial perspective it is unlikely that head-to-head trials would be instigated to compare two newly-licensed products. Furthermore, such trials are not practical at this stage in the regulatory and HTA approval timeline. Not only would the time to generate the data required for HTA assessment significantly delay patient access to the treatments, but clinical practice will have moved on and new, more relevant, questions would need to be answered.

However, this HTA provides the opportunity to develop our understanding of the comparative benefits of bortezomib and thalidomide-containing regimens. Having both regimens approved and available for clinicians to use on the NHS would enable phase IV evidence-gathering of the comparative benefits as suggested.

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15 March 2010

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