NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

Single Technology Appraisal

Lenalidomide for the treatment of myelodysplastic syndromes associated with deletion 5q cytogenetic abnormality

Final scope

Remit/appraisal objective

To appraise the clinical and cost effectiveness of lenalidomide within its licensed indication for the treatment of myelodysplastic syndromes associated with a deletion 5q cytogenetic abnormality in people with red blood cell transfusion dependence.

Background

The myelodysplastic syndromes (MDS) are a diverse group of haematological disorders in which the bone marrow functions abnormally and insufficient numbers of mature blood cells are produced. Red blood cells, white blood cells and platelets may all be affected by MDS, resulting in life threatening disease, with anaemia and increased risk of bleeding and infections. MDS affect patients' quality of life due to debilitating symptoms such as fatigue and dyspnoea, treatment regimens involving hospitalisation with intravenous drug infusions and blood transfusions, and complications such as severe infections.

MDS are caused by a cumulative acquisition of genetic errors in the bone marrow and common abnormalities include chromosomal deletions in 5q, 7, 20q, Y and trisomy 8. Other risk factors include previous cancer therapy including radiotherapy, and environmental toxins. MDS are associated with an increased risk of transformation to acute myeloid leukaemia (AML). AML is a rapidly growing cancer of the blood and bone marrow, with poor prognosis if left untreated. Around 30% of patients with MDS will progress to AML.

MDS are subdivided using the International Prognostic Scoring System (IPSS), and the French-American-British (FAB) and World Health Organisation (WHO) classification systems. Based on the proportion of leukaemic cells (or 'blasts'), bone marrow cytogenetic findings, and the presence of blood cytopenia, the IPSS classifies outcome as low-risk, intermediate-1 risk, intermediate-2 risk or high-risk. Low risk and intermediate-1 risk MDS together form approximately 70% of all MDS.

The annual incidence of MDS is estimated at 4 per 100,000, but incidence increases with age and is 30 per 100,000 per year in people over 70 years of age. Many cases remain undiagnosed. There were 1993 people newly diagnosed with MDS in England in 2004, with over 90% of patients aged over 60 at the time of diagnosis. Deletion of chromosome 5q is one of the most common cytogenetic abnormalities in MDS, occurring in between 16% to 28%

of patients. Median survival with low risk and intermediate-1 risk MDS is 5.7 years and 3.5 years respectively. It can be less than 6 months for people with high risk MDS.

The mainstay of treatment for MDS is best supportive care (transfusions, growth factors, antibiotics) to control the symptoms of bone marrow failure, low-dose standard chemotherapy or immunosuppressive therapies are used for some patients. For people with low risk MDS, often a preferred approach is one of no active treatment or 'watchful waiting' and for some people, stem cell transplantation is a potentially curative treatment option. Many patients become red blood cell transfusion dependent, particularly those with low or intermediate-1 risk MDS. A major goal of treatment is then to achieve transfusion independence and a number of treatments can be used to reduce or eliminate the transfusion need for MDS patients.

For patients with intermediate-2 or high risk MDS who are not eligible for haematopoietic stem cell transplantation, NICE technology appraisal 218 recommends azacitadine as a treatment option.

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 cell-mediated immunity, increases foetal haemoglobin production by CD34+ haematopoietic stem cells and inhibits production of pro-inflammatory cytokines. It is administered orally.

Lenalidomide does not currently have UK marketing authorisation for the treatment of MDS. It has been studied in clinical trials as monotherapy compared with standard treatment, including oral placebo tablets and supportive care, in adults who have low risk or intermediate-1 risk MDS associated with a deletion 5q cytogenetic abnormality and who are red blood cell transfusion dependent.

Intervention(s)	Lenalidomide
Population(s)	Adults with myelodysplastic syndromes (MDS) associated with a deletion 5q cytogenetic abnormality and who are red blood cell transfusion dependent
Comparators	For people with intermediate-1 or low risk MDS: • Best supportive care including blood transfusions For people with intermediate-2 and high risk MDS: • Azacitadine • Stem cell transplantation

Outcomes	The outcome measures to be considered include: • overall survival • progression-free survival (including time to transformation to AML or death) • response rates, including haematologic response and improvement • frequency of blood-transfusions (including blood-transfusion independence) • serious infections • 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. The availability of any patient access schemes for comparators should be taken into account in the economic analysis. 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 evidence allows, subgroups based on different cytogenetic profiles will be considered separately.
Related NICE recommendations	Related Technology Appraisals: Technology Appraisal 218, March 2011, 'Azacitidine for the treatment of myelodysplastic syndrome, chronic myelomonocytic leukaemia and acute myeloid leukaemia'. Review date decision February 2014. Related Guidelines: Guidance on Cancer Services, Oct 2003, 'Improving outcomes in haemato-oncology cancer'.