



Complete Summary

GUIDELINE TITLE

Epoetin alfa, epoetin beta and darbepoetin alfa for cancer treatment-induced anaemia.

BIBLIOGRAPHIC SOURCE(S)

National Institute for Health and Clinical Excellence (NICE). Epoetin alfa, epoetin beta and darbepoetin alfa for cancer treatment-induced anaemia. London (UK): National Institute for Health and Clinical Excellence (NICE); 2008 May. 36 p. (Technology appraisal guidance; no. 142).

GUIDELINE STATUS

This is the current release of the guideline.

** REGULATORY ALERT **

FDA WARNING/REGULATORY ALERT

Note from the National Guideline Clearinghouse: This guideline references drug(s) for which important revised regulatory and/or warning information has been released.

- [November 8, 2007 and January 3, 2008 Update, Erythropoiesis Stimulating Agents \(ESAs\)](#): The U.S. Food and Drug Administration (FDA) notified healthcare professionals of revised boxed warnings and other safety-related product labeling changes for erythropoiesis-stimulating agents (ESAs) stating serious adverse events, such as tumor growth and shortened survival in patients with advanced cancer and chronic kidney failure.

COMPLETE SUMMARY CONTENT

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SCOPE

DISEASE/CONDITION(S)

Anemia induced by cancer treatment

GUIDELINE CATEGORY

Assessment of Therapeutic Effectiveness
Treatment

CLINICAL SPECIALTY

Family Practice
Hematology
Internal Medicine
Oncology

INTENDED USERS

Advanced Practice Nurses
Nurses
Physician Assistants
Physicians

GUIDELINE OBJECTIVE(S)

To evaluate the clinical effectiveness and cost-effectiveness of epoetin alfa, epoetin beta, and darbepoetin alfa for cancer treatment-induced anaemia

TARGET POPULATION

Cancer patients with anemia induced by cancer treatment

INTERVENTIONS AND PRACTICES CONSIDERED

Use of erythropoietin analogues in combination with intravenous iron in specific circumstances

Note: Routine use of erythropoietin analogues for the management of cancer treatment-induced anemia was considered but not recommended.

MAJOR OUTCOMES CONSIDERED

- Clinical effectiveness
 - Anemia related outcomes including hematological response to treatment, mean hemoglobin (Hb) change, red blood cell transfusion (RBCT) requirements, including number of patients transfused, number of units transfused per patient and number of units transfused per patient per 4 weeks

- Cancer-related outcomes, including tumor response and overall survival
- Adverse events
- Quality of life
- Patient preference
- Cost-effectiveness

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Hand-searches of Published Literature (Primary Sources)
 Hand-searches of Published Literature (Secondary Sources)
 Searches of Electronic Databases
 Searches of Unpublished Data

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

Note from the National Guideline Clearinghouse (NGC): The National Institute for Health and Clinical Excellence (NICE) commissioned an independent academic centre to perform a systematic literature review on the technology considered in this appraisal and prepare an assessment report. The assessment report for this technology appraisal was prepared by West Midlands Technology Assessment Collaboration (see the "Availability of Companion Documents" field).

Clinical Effectiveness

A scoping search was undertaken to identify existing reviews and other background material and to estimate the volume and nature of primary studies. Among this literature a recent well-conducted Cochrane Review was identified, which assessed the effectiveness of epoetin alfa and beta up to 2001.

It was agreed that the review commissioned by NICE for the effectiveness part of this technology assessment would build onto the work of the Cochrane review.

Search Strategy

The Cochrane systematic review formed the basis of the Assessment Group's review regarding epoetin alfa and epoetin beta so their search strategy ran from 2000 onwards for these two drugs. In the case of darbepoetin alfa the search ran from 1996, the year before phase I trials were initiated on it. Searches ended in September 2004, studies identified after this date were acknowledged but not included in the analysis. There were no language restrictions. (Refer to Appendix 2 of the Assessment Report [see the "Availability of Companion Documents" field] for search strategies).

The main purpose of the search was to comprehensively identify completed randomised controlled trials (RCTs) of erythropoietin. To this end the following sources were searched:

- Bibliographic databases including Cochrane Library (CENTRAL), MEDLINE, EMBASE and the Science Citation Index
- Research Registers of ongoing trials including the National Research Register, Current Controlled Trials *metaRegister*, and ISRCTN database and ClinicalTrials.gov
- Citation lists of relevant studies
- Contact with experts in the field
- Invited industry submissions
- Conference proceedings

Ongoing Trials

A search for ongoing trials was also undertaken, terms for the intervention (erythropoietin, epoetin, darbepoetin) and condition of interest (anaemia/anemia) were used to search the following trials registers: National Research Register 2004 Issue 2, Current Controlled Trials *metaRegister*, ClinicalTrials.gov, National Cancer Institute PDQ database and International Cancer Research Portfolio for ongoing trials. Trials that did not relate to cancer-induced or chemotherapy-related anaemia were removed by handsorting. Finally duplicates, identified via their study identification numbers where possible, were removed, leaving a final list of 29 potentially relevant trials. (Searches carried out 5/7/2004).

Inclusion and Exclusion Criteria

Study Design

Only RCTs were included. Non-randomised trials, in particular quasi-randomised such as where allocation is based on date of birth or day of month were excluded. Also excluded were RCTs with fewer than 10 patients in any study arm.

Population

Patients had to be diagnosed with malignant disease, using clinical and histological/cytological criteria (any type of malignant disease was included, irrespective of stage or previous therapy); trials in patients with anaemia resulting from chemotherapy and/or radiotherapy or underlying malignant disease were included. Other causes of anaemia such as haemolysis, iron deficiency and occult bleeding should have been excluded in the participants of the included trials. There were no age restrictions; however, it is recognised that the licences for all three drugs do not cover erythropoietin use in children. Studies where erythropoietin was given in the context of myelo-ablative chemotherapy ahead of bone marrow or peripheral blood stem cell transplantation, or for short-term preoperative treatment to correct anaemia or to support collection of autologous blood prior to cancer surgery, were excluded.

Intervention

Epoetin alfa (Expres, Ortho biotec), epoetin beta (NeoRecormon, Roche) or darbepoetin alfa (Nesp, Amgen). Concomitant anaemia therapy such as iron or granulocyte-colony-stimulating factor (G-CSF) supplementation was permitted, as were red blood cell transfusions (RBCT).

Comparator

Within the Cochrane review any comparator was acceptable provided that the only difference between the treatment and control arms was the use of erythropoietin. However, at the NICE Consultee Meeting on 2nd September 2004, after discussion, it was felt that there may be trials in which concomitant supportive anaemia treatments such as G-CSF or iron supplementation had been given to patients receiving erythropoietin but not to patients in the control arm, which if excluded would cause valuable information to be lost. It was therefore agreed to include these trials, but also to acknowledge that these trials do have different comparators to trials where concomitant supportive anaemia treatments are given to patients equally in each arm of the trials.

It was anticipated that comparators would be either placebo or best supportive care. In both, it was anticipated that RBCT would be given when a patient's haemoglobin (Hb) fell to an unacceptably low level. Ideally a protocol for when RBCT should be instigated should have been described (i.e., "transfusion trigger"). The same rules on rescue regarding RBCT should also have been applied in the erythropoietin arm.

Outcomes

Outcomes sought from the studies fell into 4 categories: anaemia related outcomes, malignancy related outcomes, adverse events data, and patient specific outcomes such as quality of life outcomes and patients preferences.

Refer to Section 3.1.3 of the Assessment Report (see the "Availability of Companion Documents" field) for more information on outcomes.

Cost-Effectiveness

Search

The following sources were searched up to 30/7/04 to identify economic evaluations as part of wider search to identify all aspects of information on costs, cost-effectiveness and quality of life outcomes:

- MEDLINE (Ovid) 1966 – July week 4 2004
- EMBASE (Ovid) 1980 – 2004 week 30
- Database of Reviews of Effects (DARE) 2004 Issue 3
- National Health Service Economic Evaluations Database (NHS EED) 2004 Issue 3
- Office of Health Economics Health Economic Evaluation Database (OHE HEED) July 2004 issue

The search strategy, detailed in full in Appendix 2 of the Assessment Report (see the "Availability of Companion Documents" field) combined groups of terms capturing the intervention of interest (erythropoietin), with terms capturing the target condition (cancer), with terms capturing the study design of interest (cost-effectiveness, cost and quality of life). There were no language restrictions. The

submissions from the three industry sponsors were searched for additional references.

Inclusion Criteria

Originally the Assessment Group had intended to restrict the review to cost-utility studies undertaken since 2000. However, because several widely cited studies were published in the period 1995 to 2000, the search period and range of included study designs were extended. The review reported here was thus of all economic evaluations (cost-benefit, cost-utility, cost-effectiveness, and cost-consequence analyses) of erythropoietin for anaemia associated with cancer treatment from 1995 to July 2004. Inclusion decisions were made by one reviewer.

NUMBER OF SOURCE DOCUMENTS

Clinical Effectiveness

Forty-six randomized controlled trials were included.

Cost-Effectiveness

Five published economic evaluations were identified and three manufacturers' models were submitted.

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Expert Consensus

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Not applicable

METHODS USED TO ANALYZE THE EVIDENCE

Meta-Analysis
Review of Published Meta-Analyses
Systematic Review with Evidence Tables

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

Note from the National Guideline Clearinghouse (NGC): The National Institute for Health and Clinical Excellence (NICE) commissioned an independent academic centre to perform a systematic literature review on the technology considered in this appraisal and prepare an assessment report. The assessment report for this technology appraisal was prepared by West Midlands Technology Assessment Collaboration (see the "Availability of Companion Documents" field).

Clinical Effectiveness

Making Inclusion/Exclusion Decisions

Two reviewers independently extracted data from the NICE studies using a pre-designed data extraction form. For consistency with the Cochrane review the data extraction was based on the original Cochrane data extraction form and data for outcomes of haematological response (HaemR), Hb change, and RBCT were identical to that sought by the Cochrane review. For health-related quality of life (HRQoL) and survival outcomes a more detailed extraction form to that used in the Cochrane review was used. Disagreements were resolved by discussion, consulting with a third party where interpretation was difficult. Data from studies with multiple publications were extracted and reported as a single study; in the case of reported discrepancies the most recent publication was utilized. Data reported here derived from the Cochrane studies was obtained from the Cochrane review unless otherwise stated.

Two reviewers independently assessed quality for the NICE studies judged on the following criteria taken from the assessment utilized in the Cochrane Review:

- Treatment allocation
- Similarity of groups
- Implementation of masking
- Completeness of trial

Methods of Analysis/Synthesis

A descriptive analysis of included studies was undertaken, and relevant evidence categorized and summarised in tables. Where appropriate, in the absence of substantial clinical and statistical heterogeneity, results from individual studies were quantitatively pooled by meta-analysis (using MetaView 4.1 – Cochrane Collaboration). Identified research evidence was interpreted according to the assessment of methodological strengths and weaknesses and the possibility of potential biases. Publication bias for the main outcomes was assessed using funnel plots.

The following sub-group analyses were undertaken:

- Study quality
- Degree of anaemia
- Underlying malignancies and therapy
- Differences in intervention
- Concomitant treatments

The X^2 test for interaction is presented (test for heterogeneity between groups) and in addition the more exacting F test, which compares the amount of the total heterogeneity falling between groups with that remaining within the groups (essentially a univariate meta-regression). Where there is substantial heterogeneity in the overall dataset, high values of F suggest that the characteristic may help to explain that heterogeneity.

The general purpose of the sub-group analyses was to form part of a sensitivity analyses to test the robustness of the data and interpretation of results and/or for exploring heterogeneity.

Refer to Sections 3.1.4 and 3.1.5 of the Assessment Report (see the "Availability of Companion Documents" field) for details on quality assessment and methods of analysis/synthesis.

Cost-Effectiveness

Review of Previous Economic Evaluation

Data Abstraction and Appraisal Strategy

Key details of the included studies were abstracted using the framework developed and applied in past technology appraisals undertaken by the West Midlands group. Judgements about quality were made on the basis of the checklist suggested by Drummond et al. One point was allocated for each question in the checklist (with the exception of question 10, which is open) to give a summary mark out of 10. The primary data abstraction was undertaken by one reviewer with checking of data by a second reviewer.

Analysis

This was qualitative, based on the patterns in the tabulated extracted data. Draft conclusions from the initial reviewer, in particular addressing the objective to identify the reasons for variation in results were independently scrutinised and amended by two other reviewers.

Quality of Previous Evaluations

The quality assessment recorded in Table 27 of the Assessment Report (see the "Availability of Companion Documents" field) demonstrates that in general terms all studies were well conducted as judged by the criteria suggested in the Drummond checklist.

Refer to Section 5.2 and 5.3 of the Assessment Report (see the "Availability of Companion Documents" field) for information about the manufacturers' models and the Assessment Group model, respectively.

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Expert Consensus

DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

Considerations

Technology appraisal recommendations are based on a review of clinical and economic evidence.

Technology Appraisal Process

The National Institute for Health and Clinical Excellence (NICE) invites 'consultee' and 'commentator' organisations to take part in the appraisal process. Consultee organisations include national groups representing patients and carers, the bodies representing health professionals, and the manufacturers of the technology under review. Consultees are invited to submit evidence during the appraisal and to comment on the appraisal documents.

Commentator organisations include manufacturers of the products with which the technology is being compared, the National Health Service (NHS) Quality Improvement Scotland and research groups working in the area. They can comment on the evidence and other documents but are not asked to submit evidence themselves.

NICE then commissions an independent academic centre to review published evidence on the technology and prepare an 'assessment report'. Consultees and commentators are invited to comment on the report. The assessment report and the comments on it are then drawn together in a document called the evaluation report.

An independent Appraisal Committee then considers the evaluation report. It holds a meeting where it hears direct, spoken evidence from nominated clinical experts, patients and carers. The Committee uses all the evidence to make its first recommendations, in a document called the 'appraisal consultation document' (ACD). NICE sends all the consultees and commentators a copy of this document and posts it on the NICE website. Further comments are invited from everyone taking part.

When the Committee meets again it considers any comments submitted on the ACD; then it prepares its final recommendations in a document called the 'final appraisal determination' (FAD). This is submitted to NICE for approval.

Consultees have a chance to appeal against the final recommendations in the FAD. If there are no appeals, the final recommendations become the basis of the guidance that NICE issues.

Who is on the Appraisal Committee?

NICE technology appraisal recommendations are prepared by an independent committee. This includes health professionals working in the NHS and people who are familiar with the issues affecting patients and carers. Although the Appraisal Committee seeks the views of organisations representing health professionals, patients, carers, manufacturers and government, its advice is independent of any vested interests.

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Not applicable

COST ANALYSIS

Three of the five published economic analyses contained a cost–utility analysis. One published cost–utility analysis was performed from a UK health service perspective and considered the use of erythropoietin analogues versus the use of blood transfusions in people with stage IV breast cancer. This analysis incorporated a survival benefit associated with erythropoietin analogue treatment (hazard ratio [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 pounds sterling per additional quality-adjusted life year (QALY) gained. The ICERs from the two remaining cost–utility analyses were both higher than US \$100,000.

The manufacturer of epoetin alfa compared the use of this treatment (with the possibility of blood transfusion) with the use of blood transfusions. A 3-year time horizon was used and the model included a survival advantage associated with erythropoietin analogues (HR = 0.64). Base-case ICERs were presented separately for different haemoglobin subgroups and for different tumour types, and were less than 16,000 pounds sterling per additional QALY gained.

The manufacturer of epoetin beta presented separate ICERs for solid tumours and haematological cancers, together with tumour-specific survival gains associated with erythropoietin analogues (solid tumours HR = 0.49; haematological cancers HR = 1). The associated ICERs were approximately 28,000 pounds sterling and 84,000 pounds sterling per additional QALY gained, respectively.

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. 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 pounds sterling and 24,000 pounds sterling per additional QALY gained, respectively.

The Assessment Group's economic evaluation used a 3-year time horizon. The model evaluated the use of erythropoietin analogues (with the possibility of blood transfusion) versus blood transfusion alone. People included in the model were characterised only by their baseline haemoglobin concentration at the start of chemotherapy.

In the base case of the Assessment Group's economic analysis, 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 more than 100,000 pounds sterling per additional QALY gained. The results of the sensitivity analysis demonstrated that erythropoietin analogues became more cost effective as the threshold haemoglobin concentration for initiating an erythropoietin analogue was reduced to lower levels, but the ICERs still remained high. The most favourable ICERs were obtained if a baseline haemoglobin concentration of 8 g/100 mL was assumed for all participants. These were in the range of 65,000 to 80,000 pounds sterling per additional QALY gained.

Following a reduction in the published price of erythropoietin analogues, further analyses were performed using the lowest list price of the erythropoietin analogues available for this indication (that is, 62.85 pounds sterling for each

10,000 international units [IU] prefilled syringe). Based on a baseline haemoglobin of 8 g/100 mL or less and assuming no effect in terms of survival (that is, HR = 1) the ICERs obtained were 30,600 pounds sterling and 26,200 pounds sterling per additional QALY for the subgroup receiving platinum-based chemotherapy for any type of cancer and women receiving platinum-based chemotherapy for ovarian cancer, respectively.

The cost-effectiveness estimates for a treatment strategy including intravenous iron supplementation were highly sensitive to the clinical effectiveness inputs used in the analysis. Two scenarios, both using a baseline haemoglobin of 8 g/100 mL or less, were considered by applying the results of two studies that reported the outcomes needed to estimate the haematological parameters for the cost-effectiveness model. This analysis produced ICERs of 30,000 pounds sterling per QALY gained and in excess of 53,000 pounds sterling per QALY gained depending on which study was used. This analysis incorporated the lowest price following the reduction in the list price of erythropoietin analogues as above. If the assumption was included in the sensitivity analysis that 25% of people with cancer receiving blood transfusions would require an overnight stay (based on a UK study conducted between December 1996 and January 1998), the ICERs were reduced to 25,000 pounds sterling per additional QALY gained for the optimistic scenario. ICERs for the conservative case were still in excess of 53,000 pounds sterling per additional QALY gained.

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 people with cancer. Nevertheless, it concluded that erythropoietin analogues were very unlikely to be cost effective if the benefits from their use for cancer treatment-induced anaemia were considered in terms of changes in quality of life alone, and it noted that the majority of the cost-effectiveness results indicated that this was the case.

The Committee discussed the clinical and cost effectiveness of the use of the erythropoietin analogues in conjunction with intravenous iron supplementation. The Committee discussed the impact on the cost-effectiveness estimates and considered the analyses of trial data of both the most optimistic and conservative cases in which intravenous iron supplementation had been given. The Committee noted that applying the most optimistic estimates of response to erythropoietin analogues with intravenous iron supplementation produced an ICER of 30,000 pounds sterling per additional QALY gained, whereas taking into consideration the conservative scenario produced an ICER in excess of 53,000 pounds sterling per additional QALY gained. Therefore, the Committee concluded that the realistic ICER value was likely to be between these limits and thus was unlikely to fall within the range normally considered to be a cost-effective use of NHS resources. However, the Committee accepted that the additional effect of intravenous iron remained plausible and was likely to enhance the clinical and cost effectiveness of erythropoietin analogues.

The Committee understood that women with ovarian cancer receiving platinum-based chemotherapy may be at risk of more profound anaemia than other people with cancer because of the particularly intense treatment schedules associated with the use of platinum therapy for ovarian cancer. The Committee next

considered both cost-effectiveness estimates presented for the subgroup of people with ovarian cancer who received platinum chemotherapy. It acknowledged that these estimates referred to an analysis in a group with a baseline haemoglobin of 8 g/100 mL or lower. The Committee noted that the principal reason for the favourable ICER in this group was the apparent survival benefit seen with erythropoietin analogues in these people. Having considered the special characteristics associated with the use of platinum-based chemotherapy for ovarian cancer, the Committee was not persuaded by the evidence presented that a survival advantage from the use of the erythropoietin analogues had been demonstrated for this group.

However, the Committee noted that after the reduction in the list price of erythropoietin analogues was incorporated into the analysis, even if no survival benefit was assumed for the subgroup of people with ovarian cancer receiving platinum-based chemotherapy, the ICER produced was in the region of 26,000 pounds sterling. The Committee also recognised that this analysis applied to people with a baseline haemoglobin concentration of 8 g/100 mL or lower. The Committee concluded that, in the context of the use of the least costly product, it was appropriate to recommend the use of erythropoietin for this subgroup if used in combination with intravenous iron supplementation which would be expected to reduce the ICER still further.

Refer to Section 4 of the original guideline document for details of the economic analyses provided by the manufacturers, the Assessment Group comments, and the Appraisal Committee considerations.

METHOD OF GUIDELINE VALIDATION

External Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

Consultee organizations from the following groups were invited to comment on the draft scope, Assessment Report and the Appraisal Consultation Document (ACD) and were provided with the opportunity to appeal against the Final Appraisal Determination.

- Manufacturer/sponsors
- Professional/specialist and patient/carer groups
- Commentator organisations (without the right of appeal)

In addition, individuals selected from clinical expert and patient advocate nominations from the professional/specialist and patient/carer groups were also invited to comment on the ACD.

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

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

During this appraisal the regulatory health authorities have conducted reviews into the safety of erythropoietin analogues. This guidance was produced taking the conclusions of those reviews into consideration, and should be read in conjunction with the reports published by the regulatory health authorities.

Guidance

Erythropoietin analogues are not recommended for routine use in the management of cancer treatment-induced anaemia, except in the circumstances described below.

Erythropoietin analogues are recommended in combination with intravenous iron as an option for the management of cancer treatment-induced anaemia in women receiving platinum-based chemotherapy for ovarian cancer who have symptomatic anaemia with a haemoglobin level of 8 g/100 mL or lower. The use of erythropoietin analogues does not preclude the use of existing approaches to the management of anaemia, including blood transfusion where necessary.

Erythropoietin analogues in combination with intravenous iron may be considered for people who cannot be given blood transfusions and who have profound cancer treatment-related anaemia that is likely to have an impact on survival.

In the circumstances outlined above, the erythropoietin analogue with the lowest acquisition cost should be used.

People who are currently being treated with erythropoietin analogues for the management of cancer treatment-related anaemia but who do not fulfil the criteria outlined above should have the option to continue their therapy until they and their specialists consider it appropriate to stop.

CLINICAL ALGORITHM(S)

None provided

EVIDENCE SUPPORTING THE RECOMMENDATIONS

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The type of evidence supporting the recommendations is not specifically stated.

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

Appropriate use of epoetin alfa, epoetin beta, and darbepoetin alfa for cancer treatment-induced anemia

POTENTIAL HARMS

There is uncertainty about the potential side effects of erythropoietin analogues in people with anaemia who are receiving treatments for cancer. The European Medicines Agency (EMA) has recently reviewed the safety of erythropoietin analogues based on new data from both published and unpublished studies. These studies suggest an increased risk of serious cardiovascular complications in people with chronic renal failure and a possible effect on tumour progression in people with cancer. An earlier safety review by the EMA resulted in revised dosing recommendations for people receiving chemotherapy and in new safety warnings regarding possible stimulating effects on tumour progression.

For full details of side effects and contraindications, see the summary of product characteristics (SPCs).

QUALIFYING STATEMENTS

QUALIFYING STATEMENTS

- This guidance represents the view of the Institute, which was arrived at after careful consideration of the evidence available. Healthcare professionals are expected to take it fully into account when exercising their clinical judgement. The guidance does not, however, override the individual responsibility of healthcare professionals to make decisions appropriate to the circumstances of the individual patient, in consultation with the patient and/or guardian or carer.
- Implementation of this guidance is the responsibility of local commissioners and/or providers. Commissioners and providers are reminded that it is their responsibility to implement the guidance, in their local context, in light of their duties to avoid unlawful discrimination and to have regard to promoting equality of opportunity. Nothing in this guidance should be interpreted in a way which would be inconsistent with compliance with those duties.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

- The Healthcare Commission assesses the performance of National Health Service (NHS) organizations in meeting core and developmental standards set by the Department of Health in "Standards for Better Health" issued in July 2004. The Secretary of State has directed that the NHS provides funding and resources for medicines and treatments that have been recommended by the National Institute for Health and Clinical Excellence (NICE) technology appraisals normally within 3 months from the date that NICE publishes the guidance. Core standard C5 states that healthcare organisations should ensure they conform to NICE technology appraisals.
- "Healthcare Standards for Wales" was issued by the Welsh Assembly Government in May 2005 and provides a framework both for self-assessment by healthcare organisations and for external review and investigation by Healthcare Inspectorate Wales. Standard 12a requires healthcare organisations to ensure that patients and service users are provided with

effective treatment and care that conforms to NICE technology appraisal guidance. The Assembly Minister for Health and Social Services issued a Direction in October 2003 which requires Local Health Boards and NHS Trusts to make funding available to enable the implementation of NICE technology appraisal guidance, normally within 3 months.

- NICE has developed tools to help organisations implement this guidance (listed below). These are available on the [NICE Web site](#) (see also the "Availability of Companion Documents" field).
 - A costing statement explaining the resource impact of this guidance.
 - Audit support for monitoring local practice

IMPLEMENTATION TOOLS

Audit Criteria/Indicators
Patient Resources
Quick Reference Guides/Physician Guides

For information about [availability](#), see the "Availability of Companion Documents" and "Patient Resources" fields below.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Getting Better
Living with Illness

IOM DOMAIN

Effectiveness
Patient-centeredness

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

National Institute for Health and Clinical Excellence (NICE). Epoetin alfa, epoetin beta and darbepoetin alfa for cancer treatment-induced anaemia. London (UK): National Institute for Health and Clinical Excellence (NICE); 2008 May. 36 p. (Technology appraisal guidance; no. 142).

ADAPTATION

Not applicable: The guideline was not adapted from another source.

DATE RELEASED

2008 May

GUIDELINE DEVELOPER(S)

National Institute for Health and Clinical Excellence (NICE) - National Government Agency [Non-U.S.]

SOURCE(S) OF FUNDING

National Institute for Health and Clinical Excellence (NICE)

GUIDELINE COMMITTEE

Appraisal Committee

COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE

Committee Members: Professor Keith Abrams, Professor of Medical Statistics, University of Leicester; Dr Jeff Aronson, Reader in Clinical Pharmacology, Department of Primary Health Care, University of Oxford; Dr Darren Ashcroft, Reader in Medicines Usage and Safety, 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; Professor Stirling Bryan, Head, Department of Health Economics, University of Birmingham; Professor John Cairns, Public Health and Policy, London School of Hygiene and Tropical Medicine; Dr Mark Charkravarty, Director, External Relations, Procter and Gamble Health Care, Europe; Professor Jack Dowie, Health Economist, London School of Hygiene and Tropical Medicine; Ms Lynn Field, Nurse Director, Pan Birmingham Cancer Network; Professor Christopher Fowler, Professor of Surgical Education, Barts and The London School of Medicine and Dentistry, Queen Mary, University of London; Dr Fergus Gleeson, Consultant Radiologist, Churchill Hospital, Oxford; Ms Sally Gooch, Independent Nursing and Healthcare Consultant; Mrs Barbara Greggains, Lay member; Mr Sanjay Gupta, Former Service Manager in Stroke, Gastroenterology, Diabetes and Endocrinology, Basildon and Thurrock University Hospitals Foundation NHS Trust; Mr Terence Lewis, Lay member; Professor Gary McVeigh, Professor of Cardiovascular Medicine, Queens University, Belfast; Consultant Physician, Belfast Trust; Dr Ruairidh Milne, Senior Lecturer in Public Health, National Coordinating Centre for Health Technology, University of Southampton; Dr Neil Milner, General Medical Practitioner, Tramways Medical Centre, Sheffield; Dr Rubin Minhas, General Practitioner, CHD Clinical Lead, Medway Primary Care Trust; Dr John Pounsford, Consultant Physician, Frenchay Hospital, Bristol; Dr Rosalind Ramsay, Consultant Psychiatrist, Adult Mental Health Services, Maudsley Hospital; Dr Stephen Saltissi, Consultant Cardiologist, Royal Liverpool University Hospital; Dr Lindsay Smith, General Practitioner, East Somerset Research Consortium; Mr Roderick Smith, Director of Finance, West Kent PCT; Mr Cliff Snelling, Lay member; Professor Ken Stein (*Vice-Chair*), Professor of Public Health, Peninsula College of Medicine and Dentistry, University of Exeter; Professor Andrew Stevens, Professor of Public Health, Department of Public Health and Epidemiology, University of Birmingham; Dr Rod Taylor, Associate Professor in Health Services Research, Peninsula Medical School, Universities of Exeter and Plymouth

FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

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.

GUIDELINE STATUS

This is the current release of the guideline.

GUIDELINE AVAILABILITY

Electronic copies: Available in Portable Document Format (PDF) format from the [National Institute for Health and Clinical Excellence \(NICE\) Web site](#).

AVAILABILITY OF COMPANION DOCUMENTS

The following are available:

- Epoetin alfa, epoetin beta and darbepoetin alfa for cancer treatment-induced anaemia. Quick reference guide. London (UK): National Institute for Health and Clinical Excellence (NICE); 2008 May. 2 p. (Technology appraisal 142). Available in Portable Document Format (PDF) from the [National Institute for Health and Clinical Excellence \(NICE\) Web site](#).
- Epoetin alfa, epoetin beta and darbepoetin alfa for cancer treatment-induced anaemia. Costing template. London (UK): National Institute for Health and Clinical Excellence (NICE); 2008 May. 3 p. (Technology appraisal 142). Available in Portable Document Format (PDF) from the [NICE Web site](#).
- Epoetin alfa, epoetin beta and darbepoetin alfa for cancer treatment-induced anaemia. Audit support. London (UK): National Institute for Health and Clinical Excellence (NICE); 2008. 7 p. (Technology appraisal 142). Available in Portable Document Format (PDF) from the [NICE Web site](#).
- 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. A systematic review and economic evaluation. London (UK): National Institute for Health and Clinical Excellence (NICE); 2005. 306 p. (Technology appraisal 142). Available in Portable Document Format (PDF) from the [NICE Web site](#).

Print copies: Available from the National Health Service (NHS) Response Line 0870 1555 455. ref: N1563. 11 Strand, London, WC2N 5HR.

PATIENT RESOURCES

The following is available:

- Erythropoietin analogues for anaemia caused by cancer treatment. Understanding NICE guidance - Information for people who use NHS services. London (UK): National Institute for Health and Clinical Excellence (NICE); 2008 May. 4 p. (Technology appraisal 142). Available in Portable Document Format (PDF) from the [National Institute for Health and Clinical Excellence \(NICE\) Web site](#).

Print copies: Available from the National Health Service (NHS) Response Line 0870 1555 455. ref: N1564. 11 Strand, London, WC2N 5HR.

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