NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Review Proposal Project (RPP) decision paper

Review of TA322; Lenalidomide for treating myelodysplastic syndromes associated with an isolated deletion 5q cytogenetic abnormality

Final recommendation post consultation
The guidance should be transferred to the 'static guidance list'.

1. Background

This guidance was issued in September 2014

At the Guidance Executive meeting of 22 August 2017 it was agreed that we would consult on the recommendations made in the GE proposal paper. A four week consultation has been conducted with consultees and commentators and the responses are presented below.

2. Proposal put to consultees and commentators

The guidance should be transferred to the 'static guidance list'. That we consult on this proposal.

3. Rationale for selecting this proposal

New evidence is not expected to lead to a change in the recommendations in the original guidance. The main uncertainties in the appraisal were:

- the proportion of people eligible for the patient access scheme (PAS), that is, they remain on treatment beyond 26 cycles and
- the overall survival and health related quality of life benefits generated by lenalidomide.

Since the appraisal, data provided by the company suggest that the PAS is operating without any problems. The average proportion of patients on treatment at 26 cycles is greater than that estimated by the company in the appraisal, therefore improving the value proposition of lenalidomide to the NHS. The company do not have plans to change the PAS.

The estimates of overall survival used in the appraisal were taken from trial evidence which was deemed uncertain by the committee. The evidence suggested that there was not a statistically significant difference in terms of overall survival for those on lenalidomide compared with placebo. Since the appraisal a meta-analysis of over 2000 patients, examined the efficacy and safety results of lenalidomide. The results of this study found that treatment with lenalidomide significantly improved overall survival (HR=0.62) compared with placebo, erythropoiesis-stimulating agents or thalidomide. This finding is unlikely to change the current recommendation.

Two relevant ongoing trials were identified, both looking at the safety and efficacy of lenalidomide. One trial is collecting overall survival outcomes for lenalidomide, however it is a single arm trial and so it is not expected that results from this trial could help to resolve the uncertainty of the overall survival benefits for lenalidomide compared with best supportive care.

In conclusion much of the new evidence relates to the use of lenalidomide in a broader population than its marketing authorisation (people with del 5q), and of the evidence which is relevant to this population nothing is likely to change the previous recommendation.

4. Summary of consultee and commentator responses

Comments received in the course of consultations carried out by NICE are published in the interests of openness and transparency, and to promote understanding of how recommendations are developed. The comments are published as a record of the submissions that NICE has received, and are not endorsed by NICE, its officers or advisory committees.

Respondent: Department of Health **Response to proposal:** No comment	**Comment from Technology Appraisals** Comment noted.

Respondent: NCRI-ACP-RCP	**Comment from Technology Appraisals**
Response to proposal: The NCRI-ACP-RCP is grateful for the opportunity to respond to the above consultation. We have liaised with our experts and would like to make the following comments. One change that potentially impinges on the interpretation of the original guidance in practice is that the new WHO classification of myeloid malignancies (2016) has included patients with del(5q) plus one additional cytogentic abnormality (providing it is not a chromosome 7 abnormality) in the diagnosis of 'MDS with isolated del (5q)'. This is because in recent data the prognosis is shown to be no different for del(5q) alone or del(5q) plus one additional abnormality. This inclusion of both entities under the one WHO diagnostic category gives some flexibility to clinicians interpreting the use of lenalidomide within the context of the license and the NICE guidance. The use of lenalidomide may, therefore, increase with the application of the new WHO classification in the MDT.	Comment noted.

Respondent: Celgene Limited	**Comment from Technology Appraisals**
Response to proposal: Celgene agrees with NICE's proposal to move NICE Technology Appraisal Guidance No.322; Lenalidomide for treating myelodysplastic syndromes associated with an isolated deletion 5q cytogenetic abnormality to the static list.	Comment noted.

Paper signed off by: Jenniffer Prescott, 06 November 2017

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