Myeloma UK, Leukaemia CARE, Leukaemia Research and the Rarer Cancers Forum

Joint response to the Appraisal Consultation Document on lenalidomide for the treatment of myeloma

i) Do you consider that all of the relevant evidence has been taken into account?

1.1 Lenalidomide is the subject of two high-quality randomised controlled trials out of which has come a substantial body of impressive data. The body of data appears to have been considered in full and whilst we are pleased that lenalidomide has been recognised as a clinically effective treatment, we are frustrated that the Institute and the manufacturer remain unable to remove the uncertainty around the effectiveness of a treatment that is the subject of crossover in trials.

The ERG report states "the main threat to validity for clinical effectiveness data is the high level of crossover in the trials…This is a problem in many assessments of new chemotherapy in end stage cancer and it would be unethical to undertake trials that did not allow for such crossover. However, this does introduce uncertainty into the results".

Given the admitted frequency of crossover and its substantial consequence on the validity of trial data, we recommend the Institute establishes a standard method to more justly assess treatments which are penalised by the current appraisal process for being the focus of trials unblinded early because of their superior clinical effectiveness.

That the Appraisal Committee and the manufacturer cannot reduce the uncertainty around the data for a treatment that has such an impressive body of evidence supporting it is surely incongruous with their necessary skill sets.

1.2 We applaud the improved understanding of myeloma that is demonstrated by the Committee, recognising the heterogeneous nature of the disease and that choice of therapy for patients is influenced by several factors. The Committee also notes that the optimal sequence of treatments is "as yet unclear".

Given the acknowledged nature of the disease and the impressive body of evidence for lenalidomide, we urge the Institute, the Department of Health and the manufacturer to discuss ways in which the NHS price can be reduced and / or an appropriate risk share scheme can be introduced to reduce uncertainty in a timeframe that is in the best interests of patients.

ii) Do you consider that the summaries of clinical and cost effectiveness are reasonable interpretations of the evidence, and that the preliminary views on the resource impact and implications for the NHS are appropriate?

2.1 We note that the ERG considered that the "approach taken to modelling is reasonable" and that the randomised controlled trials are "good quality". Further, the Committee recognises that a good job has been done within the manufacturer's model with regards attempting to account for the crossover in the trials, and acknowledges the appropriate use of the historical

MRC data. The Committee "accepted that these data represented the best available survival data for people with multiple myeloma to be used in extrapolation of overall survival".

Despite this, it is clear that there is also an inherent distrust of the manufacturer's submission, with the Committee considering that the ERG's approach "resulted in more plausible estimates of cost effectiveness than those presented by the manufacturer".

What justification can the Institute supply that the ERG modelling is more valid? It is evident from the ERG report that the manufacturer corrected errors throughout the process; we assume therefore that the manufacturer is willing for the evidence to be the best it can be. It is unclear to us why or how we can be confident that the ERG is not making negative and pessimistic assumptions about the data to the detriment of patients. In the same way that the Institute may assume that the manufacturer overestimates the value of their product, those externally may assume that the ERG would underestimate the benefits. For is it not the case that the clash between the manufacturer and the ERG is all about different interpretations of what is scientifically most appropriate?

Indeed, the ERG states that its own modelling has many "matters of judgement and preferred assumptions" throughout it.

As informed stakeholders, we imagine that the likely QALY is in between the two estimates, which would surely bring the QALY of lenalidomide within an acceptable range for further discussion.

Ultimately, we find it unacceptable for the Institute to turn a treatment down on the basis of uncertainty which is determined by an evidence review group who admit that its own considerations were tainted with uncertainties.

2.2 Regardless of whose modelling is interpreted as 'more accurate', we recognise that lenalidomide is an expensive treatment. However, even if the ERG modelling is considered the most plausible, the QALYs for patients who have had >1 prior therapy with and without prior exposure to thalidomide are still within touching distance of what NICE deems acceptable.

In view of the undisputed clinical evidence a 'no' at FAD stage would represent a huge failure from all involved to effectively interpret an impressive set of data and show willing to strive for the best for all patients.

There is now also a window of opportunity for NICE, the company and the Department of Health to find a solution together. Such an approach would complement the national agenda of promoting more flexible pricing and availability of new drugs, as set out in Prof Mike Richard's report *Improving access to medicines for NHS patients*.

iii) Do you consider that the provisional recommendations of the Appraisal Committee are sound and constitute a suitable basis for the preparation of guidance to the NHS?

3.1 We do not. As the recommendation stands, patients who are suitable for lenalidomide will not routinely get access to it.

It is now government policy that patients can pay for treatments out of their own pockets if the NHS does not provide them. It is clear that where a treatment costs only a few pounds a day, 'topping up' is unlikely to prove a serious financial burden. Lenalidomide, however, costs £4368 per month; this top-up cost will be affordable to very few people.

A failure by NICE to reconsider its draft will make it increasingly difficult for patients to get access to this important advance in the treatment of myeloma. For this to remain a 'no' at FAD stage will effectively mean that the Institute are folding into their guidance the impossible choice between financial hardship and less efficacious treatment for relapsing myeloma patients.

iv) Are there any equality related issues that need special consideration that are not covered in the ACD?

4.1 The ACD explains that the utility values used to generate the lenalidomide QALY were based on the utility of the general public at a median age of 54. In point 4.12 the Committee communicates its unease that someone of 54 is "considerably younger than the average population at age of people who usually developed multiple myeloma". Here the Institute is implying that because myeloma patients are generally older than 54, it is not prudent to correlate health gains that a 54 year old might enjoy to a myeloma patient because health gain is not worth as much in older people that in younger people. It is our view that with this statement the Institute is exercising age discrimination.

4.2 Further, Myeloma UK wishes to point out that in the bortezomib monotherapy appraisal the Institute directed Johnson & Johnson to use this same utility value when converting Life Years Gained into QALYs. That the ERG wants consistency between the appraisals with regards the administration and medical management costs for bortezomib but employs unexplained misgivings about the manufacturer using identical utility values to the bortezomib appraisal is spurious. It implies that the ERG wants the manufacturer to comply only with the component of the bortezomib appraisal that discredits the cost effectiveness of lenalidomide.

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