NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

Single Technology Appraisal

Lenalidomide for the treatment of newly diagnosed multiple myeloma

Final scope

Remit/appraisal objective

To appraise the clinical and cost effectiveness of lenalidomide within its licensed indication as initial and maintenance therapy for newly diagnosed multiple myeloma in people for whom autologous stem cell transplant is not appropriate.

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 blood clotting, carrying oxygen around the body and fighting infections. 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 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 3 and 5 years, but covers a wide range that can be beyond 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 initial treatment, in the form of high-dose chemotherapy with stem-cell transplantation, may be possible for people in good general health. However, this approach is too intensive for most people with multiple myeloma (fewer than 20% receive stem-cell transplantation), so alternative first-line treatments are necessary. The most common approach for newly diagnosed multiple myeloma patients is to give a combination of drugs as induction chemotherapy (that is, treatment that aims to kill as many cancer cells as possible straightaway). Often, the chemotherapeutic regimen will comprise an alkylating agent (such as melphalan or cyclophosphamide), a biological therapy (such as thalidomide) and a corticosteroid (usually

dexamethasone or prednisolone). NICE technology appraisal 228 recommends thalidomide in combination with an alkylating agent and a corticosteroid as an option for the first-line treatment of multiple myeloma in people for whom high-dose chemotherapy with stem cell transplantation is considered inappropriate. Bortezomib is also recommended as a first-line biological treatment for these patients if they are also unable to tolerate or have contraindications to thalidomide. The most commonly used regimens in UK clinical practice are cyclophosphamide, thalidomide and attenuated dexamethasone (CTDa), melphalan, prednisolone and thalidomide (MPT) and melphalan, prednisolone and bortezomib (MPV). When induction chemotherapy is complete, some people receive ongoing (maintenance) treatment, where a regular dose of chemotherapy is given to prevent cancer cells from building up again for as long as possible.

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 and inhibits production of pro-inflammatory cytokines. Lenalidomide is administered orally.

Lenalidomide does not currently have a UK marketing authorisation for the treatment of newly diagnosed multiple myeloma. It is being studied in clinical trials as initial therapy in combination with alkylating agents (cyclophosphamide or melphalan) and corticosteroids (dexamethasone or prednisolone). It is also being studied in clinical trials as maintenance therapy, both on its own (monotherapy) and in combination with corticosteroids.

Lenalidomide has a UK marketing authorisation for the treatment of multiple myeloma in people who have received at least one prior therapy. NICE technology appraisal guidance No. 171 recommends lenalidomide in combination with dexamethasone as a possible treatment for people with multiple myeloma who have received at least two prior therapies.

Intervention(s)	Initial treatment with lenalidomide in combination with melphalan and prednisolone followed by maintenance treatment with lenalidomide alone
Population(s)	People with newly diagnosed or previously untreated multiple myeloma for whom autologous stem cell transplantation is not appropriate

Comparators	• Initial treatment with a combination of cyclophosphamide, thalidomide and attenuated dexamethasone (CTDa) followed by best supportive care • Initial treatment with a combination of melphalan, thalidomide and prednisolone (MPT) followed by best supportive care For people who are unable to tolerate, or have contraindications to thalidomide: • Initial treatment with a combination of melphalan, bortezomib and prednisolone (MPV) followed by best supportive care For people who are unable to tolerate, or have contraindications to bortezomib and thalidomide: • Initial treatment with a combination of melphalan and prednisolone (MP) followed by best supportive care
Outcomes	The outcome measures to be considered include: • overall survival • progression-free survival and/or time to progression • response rates • time to response • 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	If the evidence allows, the following subgroups will be considered: • people with neurological conditions that contraindicate the use of thalidomide and bortezomib The costs in the economic model should take into account patient access schemes where relevant. 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: mid-2011. 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: mid-2011. Technology Appraisal No. 228, July 2011, 'Bortezomib and thalidomide for the first-line treatment of multiple myeloma.' Review date: July 2014. Proposed Technology Appraisal, 'Lenalidomide for the maintenance treatment of multiple myeloma after autologous stem cell transplantation' Publication TBC. Related Guidelines: Cancer Service Guidance, October 2003, 'Improving Outcomes in Haematological Cancer.'