NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

Health Technology Appraisal

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

Draft scope

Draft 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 by the human body (mainly in the kidney), but can also be manufactured for clinical use using recombinant DNA technology.

Anaemia is a common side-effect of cancer treatments. It 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 and 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 70% 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

[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

severe anaemia. NICE technology appraisal guidance 142 ‘Epoetin alfa, 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 • 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.

Other considerations	If the evidence allows the following subgroups will be considered. These include cancer type and status, and chemotherapy. Guidance will only be issued in accordance with the marketing authorisation.
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

Questions for consultation

Are the interventions listed in the technology section the only epoetin analogues used in UK practice?

How should best supportive care be defined?

Are the subgroups suggested in 'other considerations' appropriate?

Are there any other subgroups of people in whom the technology is expected to be more clinically effective and cost effective or other groups that should be examined separately?

NICE is committed to promoting equality of opportunity, eliminating unlawful discrimination and fostering good relations between people with particular protected characteristics and others. Please let us know if you think that the proposed remit and scope may need changing in order to meet these aims. In particular, please tell us if the proposed remit and scope:

- could exclude from full consideration any people protected by the equality legislation who fall within the patient population for which epoetin and darbepoetin are licensed;
- could lead to recommendations that have a different impact on people protected by the equality legislation than on the wider population, e.g. by making it more difficult in practice for a specific group to access the technology;
- could have any adverse impact on people with a particular disability or disabilities.

Please tell us what evidence should be obtained to enable the Committee to identify and consider such impacts.

Do you consider the technologies to be innovative in their potential to make a significant and substantial impact on health-related benefits and how they might improve the way that current need is met (is this a 'step-change' in the management of the condition)?

Do you consider that the use of the technologies can result in any potential significant and substantial health-related benefits that are unlikely to be included in the QALY calculation?

Please identify the nature of the data which you understand to be available to enable the Appraisal Committee to take account of these benefits