



*National Institute for
Health and Clinical Excellence*

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Anaemia management in people with chronic kidney disease

NICE clinical guideline 39

Developed by the National Collaborating Centre for Chronic Conditions

NICE clinical guideline 39
Anaemia management in people with chronic kidney disease

Ordering information

You can download the following documents from www.nice.org.uk/CG039

- The NICE guideline (this document) – all the recommendations.
- A quick reference guide – a summary of the recommendations for healthcare professionals.
- ‘Understanding NICE guidance’ – information for patients and carers.
- The full guideline – all the recommendations, details of how they were developed, and summaries of the evidence they were based on.

For printed copies of the quick reference guide or ‘Understanding NICE guidance’, phone the NHS Response Line on 0870 1555 455 and quote:

- N1115 (quick reference guide)
- N1116 (‘Understanding NICE guidance’).

This guidance is written in the following context

This guidance represents the view of the Institute, which was arrived at after careful consideration of the evidence available. Healthcare professionals are expected to take it fully into account when exercising their clinical judgement. The guidance does not, however, override the individual responsibility of healthcare professionals to make decisions appropriate to the circumstances of the individual patient, in consultation with the patient and/or guardian or carer.

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Patient-centred care

This guideline offers best practice advice on the care of people with anaemia of chronic kidney disease (CKD).

Treatment and care should take into account patients' individual needs and preferences. People with anaemia of CKD should have the opportunity to make informed decisions about their care and treatment. Where patients do not have the capacity to make decisions, healthcare professionals should follow the Department of Health guidelines – 'Reference guide to consent for examination or treatment' (2001) (available from www.dh.gov.uk). From April 2007, healthcare professionals will need to follow a code of practice accompanying the Mental Health Act (summary available from www.dca.gov.uk/menincap/bill-summary.htm).

Good communication between healthcare professionals and patients is essential. It should be supported by the provision of evidence-based information offered in a form that is tailored to the needs of the individual patient. The treatment, care and information provided should be culturally appropriate and in a form that is accessible to people who have additional needs, such as people with physical, cognitive or sensory disabilities, and people who do not speak or read English.

Unless specifically excluded by the patient, carers and relatives (including parents where appropriate) should have the opportunity to be involved in decisions about the patient's care and treatment.

Carers and relatives should also be provided with the information and support they need.

Key priorities for implementation

The following recommendations have been identified as priorities for implementation.

When to begin treating the anaemia

- Management of anaemia should be considered in people with anaemia of chronic kidney disease (CKD) when their haemoglobin (Hb) level is less than or equal to 11 g/dl (or 10 g/dl if younger than 2 years of age).

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.

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.

Aspirational range and action thresholds for haemoglobin

- In people with anaemia of CKD, treatment should maintain stable Hb levels between 10.5 and 12.5 g/dl for adults and children older than 2 years of age, and between 10 and 12 g/dl in children younger than 2 years of age, reflecting the lower normal range in that age group. This should be achieved by:
 - adjusting treatment, typically when Hb rises above 12.0 or falls below 11.0 g/dl
 - taking patient preferences, symptoms and comorbidities into account and revising the aspirational range and action thresholds accordingly.

Age

- Age alone should not be a determinant for treatment of anaemia of CKD.

Iron supplementation: aspirational ranges

- 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.

The following guidance is based on the best available evidence. The full guideline ([add hyperlink]) gives details of the methods and the evidence used to develop the guidance (see section 5 for details).

1 Guidance

This guideline gives recommendations for both adults and children. Where the recommendations are different for children, details are given separately (recommendations 1.1.1.1, 1.3.8.1, 1.3.8.2, 1.3.10.1 and 1.3.11.1).

1.1 Diagnostic evaluation and assessment of anaemia

1.1.1 Diagnostic role of Hb levels

1.1.1.1 Management of anaemia should be considered in people with anaemia of chronic kidney disease (CKD) when their haemoglobin (Hb) level is less than or equal to 11 g/dl (or 10 g/dl if younger than 2 years of age).

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/1.73m² should trigger investigation into whether anaemia is due to CKD. When the eGFR is greater than or equal to 60 ml/min/1.73m² the anaemia is more likely to be related to other causes.

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.

1.1.3.2 Iron-deficiency anaemia should be¹:

- 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.

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.

See appendix D for the associated example management algorithm.

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.

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
3	30–59	Moderate decrease in GFR, with or without other evidence of kidney damage
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.

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.
- 1.2.1.2 In people with functional iron deficiency, iron supplements should be given concurrently when initiating ESA therapy.

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.

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.
- 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.
- 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.
- 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.
- 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.

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.

1.2.5 Androgens

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

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.

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.

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.

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

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.

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.

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).

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.

See appendix D for the associated example management algorithm.

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.

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 followed².

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.

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.

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

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.

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.

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.

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.

1.3.8 Optimal Hb levels

1.3.8.1 In people with anaemia of CKD, treatment should maintain stable Hb levels between 10.5 and 12.5 g/dl for adults and children older than 2 years of age, and between 10 and 12 g/dl in children younger than 2 years of age, reflecting the lower normal range in that age group. This should be achieved by:

- adjusting treatment, typically when Hb rises above 12.0 or falls below 11.0 g/dl
- taking patient preferences, symptoms and comorbidities into account and revising the aspirational range and action thresholds accordingly.

1.3.8.2 In people who do not achieve a Hb level above 10.5 g/dl (or 10.0 g/dl in children younger than 2 years of age) despite correction of iron deficiency and exclusion of the known causes of resistance to ESA therapy (defined as 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), lower levels of Hb may have to be accepted.

1.3.8.3 Age alone should not be a determinant for treatment of anaemia of CKD.

1.3.9 Adjusting ESA treatment

1.3.9.1 Iron status should be optimised before or coincident with the initiation of ESA administration.

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.

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.
- ESA dose and/or frequency should be increased or decreased when Hb measurements fall outside action thresholds (usually below 11.0 g/dl or above 12.0 g/dl), or for example when the rate of change of Hb suggests an established trend (for example, greater than 1 g/dl/month).

See appendix D for the associated example management algorithm.

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.

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.

See appendix D for the associated example management algorithm.

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.

See appendix D for the associated example management algorithm.

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.

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 dependant on the product used and the amount of iron given.

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

1.4.2 Monitoring haemoglobin 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.

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.

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.

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.

See appendix D for the associated example management algorithm.

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.

1.4.4.2 ESA-induced PRCA should be managed in accordance with current best practice. Specialist referral should be considered. N.B. Current best practice for this rare condition is available from the PRCA Global Scientific Advisory Board (GSAB; www.prcaforum.com/treatment.php).

See appendix D for the associated example management algorithm.

2 Notes on the scope of the guidance

All NICE guidelines are developed in accordance with a scope document that defines what the guideline will and will not cover. The scope of this guideline was established, after a period of consultation, at the start of the guideline development process; it is available from <http://www.nice.org.uk/page.aspx?o=233992>.

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.

3 Implementation in the NHS

The Healthcare Commission assesses the performance of NHS organisations in meeting core and developmental standards set by the Department of Health in 'Standards for better health' issued in July 2004. Implementation of clinical guidelines forms part of the developmental standard D2. Core standard C5 says that national agreed guidance should be taken into account when NHS organisations are planning and delivering care.

NICE has developed tools to help organisations implement this guidance (listed below). These are available on our website (www.nice.org.uk/CG039).

- *Slides* highlighting key messages for local discussion.
- Costing tools
 - *Costing report* to estimate the national savings and costs associated with implementation.
 - *Costing template* to estimate the local costs and savings involved.
- *Implementation advice* on how to put the guidance into practice and national initiatives which support this locally.

Suggested audit criteria based on the key priorities for implementation are listed in appendix C of this document (see page 26), and can be used to audit practice locally.

4 Research recommendations

The Guideline Development Group has made the following recommendations for research, on the basis of its review of the evidence. The Group regards these recommendations as the most important research areas 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 *Haemoglobin 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.

4.6 Implementation of management algorithm

An observational study of patient management in line with the initial management and maintenance algorithms given in this guideline, with the aim of formally piloting and validating them, or providing evidence for amendments when the guideline is updated.

Why this is important

Protocols and prescribing algorithms for ESAs are in use, including computerised decision support systems. Some of these have been piloted and validated, and it is important that the NICE guideline's algorithm match this standard to provide additional support at the broader scale of management strategies.

5 Other versions of this guideline

The National Institute for Health and Clinical Excellence commissioned the development of this guidance from the National Collaborating Centre for Chronic Conditions. The Centre established a Guideline Development Group, which reviewed the evidence and developed the recommendations. The members of the Guideline Development Group are listed in appendix A. Information about the independent Guideline Review Panel is given in appendix B.

The booklet 'The guideline development process: an overview for stakeholders, the public and the NHS' has more information about the Institute's guideline development process. It is available from www.nice.org.uk/guidelinesprocess.

5.1 Full guideline

The full guideline, 'Anaemia management in chronic kidney disease', is published by the National Collaborating Centre for Chronic Conditions; it is available from [website details to be added], the NICE website (www.nice.org.uk/CG039fullguideline) and the website of the National Library for Health (www.nlh.nhs.uk).

5.2 Quick reference guide

A quick reference guide for healthcare professionals is also available from the NICE website (www.nice.org/CG039quickrefguide) or from the NHS Response Line (telephone 0870 1555 455; quote reference number N1115).

5.3 Understanding NICE guidance: information for patients and carers

A version of this guideline for people with anaemia of chronic kidney disease and their carers is available from our website (www.nice.org.uk/CG039publicinfo) and the NHS Response Line (0870 1555 455; quote reference number N1116).

6 Related NICE guidance

NICE is in the process of developing the following guidance (details available from www.nice.org.uk):

- Chronic kidney disease. *NICE clinical guideline* (publication expected September 2008).
- Erythropoietin for anaemia induced by cancer treatment. *NICE technology appraisal* (publication date to be confirmed).

7 Review date

The process of reviewing the evidence is expected to begin 4 years after the date of issue of this guideline. Reviewing may begin before this if significant evidence that affects the guideline recommendations is identified. The updated guideline will be available within 2 years of the start of the review process.

Appendix A: The Guideline Development Group

Dr Penny Ackland

GP with interest in anaemia of CKD

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Anaemia Nurse Specialist Association

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UK Renal Pharmacy Group

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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.

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

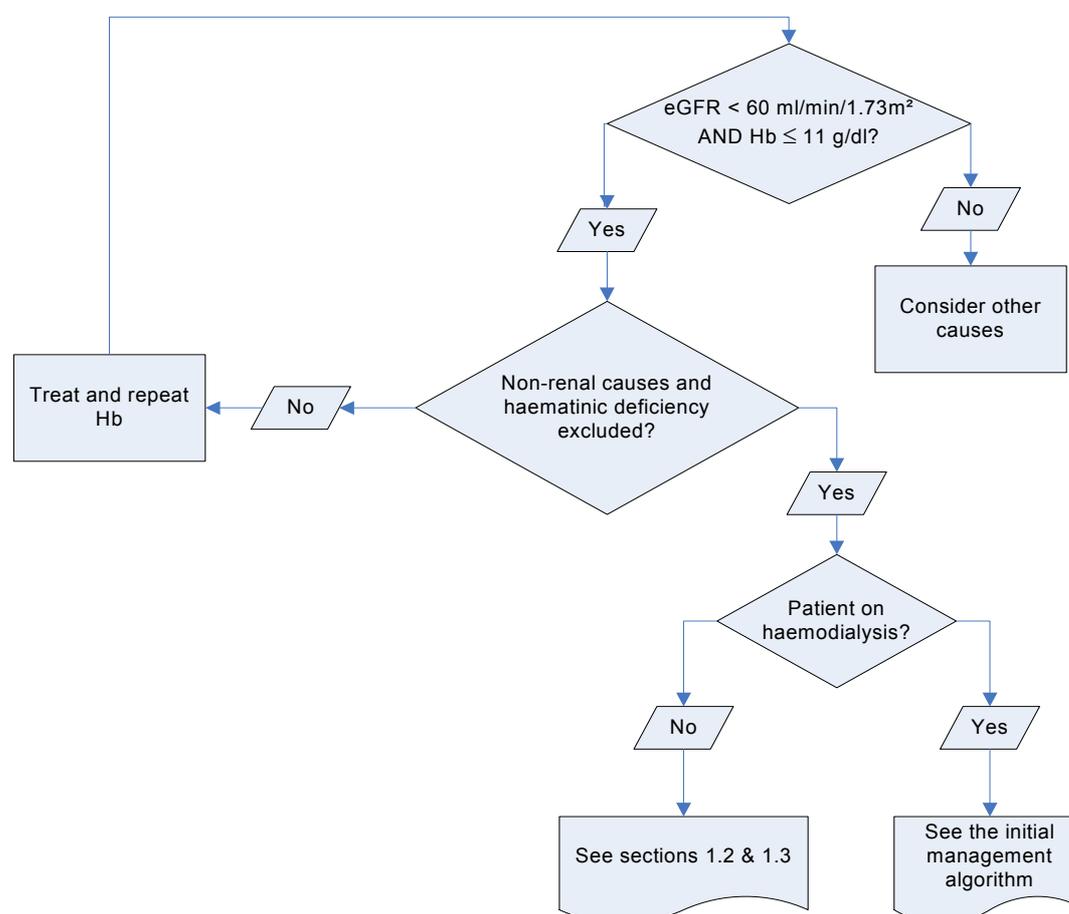
Criterion	Exception	Definition of terms
1. % of people with anaemia of CKD with recorded Hb \leq 11 g/dl (or 10 g/dl if under 2 years of age) who were started on iron/ESAs at the time, or at the following appointment.	<ul style="list-style-type: none"> Documented refusal, contraindications 	
2. % of people with anaemia of CKD with recorded Hb \leq 11 g/dl not on anaemia treatment, with a breakdown of the reasons for it not being offered or taken up by the patient.		
3. % of people with anaemia of CKD receiving anaemia treatment who are prescribed ESAs, who have a plan recorded as specified.		Patient-centred plan includes: <ul style="list-style-type: none"> 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.
4. % 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 10.5 and 12.5 g/dl for adults and children aged over 2 years, or between 10 and 12 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.	
5. 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)		

<p>6. % of people with diagnosed anaemia of CKD on maintenance therapy with ESAs who, at the time of a cross-sectional audit, have:</p> <ul style="list-style-type: none"> • 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) 		
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Appendix D: Algorithms – example management strategies

An algorithm is any set of detailed instructions that results in a predictable end state from a known beginning, ideally presented in an easy to follow decision tree format. Algorithms are only as good as the instructions given, however, and the result will be incorrect if the algorithm is not properly defined. The algorithms presented in this section are suggested management algorithms based on the known literature but importantly, they have not been tested and should be used as guides to aid development of local practice.

Diagnosis of anaemia of CKD in adults



* Test for functional iron deficiency with either:

- ferritin and transferrin saturation (TSAT), or
- ferritin and percentage of hypochromic red cells (%HRC).

Table 1 Test for functional iron deficiency with ferritin and TSAT or ferritin and %HRC

	Ferritin	TSAT%	MCV	%HRC
Functional iron deficiency	> 100 µg/l	< 20	Normal range	> 6
Absolute iron deficiency	< 100 µg/l	< 20	Low	> 6
%HRC, percentage of hypochromic red cells; MCV, mean corpuscular volume; TSAT, transferrin saturation.				

**Initial management algorithm for adult haemodialysis patients
(assumes Hb < 11g/dl)**

Iron dosage schedule

This is an example strategy for adult haemodialysis patients over 50 kg. Treatment should be tailored to individual patients according to the guideline recommendations.

Haemodialysis patients		Non-haemodialysis patients
Induction/loading dose	Maintenance dose	Iron sucrose 200 mg/fortnight × 3 doses or low molecular weight iron dextran 1 g
Either iron sucrose 200 mg/week for 5 weeks or low molecular weight iron dextran 1 g	Iron sucrose 50 mg/week or 100 mg/fortnight	

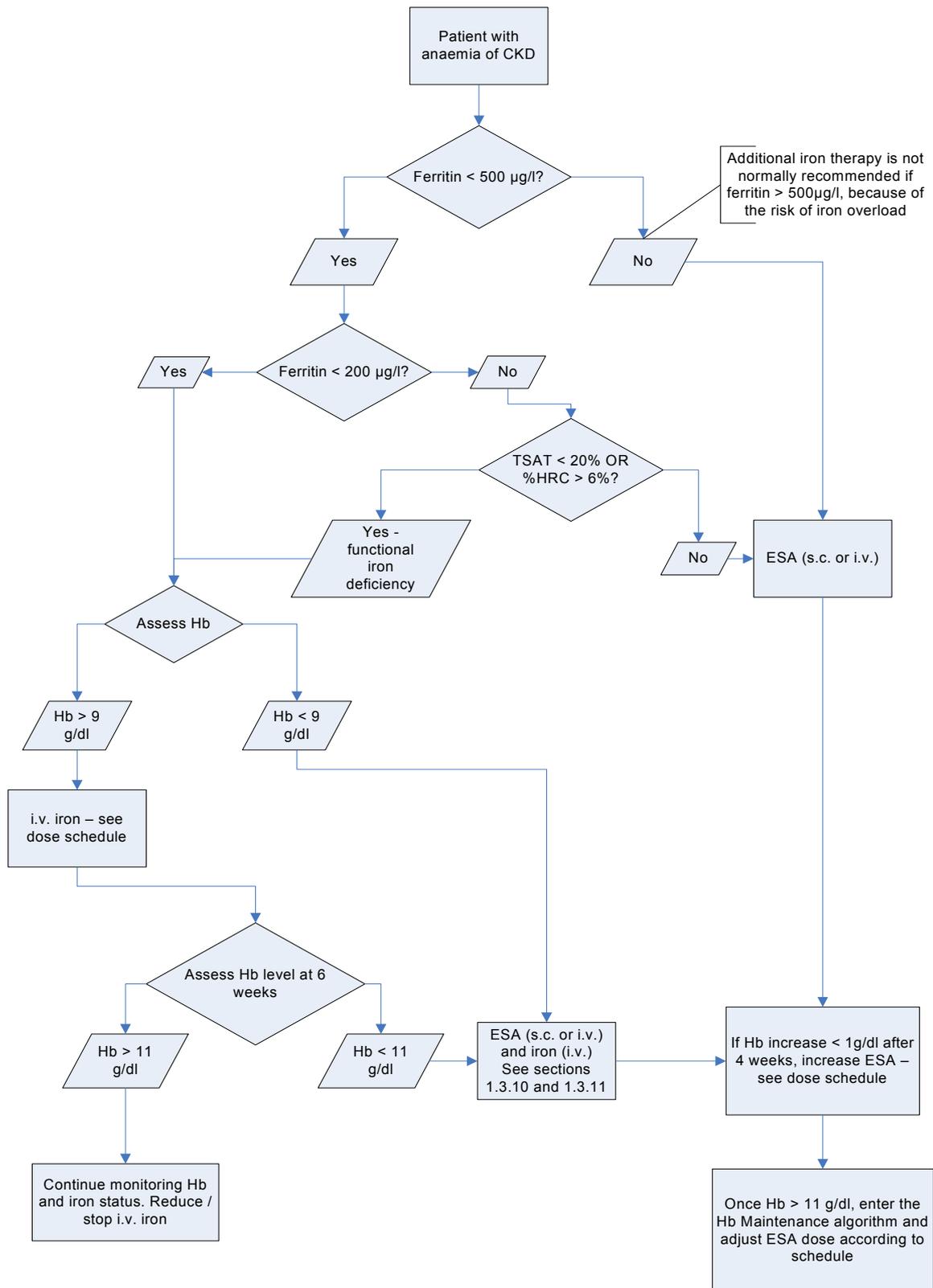
Throughout ESA induction

In people with anaemia of chronic kidney disease, haemoglobin should be monitored:

- every 2–4 weeks in the induction phase of ESA treatment
- every 4–12 weeks in the maintenance phase of ESA treatment
- more actively after an ESA dose adjustment
- in a clinical setting chosen in discussion with the patient, taking into consideration their convenience and local health care systems.

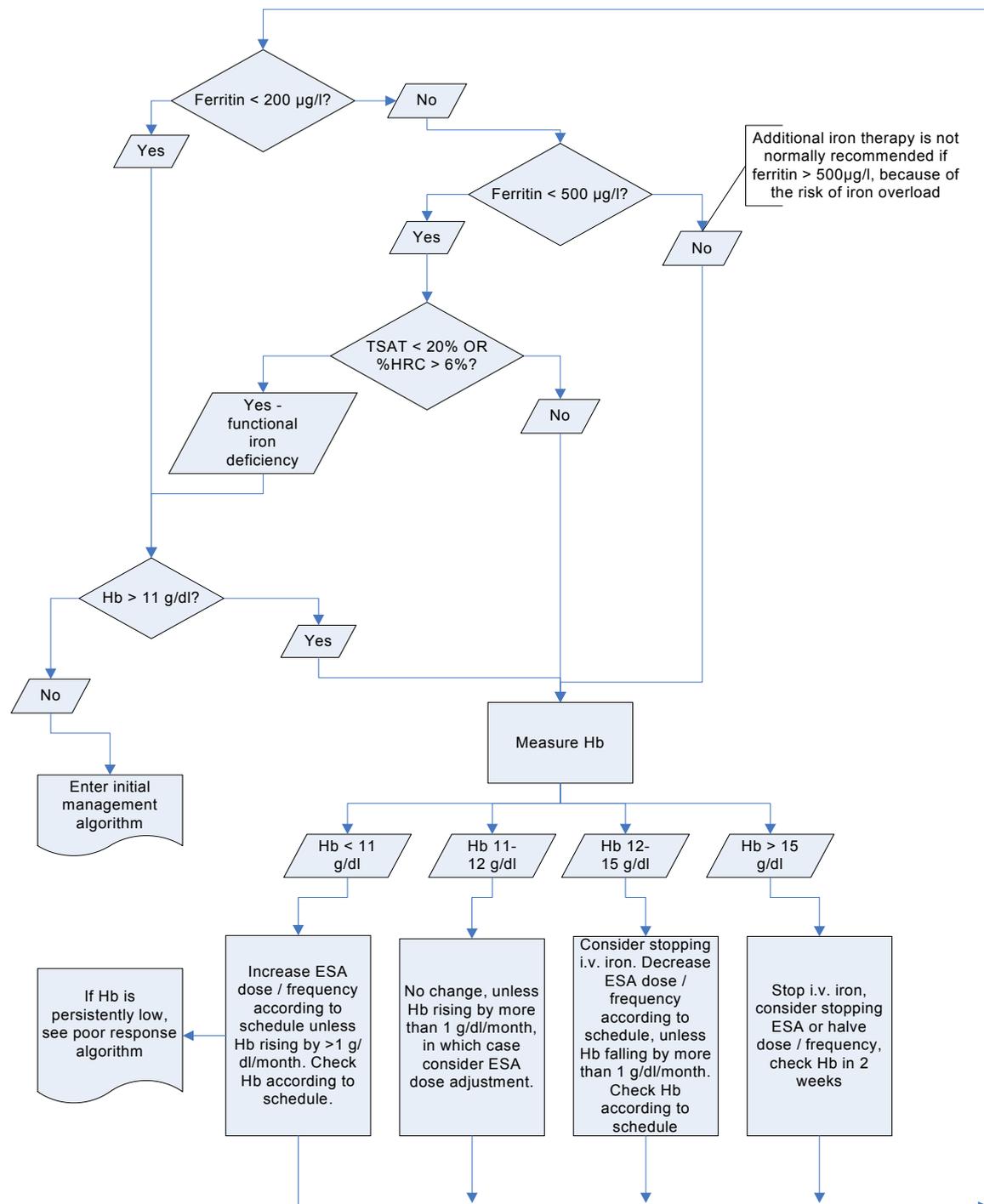
Be aware of side effects and comorbidities

On the following page is an algorithm for an example strategy for adult haemodialysis patients. Treatment should be tailored to individual patients according to the guideline recommendations.



Haemoglobin maintenance algorithm (assumes patient is receiving ESA and maintenance intravenous iron)

This is an example strategy for adult patients. Treatment should be tailored to individual patients according to the guideline recommendations.



ESA adjustment schedule for adult patients – make adjustments based on absolute Hb level and/or rate of change of Hb > 1g/dl/month

1. Erythropoietins

Current dose (units/week)	Increased dose (if single dose consider increasing dose frequency)	Decreased dose (consider reducing dose frequency, minimum weekly)
1000	2000	Suspend
2000	3000	1000
3000	4000	2000
4000	6000	3000
6000	9000	4000
9000	12000	6000
12000	Seek advice	9000
> 12000	Seek advice	Seek advice

2. Darbepoetin

Current dose (µg/week)	Increased dose (consider increasing dose frequency)	Decreased dose (consider reducing dose frequency, minimum monthly)
10	15	suspend
15	20	10
20	30	15
30	40	20
40	50	30
50	60	40
60	80	50
80	Seek advice	60
> 80	Seek advice	Seek advice

Frequency of haemoglobin monitoring in adults

1. Haemodialysis patients

Haemoglobin level and rate of change	Monitoring frequency
< 11 g/dl, rate of change \leq 1 g/dl/month	4 weeks
< 11 g/dl, rate of change > 1 g/dl/month	2 weeks
11–12 g/dl, rate of change \leq 1 g/dl/month	4 weeks
11–12 g/dl, rate of change > 1 g/dl/month	2 weeks
> 12–15 g/dl, rate of change \leq 1 g/dl/month	4 weeks
> 12–15 g/dl, rate of change > 1 g/dl/month	2 weeks
> 15 g/dl	2 weeks

2. Peritoneal dialysis and pre-dialysis (including transplant) patients

Haemoglobin level and rate of change	Monitoring frequency
< 11 g/dl, rate of change \leq 1 g/dl/month	4 weeks
< 11 g/dl, rate of change > 1 g/dl/month	2 weeks
11–12 g/dl, rate of change \leq 1 g/dl/month	4–12 weeks
11–12 g/dl, rate of change > 1 g/dl/month	2 weeks
> 12–15 g/dl, rate of change \leq 1 g/dl/month	4–12 weeks
> 12–15 g/dl, rate of change > 1 g/dl/month	2 weeks
> 15 g/dl	2 weeks

Algorithm for adult patients with poor response to ESAs

