

# Chronic kidney disease: managing anaemia

NICE guideline

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## Your responsibility

The recommendations in this guideline represent the view of NICE, arrived at after careful consideration of the evidence available. When exercising their judgement, professionals and practitioners are expected to take this guideline fully into account, alongside the individual needs, preferences and values of their patients or the people using their service. It is not mandatory to apply the recommendations, and the guideline does not override the responsibility to make decisions appropriate to the circumstances of the individual, in consultation with them and their families and carers or guardian.

Local commissioners and providers of healthcare have a responsibility to enable the guideline to be applied when individual professionals and people using services wish to use it. They should do so in the context of local and national priorities for funding and developing services, and in light of their duties to have due regard to the need to eliminate unlawful discrimination, to advance equality of opportunity and to reduce health inequalities. Nothing in this guideline should be interpreted in a way that would be inconsistent with complying with those duties.

Commissioners and providers have a responsibility to promote an environmentally sustainable health and care system and should assess and reduce the environmental impact of implementing NICE recommendations wherever possible.

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This guideline replaces CG114.

## Overview

This guideline covers diagnosing, assessing, managing and monitoring anaemia in people with chronic kidney disease. It aims to improve care for people with chronic kidney disease by specifying how to assess when their anaemia needs treating, and by making detailed recommendations on treatment with erythropoietic stimulating agents (ESAs) and iron. It also covers detecting and managing ESA-resistant anaemia.

## *Who is it for?*

- Healthcare professionals
- Commissioners and providers
- People with chronic kidney disease and their families and carers

## Introduction

Anaemia is defined as a state in which the quality or quantity of circulating red blood cells is below normal. Blood haemoglobin (Hb) concentration serves as the key indicator for anaemia because it can be measured directly and has an international standard. A major cause of anaemia of chronic kidney disease (CKD) is a reduction in erythropoietin production due to kidney damage. Erythropoietin stimulates the bone marrow to produce red blood cells, and it is produced by the kidney in response to low tissue oxygen levels.

Possible adverse effects of anaemia include reduced oxygen use, increased cardiac output, left ventricular hypertrophy, reduced cognition and concentration, reduced libido and reduced immune responsiveness.

The guideline development group for this 2015 update considered the evidence in several areas that provide challenges for clinicians managing anaemia of CKD. Recombinant human erythropoietin (also called EPO, an erythropoietic stimulating agent or ESA) for treating anaemia of CKD is an important tool in managing the condition. But some CKD patients with anaemia who are offered an ESA are 'ESA resistant' – that is, their condition consistently fails to respond to the ESA treatment. These patients often receive large doses of ESA, sometimes with blood transfusion, with limited benefits and at significant cost to the NHS. Many CKD patients with anaemia receiving an ESA are admitted with an intercurrent illness – such as pneumonia – which may temporarily render them acutely hyporesponsive to that ESA. There is uncertainty about the management of these groups of patients, and these areas were considered in the update. The update once again highlighted the often limited trial evidence in nephrology, compared with other specialities.

Over the past decade attention has shifted to the role and management of iron deficiency in anaemia of CKD. In CKD patients there is often a complex inflammatory state that makes it difficult to diagnose iron deficiency when using its standard markers, such as serum iron, serum total iron binding capacity or ferritin. In recent years evidence has been published on newer markers of iron deficiency and intravenous iron preparations. In this 2015 update, the guideline development group reassessed the diagnosis and management of iron deficiency in CKD, and made several recommendations in these areas.

This guideline covers the management of anaemia in adults, children and young people with a clinical diagnosis of anaemia associated with CKD. It does not cover people with anaemia not principally caused by CKD. All parts of the care pathway are covered in the guideline.

There is no universally accepted classification for categorising the population with anaemia of CKD by age. However, for the purposes of this guideline the Guideline Development Group agreed on a pragmatic classification based on the licensing of iron preparations in different age groups. The age groups defined in this guideline are as follows:

- children: 0–13 years
- young people: 14–17 years
- adults: 18 years and over.

### *Safeguarding children*

Remember that child maltreatment:

- is common
- can present anywhere
- may co-exist with other health problems, including anaemia of chronic kidney disease.

See the NICE guideline on [child maltreatment](#) for clinical features that may be associated with maltreatment.

### *Medicines*

The guideline will assume that prescribers will use a medicine's summary of product characteristics to inform decisions made with individual patients.

This guideline recommends some medicines for indications for which they do not have a UK marketing authorisation at the date of publication, if there is good evidence to support that use. The prescriber should follow relevant professional guidance, taking full responsibility for the decision. The patient (or those with authority to give consent on their behalf) should provide informed consent, which should be documented. See the General Medical Council's [Prescribing guidance: prescribing unlicensed medicines](#) for further information. Where recommendations have been made for the use of medicines outside their licensed indications ('off-label use'), these medicines are marked with a footnote in the recommendations.

## Patient-centred care

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

Patients and healthcare professionals have rights and responsibilities as set out in the [NHS Constitution for England](#) – all NICE guidance is written to reflect these. Treatment and care should take into account individual needs and preferences. Patients should have the opportunity to make informed decisions about their care and treatment, in partnership with their healthcare professionals. If the patient is under 16, their family or carers should also be given information and support to help the child or young person to make decisions about their treatment. If it is clear that the child or young person fully understands the treatment and does not want their family or carers to be involved, they can give their own consent. Healthcare professionals should follow the [Department of Health's advice on consent](#). If someone does not have capacity to make decisions, healthcare professionals should follow the [code of practice that accompanies the Mental Capacity Act](#) and the supplementary [code of practice on deprivation of liberty safeguards](#).

NICE has produced guidance on the components of good patient experience in adult NHS services. All healthcare professionals should follow the recommendations in [patient experience in adult NHS services](#).

If a young person is moving between paediatric and adult services, care should be planned and managed according to the best practice guidance described in the Department of Health's [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. The full list of recommendations is in [section 1](#).

### *Diagnostic evaluation and assessment of anaemia*

- Carry out testing to diagnose iron deficiency and determine potential responsiveness to iron therapy and long-term iron requirements every 3 months (every 1–3 months for people receiving haemodialysis).
  - Use percentage of hypochromic red blood cells (% HRC; more than 6%), but only if processing of blood sample is possible within 6 hours.
  - If using percentage of hypochromic red blood cells is not possible, use reticulocyte haemoglobin (Hb) content (CHr; less than 29 pg) or equivalent tests – for example, reticulocyte Hb equivalent.
  - If these tests are not available or the person has thalassaemia or thalassaemia trait, use a combination of transferrin saturation (less than 20%) and serum ferritin measurement (less than 100 micrograms/litre). [new 2015]
- Do not request transferrin saturation or serum ferritin measurement alone to assess iron deficiency status in people with anaemia of chronic kidney disease (CKD). [new 2015]

### *Assessment and optimisation of erythropoiesis*

#### Benefits of treatment with erythropoietic stimulating agents

- Offer treatment with erythropoietic stimulating agents (ESAs) to people with anaemia of CKD who are likely to benefit in terms of quality of life and physical function. [2006]

#### Optimal Hb levels

- The correction to normal levels of Hb with ESAs is not usually recommended in people with anaemia of CKD.
  - Typically<sup>[1]</sup> maintain the aspirational Hb range between 100 and 120 g/litre for adults, young people and children aged 2 years and older, and between 95 and 115 g/litre 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 5 g/litre of the range's limits). [2011, amended 2015]

## ESAs: monitoring iron status during treatment

- Offer iron therapy to people<sup>[2]</sup> receiving ESA maintenance therapy to keep their<sup>[3]</sup>:
  - percentage of hypochromic red blood cells less than 6% (unless serum ferritin is greater than 800 micrograms/litre)
  - reticulocyte Hb count or equivalent tests above 29 pg (unless serum ferritin is greater than 800 micrograms/litre)
  - transferrin saturation level above 20% and serum ferritin level above 100 micrograms/litre (unless serum ferritin is greater than 800 micrograms/litre).

The marker of iron status should be monitored every 1–3 months in people receiving haemodialysis.

In people who are pre-dialysis<sup>[4]</sup> or receiving peritoneal dialysis, levels are typically monitored every 3 months. If these people have a normal full blood count there is little benefit in checking iron status. [new 2015]

## Iron therapy for people who are iron deficient and not on ESA therapy

- Offer iron therapy to people<sup>[2]</sup> with anaemia of CKD who are iron deficient and who are not receiving ESA therapy, before discussing ESA therapy.
  - Discuss the risks and benefits of treatment options. Take into account the person's choice.
  - For people who are not receiving haemodialysis, consider a trial of oral iron before offering intravenous iron therapy. If they are intolerant of oral iron or target Hb levels are not reached within 3 months, (see [recommendation 1.3.11](#)) offer intravenous iron therapy.
  - For people who are receiving haemodialysis, offer intravenous iron therapy. Offer oral iron therapy to people who are receiving haemodialysis only if:
    - ◇ intravenous iron therapy is contraindicated or

- ◊ the person chooses not to have intravenous iron therapy after discussing the relative efficacy and side effects of oral and intravenous iron therapy. [new 2015]
- Discuss the results of the iron therapy with the person or, where appropriate, with their family or carers and offer ESA therapy if needed (see [recommendation 1.3.1](#)). [new 2015]

### Iron therapy for people who are iron deficient and receiving ESA therapy

- Offer iron therapy to people<sup>[2]</sup> with anaemia of CKD who are iron deficient and who are receiving ESA therapy.
  - Discuss the risks and benefits of treatment options. Take into account the person's choice.
  - For adults and young people, offer intravenous iron therapy.
  - For children who are receiving haemodialysis, offer intravenous iron therapy.
  - For children who are not receiving haemodialysis, consider oral iron. If the child is intolerant of oral iron or target Hb levels are not reached within 3 months (see [recommendation 1.3.11](#)), offer intravenous iron therapy. [new 2015]
- When offering intravenous iron therapy to people not receiving haemodialysis, consider high-dose low-frequency<sup>[5]</sup> intravenous iron as the treatment of choice for adults and young people when trying to achieve iron repletion. Take into account all of the following:
  - preferences of the person with anaemia of CKD or, where appropriate, their family or carers
  - nursing and administration costs
  - cost of local drug supply
  - provision of resuscitation facilities.

Intravenous iron administered at a low dose and high frequency<sup>[6]</sup> may be more appropriate for all children<sup>[2]</sup> and for adults who are receiving in-centre haemodialysis. [new 2015]

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<sup>[1]</sup>The [Medicines and Healthcare products Regulatory Agency \(MHRA\) guidance](#) (2007) notes that using ESAs to achieve Hb levels greater than 120 g/litre is associated with an increased risk of death and serious cardiovascular events in people with CKD. The MHRA advises that Hb levels

greater than this should be avoided, and that patients should be monitored closely to ensure that the lowest approved dose of ESA is used to provide adequate control of the symptoms of anaemia. Use of ESAs to achieve Hb levels greater than 120 g/litre is not consistent with UK marketing authorisations for ESAs. If such use is considered, the prescriber should follow relevant professional guidance, taking full responsibility for the decision. Informed consent should be obtained and documented. See the General Medical Council's [Prescribing guidance: prescribing unlicensed medicines](#) for further information.

<sup>[2]</sup> Refer to the Summary of Product Characteristics for the prescription of individual iron preparations. In particular, note that, at the time of publication (June 2015), intravenous iron products available in the UK did not have a UK marketing authorisation for all ages of children and young people for this indication. The prescriber should follow relevant professional guidance, taking full responsibility for the decision. Informed consent should be obtained and documented. See the General Medical Council's [Prescribing guidance: prescribing unlicensed medicines](#) for further information. Note that the marketing authorisation for ferumoxytol in the EU was withdrawn by the manufacturer in March 2015.

<sup>[3]</sup> See recommendation 1.1.3 for tests of choice to determine iron deficiency.

<sup>[4]</sup> There is no accepted definition of pre-dialysis. It is usually regarded to be CKD stages 4 and 5. Pre-dialysis includes people with a failing transplant and people having conservative management.

<sup>[5]</sup> The Guideline Development Group considered this to be a maximum of 2 infusions. For adults, the GDG considered there would be a minimum of 500 mg of iron in each infusion. Refer to the Summary of Product Characteristics for the prescription of individual iron preparations.

<sup>[6]</sup> The Guideline Development Group considered this to be more than 2 infusions. For adults, the GDG considered there would typically be 100 to 200 mg of iron in each infusion. Refer to the Summary of Product Characteristics for the prescription of individual iron preparations.

## 1 Recommendations

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.

The wording used in the recommendations in this guideline (for example, words such as 'offer' and 'consider') denotes the certainty with which the recommendation is made (the strength of the recommendation). See [about this guideline](#) for details.

### 1.1 *Diagnostic evaluation and assessment of anaemia*

#### Diagnostic role of haemoglobin levels

1.1.1 Consider investigating and managing anaemia in people with chronic kidney disease (CKD) if:

- their haemoglobin (Hb) level falls to 110 g/litre or less (or 105 g/litre or less if younger than 2 years) or
- they develop symptoms attributable to anaemia (such as tiredness, shortness of breath, lethargy and palpitations). [2011]

#### Diagnostic role of glomerular filtration rate

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

#### Diagnostic tests to determine iron status and predict response to iron therapy

1.1.3 Carry out testing to diagnose iron deficiency and determine potential responsiveness to iron therapy and long-term iron requirements every 3 months (every 1–3 months for people receiving haemodialysis).

- Use percentage of hypochromic red blood cells (% HRC; more than 6%), but only if processing of blood sample is possible within 6 hours.

- If using percentage of hypochromic red blood cells is not possible, use reticulocyte Hb content (CHR; less than 29 pg) or equivalent tests – for example, reticulocyte Hb equivalent.
- If these tests are not available or the person has thalassaemia or thalassaemia trait, use a combination of transferrin saturation (less than 20%) and serum ferritin measurement (less than 100 micrograms/litre). [new 2015]

1.1.4 Do not request transferrin saturation or serum ferritin measurement alone to assess iron deficiency status in people with anaemia of CKD. [new 2015]

## Measuring erythropoietin

1.1.5 Do not routinely consider measurement of erythropoietin levels for the diagnosis or management of anaemia in people with anaemia of CKD. [2006]

## 1.2 *Managing anaemia*

### Initiation of ESA therapy in iron-deficient patients

1.2.1 ESA (erythropoietic stimulating agent) therapy should not be initiated in the presence of absolute iron deficiency without also managing the iron deficiency. [2006]

### Maximum iron levels in people with anaemia of CKD

1.2.2 In people treated with iron, serum ferritin levels should not rise above 800 micrograms/litre. In order to prevent this, review the dose of iron when serum ferritin levels reach 500 micrograms/litre. [2006]

### Clinical utility of ESA therapy in iron-replete patients

1.2.3 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]

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

- 1.2.5 Initiate a trial of anaemia correction when there is uncertainty over whether the presence of comorbidities, or the prognosis, would negate benefit from correcting the anaemia with ESAs. [2006]
- 1.2.6 Where a trial of ESA therapy has been performed, assess the effectiveness of the trial 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]
- 1.2.7 Review all people started on ESA therapy after an agreed interval in order to decide whether or not to continue using ESAs. [2006]

### **Nutritional supplements**

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

### **Androgens**

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

### **Hyperparathyroidism**

- 1.2.10 In people with anaemia of CKD, treat clinically relevant hyperparathyroidism to improve the management of the anaemia. [2006]

### **Patient-centred care: ESAs**

- 1.2.11 Give people offered ESA therapy and their GPs information about why ESA therapy is required, how it works and what benefits and side effects may be experienced. [2006]
- 1.2.12 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]
- 1.2.13 Inform people receiving ESA therapy about the importance of concordance with therapy and the consequences of poor concordance. [2006]

- 1.2.14 When prescribing ESA therapy, take into account patient preferences about supervised- or self-administration, dose frequency, pain on injection, method of supplying ESA and storage. [2006]
- 1.2.15 In order for people to self-administer their ESA in a way that is clinically effective and safe, make arrangements to provide ready, reasonable and uninterrupted access to supplies. [2006]

## Patient education programmes

- 1.2.16 Offer culturally and age-appropriate patient education programmes 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*

### Benefits of treatment with ESAs

- 1.3.1 Offer treatment with ESAs to people with anaemia of CKD who are likely to benefit in terms of quality of life and physical function. [2006]

### Blood transfusions

- 1.3.2 Avoid blood transfusions where possible in people with anaemia of CKD in whom kidney transplant is a treatment option. [2006]



- 1.3.3 In people with anaemia of CKD, there may be situations where a transfusion is indicated clinically. In these cases, follow the relevant national guidance<sup>[7]</sup>. [2006, amended 2015]

## Comparisons of ESAs

- 1.3.4 Discuss the choice of ESA 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]

## Coordinating care

- 1.3.5 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]

## Providing ESAs

- 1.3.6 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]

## ESAs: optimal route of administration

1.3.7 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]

1.3.8 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]

## ESAs: dose and frequency

1.3.9 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 10 and 20 g/litre/month. [2006]

## Optimal Hb levels

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

- patient preferences

- symptoms and comorbidities
- the required treatment. [2011]

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

- Typically maintain<sup>[6]</sup> the aspirational Hb range between 100 and 120 g/litre for adults, young people and children aged 2 years and older, and between 95 and 115 g/litre 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 5 g/litre of the range's limits). [2011, amended 2015]

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

- high doses<sup>[9]</sup> of ESAs are required to achieve the aspirational range or
- the aspirational range is not achieved despite escalating ESA doses. [2011]

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

## Adjusting ESA treatment

1.3.14 Optimise iron status before or coincident with the initiation of ESA administration and during maintenance treatment with ESAs. [2006, amended 2011]

1.3.15 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]

1.3.16 Take into account Hb measurements when determining the dose and frequency of ESA administration.

- Investigate the cause of an unexpected change in Hb level (that is, intercurrent illness, bleeding) to enable intervention and optimise iron status.

- Increase or decrease ESA dose and/or frequency when Hb measurements fall outside action thresholds (usually below 105 g/litre or above 115 g/litre), or for example when the rate of change of Hb suggests an established trend (for example, greater than 10 g/litre/month). [2006, amended 2011]

## Treating iron deficiency: correction

1.3.17 Offer people with anaemia of CKD who are receiving ESAs iron therapy to achieve<sup>[10]</sup>:

- percentage of hypochromic red blood cells less than 6% (unless ferritin is greater than 800 micrograms/litre)
- reticulocyte Hb count or equivalent tests above 29 pg (unless serum ferritin is greater than 800 micrograms/litre).

If the above tests are not available or the person has thalassaemia or thalassaemia trait, iron therapy should maintain transferrin saturation greater than 20% and serum ferritin level greater than 100 micrograms/litre (unless serum ferritin is greater than 800 micrograms/litre).

Most patients will need 500–1000 mg of iron for adults or equivalent doses for children<sup>[11]</sup>, in a single or divided dose depending on the preparation. Intravenous iron should be administered in a setting with facilities for resuscitation. [new 2015]

## Treating iron deficiency: maintenance

1.3.18 Once percentage of hypochromic red blood cells is less than 6%, reticulocyte Hb count or equivalent tests are above 29 pg, or transferrin saturation is greater than 20% and serum ferritin level is greater than 100 micrograms/litre, offer maintenance iron to people with anaemia of CKD who are receiving ESAs.

The dosing regimen will depend on modality, for example haemodialysis patients will need the equivalent of 50–60 mg intravenous iron per week (or an equivalent dose in children<sup>[11]</sup> of 1 mg/kg/week). [new 2015]

## ESAs: monitoring iron status during treatment

1.3.19 Offer iron therapy to people<sup>[11]</sup> receiving ESA maintenance therapy to keep their<sup>[10]</sup>:

- percentage of hypochromic red blood cells less than 6% (unless serum ferritin is greater than 800 micrograms/litre)
- reticulocyte Hb count or equivalent tests above 29 pg (unless serum ferritin is greater than 800 micrograms/litre)
- transferrin saturation level above 20% and serum ferritin level above 100 micrograms/litre (unless serum ferritin is greater than 800 micrograms/litre).

The marker of iron status should be monitored every 1–3 months in people receiving haemodialysis.

In people who are pre-dialysis<sup>[12]</sup> or receiving peritoneal dialysis, levels are typically monitored every 3 months. If these people have a normal full blood count there is little benefit in checking iron status. [new 2015]

## Iron therapy for people who are iron deficient and not on ESA therapy

1.3.20 Offer iron therapy to people<sup>[11]</sup> with anaemia of CKD who are iron deficient and who are not receiving ESA therapy, before discussing ESA therapy.

- Discuss the risks and benefits of treatment options. Take into account the person's choice.
- For people who are not receiving haemodialysis, consider a trial of oral iron before offering intravenous iron therapy. If they are intolerant of oral iron or target Hb levels are not reached within 3 months (see recommendation 1.3.11), offer intravenous iron therapy.
- For people who are receiving haemodialysis, offer intravenous iron therapy. Offer oral iron therapy to people who are receiving haemodialysis only if:
  - intravenous iron therapy is contraindicated or
  - the person chooses not to have intravenous iron therapy after discussing the relative efficacy and side effects of oral and intravenous iron therapy. [new 2015]

1.3.21 Discuss the results of the iron therapy with the person or, where appropriate, with their family or carers and offer ESA therapy if needed (see recommendation 1.3.1). [new 2015]

## Iron therapy for people who are iron deficient and receiving ESA therapy

1.3.22 Offer iron therapy to people<sup>[11]</sup> with anaemia of CKD who are iron deficient and who are receiving ESA therapy.

- Discuss the risks and benefits of treatment options. Take into account the person's choice.
- For adults and young people, offer intravenous iron therapy.
- For children who are receiving haemodialysis, offer intravenous iron therapy.
- For children who are not receiving haemodialysis, consider oral iron. If the child is intolerant of oral iron or target Hb levels are not reached within 3 months (see recommendation 1.3.11), offer intravenous iron therapy. [new 2015]

1.3.23 Offer oral iron therapy to adults and young people who are receiving ESA therapy only if:

- intravenous iron therapy is contraindicated or
- the person chooses not to have intravenous iron therapy after discussing the relative efficacy and side effects of oral and intravenous iron therapy. [new 2015]

1.3.24 When offering intravenous iron therapy to people not receiving haemodialysis, consider high-dose low-frequency<sup>[13]</sup> intravenous iron as the treatment of choice for adults and young people when trying to achieve iron repletion. Take into account all of the following:

- preferences of the person with anaemia of CKD or, where appropriate, their family or carers
- nursing and administration costs
- cost of local drug supply
- provision of resuscitation facilities.

Intravenous iron administered at a low dose and high frequency<sup>[14]</sup> may be more appropriate for all children<sup>[11]</sup> and for adults who are receiving in-centre haemodialysis. [new 2015]

## 1.4 *Monitoring treatment of anaemia of CKD*

### Monitoring iron status

- 1.4.1 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]
- 1.4.2 Routine monitoring of iron stores to prevent iron overload using serum ferritin should be at intervals of 1–3 months. [2006, amended 2015]

### Monitoring Hb levels

- 1.4.3 In people with anaemia of CKD, monitor Hb:
- 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]

### Detecting ESA resistance

- 1.4.4 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]
- 1.4.5 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. Confirm PRCA by the presence of anti-erythropoietin antibodies

together with a lack of pro-erythroid progenitor cells in the bone marrow. [2006]

- 1.4.6 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]

### Managing ESA resistance

- 1.4.7 In haemodialysis patients with anaemia of CKD in whom aluminium toxicity is suspected, perform a desferrioxamine test and review the patient's management accordingly. [2006]
- 1.4.8 Consider specialist referral for ESA-induced PRCA. [2006, amended 2011]

### Role of blood transfusion in managing ESA resistance

- 1.4.9 Consider referring people with ESA resistance to a haematology service, particularly if an underlying haematological disorder is suspected. [new 2015]
- 1.4.10 Evaluate and discuss the risks and benefits of red cell transfusion with the person or, where appropriate, with their family or carers. [new 2015]
- 1.4.11 Take into account the person's symptoms, quality of life, underlying conditions and the chance of a future successful kidney transplant, in addition to Hb levels, when thinking about the need for red cell transfusion. [new 2015]
- 1.4.12 Review the rate of red cell transfusion and consider a trial period of stopping ESA in people who have ESA resistance (typically on haemodialysis and on high-dose ESA) and are having frequent transfusions when:
- all reversible causes of ESA resistance have been taken into account and excluded and
  - the person's condition is otherwise 'stable' (without intercurrent illness such as infection) and
  - the person is receiving adequate dialysis.

Review the rate of red cell transfusion between 1 and 3 months after stopping ESA



therapy. If the rate of transfusion has increased, consider restarting ESA therapy. [new 2015]

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<sup>[7]</sup> NICE is developing the guideline 'Blood transfusion' (publication expected November 2015).

<sup>[8]</sup> The [Medicines and Healthcare products Regulatory Agency \(MHRA\) guidance](#) (2007) notes that using ESAs to achieve Hb levels greater than 120 g/litre is associated with an increased risk of death and serious cardiovascular events in people with CKD. The MHRA advises that Hb levels greater than this should be avoided, and that patients should be monitored closely to ensure that the lowest approved dose of ESA is used to provide adequate control of the symptoms of anaemia. Use of ESAs to achieve Hb levels greater than 120 g/litre is not consistent with UK marketing authorisations for ESAs. If such use is considered, the prescriber should follow relevant professional guidance, taking full responsibility for the decision. Informed consent should be obtained and documented. See the General Medical Council's [Prescribing guidance: prescribing unlicensed medicines](#) for further information.

<sup>[9]</sup> More than 175 international units per kg per week for haemodialysis population; more than 125 international units per kg per week for peritoneal dialysis population; more than 100 international units per kg per week for non-dialysis population. (Data provided by the UK Renal Registry and Guideline Development Group expert opinion.)

<sup>[10]</sup> See recommendation 1.1.3 for tests of choice to determine iron deficiency.

<sup>[11]</sup> Refer to the Summary of Product Characteristics for the prescription of individual iron preparations. At the time of publication (June 2015), intravenous iron products available in the UK did not have a UK marketing authorisation for all ages of children and young people for this indication. The prescriber should follow relevant professional guidance, taking full responsibility for the decision. Informed consent should be obtained and documented. See the General Medical Council's [Prescribing guidance: prescribing unlicensed medicines](#) for further information. Note that the marketing authorisation for ferumoxytol in the EU was withdrawn by the manufacturer in March 2015.

<sup>[12]</sup> There is no accepted definition of pre-dialysis. It is usually regarded to be CKD stages 4 and 5. Pre-dialysis includes people with a failing transplant and people having conservative management.

<sup>[13]</sup> The Guideline Development Group (GDG) considered this to be a maximum of 2 infusions. For adults, the GDG considered there would be a minimum of 500 mg of iron in each infusion. Refer to the Summary of Product Characteristics for the prescription of individual iron preparations.

<sup>[14]</sup> The Guideline Development Group (GDG) considered this to be more than 2 infusions. For adults, the GDG considered there would typically be 100–200 mg of iron in each infusion. Refer to the Summary of Product Characteristics for the prescription of individual iron preparations.

## 2 Research recommendations

The Guideline Development Group has made the following recommendations for research, based on its review of evidence, to improve NICE guidance and patient care in the future.

### 2.1 *Management of anaemia of chronic kidney disease with concurrent illness*

What is the optimal management (in terms of clinical and cost effectiveness) of anaemia of chronic kidney disease (CKD) in patients who are receiving erythropoietic stimulating agents (ESAs) and have a significant concurrent acute infectious illness?

#### **Why this is important**

Chronic kidney disease is a risk factor for mortality in patients who develop acute illness. Acute illness in CKD patients is associated with development, or worsening, of anaemia.

The anaemia of end-stage renal disease is managed primarily with ESAs and intravenous iron. When CKD patients develop acute illness, their anaemia becomes difficult to control. Acute inflammatory response usually renders patients hyporesponsive to treatments for anaemia. In addition, intravenous iron might promote bacterial infection. Many patients may end up having a blood transfusion – in part because of the lack of established guidelines on managing anaemia in CKD patients with acute illness. Little is known about the relative safety of transfusion compared with parenteral iron therapy, with or without ESA therapy.

There is a need for long-term observational studies, as well as prospective randomised controlled trials to compare the effectiveness and safety of treating anaemia in acutely ill CKD patients with parenteral iron, erythropoiesis stimulating agents, blood transfusion or a combination of the 3 different therapies. A large epidemiological or cohort study is needed with a control group (for example, patients admitted to hospital as an emergency with an acute illness, but without anaemia). The study should be adequately powered to detect factors predictive of important end points such as patient survival, deterioration of renal function, the need to initiate renal replacement therapy and prolonged hospital stay.

### 2.2 *Treatment of ESA resistance*

In people with chronic ESA-resistant anaemia of CKD, what is the clinical and cost effectiveness of treating with high-dose ESA compared with blood transfusion?

### **Why this is important**

People with ESA hyporesponsiveness show evidence of increased morbidity and mortality compared with those who respond well to ESA therapy. Poor response to ESA therapy during the haemodialysis treatment period is thought to be associated with worse post-transplant long-term outcomes, including increased all-cause death and higher risk of graft failure. Little is known about the potential risks of maintaining people with CKD on high doses of ESA therapy while they are waiting for a kidney transplant. It is unclear whether high-dose ESA should be continued in people with ESA resistance in an attempt to limit the number of blood transfusions, or whether people should stop ESA treatment and be treated with transfusions alone. The adverse effects differ between the strategies and are likely to have implications for cost and quality of life.

Further research is needed to understand the clinical and cost-effectiveness of these 2 strategies. Long-term prospective observational or matched case-controlled studies are needed to assess the relative safety of large-dose ESA versus no ESA, with or without blood transfusions, on long-term patient and graft survival.

## **2.3 *Treatment of ESA resistance in haemodialysis patients***

What is the most effective type of intervention to treat haemodialysis patients with ESA-resistant anaemia?

### **Why this is important**

Around 5% to 10% of patients with end-stage renal disease show resistance to ESAs. ESA hyporesponsiveness in chronic haemodialysis patients may be associated with increased morbidity and mortality. In addition, pre-transplantation ESA hyporesponsiveness is thought to be associated with increased kidney allograft failure and patient mortality. Studies have shown that immunosuppressants, antioxidants, anti-cytokine therapies and high-flux membranes vary in how much they improve responsiveness to ESA therapy, but all the studies used a small sample size. There is inadequate evidence identified from available literature to inform recommending any intervention to improve ESA responsiveness.

Adequately powered randomised controlled trials are needed to establish the safety and efficacy of interventions to improve responsiveness to ESA therapy.

## 2.4 *Iron therapies for conservative care of anaemia of CKD*

What is the clinical and cost effectiveness of different iron therapies for people with anaemia of CKD opting for conservative care (defined in relation to haemodialysis)?

### **Why this is important**

Conservative care for end-stage renal disease aims to provide control of symptoms, with an emphasis on maintaining the person's quality of life. Anaemia management is a key element of conservative care. People opting for conservative care may prefer to receive treatment closer to home rather than in hospital, even if the treatments available in hospital are more effective. It is important to take into account quality of life and patient choice, as well as medical risks and benefits, when deciding on an anaemia treatment plan. Further research is needed into the clinical and cost-effectiveness of different iron therapies for people opting for conservative care.

## 2.5 *Target haemoglobin levels in conservative management of anaemia of CKD*

In people with anaemia of CKD opting for conservative management, what is the clinical and cost effectiveness of treating to differing target haemoglobin (Hb) levels?

### **Why this is important**

Most studies of ESA therapy involved people who differ considerably from those opting for conservative management. Trial evidence relates to people who tend to be younger, with fewer comorbidities. There are many people, mainly older people in their later seventies and eighties, who opt for conservative management of CKD instead of haemodialysis. They often have several comorbidities. They will usually be treated with an ESA in accordance with guidelines for anaemia management in CKD, with the standard target Hb range, although there is little information on the best target Hb level for this relatively older, less active group of people. A 'usual' target Hb level might reduce their anaemia symptoms. However, a lower target level might have no adverse impact on their health-related quality of life, while reducing the need for healthcare interventions that impair quality of life. A 'lower than usual' or 'permissive' target Hb level might reduce the need for intravenous iron, ESA and hospital or clinic appointments. A trial is needed to compare a 'usual' target Hb level with a 'permissive' target Hb level.

## 3 Other information

### 3.1 *Scope and how this guideline was developed*

NICE guidelines are developed in accordance with a [scope](#) that defines what the guideline will and will not cover.

#### How this guideline was developed

NICE commissioned the National Clinical Guideline Centre to develop this guideline. The Centre established a Guideline Development Group (see [section 4](#)), which reviewed the evidence and developed the recommendations.

The methods and processes for developing NICE clinical guidelines are described in the [guidelines manual](#).

### 3.2 *Related NICE guidance*

Details are correct at the time of publication of the guideline (June 2015). Further information is available on the [NICE website](#).

#### Published

##### *General*

- [Patient experience in adult NHS services](#) (2012) NICE guideline CG138
- [Medicines adherence](#) (2009) NICE guideline CG76

##### *Condition-specific*

- [Chronic kidney disease](#) (2014) NICE guideline CG182
- [Erythropoiesis-stimulating agents \(epoetin and darbepoetin\) for treating anaemia in people with cancer having chemotherapy](#) (2014) NICE technology appraisal guidance 323
- [Acute kidney injury](#) (2013) NICE guideline CG169
- [Peritoneal dialysis](#) (2011) NICE guideline CG125
- [Guidance on home compared with hospital haemodialysis for patients with end-stage renal failure](#) (2002) NICE technology appraisal guidance 48

## Under development

NICE is developing the following guidance:

- Blood transfusion. NICE guideline. Publication expected November 2015.

## 4 The Guideline Development Group, National Collaborating Centre and NICE project team

### 4.1 *Guideline Development Group*

The Guideline Development Group members listed are those for the 2015 update. For the composition of previous Guideline Development Groups, see the full guideline.

#### **Christopher Brown**

Highly Specialist Clinical Lead Pharmacist for Nephrology, Abertawe Bro Morgannwg University Health Board, Swansea

#### **Roy Connell**

Clinical Nurse Specialist, Children's Renal and Urology Unit, Nottingham University Hospitals

#### **Jan Cooper**

Patient and Carer Member, Kidney Research UK and Kidney Patients Association West Midlands Renal Network

#### **Mark Devonald**

Consultant Nephrologist, Nottingham University Hospitals

#### **Belinda Dring**

Anaemia Nurse Specialist, Nottingham University Hospitals

#### **Damian Fogarty**

Senior Lecturer and Consultant Nephrologist, Queen's University Belfast and Chairman, United Kingdom Renal Registry

#### **Kathryn Griffith**

General Practitioner, Unity Health, York

#### **Ashraf Mikhail**

Consultant Renal Physician, Morriston Hospital, Swansea

#### **Nicholas Palmer**

Patient and Carer Member, National Kidney Federation



**Mark Prentice**

Advance Renal Nurse Practitioner, James Paget University Hospital, Great Yarmouth

**Laura Ratcliffe**

Specialist Trainee, Department of Physiology and Pharmacology, University of Bristol

**Suzanne Stephens**

Consultant Paediatric Nephrologist, Birmingham Children's Hospital

**Mark Thomas (Chair)**

Consultant Physician and Nephrologist, Heart of England NHS Foundation Trust

**Wayne Thomas**

Consultant Haematologist, Derriford Hospital, Plymouth

## 4.2 *National Clinical Guideline Centre*

**Susan Latchem (until November 2014)**

Operations Director and Guideline Lead

**Smita Padhi**

Senior Research Fellow

**Jessica Glen**

Research Fellow

**Grace Marsden (until June 2014)**

Senior Health Economist

**David Wonderling**

Head of Health Economics (from June 2014)

Guideline Lead (from November 2014)

**Saoussen Ftouh (until March 2014)**

Senior Research Fellow/Project Manager

**Ben Pordes (from April 2014)**

Project Manager

**Bethany King (from July 2014)**

Document Editor/Process Assistant

**Joanna Ashe**

Information Scientist

### **4.3** *NICE project team*

**Sarah Willett**

Guideline Lead

**Martin Allaby**

Clinical Adviser

**Louise Shires**

Guideline Commissioning Manager

**Joy Carvill**

Guideline Coordinator

**Beth Shaw**

Technical Lead

**Paul Crosland**

Health Economist

**Annette Mead**

Editor

### **4.4** *Declarations of interests*

The following members of the Guideline Development Group made declarations of interests. All other members of the Group stated that they had no interests to declare. The conflicts of interest policy (2007) was followed until September 2014, when an [updated policy](#) was published.

Member	Interest declared	Type of interest	Decision taken
Mark Thomas (Chair)	Local investigator for an Amgen sponsored trial of fortnightly versus monthly darbepoetin dosing in CKD. This has resulted in standard trial fees paid into the departmental Research Fund for research nurse, physician and other costs. The last invoice was paid in May 2012. He has been UK chief investigator for this multinational study, a role that is nominal as it has not required any work or resulted in any payment.	Non-personal, non-specific pecuniary	Declare and participate
Mark Thomas (Chair)	Local investigator for a Vifor sponsored RCT of intravenous Ferinject (ferric carboxymaltose) versus oral iron therapy in treatment of iron deficiency of CKD (the FIND-CKD study). This has resulted in standard trial fees paid into the departmental Research Fund for research nurse, physician and other costs.	Non-personal, specific pecuniary	Passed responsibility for the trial to a colleague
Mark Thomas (Chair)	Attended a meeting at the Birmingham Nephrology Club, sponsored by Amgen, which included a meal, on 03/07/2014.	Personal, non-specific pecuniary	Declare and participate
Mark Thomas (Chair)	His department is involved in PIVOTAL.	Non-personal specific pecuniary	Declare and participate
Roy Connell	Organised the paediatric nephrology nurses conference (March 2014) at which Amgen contributed to the cost of hosting the education day.	Non-personal, non-specific, pecuniary	Declare and participate
Mark Devonald	He was sponsored by Janssen to attend the American Society of Nephrology meeting in November 2012.	Personal, non-specific pecuniary	Declare and participate

Mark Devonald	He is the organiser of the Nottingham acute kidney injury course which received unrestricted educational grants from MSD, Amgen, Boehringer Ingelheim and Shire.	Non-personal, non-specific pecuniary	Declare and participate
Mark Devonald	He is organising an Acute Kidney Injury course which is sponsored by Amgen who manufacture ESAs. The funding is specifically for the course and he will not be receiving any money.	Non-personal, non-specific, pecuniary	Declare and participate
Belinda Dring	Between October 2012 and March 2013: she has undertaken consultancy work for Takeda providing 2 teaching sessions on renal anaemia and processes to negotiate tariff to the sales team. She has also had sponsorship from Janssen-Cilag to attend British Renal Society. She is also an executive member of Anaemia Nurse Specialist Association (ANSA).	Personal, non-specific pecuniary	Declare and participate
Belinda Dring	Co-wrote an article for the Nursing Times on CKD published in the February 2015 issue of the Nursing Times. Received a payment.	Personal, non-specific, pecuniary	Declare and participate
Damian Fogarty	He has previously delivered educational lectures for various pharmaceutical companies on the epidemiology and generic management of CKD and diabetic nephropathy. These were paid by modest honoraria to him directly and were delivered largely to GPs but occasionally related medicine and surgical specialities such as diabetes and vascular surgery. He has also been invited to consultancy and advisory boards on an ad hoc basis usually once per annum. These were also paid by modest honoraria to him directly.	Personal, non-specific, pecuniary	Declare and participate
Damian Fogarty	He attended an investigators' meeting for the PIVOTAL trial of IV iron. This was for Belfast to participate as a recruitment centre.	Non-personal, non-specific, pecuniary	Declare and participate

Kathryn Griffith	<p>25/9/13 Speaker at meeting in Birmingham on atrial fibrillation. Fee and travel expenses paid by Omnium Medical Meetings.</p> <p>26/9/13 Speaker at BMJ Masterclass in Manchester with fee and travel paid by BMJ Education.</p> <p>2/10/13 Speaker at meeting in Bradford on anticoagulation choices for atrial fibrillation. Travel and fee paid by Leeds University pharmacy course.</p>	Personal, non-specific, pecuniary	Declare and participate
Kathryn Griffith	<p>7/9/13 Speaker at meeting on atrial fibrillation arranged by EH Medical Meetings. But sponsored by Bayer. Fee paid to The Society for Professionals with an interest in Cardiovascular Disease in General Practice (CVGP).</p> <p>8/10/13 Speaker at primary care meeting on atrial fibrillation. Fee paid to Unity Health by Boehringer Ingelheim.</p>	Non-personal, non-specific, pecuniary interest	Declare and participate
Kathryn Griffith	<p>14/9/13 Speaker at CVGP meeting in Cambridge sponsored by CVGP and accommodation provided by CVGP.</p> <p>14/10/13 Attended Northern Lights meeting of CVGP which was sponsored by Pfizer but paid for own refreshments and travel.</p>	Personal, non-specific, non-pecuniary	Declare and participate
Kathryn Griffith	Attended the American College of Cardiology in Washington 28–31 March 2014. Travel and accommodation were funded by Boehringer Ingelheim.	Personal, non-specific, pecuniary	Declare and participate

Ashraf Mikhail	<p>He received travel bursary from Johnson &amp; Johnson to attend the European Dialysis and Transplant Association meeting in July 2013.</p> <p>He also helped Xenetics Bio to design a phase II trial in January 2013.</p> <p>He is a member of the Clinical Research Centre (anaemia) within Kidney Research UK</p> <p>He is a co-author on the Renal Association anaemia clinical practice guidelines.</p>	Personal, non-specific, pecuniary	Declare and participate
Ashraf Mikhail	<p>Attended a Kidney Disease Improving Global Outcomes (KDIGO) conference on 'Controversies in iron management'. His food and accommodation were provided by KDIGO.</p>	Personal, non-specific, pecuniary	Declare and participate
Ashraf Mikhail	<p>Principle investigator of the PHARMACOSMOS 'Quality of life after IV iron in CK patients' phase III study starting in January 2015, after guideline development.</p> <p>Principle investigator of the Astellas 'hypoxia inducible factor for anaemia in dialysis patients' phase III study starting in March 2015.</p>	Personal, specific, pecuniary	Declare and participate
Nicholas Palmer	<p>Attended a Baxter-sponsored home dialysis round table discussion in October 2012. His hotel accommodation was paid for and he received a small fee.</p> <p>He also attended World Kidney Day event in March 2013 at Sanofi to provide information on CKD and acute kidney injury. His expenses were paid.</p> <p>He attended a Fresenius sponsored discussion on commissioning in March/April 2013. He was paid a small fee for attending.</p>	Personal, non-specific, pecuniary	Declare and participate
Nicholas Palmer	<p>Attended a holiday dialysis conference in Barcelona sponsored by Diaverum. He gave a talk at this event. The company paid for his accommodation, lunch and dinner.</p>	Personal, non-specific, pecuniary	Declare and participate

Nicholas Palmer	Attended Sanofi global meeting in Dubrovnik at the end of March/April and presented 'A patient's journey with CKD'. Expenses/transport and hotel were paid for.	Personal, non-specific, pecuniary	Declare and participate
Suzanne Stephens	Her husband is an adult haematologist and has been an advisor for Boehringer Ingelheim for work on dabigatran and has given a talk for Pfizer regarding apixaban.	Non-specific, family	Declare and participate
Wayne Thomas	Invited speaker at Sysmex Annual User Meeting. Accommodation and transport paid, but not paid to speak. Subject will be on functional iron deficiency in professional capacity – already written paper (2013).	Personal, non-specific, pecuniary	Declare and participate

## About this guideline

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

NICE guidelines are developed in accordance with a [scope](#) that defines what the guideline will and will not cover.

This guideline was developed by the National Clinical Guideline Centre. The Centre worked with a Guideline Development Group, comprising healthcare professionals (including consultants, GPs and nurses), patients and carers, and technical staff, which 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](#).

NICE produces guidance, standards and information on commissioning and providing high-quality healthcare, social care, and public health services. We have agreements to provide certain NICE services to Wales, Scotland and Northern Ireland. Decisions on how NICE guidance and other products apply in those countries are made by ministers in the Welsh government, Scottish government, and Northern Ireland Executive. NICE guidance or other products may include references to organisations or people responsible for commissioning or providing care that may be relevant only to England.

## *Update information*

This guideline updates and replaces NICE guideline CG114 (published February 2011).



Recommendations are marked as [new 2015], [2011], [2006], [2011, amended 2015] or [2006, amended 2015]:

- [new 2015] indicates that the evidence has been reviewed and the recommendation has been added or updated
- [2011] indicates that the evidence has not been reviewed since 2011
- [2006] indicates that the evidence has not been reviewed since 2006
- [2006, amended 2015] indicates that the evidence has not been reviewed since 2006, but changes have been made to the recommendation wording that change the meaning (see below)
- [2011, amended 2015] indicates that the evidence has not been reviewed since 2011, but changes have been made to the recommendation wording that change the meaning (see below)

## Recommendations from NICE guideline CG114 that have been amended

Recommendations are labelled [2006, amended 2015] or [2011, amended 2015] if the evidence has not been reviewed but changes have been made to the recommendation wording that change the meaning.

Recommendation in 2011 guideline	Recommendation in current guideline	Reason for change
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 <sup>[a]</sup> . [2006] (1.3.2.2)	In people with anaemia of CKD, there may be situations where a transfusion is indicated clinically. In these cases, follow the relevant national guidance <sup>[b]</sup> . [2006, amended 2015] (1.3.3)	The reference has been removed as this evidence has not been reviewed by NICE.  The NICE guideline on blood transfusion is currently in development and will form the basis of relevant haematology guidance in this area. This guideline is expected to publish in November 2015.

<p>The correction to normal levels of Hb with ESAs is not usually recommended in people with anaemia of CKD.</p> <ul style="list-style-type: none"> <li>• 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.</li> <li>• 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] (1.3.8.2)</li> </ul>	<p>The correction to normal levels of Hb with ESAs is not usually recommended in people with anaemia of CKD.</p> <ul style="list-style-type: none"> <li>• Typically<sup>[j]</sup> maintain the aspirational Hb range between 100 and 120 g/litre for adults, young people and children aged 2 years and older, and between 95 and 115 g/litre for children younger than 2 years of age, reflecting the lower normal range in that age group.</li> <li>• 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 5 g/litre of the range's limits). [2011, amended 2015] (1.3.11)</li> </ul>	<p>The footnote was added because it was decided to be more cautious given the findings of the review and the guidance from the <a href="#">Medicines and Health Regulatory Agency</a> with regard to the increased risk of mortality and cardiovascular morbidity associated with higher levels of haemoglobin.</p>
<p>Routine monitoring of iron stores should be at intervals of 4 weeks to 3 months. [2006] (1.4.1.2)</p>	<p>Routine monitoring of iron stores to prevent iron overload using serum ferritin should be at intervals of 1–3 months. [2006, amended 2015] (1.4.2)</p>	<p>Based on new evidence, serum ferritin is now recommended for assessment of iron overload only and not for diagnosis of iron deficiency. This recommendation has been amended to reflect this new evidence base. The frequency of monitoring is also covered elsewhere (see recommendation 1.3.19).</p>

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

<sup>[b]</sup> NICE is developing the guideline 'Blood transfusion' (publication expected November 2015).

<sup>[c]</sup> The [Medicines and Healthcare products Regulatory Agency \(MHRA\) guidance](#) (2007) notes that using ESAs to achieve Hb levels greater than 120 g/litre is associated with an increased risk of death and serious cardiovascular events in people with CKD. The MHRA advises that Hb levels greater than this should be avoided, and that patients should be monitored closely to ensure that the lowest approved dose of ESA is used to provide adequate control of the symptoms of anaemia. Use of ESAs to achieve Hb levels greater than 120 g/litre is not consistent with UK marketing authorisations for ESAs. If such use is considered, the prescriber should follow relevant professional guidance, taking full responsibility for the decision. Informed consent should be obtained and documented. See the General Medical Council's [Prescribing guidance: prescribing unlicensed medicines](#) for further information.

## *Strength of recommendations*

Some recommendations can be made with more certainty than others. The Guideline Development Group makes a recommendation based on the trade-off between the benefits and harms of an intervention, taking into account the quality of the underpinning evidence. For some interventions, the Guideline Development Group is confident that, given the information it has looked at, most patients would choose the intervention. The wording used in the recommendations in this guideline denotes the certainty with which the recommendation is made (the strength of the recommendation).

For all recommendations, NICE expects that there is discussion with the patient about the risks and benefits of the interventions, and their values and preferences. This discussion aims to help them to reach a fully informed decision (see also [patient-centred care](#)).

## **Interventions that must (or must not) be used**

We usually use 'must' or 'must not' only if there is a legal duty to apply the recommendation. Occasionally we use 'must' (or 'must not') if the consequences of not following the recommendation could be extremely serious or potentially life threatening.

## **Interventions that should (or should not) be used – a 'strong' recommendation**

We use 'offer' (and similar words such as 'refer' or 'advise') when we are confident that, for the vast majority of patients, an intervention will do more good than harm, and be cost effective. We use

similar forms of words (for example, 'Do not offer...') when we are confident that an intervention will not be of benefit for most patients.

## **Interventions that could be used**

We use 'consider' when we are confident that an intervention will do more good than harm for most patients, and be cost effective, but other options may be similarly cost effective. The choice of intervention, and whether or not to have the intervention at all, is more likely to depend on the patient's values and preferences than for a strong recommendation, and so the healthcare professional should spend more time considering and discussing the options with the patient.

## **Recommendation wording in guideline updates**

NICE began using this approach to denote the strength of recommendations in guidelines that started development after publication of the 2009 version of 'The guidelines manual' (January 2009). This does not apply to any recommendations ending [2006] (see [update information](#) above for details about how recommendations are labelled). In particular, for recommendations labelled [2006] the word 'consider' may not necessarily be used to denote the strength of the recommendation.

## *Other versions of this 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.

The recommendations from this guideline have been incorporated into a [NICE pathway](#).

We have produced [information for the public](#) about this guideline.

## *Implementation*

[Implementation tools and resources](#) to help you put the guideline into practice are also available.

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## Accreditation

