

**NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE**

**Single Technology Appraisal**

**Lenalidomide for previously untreated multiple myeloma**

**Draft scope (post-referral)**

**Remit/appraisal objective**

To appraise the clinical and cost effectiveness of lenalidomide within its marketing authorisation for treating multiple myeloma in people who have not previously received treatment and for whom stem-cell transplantation is considered inappropriate.

**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 cannot 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 2012, 4190 people were diagnosed with multiple myeloma in England (Office for National Statistics, 2012). It is most frequently diagnosed in older people, with 43% of people diagnosed aged 75 years and over. Multiple myeloma is more common in men than in women and the incidence is also higher in people of African and Caribbean family origin. There were 2303 deaths from multiple myeloma in England in 2012 (Cancer Research UK, 2014). The 5-year survival rate for adults with multiple myeloma in England and Wales is estimated to be 47% (Cancer Research UK, 2014).

The main aims of therapy are to prolong survival and improve quality of life. High-dose chemotherapy with autologous stem-cell transplantation may be an option for people with multiple myeloma in good general health; however, most people with multiple myeloma are not able to withstand such intensive treatments because of their age, poor fitness or other health problems. When stem-cell transplantation is not considered suitable, people may be offered initial treatment with either thalidomide or bortezomib, in combination with an alkylating agent (such as melphalan or cyclophosphamide) and a corticosteroid (usually dexamethasone or prednisolone). NICE technology appraisal guidance 228 recommends thalidomide in combination with an alkylating agent and a corticosteroid as an option for initial treatment of multiple myeloma in people for whom high-dose chemotherapy with stem-cell

transplantation is considered inappropriate. If the person is unable to tolerate or has contraindications to thalidomide, NICE technology appraisal guidance 228 recommends bortezomib in combination with an alkylating agent and a corticosteroid. After the initial treatment, maintenance therapy is sometimes given to prolong treatment benefits, but this is not currently standard practice in the NHS.

### 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 has a marketing authorisation in the UK for treating ‘adult patients with previously untreated multiple myeloma who are not eligible for transplant’, and further specifies use of lenalidomide (1) ‘in combination with dexamethasone until disease progression in patients who are not eligible for transplant’, or (2) ‘in combination with melphalan and prednisone followed by maintenance monotherapy in patients who are not eligible for transplant’.

Intervention	<ul style="list-style-type: none"> <li>• Initial treatment with lenalidomide in combination with melphalan and prednisone followed by maintenance monotherapy</li> <li>• Lenalidomide in combination with dexamethasone until disease progression</li> </ul>
Population	Adults with previously untreated multiple myeloma for whom stem-cell transplantation is considered inappropriate
Comparators	<ul style="list-style-type: none"> <li>• Initial treatment with thalidomide in combination with an alkylating agent and a corticosteroid followed by best supportive care</li> </ul> <p>For people who are unable to tolerate, or have contraindications to thalidomide:</p> <ul style="list-style-type: none"> <li>• Initial treatment with bortezomib in combination with melphalan and prednisolone followed by best supportive care</li> </ul> <p>For people who are unable to tolerate, or have contraindications to bortezomib and thalidomide:</p> <ul style="list-style-type: none"> <li>• Initial treatment with a combination of melphalan and prednisolone followed by best supportive care</li> </ul>

Outcomes	<p>The outcome measures to be considered include:</p> <ul style="list-style-type: none"> <li>• overall survival</li> <li>• progression-free survival</li> <li>• response rates</li> <li>• time to response</li> <li>• adverse effects of treatment</li> <li>• health-related quality of life.</li> </ul>
Economic analysis	<p>The reference case stipulates that the cost effectiveness of treatments should be expressed in terms of incremental cost per quality-adjusted life year.</p> <p>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.</p> <p>Costs will be considered from an NHS and Personal Social Services perspective.</p> <p>The availability of any patient access schemes for the intervention or comparator technologies should be taken into account.</p>
Other considerations	<p>If the evidence allows, the following subgroups will be considered:</p> <ul style="list-style-type: none"> <li>• people with neurological conditions that contraindicate the use of thalidomide and bortezomib</li> </ul> <p>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.</p>
Related NICE recommendations	<p>Related Technology Appraisals:</p> <p>Bortezomib and thalidomide for the first-line treatment of multiple myeloma (2011). NICE Technology Appraisal 228. Moved to static list, March 2015.</p> <p>Related Guidelines:</p> <p>Clinical Guideline in preparation, 'Myeloma: diagnosis and management of myeloma'. Earliest anticipated date of</p>

	<p>publication January 2016.</p> <p>Related NICE Pathway:</p> <p>Blood and bone marrow cancers:  <a href="http://pathways.nice.org.uk/pathways/blood-and-bone-marrow-cancers">http://pathways.nice.org.uk/pathways/blood-and-bone-marrow-cancers</a></p>
Related National Policy	<p>NHS England (2014). Manual for prescribed specialised services. Chapter 105: Specialist cancer services (adults):  <a href="http://www.england.nhs.uk/wp-content/uploads/2014/01/pss-manual.pdf">http://www.england.nhs.uk/wp-content/uploads/2014/01/pss-manual.pdf</a></p> <p>Department of Health, NHS Outcomes Framework 2014-2015, Nov 2013. Domains 1, 2, 4 and 5.  <a href="https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/256456/NHS_outcomes.pdf">https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/256456/NHS_outcomes.pdf</a></p>

### Questions for consultation

Which treatments are considered to be established clinical practice in the NHS for treating multiple myeloma in people who have not previously received treatment and for whom stem-cell transplantation is considered inappropriate? Have all relevant comparators for lenalidomide been included:

- for initial therapy?
- for maintenance therapy?

How should best supportive care be defined?

Is the subgroup suggested in 'other considerations appropriate? Are there any other subgroups of people in whom lenalidomide is expected to be more clinically effective and cost effective or other groups that should be examined separately?

Where do you consider lenalidomide will fit into the existing NICE pathway on blood and bone marrow cancers?

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 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;

## Appendix B

- 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 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 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.

### References

Cancer Research UK (2014) [Myeloma statistics](#). Accessed March 2014.

Office for National Statistics (2012) [Cancer Registration Statistics](#), England.