NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

Proposed Health Technology Appraisal

Lenalidomide for the maintenance treatment of multiple myeloma after autologous stem cell transplantation

Draft scope (Pre-referral)

Draft remit/appraisal objective

To appraise the clinical and cost effectiveness of lenalidomide within its licensed indication for the maintenance treatment of multiple myeloma after autologous stem cell transplantation.

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 that does not work properly and is not able to fight infection. Myeloma cells build up in the bone marrow and interfere with the production of normal blood cells, which are responsible for fighting infections, blood clotting and carrying oxygen around the body. They also have the ability to spread throughout the bone marrow and into the hard outer casing of the bone. 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.

About 3900 people were diagnosed with multiple myeloma in England and Wales in 2008. It is most frequently diagnosed in people aged 70–79 years and is uncommon in young people (fewer than 2% of diagnoses are in people less than 40 years old). Multiple myeloma is more common in men than in women. Average survival for people with multiple myeloma is between 4 and 6 years, but ranges from a few weeks to more than 20 years.

Multiple myeloma is an incurable disease. The aim of therapy is to achieve as long a period of stable disease as possible, thereby prolonging survival and maximising quality of life. Aggressive first-line treatment with high-dose chemotherapy (usually melphalan), to kill off as many myeloma cells as possible, is often considered for people in good general health. However, chemotherapy of this intensity also destroys normal, healthy bone marrow cells. To reduce the effect on healthy cells, autologous stem cell transplantation can be done. This process involves ‘harvesting’ haematopoietic stem cells (blood cells at their earliest stage of development before they become red blood cells, white blood cells and platelets) from a patient’s blood before chemotherapy treatment. The harvested stem cells are stored and then reintroduced to the patient’s blood following chemotherapy. This enables the bone marrow to recover quickly, so it can produce healthy blood cells again. In 2008, approximately 820 autologous stem cell

transplants were conducted in the UK for people with multiple myeloma (that is, approximately 20% of all people newly diagnosed that year). Maintenance treatment after autologous stem cell transplantation is often used to stimulate the immune system and slow or stop cancer cell growth. Current maintenance treatment options include interferon alpha and corticosteroids such as prednisolone and dexamethasone.

The technology

Lenalidomide (Revlimid, Celgene) is a structural analogue of thalidomide. Its mechanism of action includes anti-neoplastic, anti-angiogenic, pro-erythropoeitic, and immunomodulatory properties. Lenalidomide inhibits proliferation of certain haematopoietic tumour cells, enhances T cell- and Natural Killer (NK) cell-mediated immunity, increases foetal haemoglobin production by CD34+ haematopoietic stem cells and inhibits production of pro-inflammatory cytokines. Lenalidomide is administered orally.

Lenalidomide does not currently have a UK marketing authorisation for the maintenance treatment of multiple myeloma after autologous stem cell transplantation. It has been studied in clinical trials as a maintenance therapy compared with placebo for adults with multiple myeloma who have had autologous stem cell transplantation.

Intervention(s)	Lenalidomide maintenance treatment
Population(s)	Adults with multiple myeloma who have had autologous stem cell transplantation
Comparators	• Interferon alpha • Corticosteroids
Outcomes	The outcome measures to be considered include: • overall survival • progression-free survival and/or time to progression • 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.
Other considerations	Guidance will only be issued in accordance with the marketing authorisation.
Related NICE recommendations	Related Technology Appraisals: Technology Appraisal No. 129, October 2007, 'Bortezomib monotherapy for relapsed multiple myeloma'. Review date: October 2010. Technology Appraisal No. 171, June 2009, 'Lenalidomide for the treatment of multiple myeloma in people who have received at least one prior therapy'. Review date: October 2010. Technology Appraisal in Preparation, 'Bortezomib and thalidomide for the first-line treatment of multiple myeloma'. Earliest anticipated date of publication TBC. Technology Appraisal in Preparation, 'Denosumab for the treatment of bone metastases from solid tumours and multiple myeloma'. Earliest anticipated date of publication: January 2012. Proposed Technology Appraisal, 'Lenalidomide for the treatment of newly diagnosed multiple myeloma'. Publication TBC. Proposed Technology Appraisal, 'Vorinostat in combination with bortezomib for the treatment of refractory multiple myeloma'. Publication TBC. Related Guidelines: Cancer Service Guidance, October 2003, 'Improving Outcomes in Haematological Cancer.'

Questions for consultation

Have the most appropriate comparators for lenalidomide for the maintenance treatment of multiple myeloma after autologous stem cell transplantation, been included in the scope? Are the comparators listed routinely used in clinical practice? Are there specific corticosteroids which should be considered as comparators?

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

Please consider whether in the remit or the scope there are any issues relevant to equality. Please pay particular attention to whether changes need to be made to the remit or scope in order to promote equality, eliminate unlawful discrimination, or foster good relations between people who share a characteristic protected by the equalities legislation and those who do not share it, or if there is information that could be collected during the assessment process which would enable NICE to take account of equalities issues when developing guidance.

Do you consider the technology 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 the technology 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.

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/aboutnice/howwework/devnicetech/technologyappraisalprocessguides/technology_appraisal_process_guides.jsp)