NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Appraisal

Lenalidomide with bortezomib and dexamethasone for untreated multiple myeloma

Draft scope

Draft remit/appraisal objective

To appraise the clinical and cost effectiveness of lenalidomide with bortezomib and dexamethasone within its marketing authorisation for previously untreated multiple myeloma.

Background

Multiple myeloma is a form of cancer that arises from plasma cells (a type of white blood cell) in the bone marrow. Myeloma cells produce large quantities of an abnormal antibody, known as paraprotein. Unlike normal antibodies, paraprotein has no useful function and lacks the capacity to fight infection. Myeloma cells suppress the development of normal blood cells that are responsible for fighting infection (white blood cells), carrying oxygen around the body (red blood cells) and blood clotting (platelets). The term multiple myeloma refers to the presence of more than one site of affected bone at the time of diagnosis. People with multiple myeloma can experience bone pain, bone fractures, tiredness (due to anaemia), infections, hypercalcaemia (too much calcium in the blood) and kidney problems.

In 2015, 4,632 people were diagnosed with multiple myeloma in England.[1] It is most frequently diagnosed in older people, with 44% of new cases in England in people aged 75 years and over.[2] Multiple myeloma is more common in men than in women and the incidence is also reported to be higher in people of African family origin.[3] The 5-year survival rate for adults with multiple myeloma in England and Wales is about 47%.[4]

Treatment aims to prolong survival and maintain a good quality of life by controlling the disease and relieving symptoms. High-dose chemotherapy with autologous stem cell transplantation may be an option for some people with multiple myeloma. For those people, NICE technology appraisal guidance 311 recommends induction therapy with bortezomib in combination with either dexamethasone or dexamethasone and thalidomide, before high-dose chemotherapy and autologous stem cell transplantation.

For people for whom high-dose chemotherapy with autologous stem cell transplantation is considered inappropriate, NICE technology appraisal guidance 228 recommends, as a first-line treatment, thalidomide with an alkylating agent and a corticosteroid. If the person is unable to tolerate or has contraindications to thalidomide, NICE technology appraisal guidance 228 recommends bortezomib with an alkylating agent and a corticosteroid.

The technology

Lenalidomide (Revlimid, Celgene) is a structural analogue of thalidomide. It has anti-neoplastic, anti-angiogenic, pro-erythropoietic and immunomodulatory properties. Lenalidomide is administered orally.

Lenalidomide with bortezomib and dexamethasone does not have a marketing authorisation in the UK for previously untreated multiple myeloma. This lenalidomide combination has been studied in clinical trials compared with lenalidomide and dexamethasone in people who are ineligible for stem-cell transplantation, and separately in people who are eligible for stem-cell transplantation.

Lenalidomide with dexamethasone (without bortezomib) has a marketing authorisation in the UK for treating 'adult patients with previously untreated multiple myeloma who are not eligible for transplant'. Lenalidomide also has marketing authorisation as monotherapy for treating 'adult patients with newly diagnosed multiple myeloma who have undergone autologous stem cell transplantation' (subject to a separate ongoing NICE appraisal), and in combination with dexamethasone for treating 'adult patients who have received at least one prior therapy'.

Intervention(s)	Lenalidomide with bortezomib and dexamethasone
Population(s)	• People with previously untreated multiple myeloma who are eligible for stem-cell transplantation • People with previously untreated multiple myeloma who are not eligible for stem-cell transplantation
Comparators	For people who are eligible for stem-cell transplantation: • Bortezomib in combination For people who are not eligible for stem-cell transplantation: • Thalidomide with an alkylating agent and a corticosteroid • Bortezomib with an alkylating agent and corticosteroid (if thalidomide cannot be tolerated or is contraindicated) • Lenalidomide with dexamethasone (subject to ongoing NICE appraisal ID474)

Outcomes	The outcome measures to be considered include: • overall survival • progression-free survival • response rates • time to next treatment • time to treatment failure • adverse effects of treatment • health-related quality of life.
Economic analysis	The reference case stipulates that the cost effectiveness of treatments should be expressed in terms of incremental cost per quality-adjusted life year. The reference case stipulates that the time horizon for estimating clinical and cost effectiveness should be sufficiently long to reflect any differences in costs or outcomes between the technologies being compared. Costs will be considered from an NHS and Personal Social Services perspective. The availability of any patient access schemes for the intervention or comparator technologies will be taken into account. The availability and cost of generic products should be taken into account.
Other considerations	Guidance will only be issued in accordance with the marketing authorisation. Where the wording of the therapeutic indication does not include specific treatment combinations, guidance will be issued only in the context of the evidence that has underpinned the marketing authorisation granted by the regulator.
Related NICE recommendations and NICE Pathways	**Related Technology Appraisals:** Bortezomib and thalidomide for the first line treatment of multiple myeloma (2011). NICE technology appraisals guidance 228. Guidance on static list. Bortezomib for induction therapy in multiple myeloma before high-dose chemotherapy and autologous stem cell transplantation (2014) NICE technology appraisals guidance 311. Guidance on static list. **Appraisals in development (including suspended appraisals):** Lenalidomide in combination with dexamethasone for

	previously untreated multiple myeloma [ID474] NICE technology appraisals guidance. Publication date to be confirmed. (suspended appraisal) Lenalidomide for treating multiple myeloma after 1 prior treatment with bortezomib [ID667] NICE technology appraisals guidance. Publication date to be confirmed. [includes part review of TA171] (suspended appraisal) Lenalidomide for the maintenance treatment of multiple myeloma after autologous stem cell transplantation [ID475] NICE technology appraisal guidance. Publication date to be confirmed. (suspended appraisal) **Related Guidelines:** 'Myeloma: diagnosis and management of myeloma' (2016). NICE guideline 35. Review date to be confirmed. 'Haematological cancers – improving outcomes' (2016) NICE guideline 47 Review date to be confirmed. **Related Quality Standards:** Haematological cancers (2017) NICE quality standard 150 **Related NICE Pathways:** Myeloma (2017) NICE pathway
Related National Policy	NHS England (2017) Manual for Prescribed Specialised Services 2017/18. Blood and marrow transplantation services (adults and children) [section 29, page 79] Department of Health and Social Care, NHS Outcomes Framework 2016-2017 (published 2016): Domains 1, 4, 5.

Questions for consultation

Have all relevant comparators for lenalidomide with bortezomib and dexamethasone been included in the scope? Which treatments are considered to be established clinical practice in the NHS for previously untreated multiple myeloma?

Are the outcomes listed appropriate?

Are there any subgroups of people in whom lenalidomide with bortezomib and dexamethasone is expected to be more clinically effective and cost effective or other groups that should be examined separately?

Where do you consider for lenalidomide with bortezomib and dexamethasone will fit into the existing NICE pathway, Myeloma?

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 the proposed remit and scope may need changing in order to meet these aims. In particular, please tell us if the proposed remit and scope:

- could exclude from full consideration any people protected by the equality legislation who fall within the patient population for which lenalidomide with bortezomib and dexamethasone 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 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.

Do you consider lenalidomide with bortezomib and dexamethasone to be innovative in its potential to make a significant and substantial impact on health-related benefits and how it might improve the way that current need is met (is this a 'step-change' in the management of the condition)?

Do you consider that the use of lenalidomide with bortezomib and dexamethasone can result in any potential significant and substantial health-related benefits that are unlikely to be included in the QALY calculation?

Please identify the nature of the data which you understand to be available to enable the Appraisal Committee to take account of these benefits.

To help NICE prioritise topics for additional adoption support, do you consider that there will be any barriers to adoption of this technology into practice? If yes, please describe briefly.

NICE intends to appraise this technology through its Single Technology Appraisal (STA) Process. We welcome comments on the appropriateness of appraising this topic through this process. (Information on the Institute's Technology Appraisal processes is available at http://www.nice.org.uk/article/pmg19/chapter/1-Introduction).

NICE has published an addendum to its guide to the methods of technology appraisal (available at https://www.nice.org.uk/Media/Default/About/what-we-do/NICE-guidance/NICE-technology-appraisals/methods-guide-addendum-cost-comparison.pdf), which states the methods to be used where a cost comparison case is made.

- Would it be appropriate to use the cost comparison methodology for this topic?

- Is the new technology likely to be similar in its clinical efficacy and resource use to any of the comparators?

- Is the primary outcome that was measured in the trial or used to drive the model for the comparator(s) still clinically relevant?

- Is there any substantial new evidence for the comparator technology/ies that has not been considered? Are there any important ongoing trials reporting in the next year?

References

[1] Cancer Research UK 'Myeloma incidence by sex and UK region'. Accessed July 2018.
[2] Office of national statistics 'Cancer registration statistics, England'. Accessed July 2018.
[3] National cancer institute 'SEER Cancer Statistics Review, 1975-2008'. Accessed July 2018.
[4]Cancer Research UK 'Myeloma survival'. Accessed July 2018.