

# NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

## Final Appraisal Determination

### Erythropoietin for anaemia induced by cancer treatment

#### 1 Guidance

This guidance does not cover the use of erythropoietin (epoetin alfa, epoetin beta and darbepoetin alfa) in the management of cancer-related anaemia that is not induced by cancer treatment (chemotherapy or radiotherapy).

- 1.1 Erythropoietin is recommended for use in the management of anaemia only as part of ongoing or new clinical trials that are constructed to generate robust and relevant data in order to address the gaps in the currently available evidence as outlined in Section 5.
- 1.2 Patients currently receiving erythropoietin could experience loss of well-being if treatment is discontinued at a time they did not anticipate. Because of this, patients should have the option to continue therapy until they and their consultants consider it appropriate to stop.

#### 2 Clinical need and practice

- 2.1 Anaemia is defined as a reduction of haemoglobin concentration, red cell count or packed cell volume to below normal levels. Haemoglobin is the component of the blood that is responsible for carrying oxygen around the body, and is found in red blood cells. The World Health Organization definition states that anaemia should be considered to exist in adults whose haemoglobin levels are lower than 13 g/100 ml (males) or 12 g/100 ml (females). The US National Cancer Institute considers normal haemoglobin levels to be 12–16 g/100 ml (females) and 14–18 g/100 ml (males).

- 2.2 Anaemia in patients undergoing treatment for cancer may be caused by one or more factors associated with the cancer itself or with the treatment. Cancer may cause anaemia through mechanisms that are unrelated to treatment, for example infiltration of the bone marrow by cancer cells may impair red blood cell production. Reduced appetite associated with cancer may lead to anaemia through nutritional deficiencies (particularly of iron, folate and vitamin B<sub>12</sub>). Other mechanisms include blood loss into or from tumours, and cancer-associated kidney damage, which leads to reduced production of the hormone erythropoietin. Anti-cancer treatments can also suppress the production of red blood cells in the bone marrow. This is usually temporary, but cumulative damage can occur over several chemotherapy cycles. Some anti-cancer therapies are considered more likely to cause anaemia (for example, drugs containing platinum).
- 2.3 Anaemia in patients with cancer is associated with many symptoms, each of which has an impact on quality of life. These include dizziness, shortness of breath on exertion, palpitations, headache and depression. Severe fatigue is perhaps the most commonly reported symptom of anaemia, and can lead to an inability to perform everyday tasks. However, fatigue in patients with cancer is not always attributable to anaemia and may have other causes (for example, the disease itself, chemotherapy, radiotherapy, and anxiety or depression).
- 2.4 Many patients with cancer are anaemic at diagnosis, before any cancer treatment starts. Moreover, when anaemia is caused by treatments such as chemotherapy, the degree of anaemia often fluctuates, and is typically at its worst 2–4 weeks after chemotherapy is given. However, the degree of fluctuation depends on many factors, including the nature of the treatment and the number of courses administered. Once cancer treatments are stopped, a period of 'normalisation' is likely, during which the haemoglobin returns to pretreatment levels, depending on how successful the treatment has been.

- 2.5 In a large European survey of just under 15,000 patients with cancer, at enrolment 39% had haemoglobin below 12 g/100 ml, 10% had haemoglobin below 10 g/100 ml and 1% had haemoglobin below 8 g/100 ml. However, the percentages of patients with anaemia increased during treatment, especially during chemotherapy. The percentages also varied by tumour type – for example, they appeared substantially higher in patients who had lymphoma/myeloma and gynaecological cancers than in patients with other types of cancer.
- 2.6 Standard care options available for people with anaemia induced by cancer treatment include adjustments to the cancer treatment regimen, iron supplementation and blood transfusion. The majority of patients who become anaemic do not receive any treatment for their anaemia, but people who become moderately or severely anaemic are typically given transfusions.
- 2.7 There are a number of concerns about the use of blood transfusion, for example the potential risks of introducing a serious infection such as hepatitis C or HIV. However, current evidence suggests that the likelihood of this is negligible. Other concerns include the limited supply of blood and the possibility of giving incorrectly matched blood.

### **3 The technologies**

- 3.1 Erythropoietin is a glycoprotein hormone produced primarily by cells of the peritubular capillary endothelium of the kidney and is responsible for regulating red blood cell production. Erythropoietin for clinical use is produced by recombinant DNA technology.
- 3.2 Epoetin alfa and epoetin beta are recombinant erythropoietins, consisting of 165 amino acids in almost identical sequences to the native protein. Darbepoetin alfa is a hyperglycosylated derivative of epoetin, which has a longer half-life and may be administered less frequently than epoetin.

- 3.3 Epoetin alfa is licensed for the treatment of anaemia and for the 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. It should be administered to patients with anaemia (haemoglobin 11 g/100 ml or lower) with the aim of achieving a target haemoglobin concentration of approximately 12 g/100 ml. The recommended initial dose is 150 IU/kg given subcutaneously three times per week (see the Summary of Product Characteristics for further dosing details).
- 3.4 Epoetin beta is licensed for the treatment of symptomatic anaemia (haemoglobin 11 g/100 ml or lower) in adult patients with solid tumours who are receiving chemotherapy. It is also licensed for the treatment of symptomatic anaemia in adult patients with multiple myeloma, low-grade non-Hodgkin's lymphoma or chronic lymphocytic leukaemia who have a relative erythropoietin deficiency and who are receiving anti-tumour therapy. The recommended initial dose is 450 IU/kg body weight per week (see the Summary of Product Characteristics for further dosing details).
- 3.5 Darbepoetin alfa is licensed for the treatment of symptomatic anaemia (haemoglobin 11 g/100 ml or lower) in adult patients with non-myeloid malignancies who are receiving chemotherapy. The recommended initial dose is 6.75 micrograms/kg body weight given once every 3 weeks. Alternatively, 2.25 micrograms/kg can be given once weekly (see the Summary of Product Characteristics for further dosing details).
- 3.6 Erythropoietins are an addition to, rather than a complete replacement for, existing components of the management of anaemia induced by cancer treatment. Blood transfusion in particular may still be required.
- 3.7 There is uncertainty surrounding the side effects of recombinant erythropoietins in patients with anaemia undergoing treatments for cancer. A recent safety briefing by the US Food & Drug Administration (FDA) requested

additional clinical studies to assess the safety and optimal manner for administration of erythropoietin to patients with cancer, following recent trials that indicated a possible association between erythropoietin and impaired survival.

- 3.8 The European licences of the three products under consideration were amended by the European Medicines Agency (EMA) during 2005 as a result of the FDA safety briefing. Recommendations on starting levels, target levels and rates of increase in haemoglobin levels were made more restrictive, and warnings about the increased risk of thrombotic vascular events and the potential effect on tumour growth were inserted. For full details of side effects and contraindications, see the Summaries of Product Characteristics.
- 3.9 The cost of a course of treatment with any of the three products is approximately £2500–5000 (excluding VAT, 'British national formulary', 50th edition). This is based on the assumptions that patients weigh 70 kg and undergo erythropoietin treatment in the context of a 4-weekly chemotherapy regimen lasting for three to six courses. Costs may vary in different settings because of negotiated procurement discounts.

## **4 Evidence and interpretation**

The Appraisal Committee (appendix A) considered evidence from a number of sources (appendix B).

### **4.1 *Clinical effectiveness***

- 4.1.1 The systematic review in the Assessment Report was an update of an earlier systematic review published by the Cochrane Collaboration. The Assessment Report included a total of 46 randomised controlled trials (RCTs); 27 related to the use of epoetin alfa, 10 to the use of epoetin beta and five to the use of darbepoetin alfa. A further four RCTs either assessed the use of two different erythropoietins within the same study or did not state which product was being evaluated.

- 4.1.2 All RCTs compared the use of erythropoietin and supportive care (including the use of blood transfusions) for anaemia with supportive care alone. The types of malignancy within and across each study varied (for example, solid, haematological or mixed). Anti-cancer therapies were chemotherapy (with or without platinum) or radiotherapy, or a combination of the two. Most of the trials stated that they included patients with haemoglobin below a certain threshold level. The highest threshold for inclusion in a study was  $\leq 16$  g/100 ml and the lowest was  $< 10$  g/100 ml. The average baseline haemoglobin at the time of randomisation in the studies ranged from 8.6 g/100 ml to 11.5 g/100 ml.
- 4.1.3 For the outcome of patient survival, data were available from a total of 28 trials. Of these trials, 19 had been included in the Cochrane review where the hazard ratio (HR) associated with survival was 0.84 (95% confidence interval [CI], 0.69 to 1.02) in favour of erythropoietin. A single trial with positive results in favour of erythropoietin contributed more than half the patients in the Cochrane review. The nine trials that have been reported since the review suggest less benefit and, when analysed as a group, produced a HR of 1.15 (95% CI, 1.00 to 1.32) in favour of the control arm. Combining the data from all 28 trials produced a HR of 1.03 (95% CI, 0.88 to 1.21) in favour of the control arm. The Assessment Group did, however, report considerable clinical heterogeneity in terms of the site of cancer, setting, dose and comparator.
- 4.1.4 Given the considerable heterogeneity reported, and the discrepancy between the HR resulting from the Assessment Group's meta-analysis of all 28 trials (1.03) and that of the original Cochrane review (0.84), the Assessment Group was asked to conduct a meta-analysis on patient survival including only those studies that used erythropoietin within its licensed indications. Studies were assessed based on a checklist of criteria derived from the Summary of Product Characteristics for each product (as at 24 November 2005). The checklist was applied to each of the 28 RCTs included in the Assessment Group's meta-analysis by two researchers working independently. The

application of the method suggested by Altman for inter-rater reliability indicated that there was good agreement between the two researchers (kappa 0.74, 95% CI 0.64 to 0.84). The results of this exercise indicated that none of the studies included in the original meta-analysis were unequivocally within the licensed indications conveyed in the Summaries of Product Characteristics.

- 4.1.5 In the absence of RCTs of erythropoietin within its licensed indications, the Assessment Group subsequently grouped the RCTs according to how closely their inclusion criteria and treatment protocols matched the products' licensed indications. Seven RCTs were identified as having trial populations, doses, and starting and target haemoglobin levels that were similar to those indicated in the Summaries of Product Characteristics. The combined HR for the outcome of survival derived from these RCTs was 0.94 (95% CI, 0.68 to 1.30). A further five RCTs were identified as having trial populations and doses that were similar to those indicated in the Summaries of Product Characteristics, although the starting and target levels of haemoglobin were moderately high. The combined HR for these RCTs was 0.96 (95% CI, 0.83 to 1.11).
- 4.1.6 The pooled (fixed effects) relative risk (RR) for haematological response (defined as an increase in haemoglobin of at least 2 g/100 ml) reported by the Assessment Group was 3.40 (95% CI, 3.01 to 3.83) in favour of erythropoietin therapy with little evidence of statistical heterogeneity. Typically, 50% of patients treated with erythropoietin experienced a haematological response.
- 4.1.7 The meta-analysis in the Assessment Report showed a weighted mean difference in overall haemoglobin, between intervention and control arms, of 1.63 g/100 ml (95% CI, 1.46 to 1.80) in favour of erythropoietin.
- 4.1.8 The RR of transfusion for all trials reporting data on the number of patients receiving a transfusion was 0.63 (95% CI, 0.58 to 0.67, fixed effects) in favour of erythropoietin. For this outcome, the test for heterogeneity was highly

statistically significant ( $p = 0.0001$ ) and indicated that the type of malignancy and the type of therapy may influence the numbers of patients receiving red blood cell transfusions. Iron supplementation also appeared to confer a reduction.

- 4.1.9 In terms of the overall amount of blood transfused, very little difference between intervention and control arms was reported (weighted mean difference  $-1.05$  units; 95% CI,  $-1.32$  to  $-0.78$ ).
- 4.1.10 Change in health-related quality of life is an important measure of the effectiveness of treatments for anaemia induced by cancer treatment. However, fewer than half of the RCTs included in the Assessment Group's review of the clinical evidence base reported this outcome. Some positive results in favour of treatments were found, but in general the quality of the analyses was poor. The outcomes were often inadequately reported and a variety of different assessment scales was used, limiting comparability and making general assessments of study quality difficult. Many did not use validated health-related quality of life measures. Fewer than half of the studies included in the review were placebo controlled, meaning that bias may have been introduced as patients were not blinded to treatment.

## **4.2 Cost effectiveness**

- 4.2.1 Five published economic evaluations were available to the Committee along with evaluations from each of the three manufacturers, and one from the Assessment Group.
- 4.2.2 Three of the five published analyses contained a cost–utility analysis (CUA). One published CUA was performed from a UK Health Service perspective and considered the use of erythropoietin in patients with stage IV breast cancer versus the use of blood transfusions. This analysis incorporated a survival benefit associated with erythropoietin treatment (HR of death of approximately 0.72). Utility data were collected from 30 oncology nurses. The associated incremental cost-effectiveness ratio (ICER) from this study was

approximately £9000 per additional quality-adjusted life year (QALY). The ICERs from the two remaining CUAs were both greater than US\$100,000.

- 4.2.3 The manufacturer of epoetin alfa compared the use of this treatment (with the possibility of blood transfusion) against the use of blood transfusions. A 3-year time horizon was assumed and the model included a survival advantage associated with erythropoietin (HR 0.64). ICERs, which were presented separately for different haemoglobin subgroups and for different tumour types, were mostly below £16,000 per additional QALY.
- 4.2.4 The manufacturer of darbepoetin alfa submitted an economic evaluation that included two scenarios. In the first, the use of darbepoetin alfa was considered over 25 weeks, whereas the second included a time horizon of almost 3 years coupled with a treatment survival advantage (mean HR 0.88). The associated ICERs for the two scenarios were approximately £160,000 and £24,000 per additional QALY, respectively.
- 4.2.5 The manufacturer of epoetin beta presented separate ICERs for solid tumours and haematological cancers along with tumour-specific survival gains associated with erythropoietin (solid tumours HR 0.49; haematological cancers HR 1). The associated ICERs were £28,000 and £84,000 per additional QALY, respectively.
- 4.2.6 The Assessment Group's economic evaluation used a 3-year time horizon. The model evaluated the use of erythropoietin (with the possibility of blood transfusion) versus blood transfusion alone. Patients included in the model were characterised only by their baseline haemoglobin level at the start of chemotherapy. No other characteristics, such as cancer type or type of anti-cancer treatment, were assumed to influence outcome. In the treatment arm, erythropoietin was assumed to be given when haemoglobin levels fell below 13 g/100 ml. A full dose was assumed when haemoglobin levels were less than 12 g/100 ml and half doses when haemoglobin levels were between 12 and 13 g/100 ml. The baseline distribution of haemoglobin was restricted

to levels less than or equal to 11 g/100 ml in sensitivity analyses, following the change to the licensed indications during 2005 (starting haemoglobin restricted to 11 g/100 ml or lower for all products). Erythropoietin treatment was assumed to stop if and when haemoglobin levels reached 13 g/100 ml. Response to erythropoietin was defined as a 2 g/100 ml increase in a given haemoglobin level. Blood transfusion was considered when haemoglobin levels were below 10 g/100 ml.

- 4.2.7 The Assessment Group's meta-analysis suggested that there was almost no difference in survival between patients treated with erythropoietin and controls (HR 1.03; 95% CI, 0.88 to 1.21). Further meta-analyses of RCTs, the inclusion criteria and treatment protocols of which were similar to the licensed indications, resulted in HRs of 0.94 (95% CI, 0.68 to 1.30) and 0.96 (95% CI, 0.83 to 1.11) when studies with moderately high starting or target levels of haemoglobin were considered. Therefore, in the base case of the economic evaluation, patient survival was assumed to be the same for both treatment and control arms (that is, a HR of 1 was used). This produced an ICER of over £100,000 per additional QALY. The results of the sensitivity analysis demonstrated that erythropoietin became more cost effective as the baseline distribution of haemoglobin was restricted to lower levels but still remained above conventional cost-effectiveness thresholds. The most favourable ICERs were obtained when a baseline haemoglobin level of 8 g/100 ml was assumed for all patients and these were in the range of £65,000–80,000).

### **4.3 Consideration of the evidence**

- 4.3.1 The Committee reviewed the data available on the clinical and cost effectiveness of erythropoietin for people with anaemia induced by cancer treatment, having considered evidence on the nature of the condition and the value placed on the benefits of erythropoietin by people with the condition, those who represent them, and clinical experts. It was also mindful of the need to take account of the effective use of NHS resources.

- 4.3.2 The Committee heard from the clinical and patient experts about the consequences of fatigue due to anaemia induced by cancer treatment, and that fatigue related to cancer treatment was often inadequately assessed and treated. However, they understood that fatigue in patients with cancer has a number of potential contributory factors; and that deciding in the clinical setting the exact contribution of anaemia to this symptom is very difficult. The Committee heard from the experts that it was difficult to predict which patients would benefit from treatment of their anaemia, with either blood transfusion or erythropoietin, on the basis of haemoglobin levels alone. Currently these decisions are made on a case-by-case basis taking account of symptoms, haemoglobin level and patient/clinician preferences. The Committee also noted that typically only around 50% of patients experience a haematological response to erythropoietin treatment.
- 4.3.3 The Committee noted that some patients preferred to avoid blood transfusions and that blood transfusions could be inconvenient because of the need to attend hospital.
- 4.3.4 The Committee considered the evidence from the randomised studies and noted the effects of erythropoietin on various measures of health-related quality of life. The Committee noted that these studies had methodological weaknesses and that in many studies patients had not been blinded to treatment allocation. Most studies suggested that erythropoietin improved health-related quality of life, but the additional benefits over standard care (that is, blood transfusions and iron therapy where indicated) were small. The Committee was aware that standard care within the trials was occasional blood transfusion as needed. They understood that, in the trials, erythropoietin therapy reduced the requirement for blood transfusions by approximately one unit per patient overall.
- 4.3.5 The Committee discussed the use of regular and directed blood transfusions to achieve target haemoglobin levels as a possible comparator for the use of erythropoietin in anaemia induced by cancer treatment. They were aware that

this comparison was not part of any of the clinical trials and thus it was not possible to assess the true effect on quality of life of erythropoietin compared with intensive blood transfusion therapy. The Committee was, however, persuaded that transfusion therapy to achieve a sustained and prolonged increase in haemoglobin levels would be time consuming and inconvenient for most patients, and trials of this type would be difficult to undertake.

- 4.3.6 The Committee discussed the effect of erythropoietin on survival, noting the Assessment Group's finding that none of the studies included in the Assessment Report's meta-analysis of survival was unequivocally within the products' current licensed indications. The Committee carefully considered the various survival estimates associated with the use of erythropoietin for anaemia induced by cancer treatment that were submitted. These included the meta-analysis of all studies included within the Assessment Report; the further work undertaken by the Assessment Group, which categorised the trials according to how closely they matched the licensed indications; and several survival meta-analyses submitted by Consultees.
- 4.3.7 The Committee was aware that some studies had shown benefits with erythropoietin in terms of improved survival, but that the results of other studies were consistent with a detrimental effect. The Committee considered various explanations for the opposing effects on survival, including the use of unlicensed doses of erythropoietin, the use of erythropoietin to produce inappropriately high haemoglobin levels, or use in patients with inappropriately high starting levels of haemoglobin. The Committee also heard that there was considerable international debate about the safety of erythropoietin, and that there were biologically plausible reasons to suggest possible growth-enhancing effects of erythropoietin on some tumours. The Committee therefore concluded that the true effect of erythropoietin on survival remains unknown. On the basis of the currently available evidence, and having considered the estimates of survival from the studies that most

closely reflected the licensed indications, the Committee felt that the effect of erythropoietin on survival could not be assumed to be positive.

4.3.8 The Committee considered the various cost-effectiveness analyses from the manufacturers and the Assessment Group. The Committee was conscious that improvements in quality of life, however small, are highly valued by patients. Nevertheless, they concluded that erythropoietin was very unlikely to be cost effective if the benefits from its use for anaemia induced by cancer treatment were considered in terms of changes in quality of life alone, and noted that the majority of the cost-effectiveness models presented indicated that this was the case.

4.3.9 The Committee discussed in detail the possibility that there may be subgroups of patients with anaemia induced by cancer treatment for whom erythropoietin therapy might be particularly beneficial. The Committee noted, as above, that there were biologically plausible mechanisms by which erythropoietin might harm some people with certain types of tumour by interacting with specific receptors on tumour cells. They accepted that survival benefit could therefore be related to tumour type but were not persuaded that the current evidence was sufficient to allow them to make specific recommendations for different tumour types. The Committee was also aware that some types of cancer and cancer treatments were associated with particularly severe anaemia and that there may be groups of patients who might therefore benefit particularly from erythropoietin. However, the current evidence base was insufficiently developed to allow these subgroups to be identified and for recommendations to be made about them. The Committee considered that future research should be directed to identifying these subgroups to ensure that erythropoietin therapy was used in the most clinically and cost-effective manner.

4.3.10 The Committee noted that the economic model produced by the Assessment Group had assumed baseline haemoglobin levels of less than or equal to 13 g/100 ml and that this assumption was inconsistent with the new licensed

indications for all three drugs. The Committee understood that sensitivity analyses had been conducted using lower baseline haemoglobin levels and that this had resulted in more favourable ICERs. However, the Committee concluded that the impact of this was insufficient to render erythropoietin cost effective according to conventional thresholds.

4.3.11 The Committee discussed the issue of the scarcity of blood products and noted the 'Better blood transfusion' initiative (Health service circular 2002/009), which mandates the exploration of alternatives to blood transfusions. The Committee was somewhat concerned that its guidance might run counter to these recommendations but felt that, on balance, its recommendation was sound given the currently available evidence on the clinical and cost effectiveness of erythropoietin. The Committee discussed the suggestion that the true cost of blood may not be fully reflected in the economic analyses. However, the Committee was persuaded that the full current economic cost was included in the Assessment Group's model. The Committee also concluded that it was not within the scope of this appraisal to consider the relative cost effectiveness of erythropoietin in the context of strategies that could be used to reduce the use of, or dependence on, transfusion of blood for anaemia induced by cancer treatment or other clinical situations.

4.3.12 The Committee was aware that some clinical guidelines, including those issued by the American Society for Clinical Oncology/American Society of Hematology and the European Organisation of Research and Treatment of Cancer, recommended the use of erythropoietin for cancer treatment-induced anaemia in certain circumstances. However, as these guidelines do not take cost effectiveness into account, the Committee agreed that they should not influence their decision.

## **5 Recommendations for further research**

- 5.1 Further research is required to establish the effects of erythropoietin in the management of anaemia induced by cancer treatment on health-related quality of life (specifically utility scores), including effects on fatigue.
- 5.2 Research is needed to confirm the benefits and risks associated with erythropoietin in the management of anaemia induced by cancer treatment (specifically mortality benefits and risks) and to identify patient subgroups (including those with different tumour types) in whom the possible risks are acceptable.

## **6 Implications for the NHS**

- 6.1 The NICE Costing Unit is currently developing this section. A costing template and report will be available at the time of publication of the final guidance.

## **7 Implementation and audit**

- 7.1 NHS organisations and clinicians who care for people with anaemia induced by cancer treatment should review their current practice and policies to take account of the guidance set out in section 1.

## **8 Related guidance**

- 8.1 There is no related guidance for this technology.

## **9 Review of guidance**

- 9.1 The review date for a technology appraisal refers to the month and year in which the Guidance Executive will consider whether the technology should be reviewed. This decision will be taken in the light of information gathered by the Institute, and in consultation with consultees and commentators.
- 9.2 The guidance on this technology will be considered for review in 2008.

David Barnett  
Chair, Appraisal Committee  
March 2006

## **A. Appraisal Committee members**

The Appraisal Committee is a standing advisory committee of the Institute. Its members are appointed for a 3-year term. A list of the Committee members who took part in the discussions for this appraisal appears below. The Appraisal Committee meets regularly and membership is split into two branches, with the chair, vice chair and a number of other members attending meetings of both branches. Each branch considers its own list of technologies and ongoing topics are not moved between the branches.

Committee members are asked to declare any interests in the technology to be appraised. If it is considered there is a conflict of interest, the member is excluded from participating further in that appraisal.

The minutes of each Appraisal Committee meeting, which include the names of the members who attended and their declarations of interests, are posted on the NICE website.

### **Dr Darren Ashcroft**

Senior Clinical Lecturer, School of Pharmacy and Pharmaceutical Sciences,  
University of Manchester

### **Professor David Barnett (Chair)**

Professor of Clinical Pharmacology, University of Leicester

### **Dr Peter Barry**

Consultant in Paediatric Intensive Care, Leicester Royal Infirmary

### **Mr Brian Buckley**

Vice Chairman, InContact

### **Professor John Cairns**

Public Health and Policy, London School of Hygiene and Tropical Medicine

**Professor Mike Campbell**

Statistician, University of Sheffield

**Professor David Chadwick**

Professor of Neurology, Walton Centre for Neurology and Neurosurgery

**Dr Mark Chakravarty**

Head of Government Affairs and NHS Policy, Procter and Gamble Pharmaceuticals (UK) Ltd

**Dr Peter I Clark**

Honorary Chairman, Association of Cancer Physicians

**Dr Mike Davies**

Consultant Physician, University Department of Medicine & Metabolism, Manchester Royal Infirmary

**Mr Richard Devereaux-Phillips**

Public Affairs Manager, Medtronic Ltd

**Professor Jack Dowie**

Health Economist, London School of Hygiene

**Dr Fergus Gleeson**

Consultant Radiologist, The Churchill Hospital, Oxford

**Ms Sally Gooch**

Former Director of Nursing & Workforce Development, Mid Essex Hospital Services NHS Trust

**Mr Sanjay Gupta**

Stroke Services Manager, Basildon and Thurrock University Hospitals NHS Trust

**Professor Philip Home**

Professor of Diabetes Medicine, University of Newcastle upon Tyne

**Dr Peter Jackson**

Clinical Pharmacologist, University of Sheffield

**Professor Peter Jones**

Professor of Statistics & Dean Faculty of Natural Sciences, Keele University

**Dr Mike Laker**

Medical Director, Newcastle Hospitals NHS Trust

**Dr George Levvy**

Lay representative

**Ms Rachel Lewis**

Nurse Advisor to the Department of Health

**Mr Terence Lewis**

Mental Health Consultant, National Institute for Mental Health in England

**Professor Jonathan Michaels**

Professor of Vascular Surgery, University of Sheffield

**Dr Neil Milner**

General Medical Practitioner, Sheffield

**Dr Ruairidh Milne**

Senior Lecturer in Health Technology Assessment, National Coordinating Centre for Health Technology

**Dr Rubin Minhas**

General Practitioner, Primary Care Cardiovascular Society

**Mr Miles Scott**

Chief Executive, Bradford Teaching Hospitals NHS Foundation Trust

**Dr Lindsay Smith**

General Practitioner, East Somerset Research Consortium

**Dr Ken Stein**

Senior Lecturer, Peninsula Technology Assessment Group (PenTAG), University of Exeter

**Professor Andrew Stevens**

Professor of Public Health, University of Birmingham

## **B. NICE Project Team**

Each appraisal of a technology is assigned to a Health Technology Analyst and a Technology Appraisal Project Manager within the Institute.

**Kate Burslem**

Technical Lead, NICE project team

**Cathryn Fuller**

Project Manager, NICE project team

## **Appendix B. Sources of evidence considered by the Committee for the use of erythropoietin for anaemia induced by cancer treatment**

A The assessment report for this appraisal was prepared by West Midlands Health Technology Assessment Collaboration, University of Birmingham.

I Wilson J, Hyde C, Yao G et al. 'A systematic review and economic evaluation of epoetin alfa, epoetin beta and darbepoetin alfa in anaemia associated with cancer, especially that attributable to cancer treatment', March 2005.

B The following organisations accepted the invitation to participate in this appraisal. They were invited to make submissions and comment on the draft scope, Assessment Report and Appraisal Consultation Document (ACD). Consultee organisations are provided with the opportunity to appeal against the Final Appraisal Determination.

II Manufacturers/sponsors:

- Amgen Limited
- Janssen-Cilag Limited
- Roche Products Ltd

III Professional/specialist and patient/carer groups:

- Breakthrough Breast Cancer
- British Oncology Pharmacy Association
- British Society for Haematology
- CancerBACUP

- Department of Health
- International Myeloma Foundation (UK)
- Leukaemia Care
- Macmillan Cancer Relief
- National Blood Service
- Ovacome
- Roy Castle Lung Cancer Foundation
- Royal College of Nursing
- Royal College of Pathologists
- Royal College of Physicians
- Royal Pharmaceutical Society of Great Britain
- Slough Primary Care Trust
- Tenovus The Cancer Charity
- Welsh Assembly Government
- Welsh Blood Service

IV Commentator organisations (without the right of appeal):

- British National Formulary
- Institute of Cancer Research
- National Cancer Research Institute
- National Collaborating Centre for Cancer

- National Collaborating Centre for Chronic Conditions
- National Public Health Service for Wales
- NHS Quality Improvement Scotland

C The following individuals were selected from clinical expert and patient advocate nominations from the professional/specialist and patient/carer groups. They participated in the Appraisal Committee discussions and provided evidence to inform the Appraisal Committee's deliberations. They gave their expert personal view on the use of erythropoietin for anaemia induced by cancer treatment by attending the initial Committee discussion and/or providing written evidence to the Committee. They were also invited to comment on the ACD.

- Dr Geoff Hall, Senior Lecturer in Medical Oncology/Honorary Consultant Physician, Cancer Research UK Clinical Centre, clinical expert nominated by Royal College of Physicians
- Dr Keith MO Wilson, Senior Clinical Lecturer in Haematology, clinical expert nominated by the Welsh Blood Service
- Dr Tim J Littlewood, Consultant Haematologist, John Radcliffe Hospital, clinical expert nominated by the National Blood Service
- Ms Hannah Young, patient expert nominated by Ovacome
- Mr Lawrence Doffman, patient expert nominated by International Myeloma Foundation