NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

Health Technology Appraisal

Lenalidomide for relapsed and/or refractory multiple myeloma

Draft scope (Pre-referral)

Draft remit/appraisal objective

To appraise the clinical and cost effectiveness of lenalidomide in the treatment of relapsed and/or refractory multiple myeloma.

Background

Multiple myeloma (MM), is a cancer of the plasma cells (a form of white blood cell), where a clone of abnormal plasma cell multiplies, forms tumours in the bone marrow and produces a large quantity of abnormal antibodies that accumulate in the blood or urine. Patients with MM can experience bone pain, bone fractures, fatigue, anaemia, infections, hypercalcaemia and kidney problems. 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.

In 2001 there were 3145 new cases of multiple myeloma diagnosed in England and Wales and 2317 deaths in 2002. There has been an increase in incidence of MM over the past 30 years but this may reflect improvements in diagnosis. Prevalence of MM over a period of five years for the UK has been estimated at 7893 (2002 as reference year). The likelihood of developing MM increases with age, and the median age at diagnosis is 60-65 years. It is more common in men than women and associated with poor disease prognosis and high mortality.

MM is currently an incurable illness. The natural history of myeloma is heterogeneous with survival times ranging from a few weeks to over 20 years. The prognosis is usually poor. The one-year survival rate is approximately 60% and the five-year survival rate is approximately 20%, and rates for patients with relapsed and/or refractory disease will be somewhat lower. Prognostic factors include stage of disease, serum levels of ß2-microglobulin, C-reactive protein, and albumin, atypical plasma cell morphology and abnormal cytogenetic features.

The aim of therapy is to slow disease progression, to manage symptoms and to prolong survival. Current treatments for relapsed and/or refractory disease include chemotherapy with alkylating agents and anthracyclines, bortezomib, thalidomide and corticorsteroids, alone or in combination use. Repeat high-dose chemotherapy with stem-cell rescue may be considered for certain patients. Choice of therapy for an individual patient is influenced by the previous treatment and response to it, the duration of remission, comorbidities, patient preference and cytogenetic features of disease.

The technology

Lenalidomide (Revlimid, Celgene) is an oral immuno-modulatory thalidomide analogue in development for relapsed and/or refractory multiple myeloma. Lenalidomide has been reported to have an apparent lack of some, or a decreased amount of, adverse effects associated with thalidomide, including teratogenicity.

Lenalidomide does not currently hold a UK marketing authorisation and the licensed indications are not yet specified. It has been assigned orphan drug status in the EU for multiple myeloma. In randomised controlled trials evaluating lenalidomide in multiple myeloma, lenalidomide has been administered orally at a dose of 25mg/day, on days 1-21 of a 28-day cycle. It is currently unclear how many treatment cycles would be given or required.

Intervention	Lenalidomide in combination with high dose dexamethasone
Population	People with relapsed and/or refractory multiple myeloma who have received at least one prior therapy
Standard comparators	• High dose dexamethasone • Bortezomib • Thalidomide • Repeated initial chemotherapy which may include regimens based on mephalan, cyclophosphamide or vincristine and doxorubicin • Combinations of the treatments above
Outcomes	The outcome measures to be considered include: • overall survival • progression-free survival • response rates • health-related quality of life • adverse effects of treatment

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 time horizon for the economic evaluation should reflect the period over which costs and benefits can reasonably be expected given the prognosis of multiple myeloma. 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. If clinical trial evidence allows subgroups of patient populations in whom the technology is clinically effective and cost effective should be considered. Consideration of subgroups might be related to the type and number of prior therapies, the duration of remission, the severity of disease and cytogenetic features.
Related NICE recommendations	Related Technology Appraisals in progress: Bortezomib monotherapy for relapsed multiple myeloma (single technology appraisal). Expected date of issue: TBC Related Guidelines: Cancer Service Guidance: Improving Outcomes in Haematological Cancer, October 2003

Questions for consultation

- What is the appropriate place of lenalidomide in treatment pathways for relapsed/ refractory multiple myeloma?
- The Institute would welcome comments as to whether this technology is suitable for the Single Technology Appraisal process.