NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Appraisal

Erythropoiesis-stimulating agents (epoetin and darbepoetin) for treating cancer-treatment induced anaemia (including review of TA 142)

Scope

Remit/appraisal objective[1]

To appraise the clinical and cost effectiveness of erythropoiesis-stimulating agents (epoetin and darbepoetin)[2] within their licensed indications for the treatment of cancer-treatment induced anaemia.

Background

Anaemia is defined as a reduction of haemoglobin concentration, red cell count or packed cell volume to below normal levels. The World Health Organization has defined anaemia as a haemoglobin level of less than 12 g/dl in women and less than 13 g/dl in men. A reduction in the red blood cells can result from either the defective production of red blood cells or an increased rate of loss of cells, either by premature destruction or bleeding. Production of red blood cells (erythropoiesis) is primarily stimulated and regulated by a hormone called erythropoietin. Erythropoietin is a glycoprotein hormone that is produced naturally in the kidneys, but can also be manufactured for clinical use using recombinant DNA technology.

Anaemia can lead to a marked reduction in aspects of quality of life, such as increased fatigue, reduced exercise capacity and decreased sense of well-being. Fatigue is one of the commonest symptoms of anaemia.
Anaemia is a common side-effect of cancer treatments and the anaemia-related fatigue has been shown to have a significant impact on cancer patients. Nearly 60% of patients with solid tumours undergoing chemotherapy became anaemic with a haemoglobin (Hb) <11 g/dl during their treatment. Anaemia is also common in haematological malignancies; up to 75% of patients with multiple myeloma are anaemic at diagnosis, and 70% of patients with lymphoma are anaemic by cycles 3-4 of their chemotherapy.

Cancer treatment-induced anaemia is managed by adjustments to the cancer treatment regimen, iron supplementation and blood transfusion in cases of severe anaemia. NICE technology appraisal guidance 142 ‘Epoetin alfa,

[1] The original remit was to appraise the clinical and cost effectiveness of erythropoietin alfa and beta and darbepoetin vs. best standard care, which may include the use of blood transfusions, in the treatment of cancer-treatment induced anaemia and to provide guidance to the NHS in England and Wales

[2] This appraisal includes a review of Technology Appraisal No. 142, May 2008, ‘Epoetin alfa, epoetin beta and darbepoetin alfa for cancer treatment-induced anaemia

epoetin beta and darbepoetin alfa for cancer treatment-induced anaemia' recommends erythropoietin analogues only for women receiving platinum-based chemotherapy for ovarian cancer who have a blood haemoglobin level of 8 g/100 ml or lower, and also for people who have very severe anaemia and cannot receive blood transfusions.

The technologies

Epoetin alfa, beta, theta and zeta are recombinant human erythropoietin analogues. Epoetins are used to shorten the period of symptomatic anaemia in patients receiving cytotoxic chemotherapy. They are administered by injection.

Epoetin alfa (Eprex, Janssen-Cilag) has a UK marketing authorisation for the treatment of anaemia and for the reduction of transfusion requirements in adults receiving chemotherapy for solid tumours, malignant lymphoma or multiple myeloma, who are at risk of transfusion as assessed by their general status (e.g. cardiovascular status, pre-existing anaemia at the start of chemotherapy).

Epoetin alfa (Binocrit, Sandoz) is a biosimilar medicine referenced to Eprex which contains epoetin alfa. It has a UK marketing authorisation for the treatment of anaemia and for the reduction of transfusion requirements in adults receiving chemotherapy for solid tumours, malignant lymphoma or multiple myeloma, who are at risk of transfusion as assessed by their general status (e.g. cardiovascular status, pre-existing anaemia at the start of chemotherapy).

Epoetin beta (NeoRecormon, Roche Products) has a UK marketing authorisation for the treatment of symptomatic anaemia in adult patients with non-myeloid malignancies who are receiving chemotherapy.

Epoetin theta (Eporatio, Teva UK) has a UK marketing authorisation for the treatment of symptomatic anaemia in adult cancer patients with non-myeloid malignancies receiving chemotherapy.

Epoetin zeta (Retacrit, Hospira UK) is a biosimilar medicine referenced to Eprex which contains epoetin alfa. It has a UK marketing authorisation for the treatment of anaemia and reduction of transfusion requirements in adult patients receiving chemotherapy for solid tumours, malignant lymphoma or multiple myeloma, and at risk of transfusion as assessed by the patient's general status (e.g. cardiovascular status, pre-existing anaemia at the start of chemotherapy).

Darbepoetin alfa (Aranesp, Amgen) is a hyperglycosylated derivative of epoetin that stimulates erythropoiesis by the same mechanism as the endogenous hormone. Darbepoetin alfa is administered by injection. Darbepoetin alfa has UK marketing authorisation for the treatment of

symptomatic anaemia in adult cancer patients with non-myeloid malignancies who are receiving chemotherapy.

Intervention(s)	• Epoetin alfa, beta, theta and zeta • Darbepoetin alfa
Population(s)	• People receiving chemotherapy for solid tumours, malignant lymphoma or multiple myeloma, and at risk of transfusion as assessed by the patient's general status (e.g. cardiovascular status, pre-existing anaemia at the start of chemotherapy) • People with non-myeloid malignancies who are receiving chemotherapy
Comparators	• Best supportive care (including adjustment to the cancer treatment regimen, blood transfusion and iron supplementation) • The interventions will be compared with each other in line with their marketing authorisations
Outcomes	The outcome measures to be considered include: • haematological response to treatment • need for blood transfusion after treatment • tumour response (time to cancer progression) • survival • 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. The cost effectiveness should also take into account any supplements to the erythropoietin technologies.

Other considerations	If the evidence allows subgroups will be considered, for example by cancer type and status, by chemotherapy, or by type of best supportive care received. Guidance will only be issued in accordance with the marketing authorisations.
Related NICE recommendations	Related Technology Appraisals: Technology Appraisal No. 142, May 2008, 'Epoetin alfa, epoetin beta and darbepoetin alfa for cancer treatment-induced anaemia'. Subject to this appraisal review