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Single Technology Appraisal (STA)

Lenalidomide for the treatment of multiple myeloma in people who have received at least one prior therapy with bortezomib (partial review of TA171)

Thank you for agreeing to give us a statement on your organisation's view of the technology and the way it should be used in the NHS.

Healthcare professionals can provide a unique perspective on the technology within the context of current clinical practice which is not typically available from the published literature.

To help you in making your statement, we have provided a template. The questions are there as prompts to guide you. It is not essential that you answer all of them.

Please do not exceed the 8-page limit.

About you

Your name:
Dr Faith Davies

Name of your organisation
NCR/RCP/RCR/ACP/JCCo

Are you (tick all that apply):

- a specialist in the treatment of people with the condition for which NICE is considering this technology?
-
- **yes**

- a specialist in the clinical evidence base that is to support the technology (e.g. involved in clinical trials for the technology)?

- an employee of a healthcare professional organisation that represents clinicians treating the condition for which NICE is considering the technology? If so, what is your position in the organisation where appropriate (e.g. policy officer, trustee, member etc.)?
-
chair of the NCRI Myeloma Sub group
-
- other? (please specify)

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What is the expected place of the technology in current practice?

How is the condition currently treated in the NHS? Is there significant geographical variation in current practice? Are there differences of opinion between professionals as to what current practice should be? What are the current alternatives (if any) to the technology, and what are their respective advantages and disadvantages?

Are there any subgroups of patients with the condition who have a different prognosis from the typical patient? Are there differences in the capacity of different subgroups to benefit from or to be put at risk by the technology?

In what setting should/could the technology be used – for example, primary or secondary care, specialist clinics? Would there be any requirements for additional professional input (for example, community care, specialist nursing, other healthcare professionals)?

If the technology is already available, is there variation in how it is being used in the NHS? Is it always used within its licensed indications? If not, under what circumstances does this occur?

Please tell us about any relevant **clinical guidelines** and comment on the appropriateness of the methodology used in developing the guideline and the specific evidence that underpinned the various recommendations.

Myeloma is a relapsing remitting disease which requires a personalised/individual approach to therapy to ensure prolonged periods of remission and good quality of life.

Over the last 10 years two active classes of drugs have been introduced into the clinic (IMiDs eg thalidomide, lenadlidomide and pomalidomide) and proteasome inhibitors (bortezomib). These drugs have led to increased response rates and importantly improved progression and overall survival. Consensus concerning the most effective order to deliver the drugs varies around Europe and the US. These variations are based on clinical evidence, availability of drugs within health care systems and importantly patient disease factors (eg the presence of renal disease, high risk cytogenetics, thromboembolic disease, oral vs iv preparations, side effect profile etc).

According to the current NICE guidance, the majority of myeloma patients in the UK receive a thalidomide based combination +/- high dose therapy with blood stem cell support as first line therapy, a bortezomib combination for second line therapy and a lenalidomide combination as third line therapy.

For a number of reasons some patients will receive bortezomib as front line therapy eg patients who enter a clinical trial or for clinical reasons (eg intolerance or contraindication to thalidomide, renal failure or high risk disease). When these patients relapse there is no current NICE guidance for

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treatment, as bortezomib is currently listed as NICE second line therapy. It is however available in England via the Cancer Drug fund (CDF). A longer term solution to access lenalidomide second line for these patients (rather than via the CDF) would be appropriate moving forward.

Clinicians agree that lendaliomide would be the chosen second line therapy for this group of patients. Although in some instances repeating therapy with bortezomib may be appropriate (eg for patients with a long remission to their first line bortezomib therapy), in the majority of cases this would not be appropriate.

Bortezomib has recently gained an upfront licence for both the treatment of transplant eligible and the transplant ineligible patients and NICE guidance for this area is under review. If this is accepted then this group of patients without access to lenalidomide second line may increase outside of the current scope of this appraisal (ie those intolerant or with a contraindication to thalidomide).

The advantages and disadvantages of the technology

NICE is particularly interested in your views on how the technology, when it becomes available, will compare with current alternatives used in the UK. Will the technology be easier or more difficult to use, and are there any practical implications (for example, concomitant treatments, other additional clinical requirements, patient acceptability/ease of use or the need for additional tests) surrounding its future use?

If appropriate, please give your view on the nature of any rules, informal or formal, for starting and stopping the use of the technology; this might include any requirements for additional testing to identify appropriate subgroups for treatment or to assess response and the potential for discontinuation.

If you are familiar with the evidence base for the technology, please comment on whether the use of the technology under clinical trial conditions reflects that observed in clinical practice. Do the circumstances in which the trials were conducted reflect current UK practice, and if not, how could the results be extrapolated to a UK setting? What, in your view, are the most important outcomes, and were they measured in the trials? If surrogate measures of outcome were used, do they adequately predict long-term outcomes?

What is the relative significance of any side effects or adverse reactions? In what ways do these affect the management of the condition and the patient's quality of life? Are there any adverse effects that were not apparent in clinical trials but have come to light subsequently during routine clinical practice?

The clinical trial data (009 and 010 - NEJM x 2) demonstrated the efficacy of lenalidomide and dexamethasone in the first to third relapse population, however the original NICE appraisal suggested its use at second relapse (third line).

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In addition to the supporting clinical trial data, UK clinicians agree that lendaliomide would be the chosen second line therapy for this group of patients (ie patients who were intolerant or contraindicated to thalidomide and received bortezomib first line). This is standard practice both in Europe and in the USA.

In some instances repeating therapy with bortezomib may also be appropriate (eg for patients with a long remission to their first line bortezomib therapy who had minimal side effects from therapy). In this latter instance patients would go on to access lenalidomide third line under the current NICE guidance.

I can see no obvious disadvantage to this technology in this setting.

Equality and Diversity

NICE is committed to promoting equality of opportunity, eliminating unlawful discrimination and fostering good relations between people with particular protected characteristics and others. Please let us know if you think that this appraisal:

- Could exclude from full consideration any people protected by the equality legislation who fall within the patient population for which [the treatment(s)] is/are/will be licensed;
- Could lead to recommendations that have a different impact on people protected by the equality legislation than on the wider population, e.g. by making it more difficult in practice for a specific group to access the technology;
- Could lead to recommendations that have any adverse impact on people with a particular disability or disabilities

Please tell us what evidence should be obtained to enable the Committee to identify and consider such impacts

The lack of guidance for patients who have received bortezomib upfront is currently a problem as it places patients who are intolerant or contraindicated to thalidomide, have entered a clinical trial or have renal failure/high risk disease at a significant disadvantage/risk as they have limited access to therapy at second line. In these instances patients may be given a less efficacious therapy and therefore potentially limit their clinical outcome. Therefore this STA should improve any perceived issues with equality.

Any additional sources of evidence

Can you provide information about any relevant evidence that might not be found by a technology-focused systematic review of the available trial evidence? This could be information on recent and informal unpublished evidence, or information from registries and other nationally coordinated clinical audits. Any such information must

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include sufficient detail to allow a judgement to be made as to the quality of the evidence and to allow potential sources of bias to be determined.

Implementation issues

The NHS is required by the Department of Health and the Welsh Assembly Government to provide funding and resources for medicines and treatments that have been recommended by NICE technology appraisal guidance. This provision has to be made within 3 months from the date of publication of the guidance.

If the technology is unlikely to be available in sufficient quantity, or the staff and facilities to fulfil the general nature of the guidance cannot be put in place within 3 months, NICE may advise the Department of Health and the Welsh Assembly Government to vary this direction.

Please note that NICE cannot suggest such a variation on the basis of budgetary constraints alone.

How would possible NICE guidance on this technology affect the delivery of care for patients with this condition? Would NHS staff need extra education and training? Would any additional resources be required (for example, facilities or equipment)?

No issues