NICE National Institute for Health and Care Excellence

Anaemia management in people with chronic kidney disease

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NICE clinical guideline 114

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Contents

Introduction

This guideline updates and replaces NICE clinical guideline 39.

Internationally anaemia is defined as a state in which the quality and/or quantity of circulating red blood cells are below normal. Blood haemoglobin (Hb) concentration serves as the key indicator for anaemia because it can be measured directly, has an international standard, and is not influenced by differences in technology. However, because Hb values in healthy individuals within a population show a normal distribution, a certain number of healthy individuals will fall below a given cut-off point.

Why is anaemia important in patients with chronic kidney disease (CKD)? Possible adverse effects of anaemia include reduced oxygen utilisation, increased cardiac output and left ventricular hypertrophy, increased progression of CKD, reduced cognition and concentration, reduced libido and reduced immune responsiveness. How much these adverse effects translate into adverse outcomes such as impaired quality of life, increased hospitalisation, increased cardiovascular events and increased cardiovascular and all-cause mortality has been debated for several years. What is incontrovertible is that since the introduction of human recombinant erythropoietin for treating CKD-related anaemia over 2 decades ago we have had the tools to significantly influence anaemia management. The phenotype of the kidney patient with Hb levels between 5–8 g/dl, rendered massively iron over-loaded and virtually un-transplantable as a result of multiple transfusions, has thankfully become unrecognisable. Attention has shifted from treating severe anaemia in dialysis patients to preventing anaemia pre-dialysis and to correcting of anaemia to higher Hb levels.

It is well established that Hb levels fall as kidney function declines but there is significant heterogeneity at each level of kidney dysfunction. Although normal values for Hb in the general population differ by gender this has not been addressed in most study designs of anaemia in CKD. Observational data suggest that lower Hb values are associated with increased cardiovascular abnormalities/events, increased hospitalisation, increased mortality, increased transfusion requirements and reduced quality of life. Major criticisms levelled at observational studies have been their heterogeneity and the variation in adjustment for confounders. Randomised controlled clinical trials of correction of anaemia to higher versus lower levels of Hb have failed to demonstrate the expected improved outcomes, even suggesting potential harm. These too have been criticised, particularly on the basis that the treatment required to achieve Hb levels in the different studies has also been subject to confounding; these trials have served

to highlight the potential importance of erythropoietin dose and individual responsiveness to anaemia treatment.

When 'Anaemia management in people with chronic kidney disease' (NICE clinical guideline 39) was published in 2006, guidance on limiting the upper level of Hb was primarily driven by health economics and a lack of evidence of additional benefit in people treated to levels of Hb greater than 12.5 g/dl. However, studies published after the guidance were consistent with a relative lack of benefit and possible harm in the process of aspiring to higher Hb levels, dictating a review of published recommendations.

New recommendations have been added for the diagnostic evaluation and assessment of anaemia and the assessment and optimisation of erythropoiesis.

Recommendations are marked as **[2006]**, **[2006, amended 2011]** or **[new 2011].**

- **[2006]** indicates that the evidence has not been updated and reviewed since 2006.
- **[2006, amended 2011]** indicates recommendations where the evidence has not been reviewed since the original guideline but they have been amended because of GDG consensus that they no longer reflect clinical practice or to add clarity; **or** recommendations that need amending to be consistent with new recommendations.

Patient-centred care

This guideline offers best practice advice on the care of people with anaemia of CKD.

Treatment and care should take into account patients' needs and preferences. People with anaemia of CKD should have the opportunity to make informed decisions about their care and treatment, in partnership with their healthcare professionals. If patients do not have the capacity to make decisions, healthcare professionals should follow the Department of Health's advice on consent and the code of practice that accompanies the Mental Capacity Act. In Wales, healthcare professionals should follow advice on consent from the Welsh Government.

If the patient is under 16, healthcare professionals should follow the guidelines in the Department of Health's Seeking consent: working with children.

Good communication between healthcare professionals and patients is essential. It should be supported by evidence-based written information tailored to the patient's needs. Treatment and care, and the information patients are given about it, should be culturally appropriate. It should also be accessible to people with additional needs such as physical, sensory or learning disabilities, and to people who do not speak or read English.

If the patient agrees, families and carers should have the opportunity to be involved in decisions about treatment and care.

Families and carers should also be given the information and support they need.

Care of young people in transition between paediatric and adult services should be planned and managed according to the best practice guidance described in Transition: getting it right for young people..

Adult and paediatric healthcare teams should work jointly to provide assessment and services to young people with anaemia of CKD. Diagnosis and management should be reviewed throughout the transition process, and there should be clarity about who is the lead clinician to ensure continuity of care.

Key priorities for implementation

The following recommendations have been identified as priorities for implementation.

When to begin treating the anaemia

- Consider investigating and managing anaemia in people with CKD if:
  - their Hb level falls to 11 g/dl or less (or 10.5 g/dl or less if younger than 2 years) **or**
  - they develop symptoms attributable to anaemia (such as tiredness, shortness of breath, lethargy and palpitations). **[new 2011]**

Who should receive ESAs

- Treatment with erythropoiesis-stimulating agents (ESAs) should be offered to people with anaemia of CKD who are likely to benefit in terms of quality of life and physical function. **[2006]**

Agreeing a plan for ESA treatment

- ESA treatment should be clinically effective, consistent and safe in people with anaemia of CKD. To achieve this, the prescriber and patient should agree a plan that is patient-centred and includes:
  - continuity of drug supply
  - flexibility of where the drug is delivered and administered
  - the lifestyle and preferences of the patient
  - cost of drug supply
  - desire for self-care where appropriate
  - regular review of the plan in light of changing needs. **[2006]**

Aspirational range and action thresholds for Hb

- When determining individual aspirational Hb ranges for people with anaemia of CKD, take into account:
  - patient preferences
  - symptoms and comorbidities
  - the required treatment. **[new 2011]**
- The correction to normal levels of Hb with ESAs is not usually recommended in people with anaemia of CKD.
  - Typically maintain the aspirational Hb range between 10 and 12 g/dl for adults, young people and children aged 2 years and older, and between 9.5 and 11.5 g/dl for children younger than 2 years of age, reflecting the lower normal range in that age group.
  - To keep the Hb level within the aspirational range, do not wait until Hb levels are outside the aspirational range before adjusting treatment (for example, take action when Hb levels are within 0.5 g/dl of the range's limits). **[new 2011]**

Age

- Age alone should not be a determinant for treatment of anaemia of CKD. **[2006]**

Iron supplementation: aspirational ranges

- People receiving ESA maintenance therapyshould be given iron supplements to keep their:
  - serum ferritin levels between 200 and 500 micrograms/l in both haemodialysis and non-haemodialysis patients, **and either**
    - transferrin saturation level above 20% (unless ferritin is greater than 800 micrograms/l) **or**
    - percentage hypochromic red cells (%HRC) less than 6% (unless ferritin is greater than 800 micrograms/l).

      In practice it is likely this will require intravenous iron. **[2006]**

1 Guidance

The following guidance is based on the best available evidence. The full guideline gives details of the methods and the evidence used to develop the guidance.

This guideline gives recommendations for adults, young people and children. Where the recommendations are different for children, details are given separately.

1.1 Diagnostic evaluation and assessment of anaemia

1.1.1 Diagnostic role of Hb levels

1.1.1.1 Consider investigating and managing anaemia in people with CKD if:

- their Hb level falls to 11 g/dl or less (or 10.5 g/dl or less if younger than 2 years) **or**
- they develop symptoms attributable to anaemia (such as tiredness, shortness of breath, lethargy and palpitations). **[new 2011]**

1.1.2 Diagnostic role of glomerular filtration rate

1.1.2.1 An estimated glomerular filtration rate (eGFR) of less than 60 ml/min/1.73m^2 should trigger investigation into whether anaemia is due to CKD. When the eGFR is greater than or equal to 60 ml/min/1.73m^2 the anaemia is more likely to be related to other causes. **[2006]**

1.1.3 Diagnostic tests to determine iron status

1.1.3.1 Serum ferritin levels may be used to assess iron deficiency in people with CKD. Because serum ferritin is an acute-phase reactant and frequently raised in CKD, the diagnostic cut-off value should be interpreted differently to non-CKD patients. **[2006]**

1.1.3.2 Iron-deficiency anaemia should be[1]:

- diagnosed in people with stage 5 CKD with a ferritin level of less than 100 micrograms/l

- considered in people with stage 3 and 4 CKD if the ferritin level is less than 100 micrograms/l. **[2006]**

1.1.3.3 In people with CKD who have serum ferritin levels greater than 100 micrograms/l, functional iron deficiency (and hence, those patients who are most likely to benefit from intravenous iron therapy) should be defined by:

- percentage of hypochromic red cells greater than 6%, where the test is available **or**
- transferrin saturation less than 20%, when the measurement of the percentage of hypochromic red cells is unavailable. **[2006]**

1.1.4 Measurement of erythropoietin

1.1.4.1 Measurement of erythropoietin levels for the diagnosis or management of anaemia should not be routinely considered for people with anaemia of CKD.**[2006]**

1.2 Management of anaemia

1.2.1 Initiation of ESA therapy in iron-deficient patients

1.2.1.1 ESA therapy should not be initiated in the presence of absolute iron deficiency without also managing the iron deficiency. **[2006]**

1.2.1.2 In people with functional iron deficiency, iron supplements should be given concurrently when initiating ESA therapy. **[2006]**

1.2.2 Maximum iron levels in people with anaemia of CKD

1.2.2.1 In people treated with iron, serum ferritin levels should not rise above 800 micrograms/l. In order to prevent this, the dose of iron should be reviewed when serum ferritin levels reach 500 micrograms/l. **[2006]**

1.2.3 Clinical utility of ESA therapy in iron-replete patients

1.2.3.1 The pros and cons of a trial of anaemia management should be discussed between the clinician, the person with anaemia of CKD, and their families and carers if applicable. **[2006]**

1.2.3.2 ESAs need not be administered where the presence of comorbidities, or the prognosis, is likely to negate the benefits of correcting the anaemia. **[2006]**

1.2.3.3 A trial of anaemia correction should be initiated when there is uncertainty over whether the presence of comorbidities, or the prognosis, would negate benefit from correcting the anaemia with ESAs. **[2006]**

1.2.3.4 Where a trial of ESA therapy has been performed, the effectiveness of the trial should be assessed after an agreed interval. Where appropriate, a mutual decision should be agreed between the clinician, the person with anaemia of CKD and their families and carers on whether or not to continue ESA therapy. **[2006]**

1.2.3.5 All people started on ESA therapy should be reviewed after an agreed interval in order to decide whether or not to continue using ESAs. **[2006]**

1.2.4 Nutritional supplements

1.2.4.1 Supplements of vitamin C, folic acid or carnitine should not be prescribed as adjuvants specifically for the treatment of anaemia of CKD. **[2006]**

1.2.5 Androgens

1.2.5.1 In people with anaemia of CKD, androgens should not be used to treat the anaemia. **[2006]**

1.2.6 Hyperparathyroidism

1.2.6.1 In people with anaemia of CKD, clinically relevant hyperparathyroidism should be treated to improve the management of the anaemia. **[2006]**

1.2.7 Patient-centred care: ESAs

1.2.7.1 People offered ESA therapy and their GPs should be given information about why ESA therapy is required, how it works and what benefits and side effects may be experienced. **[2006]**

1.2.7.2 When managing the treatment of people with anaemia of CKD, there should be agreed protocols defining roles and responsibilities of healthcare professionals in primary and secondary care. **[2006]**

1.2.7.3 People receiving ESA therapy should be informed about the importance of concordance with therapy and the consequences of poor concordance. **[2006]**

1.2.7.4 When prescribing ESA therapy, healthcare professionals should take into account patient preferences about supervised- or self-administration, dose frequency, pain on injection, method of supplying ESA and storage. **[2006]**

1.2.7.5 In order for people to self-administer their ESA in a way that is clinically effective and safe, arrangements should be made to provide ready, reasonable and uninterrupted access to supplies. **[2006]**

1.2.8 Patient education programmes

1.2.8.1 Culturally and age-appropriate patient education programmes should be offered to all people diagnosed with anaemia of CKD (and their families and carers). These should be repeated as requested, and according to the changing circumstances of the patient. They should include the following key areas.

- Practical information about how anaemia of CKD is managed.
- Knowledge (for example, about symptoms, iron management, causes of anaemia, associated medications, phases of treatment).
- Professional support (for example, contact information, community services, continuity of care, monitoring, feedback on progress of results).

- Lifestyle (for example, diet, physical exercise, maintaining normality, meeting other patients).
- Adaptation to chronic disease (for example, previous information and expectations, resolution of symptoms). **[2006]**

1.3 Assessment and optimisation of erythropoiesis

1.3.1 Benefits of treatment with ESAs

1.3.1.1 Treatment with ESAs should be offered to people with anaemia of CKD who are likely to benefit in terms of quality of life and physical function. **[2006]**

1.3.2 Blood transfusions

1.3.2.1 In people with anaemia of CKD in whom kidney transplant is a treatment option, blood transfusions should be avoided where possible. **[2006]**

1.3.2.2 In people with anaemia of CKD, there may be situations where a transfusion is indicated clinically. In these cases, the relevant haematology guidelines should be followed[-]. **[2006]**

1.3.3 Comparison of ESAs

1.3.3.1 The choice of ESA should be discussed with the person with anaemia of CKD when initiating treatment and at subsequent review, taking into consideration the patient's dialysis status, the route of administration and the local availability of ESAs. There is no evidence to distinguish between ESAs in terms of efficacy. **[2006]**

1.3.4 Coordinating care

1.3.4.1 People with anaemia of CKD should have access to a designated contact person or persons who have principal responsibility for their anaemia management and who have skills in the following activities.

- Monitoring and managing a caseload of patients in line with locally agreed protocols.

- Providing information, education and support to empower patients and their families and carers to participate in their care.
- Coordinating an anaemia service for people with CKD, working between secondary and primary care and providing a single point of contact, to ensure patients receive a seamless service of the highest standard.
- Prescribing medicines related to anaemia management and monitoring their effectiveness. **[2006]**

1.3.5 Providing ESAs

1.3.5.1 ESA therapy should be clinically effective, consistent and safe in people with anaemia of CKD. To achieve this, the prescriber and patient should agree a plan that is patient-centred and includes:

- continuity of drug supply
- flexibility of where the drug is delivered and administered
- the lifestyle and preferences of the patient
- cost of drug supply
- desire for self-care where appropriate
- regular review of the plan in light of changing needs. **[2006]**

1.3.6 ESAs: optimal route of administration

1.3.6.1 The person with anaemia of CKD and the prescriber should agree (and revise as appropriate) the route of administration of ESAs, taking into account the following factors:

- patient population (for example, haemodialysis patients)
- pain of injection
- frequency of administration
- the lifestyle and preferences of the patient

- efficacy (for example, subcutaneous versus intravenous administration, or long-acting versus short-acting preparations)
- cost of drug supply. **[2006]**

1.3.6.2 The prescriber should take into account that when using short-acting ESAs, subcutaneous injection allows the use of lower doses of drugs than intravenous administration. **[2006]**

1.3.7 ESAs: dose and frequency

1.3.7.1 When correcting anaemia of CKD, the dose and frequency of ESA should be:

- determined by the duration of action and route of administration of the ESA
- adjusted to keep the rate of Hb increase between 1 and 2 g/dl/month. **[2006]**

1.3.8 Optimal Hb levels

1.3.8.1 When determining individual aspirational Hb ranges for people with anaemia of CKD, take into account:

- patient preferences
- symptoms and comorbidities
- the required treatment. **[new 2011]**

1.3.8.2 The correction to normal levels of Hb with ESAs is not usually recommended in people with anaemia of CKD.

- Typically maintain the aspirational Hb range between 10 and 12 g/dl for adults, young people and children aged 2 years and older, and between 9.5 and 11.5 g/dl for children younger than 2 years of age, reflecting the lower normal range in that age group.
- To keep the Hb level within the aspirational range, do not wait until Hb levels are outside the aspirational range before adjusting treatment (for example, take action when Hb levels are within 0.5 g/dl of the range's limits). **[new 2011]**

1.3.8.3 Consider accepting Hb levels below the agreed aspirational range if:

- high doses[3] of ESAs are required to achieve the aspirational range **or**
- the aspirational range is not achieved despite escalating ESA doses. **[new 2011]**

1.3.8.4 Consider accepting Hb levels above the agreed aspirational range when:

- these develop with iron therapy alone **or**
- these develop with low doses of ESAs **or**
- it is thought that the person might benefit (for example, if they have a physically demanding job) **or**
- the absolute risk of cerebrovascular disease is thought to be low. **[new 2011]**

1.3.8.5 Age alone should not be a determinant for treatment of anaemia of CKD. **[2006]**

1.3.9 Adjusting ESA treatment

1.3.9.1 Iron status should be optimised before or coincident with the initiation of ESA administration and during maintenance treatment with ESAs[4]. **[2006, amended 2011]**

1.3.9.2 Use of angiotensin-converting enzyme (ACE) inhibitors or angiotensin type II receptor antagonists is not precluded, but if they are used, an increase in ESA therapy should be considered. **[2006]**

1.3.9.3 Hb measurements should be taken into account when determining the dose and frequency of ESA administration.

- The cause of an unexpected change in Hb level should be investigated (that is, intercurrent illness, bleeding) to enable intervention and iron status should be optimised[5].
- ESA dose and/or frequency should be increased or decreased when Hb measurements fall outside action thresholds (usually below 10.5 g/dl or above

11.5 g/dl), or for example when the rate of change of Hb suggests an established trend (for example, greater than 1 g/dl/month).**[2006, amended 2011]**

1.3.10 Treating iron deficiency: correction

1.3.10.1 People with anaemia of CKD who are receiving ESAs should be given iron therapy to maintain:

- serum ferritin level greater than 200 micrograms/l
- transferrin saturation greater than 20% (unless ferritin is greater than 800 micrograms/l)
- percentage hypochromic red blood cells less than 6% (unless ferritin is greater than 800 micrograms/l).

Most patients will require 600–1000 mg of iron for adults or equivalent doses for children, in a single or divided dose depending on the preparation. Patients with functional iron deficiency should be treated with intravenous iron. Peritoneal dialysis and non-dialysis patients who do not respond to oral iron will require intravenous iron. In appropriate circumstances, iron treatment can also be administered in the community. **[2006]**

1.3.10.2 In non-dialysis patients with anaemia of CKD in whom there is evidence of absolute or functional iron deficiency, this should be corrected before deciding whether ESA therapy is necessary. **[2006]**

1.3.11 Treating iron deficiency: maintenance

1.3.11.1 Once ferritin levels are greater than 200 micrograms/l, and the percentage hypochromic red cells is less than 6% or transferrin saturation is greater than 20%, people with anaemia of CKD who are receiving ESAs should be given maintenance iron. The dosing regimen will depend on modality, for example haemodialysis patients will require the equivalent of 50–60 mg intravenous iron per week (or an equivalent dose in children of 1 mg/kg/week). Peritoneal dialysis and non-dialysis patients who do not respond to oral iron will require intravenous iron. **[2006]**

1.3.12 ESAs: monitoring iron status during treatment

1.3.12.1 People receiving ESA maintenance therapy should be given iron supplements to keep their:

- serum ferritin levels between 200 and 500 micrograms/l in both haemodialysis and non-haemodialysis patients, **and either**
  - transferrin saturation level above 20% (unless ferritin is greater than 800 micrograms/l) **or**
  - percentage hypochromic red cells (%HRC) less than 6% (unless ferritin is greater than 800 micrograms/l)

  In practice it is likely this will require intravenous iron. **[2006]**

1.4 Monitoring treatment of anaemia of CKD

1.4.1 Monitoring iron status

1.4.1.1 People with anaemia of CKD should not have iron levels checked earlier than 1 week after receiving intravenous iron. The length of time to monitoring of iron status is dependent on the product used and the amount of iron given. **[2006]**

1.4.1.2 Routine monitoring of iron stores should be at intervals of 4 weeks to 3 months. **[2006]**

1.4.2 Monitoring Hb levels

1.4.2.1 In people with anaemia of CKD, Hb should be monitored:

- every 2–4 weeks in the induction phase of ESA therapy
- every 1–3 months in the maintenance phase of ESA therapy
- more actively after an ESA dose adjustment
- in a clinical setting chosen in discussion with the patient, taking into consideration their convenience and local healthcare systems. **[2006]**

1.4.3 Detecting ESA resistance

1.4.3.1 After other causes of anaemia, such as intercurrent illness or chronic blood loss have been excluded, people with anaemia of CKD should be considered resistant to ESAs when:

- an aspirational Hb range is not achieved despite treatment with 300 IU/kg/week or more of subcutaneous epoetin or 450 IU/kg/week or more of intravenous epoetin or 1.5 micrograms/kg/week of darbepoetin, **or**
- there is a continued need for the administration of high doses of ESAs to maintain the aspirational Hb range. **[2006]**

1.4.3.2 In people with CKD, pure red cell aplasia (PRCA) is indicated by a low reticulocyte count, together with anaemia and the presence of neutralising antibodies. The Guideline Development Group considered that PRCA should be confirmed by the presence of anti-erythropoietin antibodies together with a lack of pro-erythroid progenitor cells in the bone marrow. **[2006]**

1.4.3.3 In people with anaemia of CKD, aluminium toxicity should be considered as a potential cause of a reduced response to ESAs after other causes, such as intercurrent illness and chronic blood loss, have been excluded. **[2006]**

1.4.4 Managing ESA resistance

1.4.4.1 In haemodialysis patients with anaemia of CKD in whom aluminium toxicity is suspected, a desferrioxamine test should be performed and the patient's management reviewed accordingly. **[2006]**

1.4.4.2 Consider specialist referral for ESA-induced PRCA. **[2006, amended 2011]**

[1] Stages of chronic kidney disease

Stage	GFR (ml/min/ 1.73m ^{2})	Description

1	> 90	Normal or increased GFR, with other evidence of kidney damage
2	60–89	Slight decrease in GFR, with other evidence of kidney damage
3a	45–59	Moderate decrease in GFR, with or without other evidence of kidney damage
3b	30–44	
4	15–29	Severe decrease in GFR, with or without other evidence of kidney damage
5	< 15	Established renal failure
Diagnosis should be on the basis of evidence of CKD for ≥ 3 months.		

[2] Chapman JF, Elliott C, Knowles SM et al. (2004) Guidelines for compatibility procedures in blood transfusion laboratories. Transfusion Medicine 14(1): 59–73.

[3] > 175 IU/kg/week for haemodialysis population; > 125 IU/kg/week for peritoneal dialysis population; > 100 IU/kg/week for non-dialysis population (Data provided by the National Renal Registry and GDG expert opinion).

[4] Amended to clarify that iron status should be monitored during ESA maintenance treatment (see 1.3.12.1).

[5] Amended to show iron status should be optimised following an unexpected change in Hb level.

2 Notes on the scope of the guidance

NICE guidelines are developed in accordance with a scope that defines what the guideline will and will not cover. The scope of this guideline is available – click on 'How this guidance was produced'.

This guideline sets out best practice guidance on the care of children and adults who have a clinical diagnosis of anaemia associated with CKD, in primary, secondary and tertiary NHS care settings. This includes the care of people with pre-dialysis CKD, people with established renal failure receiving renal replacement therapy, people with established renal failure receiving conservative management, and people after renal transplant surgery.

The guideline does not cover the care of people with anaemia with CKD where CKD is not the principal cause of the anaemia.

How this guideline was developed

NICE commissioned the National Clinical Guideline Centre to develop this guideline. The Centre established a Guideline Development Group (see appendix A), which reviewed the evidence and developed the recommendations. An independent Guideline Review Panel oversaw the development of the guideline (see appendix B).

There is more information about how NICE clinical guidelines are developed on the NICE website. A booklet, 'How NICE clinical guidelines are developed: an overview for stakeholders, the public and the NHS' is available.

3 Implementation

NICE has developed tools to help organisations implement this guidance.

4 Research recommendations

In 2006 the Guideline Development Group made the following recommendations for research, based on its review of evidence, to improve NICE guidance and patient care in the future. The Guideline Development Group's full set of research recommendations is detailed in the full guideline (see section 5).

4.1 Intravenous iron in children

A prospective study of adequate duration of intravenous iron preparations in children with anaemia of CKD, including safety, dosing and efficacy outcomes.

Why this is important

There is very little evidence relating to anaemia of CKD in children. It is known that there is a range of iron levels for adults outside which adverse outcomes become more likely, and this helps guide monitoring and treatment adjustment in anaemia correction and maintenance. In children, there is likely to be much greater variation between individuals.

4.2 Trials of ESAs in children

Trials of ESAs in children with anaemia of CKD (including darbepoetin, which is currently not licensed for use in children younger than 12 years), including safety, dosing and efficacy outcomes.

Why this is important

As for 4.1, there is very little evidence relating to anaemia of CKD in children. ESAs are a key therapy and therefore more data are needed in order to define suitable treatment regimens.

4.3 Hb levels in older people

An observational study of Hb levels and adverse outcomes in older people.

Why this is important

Evidence suggests that anaemia due to reduced erythropoiesis occurs even in early stages of CKD. This may be undetected and is associated with adverse outcomes in older people. A better understanding of the Hb levels associated with adverse outcomes in older people would enable improved detection of anaemia of CKD and reduction of risk.

4.4 ESA tolerance test

A trial of an ESA tolerance test including collection of data on ESA regimens and Hb levels achieved.

Why this is important

A better understanding of the practical impact of ESA tolerance testing on treatment and outcomes would clarify whether such tests are useful, particularly in terms of tailoring ESAs and optimal Hb levels for individual patients depending on their response.

4.5 Iron levels in pre-dialysis patients

A randomised controlled trial to assess Hb level as an outcome in pre-dialysis patients treated to serum ferritin levels lower than 200 micrograms/l versus those treated to 300–500 micrograms/l.

Why this is important

The ferritin level up to which pre-dialysis patients should be treated to achieve acceptable Hb (and at which ESAs are considered if Hb is still inadequate) is not well addressed in the evidence base.

5 Other versions of this guideline

5.1 Full guideline

The full guideline, 'Anaemia management in chronic kidney disease' contains details of the methods and evidence used to develop the guideline. It is published by the National Clinical Guideline Centre, and is available from our website.

5.2 Information for the public

NICE has produced information for the public explaining this guideline.

We encourage NHS and voluntary sector organisations to use text from this information in their own materials about anaemia in CKD.

6 Related NICE guidance

Published

- Chronic kidney disease. NICE clinical guideline 73 (2008).
- Anaemia (cancer-treatment induced) – erythropoietin (alpha and beta) and darbepoetin. NICE technology appraisal guidance 142 (2008).

7 Updating the guideline

NICE clinical guidelines are updated so that recommendations take into account important new information. New evidence is checked 3 years after publication, and healthcare professionals and patients are asked for their views; we use this information to decide whether all or part of a guideline needs updating. If important new evidence is published at other times, we may decide to do a more rapid update of some recommendations. Please see our website for information about updating the guideline.

Appendix A: The Guideline Development Group, National Collaborating Centre and NICE project team

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Ms Christine Howard
National Kidney Research Fund

Ms Karen Jenkins
Royal College of Nursing

Dr Mick Kumwenda
British Renal Society

Professor Alison MacLeod
Cochrane Renal Group

Dr Nyokabi Musila
Research Fellow, NCC-CC

Ms Debbie Nicholl
Health Economist, NCC-CC

Dr Shelagh O'Riordan
British Geriatrics Society

Mrs Alison Richards
Information Scientist, NCC-CC

Ms Alison Roche
Anaemia Nurse Specialist Association

Dr Paul Roderick
Faculty of Public Health

Dr Paul Stevens
Clinical Advisor, NCC-CC

Dr Stephen Thomas
Royal College of Physicians

Dr Eric Will
British Renal Society

Appendix B: The Guideline Review Panel

The Guideline Review Panel is an independent panel that oversees the development of the guideline and takes responsibility for monitoring adherence to NICE guideline development processes. In particular, the panel ensures that stakeholder comments have been adequately considered and responded to. The panel includes members from the following perspectives: primary care, secondary care, lay, public health and industry.

Guideline Review Panel 2011 (partial update)

Dr John Hyslop (Chair)
Consultant Radiologist, Royal Cornwall Hospital NHS Trust

Mrs Sarah Fishburn
Lay member

Mr Kieran Murphy
Health Economics and Reimbursement Manager, Johnson & Johnson Medical Devices and Diagnostics (UK)

Dr Ash Paul
Deputy Medical Director, Health Commission Wales

Professor Liam Smeeth
Professor of Clinical Epidemiology, London School of Hygiene and Tropical Medicine

Guideline Review Panel 2006

Dr Peter Rutherford (Chair)
Senior Lecturer in Nephrology, University of Wales College of Medicine

Dame Helena Shovelton
Chief Executive, British Lung Foundation

Dr Rob Higgins
Consultant in Renal and General Medicine, University Hospitals Coventry and Warwickshire NHS Trust, Coventry

Dr John Young
Medical Director, Merck Sharp & Dohme (MSD)

Appendix C: Technical detail on the criteria for audit

Criterion	Exception	Definition of terms
1. % of people with anaemia of CKD receiving anaemia treatment who are prescribed ESAs, who have a plan recorded as specified.		Patient-centred plan includes: • continuity of drug supply • flexibility of where the drug is delivered and administered • the lifestyle and preferences of the patient • cost of drug supply • desire for self-care where appropriate • regular review of the plan in light of changing needs.

2. % of people with diagnosed anaemia of CKD who have received treatment for 3 months or longer and, at the time of a cross-sectional audit, have Hb levels between 10 and 12 g/dl for adults and children aged over 2 years, or between 9.5 and 11.5 g/dl in children aged under 2 years.	Patients who have underlying causes for poor response (see section 1.4); patients who are in the induction phase of their treatment.	
3. Distribution of age across people with anaemia of CKD receiving treatment is similar to distribution of age across people with anaemia of CKD eligible for treatment (there is no discrimination on the basis of age)		
4. % of people with diagnosed anaemia of CKD on maintenance therapy with ESAs who, at the time of a cross-sectional audit, have: • serum ferritin between 200 and 500 µg/l in both haemodialysis and non-haemodialysis patients, **and either** • transferrin saturation level above 20% (unless ferritin > 800 µg/l) **or** • percentage hypochromic red cells (%HRC) less than 6% (unless ferritin > 800 µg/l)		

Appendix D: Algorithm

The recommendations from this guideline have been incorporated into a NICE Pathway. The full guideline also contains a care pathway overview and algorithms.

About this guideline

NICE clinical guidelines are recommendations about the treatment and care of people with specific diseases and conditions in the NHS in England and Wales.

The guideline was developed by the National Clinical Guideline Centre. The Centre worked with a group of healthcare professionals (including consultants, GPs and nurses), patients and carers, and technical staff, who reviewed the evidence and drafted the recommendations. The recommendations were finalised after public consultation.

The methods and processes for developing NICE clinical guidelines are described in The guidelines manual.

This guideline updates and replaces NICE clinical guideline 30 (published 2006).

The recommendations from this guideline have been incorporated into a NICE Pathway. We have produced information for the public explaining this guideline. Tools to help you put the guideline into practice and information about the evidence it is based on are also available.

Changes after publication

New recommendations have been added for the diagnostic evaluation and assessment of anaemia and the assessment and optimisation of erythropoiesis.

Recommendations are marked as **[2006]**, **[2006, amended 2011]** or **[new 2011].**

- **[2006]** indicates that the evidence has not been updated and reviewed since 2006.
- **[2006, amended 2011]** indicates recommendations where the evidence has not been reviewed since the original guideline but they have been amended because of GDG consensus that they no longer reflect clinical practice or to add clarity; **or** recommendations that need amending to be consistent with new recommendations.

January 2012: minor maintenance

May 2013: minor maintenance

Your responsibility

This guidance represents the view of NICE, 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. However, the guidance does not 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, and informed by the summary of product characteristics of any drugs they are considering.

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 that would be inconsistent with compliance with those duties.

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