NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

Health Technology Appraisal

Bortezomib and thalidomide for the first-line treatment of multiple myeloma

Final scope

Remit/appraisal objective

To appraise the clinical and cost effectiveness of bortezomib and thalidomide in combination regimens with an alkylating agent and a corticosteroid for the first-line treatment of 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. In patients with multiple myeloma, a single plasma cell becomes cancerous (myeloma) and begins to multiply. These abnormal plasma cells, also known as myeloma cells, build up in the bone marrow, reducing space for making normal white cells, red cells and platelets. Normal blood cells are responsible for fighting infections, carrying oxygen around the body and blood clotting. Myeloma cells produce large quantities of one type of abnormal antibody that does not work properly and is not able fight infection. Patients with MM can experience bone pain, bone fractures, fatigue, anaemia, infections, hypercalcaemia and kidney problems.

There were about 3500 new cases of multiple myeloma in England and Wales in 2005. The incidence of multiple myeloma is about 1.5 times as common in males as in females, and twice as common in black people than it is in white people. Multiple myeloma is most commonly diagnosed between the ages of 60 and 65 years. Multiple myeloma remains an incurable disease, with an average survival of 4 to 6 years.

Multiple myeloma is an incurable disease. The main aims of treatment are to alleviate symptoms and to achieve disease control while minimising the adverse effects of treatments. The main objective of first-line therapy is to achieve a period of stable disease (termed the plateau phase) in the majority of patients for as long as possible, thereby prolonging survival and maximising quality of life. In the current management of multiple myeloma, the choice of initial treatment depends on factors such as age and performance status. When it is suitable for the patient, high-dose chemotherapy (HDT) with autologous stem-cell transplantation are offered. Where HDT and stem-cell transplantation are not feasible, the treatment options include single agent or combination therapies, including chemotherapy such as melphalan or cyclophosphamide, corticosteroids such as prednisolone or dexamethasone, and thalidomide. Following initial treatment, patients usually experience a period of remission, but almost all patients eventually relapse, and others have disease which has been refractory (not responded) to treatment.

The technology

Bortezomib (Velcade, Janssen-Cilag) is an anticancer drug that works by reversible proteasome inhibition. By inhibiting proteasomes, multi-enzyme complexes present in all cells, bortezomib interferes with the cell cycle leading to cell death. Myeloma cells are more sensitive to the action of bortezomib than normal cells.

Bortezomib has a marketing authorisation for its use in combination with melphalan and prednisone for the treatment of patients with previously untreated multiple myeloma who are not eligible for high-dose chemotherapy with bone marrow transplant. Bortezomib is administered as an intravenous injection.

Thalidomide (Thalidomide Pharmion, Celgene) is a drug that affects the immune system. Its precise mechanism of action is unknown and under investigation but it is thought to have multiple actions, including the ability to inhibit the growth and survival of myeloma cells in various ways, anti-inflammatory activity, and to inhibit the growth of new blood vessels.

Thalidomide has a marketing authorisation for use in combination with melphalan and prednisone as first line treatment of patients with untreated multiple myeloma, aged ≥ 65 years or ineligible for high dose chemotherapy. Thalidomide is prescribed and dispensed according to the Thalidomide Pharmion Pregnancy Prevention Programme (for details, see summary of product characteristics).

Intervention(s)	• Bortezomib in combination with an alkylating agent and a corticosteroid • Thalidomide in combination with an alkylating agent and a corticosteroid
Population(s)	People with previously untreated multiple myeloma, for whom high dose chemotherapy with stem cell transplantation is not appropriate.
Comparators	The interventions will be compared with each other and the following comparators: • Melphalan or cyclophosphamide in combination with prednisolone or dexamethasone

Outcomes	The outcome measures to be considered include: • overall survival • progression-free survival • time to progression • response rates • 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	The measurement scales for assessing treatment response (for example, the European Group for Blood and Marrow Transplant criteria) used in analysis should be clearly stated and justified. If evidence allows subgroups of patient populations in whom the technology is clinically effective and cost effective should be considered. These may include subgroups by severity of disease, cytogenetic features and comorbidities such as renal impairment. Consideration should be given to number of treatment cycles and continuation rules for treatment.
Related NICE recommendations	Related Technology Appraisals: Technology Appraisal No. 129, October 2007, Bortezomib monotherapy for relapsed multiple myeloma Technology Appraisal in Preparation, 'Lenalidomide for multiple myeloma in people who have received at least one prior therapy', Earliest anticipated date of publication June 2009 Related Guidelines: Cancer Service Guidance, October 2003, Improving Outcomes in Haematological Cancer