# NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

# Guideline

# Chronic kidney disease

## Draft for consultation, January 2021

**This guideline covers** the care and treatment of people with, or at risk of developing, chronic kidney disease. It aims to prevent or delay the progression, reduce the risk of complications and cardiovascular disease. It also includes information on managing anaemia associated with chronic kidney disease and hyperphosphataemia in people with chronic kidney disease.

This guideline will update NICE guideline NG8 (published June 2015), NICE guideline CG182 (published July 2014) and NICE guideline CG157 (published March 2013).

**Who is it for?**

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

**What does it include?**

- the recommendations
- recommendations for research
- rationale and impact sections that explain why the committee made the 2021 recommendations and how they might affect practice
- the guideline context.

Information about how the guideline was developed is on the guideline's webpage. This includes the evidence reviews, the scope, details of the committee and any declarations of interest.

**New and updated recommendations**

We have reviewed the evidence on investigations, classification and frequency of monitoring for chronic kidney disease (CKD), blood pressure control for people with CKD, phosphate binders to manage mineral and bone disorder in CKD, glomerular filtration rate for diagnosing anaemia associated with CKD and intravenous iron for treating anaemia associated with CKD. You are invited to comment on the new and updated recommendations. These are marked as **[2021]**.

You are also invited to comment on recommendations that we propose to delete from the previous guidelines.

We have not reviewed the evidence for the recommendations shaded in grey, and cannot accept comments on them. In some cases, we have made minor wording changes for clarification.

See update information for a full explanation of what is being updated.

Full details of the evidence and the committee's discussion on the 2021 recommendations are in the evidence reviews. Evidence for the previous recommendations is in the full versions of the relevant guidelines: chronic kidney disease, chronic kidney disease (stage 4 or 5): management of hyperphosphataemia and chronic kidney disease: managing anaemia.

The recommendations in this guideline were largely developed before the COVID-19 pandemic. Please tell us if there are any particular issues relating to COVID-19 that we should take into account when finalising the guideline for publication. NICE has produced a COVID-19 rapid guideline on chronic kidney disease. It recommends changes to usual practice to maximise the safety of patients and protect staff from infection during the COVID-19 pandemic.

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# Contents

# Recommendations

People have the right to be involved in discussions and make informed decisions about their care, as described in NICE's information on making decisions about your care.

Making decisions using NICE guidelines explains how we use words to show the strength (or certainty) of our recommendations, and has information about prescribing medicines (including off-label use), professional guidelines, standards and laws (including on consent and mental capacity), and safeguarding.

## 1.1 Investigations for chronic kidney disease

### Measuring kidney function

### Creatinine-based estimate of glomerular filtration rate

1.1.1 Whenever a request for serum creatinine measurement is made, clinical laboratories should report an estimate of glomerular filtration rate (eGFRcreatinine) using a prediction equation (see recommendation 1.1.2) in addition to reporting the serum creatinine result.

eGFRcreatinine may be less reliable in certain situations (for example, acute kidney injury, pregnancy, oedematous states, muscle wasting disorders, and in adults who are malnourished or have had an amputation) and has not been well validated in certain ethnic groups (for example, in people of Asian family origin). **[2014]**

1.1.2 Clinical laboratories should:

- use the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) creatinine equation to estimate GFRcreatinine, using creatinine assays with calibration traceable to standardised reference material
- use creatinine assays that are specific (for example, enzymatic assays) and zero-biased compared with isotope dilution mass spectrometry (IDMS)

- participate in a UK national external quality assessment scheme for creatinine. **[2014]**

1.1.3 For adults of African-Caribbean or African family origin, multiply eGFR by 1.159 if calculated using the CKD-EPI creatinine equation. **[2021]**

For a short explanation of why the committee made this 2021 recommendation see rationale and impact section on creatinine-based estimate of GFR.

Full details of the evidence and the committee's discussion are in evidence review A: Diagnostic accuracy of eGFR calculations in adults, children, and young people from black, Asian and other minority ethnic groups with CKD.

1.1.4 Interpret eGFRcreatinine with caution in adults with extremes of muscle mass, for example, in bodybuilders, people who have had an amputation or people with muscle wasting disorders. (Reduced muscle mass will lead to overestimation and increased muscle mass to underestimation of the GFR.) **[2008]**

1.1.5 Advise adults not to eat any meat in the 12 hours before having a blood test for eGFRcreatinine. Avoid delaying the despatch of blood samples to ensure that they are received and processed by the laboratory within 12 hours of venepuncture. **[2008]**

### Reporting and interpreting GFR values

1.1.6 Clinical laboratories should report GFR either as a whole number if it is 90 ml/min/1.73 $m^2$ or less, or as 'greater than 90 ml/min/1.73 $m^2$'. **[2014]**

1.1.7 If GFR is greater than 90 ml/min/1.73 $m^2$, use an increase in serum creatinine concentration of more than 20% to infer significant reduction in kidney function. **[2014]**

1.1.8 Interpret eGFR values of 60 ml/min/1.73 $m^2$ or more with caution, bearing in mind that estimates of GFR become less accurate as the true GFR increases. **[2014]**

1.1.9 Confirm an eGFR result of less than 60 ml/min/1.73 $m^2$ in an adult not previously tested by repeating the test within 2 weeks. Allow for biological and analytical variability of serum creatinine (±5%) when interpreting changes in eGFR. **[2008]**

### When highly accurate measures of GFR are needed

1.1.10 If a highly accurate measure of GFR is needed, for example, during monitoring of chemotherapy and in the evaluation of renal function in potential living donors, consider a reference standard measure (inulin, 51Cr-EDTA, 125I-iothalamate or iohexol). **[2008]**

### Investigations for proteinuria

1.1.11 Do not use reagent strips to identify proteinuria. **[2021]**

1.1.12 For the initial detection of proteinuria in adults, children and young people:

- use urine albumin:creatinine ratio (ACR) rather than protein:creatinine ratio (PCR) because of the greater sensitivity for low levels of proteinuria
- check an ACR between 3 mg/mmol and 70 mg/mmol in a subsequent early morning sample to confirm the result.

A repeat sample is not needed if the initial ACR is 70 mg/mmol or more. **[2021]**

1.1.13 Regard a confirmed ACR of 3 mg/mmol or more as clinically important proteinuria. **[2021]**

1.1.14 Measure proteinuria with urine ACR in the following groups:

- adults, children and young people with diabetes (type 1 or type 2)
- adults with a GFR of less than 60 ml/min/1.73 $m^2$
- adults with a GFR of 60 ml/min/1.73 $m^2$ or more if there is a strong suspicion of CKD
- children and young people without diabetes and with creatinine above the upper limit of the age-appropriate reference range.

When ACR is 70 mg/mmol or more, PCR can be used as an alternative to ACR. **[2021]**

For a short explanation of why the committee made these 2021 recommendations see the rationale and impact section on investigations for proteinuria.

Full details of the evidence and the committee's discussion are in evidence review B: Accuracy of albumin:creatinine ratio versus protein:creatinine ratio measurements to quantify proteinuria in children and young people with CKD.

**Incidental finding of proteinuria on reagent strips**

1.1.15 If unexplained proteinuria is an incidental finding on a reagent strip, offer testing for CKD using eGFRcreatinine and ACR. **[2021]**

**Haematuria**

1.1.16 Use reagent strips to test for haematuria in adults, children and young people:

- Evaluate further for results of 1+ or higher.
- Do not use urine microscopy to confirm a positive result. **[2021]**

For a short explanation of why the committee made these 2021 recommendations see the rationale and impact section on reagent strips for proteinuria and haematuria.

Full details of the evidence and the committee's discussion are in evidence review C: Accuracy of reagent strips for detecting protein and blood in urine in children and young people with CKD.

### Managing isolated invisible haematuria

1.1.17 When there is the need to differentiate persistent invisible haematuria in the absence of proteinuria from transient haematuria, regard 2 out of 3 positive reagent strip tests as confirmation of persistent invisible haematuria. **[2008]**

1.1.18 Persistent invisible haematuria, with or without proteinuria, should prompt investigation for urinary tract malignancy in appropriate age groups (See the NICE guideline on suspected cancer: recognition and referral). **[2008]**

1.1.19 Persistent invisible haematuria in the absence of proteinuria should be followed up annually with repeat testing for haematuria (see recommendations 1.1.17 and 1.1.18), proteinuria or albuminuria, GFR and blood pressure monitoring as long as the haematuria persists. **[2008]**

### Who should be tested for CKD

1.1.20 Monitor GFR at least annually in adults, children and young people taking drugs known to be nephrotoxic, such as calcineurin inhibitors (for example, cyclosporin or tacrolimus), lithium and non-steroidal anti-inflammatory drugs (NSAIDs). **[2021]**

1.1.21 Offer testing for CKD using eGFRcreatinine and ACR to adults with any of the following risk factors:

- diabetes
- hypertension
- acute kidney injury

- cardiovascular disease (ischaemic heart disease, chronic heart failure, peripheral vascular disease or cerebral vascular disease)
- structural renal tract disease, recurrent renal calculi or prostatic hypertrophy
- multisystem diseases with potential kidney involvement, for example, systemic lupus erythematosus
- family history of end-stage renal disease (GFR category G5) or hereditary kidney disease
- incidental detection of haematuria or proteinuria. **[2021]**

1.1.22 Offer testing for CKD using eGFRcreatinine and ACR to children and young people with any of the following risk factors:

- acute kidney injury
- solitary functioning kidney. **[2021]**

1.1.23 Consider testing for CKD using eGFRcreatinine and ACR in children and young people with any of the following risk factors:

- low birth weight (2,500 g or lower)
- diabetes
- hypertension
- cardiac disease
- structural renal tract disease or recurrent renal calculi
- multisystem diseases with potential kidney involvement, for example, systemic lupus erythematosus
- family history of end-stage renal disease (GFR category G5) or hereditary kidney disease
- incidental detection of haematuria or proteinuria. **[2021]**

1.1.24 Do not use any of the following as risk factors indicating testing for CKD in adults, children and young people:

- age
- gender

- ethnicity
- obesity in the absence of metabolic syndrome, diabetes or hypertension. **[2021]**

1.1.25 Monitor adults, children and young people for the development or progression of CKD for at least 3 years after acute kidney injury (longer for people with acute kidney injury stage 3) even if eGFR has returned to baseline. **[2021]**

For a short explanation of why the committee made these 2021 recommendations see the rationale and impact section on who should be tested for CKD.

Full details of the evidence and the committee's discussion are in evidence review D: Children and young people who should be tested for CKD.

## 1.2 Classification of CKD in adults

1.2.1 Classify CKD in adults using a combination of GFR and ACR categories (as described in table 1). Be aware that:

- increased ACR is associated with increased risk of adverse outcomes
- decreased GFR is associated with increased risk of adverse outcomes
- increased ACR and decreased GFR in combination multiply the risk of adverse outcomes. **[2014]**

1.2.2 Do not determine management of CKD solely by age. **[2014]**

**Table 1 Risk of adverse outcomes in adults by GFR and ACR category**

| | **ACR category A1: normal to mildly increased (less than 3 mg/mmol)** | **ACR category A2: moderately increased (3 to 30 mg/mmol)** | **ACR category A3: severely increased (over 30 mg/mmol)** |
|---|---|---|---|
| **GFR category G1: normal and high (90 ml/min/1.73m$^2$ or over)** | Low risk<br>No CKD if there are no other markers of kidney damage | Moderate risk | High risk |
| **GFR category G2: mild reduction related to normal range for a young adult (60 to 89 ml/min/1.73m$^2$)** | Low risk<br>No CKD if there are no other markers of kidney damage | Moderate risk | High risk |
| **GFR category G3a: mild to moderate reduction (45 to 59 ml/min/1.73m$^2$)** | Moderate risk | High risk | Very high risk |
| **GFR category G3b: moderate to severe reduction (30 to 44 ml/min/1.73m$^2$)** | High risk | Very high risk | Very high risk |
| **GFR category G4: severe reduction (15 to 29 ml/min/1.73m$^2$)** | Very high risk | Very high risk | Very high risk |
| **GFR category G5: kidney failure (under 15 ml/min/1.73m$^2$)** | Very high risk | Very high risk | Very high risk |

Adapted with permission from the KDIGO 2012 clinical practice guideline for the evaluation and management of chronic kidney disease

Abbreviations: ACR, albumin creatinine ratio; CKD, chronic kidney disease; GFR glomerular filtration rate

**Investigating the cause of CKD and determining the risk of adverse outcomes**

1.2.3 Agree a plan to establish the cause of CKD during an informed discussion with the person with CKD, particularly if the cause may be treatable (for example, urinary tract obstruction, nephrotoxic drugs or glomerular disease). **[2014]**

1.2.4 Use the person's GFR and ACR categories (see table 1) to indicate their risk of adverse outcomes (for example, CKD progression, acute kidney

injury, all-cause mortality and cardiovascular events) and discuss this with them. **[2014]**

**Indications for renal ultrasound in adults**

1.2.5 Offer a renal ultrasound scan to all adults with CKD who:

- have accelerated progression of CKD (see recommendation 1.3.3)
- have visible or persistent invisible haematuria
- have symptoms of urinary tract obstruction
- have a family history of polycystic kidney disease and are older than 20
- have a GFR of less than 30 ml/min/1.73 $m^2$ (GFR category G4 or G5)
- are considered by a nephrologist to need a renal biopsy. **[2008, amended 2014]**

1.2.6 Advise adults with a family history of hereditary kidney disease about the implications of an abnormal result before a renal ultrasound scan is arranged for them. **[2008]**

## 1.3 Frequency of monitoring

1.3.1 If an adult, child or young person has CKD, or is at risk of it, agree the frequency of monitoring (eGFRcreatinine and ACR) with them (and their family members or carers, as appropriate), bearing in mind that CKD is not progressive in many people. **[2021]**

See the recommendations in section 1.5 on when to refer adults (recommendation 1.5.5) and children and young people (recommendation 1.5.6) for specialist assessment.

1.3.2 Use table 2 to guide the minimum frequency of GFR monitoring, but tailor it according to:

- the underlying cause of CKD
- the rate of decline in eGFR or increase in ACR (but be aware that CKD progression is often non-linear)

- other risk factors, including heart failure, diabetes and hypertension
- changes to their treatment (such as renin–angiotensin–aldosterone system [RAAS] antagonists, NSAIDs and diuretics)
- intercurrent illness
- whether they have chosen conservative management of CKD. **[2021]**

**Table 2 Minimum number of monitoring checks (eGFR) per year for adults, children and young people with or at risk of chronic kidney disease**

| | **ACR category A1: normal to mildly increased (less than 3 mg/mmol)** | **ACR category A2: moderately increased (3 to 30 mg/mmol)** | **ACR category A3: severely increased (over 30 mg/mmol)** |
|---|---|---|---|
| **GFR category G1: normal and high (90 ml/min/1.73m$^2$ or over)** | 0 to 1 | 1 | 1 or more |
| **GFR category G2: mild reduction related to normal range for a young adult (60 to 89 ml/min/1.73m$^2$)** | 0 to 1 | 1 | 1 or more |
| **GFR category G3a: mild to moderate reduction (45 to 59 ml/min/1.73m$^2$)** | 1 | 1 | 2 |
| **GFR category G3b: moderate to severe reduction (30 to 44 ml/min/1.73m$^2$)** | 1 to 2 | 2 | 2 or more |
| **GFR category G4: severe reduction (15 to 29 ml/min/1.73m$^2$)** | 2 | 2 | 3 |
| **GFR category G5: kidney failure (under 15 ml/min/1.73m$^2$)** | 4 | 4 or more | 4 or more |

Abbreviations: ACR, albumin creatinine ratio; GFR glomerular filtration rate.

For a short explanation of why the committee made these 2021 recommendations see the rationale and impact section on frequency of monitoring.

Full details of the evidence and the committee's discussion are in evidence review E: Optimal monitoring frequency and evidence review N: Defining clinically significant decline in eGFR in terms of risk of kidney disease progression.

### Defining progression in adults

1.3.3 Define accelerated progression of CKD in adults as:

- a sustained decrease in GFR of 25% or more and a change in GFR category within 12 months **or**
- a sustained decrease in GFR of 15 ml/min/1.73 $m^2$ per year. **[2014]**

1.3.4 Take the following steps to identify the rate of progression of CKD:

- Obtain a minimum of 3 GFR estimations over a period of not less than 90 days.
- In adults with a new finding of reduced GFR, repeat the GFR within 2 weeks to exclude causes of acute deterioration of GFR. For example, acute kidney injury or starting renin–angiotensin system antagonist therapy. **[2008, amended 2014]**

1.3.5 Be aware that adults with CKD are at increased risk of progression to end-stage renal disease if they have either of the following:

- a sustained decrease in GFR of 25% or more over 12 months **or**
- a sustained decrease in GFR of 15 ml/min/1.73 $m^2$ or more over 12 months. **[2008, amended 2014]**

1.3.6 When assessing CKD progression, extrapolate the current rate of decline of GFR and take this into account when planning intervention strategies,

particularly if it suggests that the person might need renal replacement therapy in their lifetime. **[2008, amended 2014]**

**Risk factors associated with CKD progression in adults**

1.3.7 Work with adults who have any of the following risk factors for CKD progression to optimise their health:

- cardiovascular disease
- proteinuria
- acute kidney injury
- hypertension
- diabetes
- smoking
- African, African-Caribbean or Asian family origin
- chronic use of NSAIDs
- untreated urinary outflow tract obstruction. **[2014]**

1.3.8 In adults with CKD the chronic use of NSAIDs may be associated with progression and acute use is associated with a reversible decrease in GFR. Exercise caution when treating people with CKD with NSAIDs over prolonged periods of time. Monitor the effects on GFR, particularly in people with a low baseline GFR and/or in the presence of other risks for progression. **[2008]**

## 1.4 Information and education for people with CKD

1.4.1 Offer people with CKD (and their family members or carers, as appropriate) education and information tailored to the severity and cause of CKD, the associated complications and the risk of progression. **[2008]**

See the information on enabling patients to actively participate in their care in NICE's guideline on patient experience in adult NHS services.

NICE is also developing a guideline on babies, children and young people's experience of healthcare (publication expected in August 2021).

1.4.2 When developing information or education programmes, involve adults with CKD in their development from the outset. The following topics are suggested.

- What is CKD and how does it affect people?
- What questions should people ask about their kidneys?
- What treatments are available for CKD, what are their advantages and disadvantages, and what complications or side effects may occur as a result of treatment or medication?
- What can people do to manage and influence their own condition?
- In what ways could CKD and its treatment affect people's daily life, social activities, work opportunities and financial situation, including benefits and allowances available?
- How can people cope with and adjust to CKD and what sources of psychological support are available?
- Information about renal replacement therapy (such as the frequency and length of time of dialysis treatment sessions or exchanges and pre-emptive transplantation) and the preparation needed (such as having a fistula or peritoneal catheter), if appropriate for the person. See the NICE guideline on renal replacement therapy and conservative management.
- Conservative management and when it may be considered. **[2008]**

1.4.3 Offer adults with CKD (and their family members or carers, as appropriate) high-quality information or education programmes as

appropriate to the severity of their condition to allow time for them to fully understand and make informed choices about their treatment. **[2008]**

1.4.4 Ensure healthcare professionals providing information and education programmes have specialist knowledge about CKD and the necessary skills to facilitate learning. **[2008]**

1.4.5 Take account of the psychological aspects of coping with CKD and offer adults with CKD access to support, for example, support groups, counselling or a specialist nurse. **[2008]**

### Lifestyle advice

1.4.6 Encourage adults with CKD to take exercise, achieve a healthy weight and stop smoking. **[2008]**

### Dietary interventions

1.4.7 Offer dietary advice about potassium, phosphate, calorie and salt intake appropriate to the severity of CKD. **[2008, amended 2014]**

1.4.8 If dietary intervention is agreed, provide it alongside education, detailed dietary assessment and supervision to ensure malnutrition is prevented. **[2008]**

### Low-protein diets

1.4.9 Do not offer low-protein diets (dietary protein intake less than 0.6 to 0.8 g/kg/day) to adults with CKD. **[2014]**

### Self-management

1.4.10 Ensure that systems are in place to:

- inform adults with CKD (and their family members or carers, as appropriate) of their diagnosis
- enable adults with CKD (and their family members or carers, as appropriate) to share in decision making about their care

- support self-management (this includes providing information about blood pressure, smoking cessation, exercise, diet and medicines) and enable adults with CKD to make informed choices. **[2014]**

1.4.11 Give adults access to their medical data (including diagnosis, comorbidities, test results, treatments and correspondence) through information systems, such as Renal PatientView, to encourage and help them to self-manage their CKD. **[2014]**

## 1.5 Risk assessment, referral criteria and shared care

### Risk assessment

1.5.1 Give adults with CKD and their family members or carers (as appropriate) information about their absolute risk and their 5-year risk of needing renal replacement therapy (measured using the 4-variable Kidney Failure Risk Equation).
Follow the recommendations on shared decision making in NICE's guideline on patient experience in adult NHS services when communicating risk. **[2021]**

1.5.2 Use every day, jargon-free language to communicate information on risk. If technical terms are used, explain them clearly. **[2021]**

1.5.3 Set aside enough time during the consultation to give information on risk assessment and to answer any questions. Arrange another appointment for more discussion if this is needed. **[2021]**

1.5.4 Document the discussion on risk assessment and any decisions the person makes. **[2021]**

### Referral criteria

1.5.5 Refer adults with CKD for specialist assessment (taking into account their wishes and comorbidities) if they have any of the following:

- a 5-year risk of needing renal replacement therapy of greater than 5% (measured using the 4-variable Kidney Failure Risk Equation)

- an ACR of 70 mg/mmol or more, unless known to be caused by diabetes and already treated
- an ACR of 30 mg/mmol or more (ACR category A3), together with haematuria
- a sustained decrease in GFR of 25% or more and a change in GFR category within 12 months
- a sustained decrease in GFR of 15 ml/min/1.73 $m^2$ or more per year
- hypertension that remains poorly controlled (above the person's individual target) despite the use of at least 4 antihypertensive drugs at therapeutic doses (see also NICE's guideline on hypertension in adults)
- known or suspected rare or genetic causes of CKD
- suspected renal artery stenosis. **[2021]**

1.5.6 Refer children and young people with CKD for specialist assessment if they have any of the following:

- an ACR of 3 mg/mmol or more, confirmed on a repeat early morning urine sample
- haematuria
- any decrease in GFR
- hypertension
- known or suspected rare or genetic causes of CKD
- suspected renal artery stenosis
- renal outflow obstruction. **[2021]**

1.5.7 Consider discussing management with a specialist by letter, email or telephone if there are concerns but the person with CKD does not need to see a specialist. **[2021]**

1.5.8 Refer people with CKD and renal outflow obstruction to urological services, unless urgent treatment is needed (for example, for hyperkalaemia, severe uraemia, acidosis or fluid overload). **[2021]**

**Shared care**

1.5.9 After referral:

- Agree a care plan with the person with CKD or their family member or carer (as appropriate).
- Consider routine follow up at the GP surgery rather than in a specialist clinic.
- Specify criteria for future referral and re-referral if GP follow up is agreed; for children and young people, these criteria should be agreed between the GP and secondary care services. **[2021]**

For a short explanation of why the committee made these 2021 recommendations see the rationale and impact section on risk assessment, referral criteria and shared care.

Full details of the evidence and the committee's discussion are in evidence review F: The best combination of measures to identify increased risk of progression in adults, children and young people.

## 1.6 Pharmacotherapy

**Blood pressure control**

See NICE's guideline on hypertension in adults for advice on blood pressure control in people with frailty and multimorbidity.

1.6.1 In adults with CKD and an ACR under 70 mg/mmol, aim for a systolic blood pressure below 140 mmHg (target range 120 to 139 mmHg) and a diastolic blood pressure below 90 mmHg. **[2021]**

1.6.2 In adults with CKD and an ACR of 70 mg/mmol or more, aim for a systolic blood pressure below 130 mmHg (target range 120 to 129 mmHg) and a diastolic blood pressure below 80 mmHg. **[2021]**

1.6.3 In children and young people with CKD and an ACR of 70 mg/mol or more, aim for a systolic blood pressure below the 50th percentile for height. **[2021]**

For a short explanation of why the committee made these 2021 recommendations see the rationale and impact section on pharmacotherapy for blood pressure control.

Full details of the evidence and the committee's discussion are in evidence review G: Optimal blood pressure targets

**Pharmacotherapy for hypertension**

1.6.4 Follow the recommendations on treating hypertension in NICE's guideline on hypertension in adults for adults with CKD, hypertension and an ACR of less than 30 mg/mmol (ACR categories A1 and A2). **[2014, amended 2021]**

1.6.5 Offer an angiotensin-receptor blocker (ARB) or an angiotensin-converting enzyme (ACE) inhibitor to adults, children and young people with CKD who have hypertension and an ACR over 30 mg/mmol (ACR category A3 or above). **[2021]**

**Pharmacotherapy for proteinuria**

1.6.6 For adults with CKD and diabetes (type 1 or type 2), offer:

- an ACE inhibitor or an ARB if ACR is 3 mg/mmol or more
- an SGLT2 inhibitor, in addition to an ACE inhibitor or an ARB, if they have type 2 diabetes, an ACR of 30 mg/mmol or more and meet the

criteria in the marketing authorisation (including relevant eGFR thresholds); monitor for volume depletion and eGFR decline.

In June 2021, not all SGLT2 inhibitors were licensed for this indication. See NICE's information on prescribing medicines. **[2021]**

1.6.7 For children and young people with CKD, an ACR of 3 mg/mmol or more and diabetes (type 1 or 2), offer an ACE inhibitor or an ARB. **[2021]**

1.6.8 For adults with CKD but without diabetes:

- refer for nephrology assessment and offer an ACE inhibitor or ARB, if ACR is 70 mg/mmol or more
- monitor in line with recommendations 1.3.1 and 1.3.2 if ACR is between 30 and 70 mg/mmol; consider discussing with a nephrologist if eGFR declines or ACR increases. **[2021]**

1.6.9 For children and young people with CKD but without diabetes:

- offer an ACE inhibitor or ARB if ACR is 70 mg/mol or more
- monitor in line with recommendations 1.3.1 and 1.3.2 if ACR is between 30 and 70 mg/mmol; consider discussing with a nephrologist if eGFR declines or ACR increases. **[2021]**

1.6.10 When offering medicines to lower proteinuria to people with frailty, comorbidities or who are taking many other prescribed medicines, follow the recommendations in NICE's guideline on medicines optimisation to ensure the best possible outcomes. Seek specialist advice if needed, for example, from a consultant in care of the elderly. **[2021]**

For a short explanation of why the committee made these 2021 recommendations see the rationale and impact section on pharmacotherapy for proteinuria and choice of antihypertensive agent.

Full details of the evidence and the committee's discussion are in evidence review H: Interventions to lower proteinuria.

### Renin-angiotensin system antagonists

1.6.11 Do not offer a combination of renin–angiotensin system antagonists to adults with CKD. **[2014]**

1.6.12 Explain to adults with CKD (and their family members or carers, as appropriate) who are prescribed renin–angiotensin system antagonists about the importance of:

- achieving the optimal tolerated dose of renin–angiotensin system antagonists **and**
- monitoring eGFR and serum potassium in achieving this safely. **[2008]**

1.6.13 Measure serum potassium concentrations and estimate the GFR before starting renin–angiotensin system antagonists in people with CKD. Repeat these measurements between 1 and 2 weeks after starting renin–angiotensin system antagonists and after each dose increase. **[2008]**

1.6.14 Do not routinely offer a renin–angiotensin system antagonist to adults with CKD if their pretreatment serum potassium concentration is greater than 5.0 mmol/litre. **[2008, amended 2014]**

1.6.15 If an adult cannot use renin–angiotensin system antagonists because of hyperkalaemia:

- assess for and treat any other factors that promote hyperkalaemia **and**
- recheck serum potassium concentration. **[2008]**

1.6.16 Be aware that more frequent monitoring of serum potassium concentration may be needed if drugs known to promote hyperkalaemia

are prescribed for use in people alongside renin–angiotensin system antagonists. **[2008]**

1.6.17 Stop renin–angiotensin system antagonists in adults if the serum potassium concentration increases to 6.0 mmol/litre or more and other drugs known to promote hyperkalaemia have been discontinued. **[2008]**

1.6.18 After introducing or increasing the dose of renin–angiotensin system antagonists in adults, do not modify the dose if either:

- the GFR decrease from pretreatment baseline is less than 25% **or**
- the serum creatinine increase from baseline is less than 30%. **[2008]**

1.6.19 If there is a decrease in eGFR or increase in serum creatinine after starting or increasing the dose of renin–angiotensin system antagonists, but it is less than 25% (eGFR) or 30% (serum creatinine) of baseline, repeat the test in 1 to 2 weeks. Do not modify the renin–angiotensin system antagonist dose if the change in eGFR is less than 25% or the change in serum creatinine is less than 30%. **[2008]**

1.6.20 If an adult's eGFR change is 25% or more, or the change in serum creatinine is 30% or more:

- investigate other causes of a deterioration in renal function, such as volume depletion or concurrent medication (for example, NSAIDs)
- if no other cause for the deterioration in renal function is found, stop the renin–angiotensin system antagonist or reduce the dose to a previously tolerated lower dose, and add an alternative antihypertensive medication if needed. **[2008]**

### Statins for adults

1.6.21 Follow the recommendations in NICE's guideline on cardiovascular disease: risk assessment and reduction, including lipid modification for the use of statins in adults with CKD. **[2014]**

### Oral antiplatelets and anticoagulants for adults

1.6.22 Offer antiplatelet drugs to adults with CKD for the secondary prevention of cardiovascular disease, but be aware of the increased risk of bleeding. **[2014]**

1.6.23 Consider apixaban in preference to warfarin in adults with a confirmed eGFR of 30–50 ml/min/1.73 $m^2$ and non-valvular atrial fibrillation who have 1 or more of the following risk factors:

- prior stroke or transient ischaemic attack
- age 75 years or older
- hypertension
- diabetes mellitus
- symptomatic heart failure. **[2014]**

## 1.7 Diagnosing and assessing anaemia

### Diagnostic role of haemoglobin levels

1.7.1 Consider investigating and managing anaemia in adults, children and young people with 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

1.7.2 In adults, children and young people with anaemia:

- If eGFR is above 60 ml/min/1.73 $m^2$, investigate other causes of anaemia as it is unlikely to be caused by CKD.

- If eGFR is between 30 and 60 ml/min/1.73 $m^2$:
  - investigate other causes of anaemia, but
  - use clinical judgement to decide how extensive this investigation should be, because the anaemia may be caused by CKD.
- If eGFR is below 30 ml/min/1.73 $m^2$, think about other causes of anaemia but note that the anaemia is likely to be caused by CKD. **[2021]**

For a short explanation of why the committee made this 2021 recommendation see the rationale and impact section on diagnostic role of glomerular filtration rate.

Full details of the evidence and the committee's discussion are in evidence review I: eGFR threshold for the investigation of anaemia due to CKD.

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

1.7.3 Carry out testing to diagnose iron deficiency and determine potential responsiveness to iron therapy and long-term iron requirements every 3 months (every 1 to 3 months for people having 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). **[2015]**

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

1.7.5 Do not routinely measure erythropoietin levels for the diagnosis or management of anaemia in people with anaemia of CKD. **[2006]**

## 1.8 Managing anaemia

### Starting erythropoietic stimulating agent therapy in iron-deficiency

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

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

1.8.2 In adults, children and young 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 people with sufficient iron

1.8.3 Discuss the pros and cons of a trial of anaemia management with the person with anaemia of CKD, and their families and carers if agreed. **[2006]**

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

1.8.5 Start 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]**

1.8.6 If a trial of ESA therapy is carried out, assess the effectiveness of the trial after an agreed interval. Agree with the person with anaemia of CKD (and

their families and carers, if appropriate) whether or not to continue ESA therapy. **[2006]**

1.8.7 Review treatment in all people started on ESA therapy after an agreed interval to decide whether or not to continue using ESAs. **[2006]**

### Nutritional supplements

1.8.8 Do not prescribe supplements of vitamin C, folic acid or carnitine as adjuvants specifically for the treatment of anaemia of CKD. **[2006]**

### Androgens

1.8.9 Do not use androgens to treat anaemia in with anaemia of CKD. **[2006]**

### Hyperparathyroidism

1.8.10 Treat clinically relevant hyperparathyroidism in adults, children and young people with CKD to improve the management of the anaemia. **[2006]**

### Person-centred care and ESAs

1.8.11 Give adults, children and young people offered ESA therapy and their GPs information about why ESA therapy is needed, how it works and what benefits and side effects may be experienced. **[2006]**

1.8.12 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]**

1.8.13 Explain to people receiving ESA therapy about the importance of concordance with therapy and the consequences of poor adherence. **[2006]**

1.8.14 When prescribing ESA therapy, take into account the person's preferences about supervised- or self-administration, dose frequency, pain on injection, method of supplying ESA and storage. **[2006]**

1.8.15 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

1.8.16 Offer culturally and age-appropriate patient education programmes to all adults, children and young people diagnosed with anaemia of CKD (and their families and carers). These should be repeated as requested, and according to the person's changing circumstances. 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 people with the condition).
- Adaptation to chronic disease (for example, previous information and expectations, resolution of symptoms). **[2006]**

## 1.9 Assessing and optimising erythropoiesis in people with anaemia

### Benefits of treatment with ESAs

1.9.1 Offer treatment with ESAs to adults, children and young people with anaemia of CKD who are likely to benefit in terms of quality of life and physical function. **[2006]**

### Blood transfusions

1.9.2 Avoid blood transfusions if possible in people with anaemia of CKD in whom kidney transplant is a treatment option. **[2006]**

1.9.3 If a transfusion is indicated clinically in a person with anaemia of CKD, follow the NICE guideline on blood transfusion. **[2006, amended 2015]**

### Comparisons of ESAs

1.9.4 Discuss the choice of ESA with the person with anaemia of CKD when starting treatment and at subsequent review, taking into account:

- the person's dialysis status
- the route of administration
- the local availability of ESAs
- the lack of evidence comparing the efficacy of ESAs. **[2006]**

### Coordinating care

1.9.5 Ensure people with anaemia of CKD have access to a designated contact person or people who have principal responsibility for their anaemia management and who have skills in the following activities:

- Monitoring and managing a caseload in line with locally agreed protocols.
- Providing information, education and support to empower people 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 people receive a seamless service of the highest standard.

- Prescribing medicines related to anaemia management and monitoring their effectiveness. **[2006]**

### Providing ESAs

1.9.6 Agree a treatment plan between the prescriber and the person with anaemia of CKD that ensures ESA therapy is clinically effective, consistent and safe. The plan should be person-centred and include:

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

### ESAs: optimal route of administration

1.9.7 Agree the route of administration of ESAs between the person with anaemia of CKD and the prescriber, and revise as appropriate. Take into account the following factors:

- patient population (for example, people having haemodialysis)
- pain of injection
- frequency of administration
- the person's lifestyle and preferences
- efficacy (for example, subcutaneous compared with intravenous administration, or long-acting compared with short-acting preparations)
- cost of drug supply. **[2006]**

1.9.8 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

1.9.9 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

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

- their preferences
- symptoms and comorbidities
- the necessary treatment. **[2011]**

1.9.11 Do not routinely correct Hb to normal levels with ESAs in adults, children and young people with anaemia of CKD.

- Typically maintain the aspirational Hb range between 100 and 120 g/litre for adults, young people and children aged 2 years and over, and between 95 and 115 g/litre for children under 2 years, 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).

Follow the MHRA safety advice on recombinant human erythropoietins, particularly the advice to avoid Hb levels above 120 g/litre because of the increased risk of death and serious adverse cardiovascular events

in people with CKD. People should have close monitoring to ensure that the lowest approved dose of ESA is used to provide adequate control of the anaemia symptoms. **[2021]**

For a short explanation of why the committee made this 2021 recommendation see the rationale and impact section on optimal Hb levels.

Full details of the evidence and the committee's discussion are in evidence review J: Aspirational haemoglobin target range for children and young people with CKD.

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

- high doses of ESAs are needed to achieve the aspirational range **or**
- the aspirational range is not achieved despite escalating ESA doses.

High doses are more than 175 IU/kg per week for people having haemodialysis; more than 125 IU/kg per week for people having peritoneal dialysis; more than 100 IU/kg per week for people not having dialysis. **[2011]**

1.9.13 Do not use age alone to determine treatment of anaemia of CKD. **[2006]**

### Adjusting ESA treatment

1.9.14 Optimise iron status before or at the same time as starting ESAs and during maintenance treatment with ESAs. **[2006, amended 2011]**

1.9.15 Use of 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]**

1.9.16 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 or 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]**

### Correcting iron deficiency

1.9.17 Offer iron therapy to adults, children and young people with anaemia of CKD who are receiving ESAs to achieve:

- 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 these 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 adults will need 500 to 1,000 mg of iron (equivalent doses for children) in a single or divided dose depending on the preparation. Intravenous iron should be administered in a setting with facilities for resuscitation. **[2015]**

In June 2021, this was an off-label use of intravenous iron products for some ages of children and young people. See NICE's information on prescribing medicines.

1.9.18 Offer a high-dose intravenous iron regimen to adults, children and young people with stage 5 CKD on in-centre (hospital or satellite unit) haemodialysis, if they have iron deficiency (see recommendation 1.7.3).

See table 3 for an example of a high-dose intravenous iron regimen for adults or use a bioequivalent dose of iron. For children and young people, use the maximum dosing regimen in the BNFc unless serum ferritin is greater than 800 micrograms/litre when the dose should be withheld.

In June 2021, this was an off-label use of intravenous iron products for some children and young people. See NICE's information on prescribing medicines. **[2021]**

**Table 3 Example of high-dose intravenous iron regimen for adults**

| **Iron status** | **Intravenous iron sucrose (high-dose regimen)** |
|---|---|
| First month | 600 mg divided equally over 3 haemodialysis sessions |
| Second month onwards if ferritin 700 micrograms/litre or less | 200 mg during each of the first 2 dialysis sessions |
| Second month onwards if ferritin over 700 micrograms/litre and/or transferrin saturation 40% or more and/or C-reactive protein (CRP) over 50 mg/litre | Withhold iron dose |

Intravenous iron sucrose based on the high-dose iron regimen in the PIVOTAL trial (Macdougall 2019), which included people with serum ferritin below 400 micrograms/litre, a transferrin saturation below 30% and a CRP below 50 mg/litre and on ESA.

For a short explanation of why the committee made this 2021 recommendation see the rationale and impact section on correcting iron deficiency.

Full details of the evidence and the committee's discussion are in evidence review K: Anaemia – IV iron.

**Maintaining iron levels after a deficiency is corrected**

1.9.19 Once the 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 people having haemodialysis will need the equivalent of 50 to 60 mg intravenous iron per week (or an equivalent dose in children of 1 mg/kg/week). **[2015]**

In June 2021, this was an off-label use of intravenous iron products for some ages of children and young people. See NICE's information on prescribing medicines.

**Monitoring iron status during ESA treatment**

1.9.20 Offer iron therapy to adults, children and young people receiving ESA maintenance therapy to keep their:

- 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 to 3 months in

people having haemodialysis.

In people who are pre-dialysis 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. **[2015]**

In June 2021, this was an off-label use of intravenous iron products for some ages of children and young people. See NICE's information on prescribing medicines.

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

1.9.21 Offer iron therapy to adults, children and young people with anaemia of CKD who are iron deficient and who are not receiving ESA therapy, before discussing ESA therapy. (In June 2021, this was an off-label use of intravenous iron products for some ages of children and young people. See NICE's information on prescribing medicines).

- Discuss the risks and benefits of treatment options. Take into account the person's choice.
- For people who are not having 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 1.9.11), offer intravenous iron therapy.
- For people who are having haemodialysis, offer intravenous iron therapy. Offer oral iron therapy to people who are having 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. **[2015]**

1.9.22 Discuss the results of the iron therapy with the person or, if appropriate, with their family or carers and offer ESA therapy if needed (see recommendation 1.7.22). **[2015]**

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

1.9.23 Offer iron therapy to adults, children and young people with anaemia of CKD who are iron deficient and who are receiving ESA therapy. (In June 2021, this was an off-label use of intravenous iron products for some ages of children and young people. See NICE's information on prescribing medicines).

- 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 having haemodialysis, offer intravenous iron therapy.
- For children who are not having haemodialysis, consider oral iron. If the child is intolerant of oral iron or target Hb levels are not reached within 3 months (see recommendation 1.9.11), offer intravenous iron therapy. **[2015]**

1.9.24 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. **[2015]**

1.9.25 When offering intravenous iron therapy to people not having haemodialysis, consider high-dose low-frequency 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, if 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 may be more appropriate for all children and for adults who are having in-centre haemodialysis.

High dose and low frequency iron is a maximum of 2 infusions, with a minimum of 500 mg of iron in each infusion for adults. Low dose and high frequency is more than 2 infusions with 100 mg to 200 mg of iron in each infusion for adults. **[2015]**

In June 2021, this was an off-label use of intravenous iron products for some ages of children and young people. See NICE's information on prescribing medicines.

## 1.10 Monitoring anaemia treatment

### Monitoring iron status

1.10.1 Do not check iron levels earlier than 1 week after administering intravenous iron in adults, children and young people with anaemia of CKD. The length of time to monitoring of iron status is dependent on the product used and the amount of iron given. **[2006]**

1.10.2 Carry out routine monitoring of iron stores to prevent iron overload using serum ferritin at intervals of 1 to 3 months. **[2006, amended 2015]**

### Monitoring Hb levels

1.10.3 In adults, children and young people with anaemia of CKD, monitor Hb:

- every 2 to 4 weeks in the induction phase of ESA therapy
- every 1 to 3 months in the maintenance phase of ESA therapy
- more frequently after an ESA dose adjustment

- in a clinical setting chosen in discussion with the person, taking into account their convenience and local healthcare systems. **[2006]**

### Detecting ESA resistance

1.10.4 After other causes of anaemia, such as intercurrent illness or chronic blood loss have been excluded, regard people with anaemia of CKD as 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]**

1.10.5 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]**

1.10.6 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

1.10.7 If aluminium toxicity is suspected in an adult, child or young person with anaemia of CKD having haemodialysis, perform a desferrioxamine test and review the management of their condition accordingly. **[2006]**

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

### Role of blood transfusion in managing ESA resistance

1.10.9 Consider referring adults, children and young people with ESA resistance to a haematology service, particularly if an underlying haematological disorder is suspected. **[2015]**

1.10.10 Evaluate and discuss the risks and benefits of red cell transfusion with the person or, if appropriate, with their family or carers. **[2015]**

1.10.11 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. **[2015]**

1.10.12 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. **[2015]**

## 1.11 Hyperphosphataemia in people with CKD stage 4 or 5

### Dietary management for adults, children and young people

1.11.1 A specialist renal dietitian, supported by healthcare professionals with the necessary skills and competencies, should carry out a dietary assessment and give individualised information and advice on dietary phosphate management. **[2013]**

1.11.2 Tailor advice on dietary phosphate management to the person's learning needs and preferences, rather than using a generalised or complex multicomponent programme of delivery. **[2013]**

1.11.3 Give information about controlling intake of phosphate-rich foods (in particular, foods with a high phosphate content per gram of protein, as well as food and drinks with high levels of phosphate additives) to control serum phosphate, while avoiding malnutrition by maintaining a protein intake at or above the minimum recommended level. For people on dialysis, take into account possible dialysate protein losses. **[2013]**

1.11.4 If a nutritional supplement is needed to maintain protein intake in children and young people with hyperphosphataemia, offer a supplement with a lower phosphate content, taking into account the person's preference and other nutritional requirements. **[2013]**

### Before starting phosphate binders for adults, children and young people

1.11.5 Before starting phosphate binders for adults, children and young people with CKD stage 4 or 5, optimise:

- diet (see recommendations 1.4.7 to 1.4.9 for adults)
- dialysis, for people who are having this. **[2021]**

1.11.6 When offering a phosphate binder, explain to people and their family members or carers (as appropriate):

- the reason for offering phosphate binders
- the risks if they are not taken and
- the need to take phosphate binders with food (including, for example, high-protein snacks). **[2021]**

1.11.7 If the person has problems taking the first phosphate binder offered, consider switching to the next recommended one (see recommendations 1.11.8 to 1.11.14). **[2021]**

**Phosphate binders for children and young people**

1.11.8 Offer children and young people with CKD stage 4 or 5 and hyperphosphataemia, a calcium-based phosphate binder to control serum phosphate levels. **[2021]**

1.11.9 If serum calcium increases towards, or above, the age-adjusted upper normal limit:

- investigate possible causes other than the phosphate binder
- consider reducing the dose of the calcium-based phosphate binder and adding sevelamer carbonate or switching to sevelamer carbonate alone.

  In June 2021, this was an off-label use of sevelamer carbonate. See NICE's information on prescribing medicines. **[2021]**

1.11.10 For all children and young people who are taking more than one phosphate binder, titrate the dosage to achieve the best possible control

of serum phosphate while keeping serum calcium levels below the upper normal limit. **[2021]**

### Phosphate binders for adults

#### First phosphate binder for adults

1.11.11 Offer adults with CKD stage 4 or 5 and hyperphosphataemia, calcium acetate to control serum phosphate levels.

In June 2021, this was an off-label use of calcium acetate in people not on dialysis. See NICE's information on prescribing medicines. **[2021]**

1.11.12 Offer sevelamer carbonate if calcium acetate is not indicated (for example, because of hypercalcaemia or low serum parathyroid hormone levels) or not tolerated.

In June 2021, this was an off-label use of sevelamer carbonate. See NICE's information on prescribing medicines. **[2021]**

1.11.13 If calcium acetate and sevelamer carbonate cannot be used, consider:

- sucroferric oxyhydroxide, for adults on dialysis if a calcium-based phosphate binder is not needed **or**
- calcium carbonate, if a calcium-based phosphate binder is needed.

  In June 2021, this was an off-label use of these phosphate binders in people not on dialysis. See NICE's information on prescribing medicines. **[2021]**

1.11.14 Only consider lanthanum carbonate for adults with CKD stage 4 or 5 if other phosphate binders cannot be used.

In June 2021, this was an off-label use of lanthanum carbonate phosphate binders in people not on dialysis and with serum phosphate levels less

than 1.78 mmol/l. See NICE's information on prescribing medicines. **[2021]**

### Combinations of phosphate binders for adults

1.11.15 If adults with CKD stage 4 or 5 remain hyperphosphataemic after taking the maximum dose recommended in the BNF (or the maximum dose they can tolerate if that is lower), of a calcium-based phosphate binder:

- check they are taking it as prescribed
- consider combining a calcium-based phosphate binder with a non-calcium-based phosphate binder. **[2021]**

1.11.16 For all adults who are taking more than one phosphate binder, titrate the dosage to achieve the best possible control of serum phosphate while keeping serum calcium levels below the upper normal limit. **[2021]**

### Review of treatments in adults, children and young people

1.11.17 At every routine clinical review, assess the person's serum phosphate control, taking into account:

- diet
- whether they are taking the phosphate binders as prescribed
- other relevant factors, such as vitamin D levels, serum parathyroid hormone levels or dialysis. **[2021]**

For a short explanation of why the committee made these 2021 recommendations see the rationale and impact section on hyperphosphataemia in people with CKD stage 4 or 5.

Full details of the evidence and the committee's discussion are in evidence review L: Use of phosphate binders.

## 1.12 Other complications in adults

### Bone metabolism and osteoporosis

1.12.1 Do not routinely measure calcium, phosphate, parathyroid hormone and vitamin D levels in adults with a GFR of 30 ml/min/1.73 $m^2$ or more (GFR category G1, G2 or G3). **[2008]**

1.12.2 Measure serum calcium, phosphate and parathyroid hormone concentrations in adults with a GFR of less than 30 ml/min/1.73 $m^2$ (GFR category G4 or G5). Determine the subsequent frequency of testing by the measured values and the clinical circumstances. If doubt exists, seek specialist opinion. **[2008]**

1.12.3 Offer bisphosphonates if indicated for the prevention and treatment of osteoporosis in adults with a GFR of 30 ml/min/1.73 $m^2$ or more (GFR category G1, G2 or G3). **[2008]**

### Vitamin D supplements in the management of CKD–mineral and bone disorders

Detailed advice on the management of CKD–mineral and bone disorders is beyond the scope of this guideline. If uncertain, seek advice from your local renal service.

1.12.4 Do not routinely offer vitamin D supplementation to manage or prevent CKD–mineral and bone disorders. **[2014]**

1.12.5 Offer colecalciferol or ergocalciferol to treat vitamin D deficiency in people with CKD and vitamin D deficiency. **[2014]**

1.12.6 If vitamin D deficiency has been corrected and symptoms of CKD–mineral and bone disorders persist, offer alfacalcidol (1-alpha-hydroxycholecalciferol) or calcitriol

(1-25-dihydroxycholecalciferol) to people with a GFR of less than 30 ml/min/1.73 $m^2$ (GFR category G4 or G5). **[2014]**

1.12.7 Monitor serum calcium and phosphate concentrations in people receiving alfacalcidol or calcitriol supplements. **[2014]**

**Oral bicarbonate supplements in the management of metabolic acidosis**

Detailed advice on the management of metabolic acidosis is beyond the scope of this guideline. If uncertain, seek advice from your local renal service.

1.12.8 Consider oral sodium bicarbonate supplementation for adults with both:

- a GFR less than 30 ml/min/1.73 $m^2$ (GFR category G4 or G5) and
- a serum bicarbonate concentration of less than 20 mmol/litre. **[2014]**

## Terms used in this guideline

This section defines terms that have been used in a particular way for this guideline. For other definitions see the NICE glossary.

**Chronic kidney disease (CKD)**

Abnormalities of kidney function or structure present for more than 3 months, with implications for health. This includes all people with markers of kidney damage and those with a glomerular filtration rate (GFR) of less than 60 ml/min/1.73 $m^2$ on at least 2 occasions separated by a period of at least 90 days (with or without markers of kidney damage).

**Classification of CKD**

CKD is classified according to estimated GFR (eGFR) and albumin:creatinine ratio (ACR) (see table 1), using 'G' to denote the GFR category (G1 to G5, which have the same GFR thresholds as the CKD stages 1 to 5 recommended previously) and 'A' for the ACR category (A1 to A3), for example:

- A person with an eGFR of 25 ml/min/1.73 $m^2$ and an ACR of 15 mg/mmol has CKD G4A2.
- A person with an eGFR of 50 ml/min/1.73 $m^2$ and an ACR of 35 mg/mmol has CKD G3aA3.

- An eGFR of less than 15 ml/min/1.73 $m^2$ (GFR category G5) is referred to as kidney failure.

**Glomerular filtration rate (GFR)**

This is abbreviated in the following way in this guideline:

- GFR: either a measured or an estimated GFR
- eGFR: estimated GFR (without indicating the method of estimation)
- eGFRcreatinine: an estimation of GFR using serum creatinine

**4-variable Kidney Failure Risk Equation**

A person's 5-year risk of needing renal replacement therapy (defined as the need for dialysis or transplant) is estimated, as in Major 2019, as:

$$1 - 0.9570^{\exp(\beta sum)}$$

$$\beta sum = \left[-0.2201 * \left(\frac{age}{10} - 7.036\right)\right] + [0.2467 * (male - 0.5642)] - \left[0.5567 * \left(\frac{eGFR}{5} - 7.222\right)\right] + [0.4510 * (\log(ACR) - 5.137)]$$

In the above, eGFR is reported in ml/min/1.73$m^2$ and ACR in mg/g

**Markers of kidney disease**

These include albuminuria (ACR more than 3 mg/mmol), urine sediment abnormalities, electrolyte and other abnormalities due to tubular disorders, abnormalities detected by histology, structural abnormalities detected by imaging, and a history of kidney transplantation.

**People**

Some recommendations in this guideline apply to adults only, and we have specified 'adults' in these individual recommendations. When a recommendation applies to children and young people only, we have also specified this in the recommendation. When recommendations apply to adults, children and young people we have specified this in recommendations at the beginning of a section. But for brevity, we have used 'people' for later recommendations. When a recommendation refers to 'people', this means adults, children and young people.

**Pre-dialysis**

Usually regarded to be CKD stages 4 and 5, although there is no accepted definition. Pre-dialysis includes people with a failing transplant and people having conservative management.

**Renin–angiotensin–aldosterone system antagonist**

A drug that blocks or inhibits the renin–angiotensin–aldosterone system, including angiotensin-converting enzyme (ACE) inhibitors, angiotensin-receptor blockers (ARBs), direct renin inhibitors and aldosterone antagonists.

**Renin–angiotensin system antagonist**

A drug that blocks or inhibits the renin–angiotensin system, including ACE inhibitors, ARBs and direct renin inhibitors. This group of drugs does not include aldosterone antagonists.

# Recommendations for research

As part of the 2021 update, the guideline committee made 18 research recommendations on chronic kidney disease. They prioritised 5 key research recommendations. They also retained some research recommendations from previous guidelines.

## Key recommendations for research

### 1 Creatinine-based estimate of eGFR – existing calculations

In adults, children and young people from black, Asian and other minority ethnic groups with chronic kidney disease (CKD) living in the UK, which existing eGFR calculations are the most accurate? **[2021]**

### 2 Creatinine-based estimate of eGFR – improving accuracy of calculations

In adults, children and young people from black, Asian and other minority ethnic groups with CKD living in the UK, what biomarkers or factors, other than ethnicity, improve the diagnostic accuracy of eGFR calculations? **[2021]**

For a short explanation of why the committee made these recommendations see the rationale section on creatinine-based estimate of GFR.

Full details of the evidence and the committee's discussion are in evidence review A: Diagnostic accuracy of eGFR calculations in adults, children, and young people from black, Asian and other minority ethnic groups with CKD.

### 3 Risk assessment for black, Asian and minority ethnic groups

What is the accuracy of the 4-variable Kidney Failure Risk Equation in adults, children and young people with CKD from black, Asian and minority ethnic groups living in the UK? **[2021]**

For a short explanation of why the committee made this recommendation see the rationale section on risk assessment, referral criteria and shared care.

Full details of the evidence and the committee's discussion are in evidence review F: The best combination of measures to identify increased risk of progression in adults, children and young people.

### 4 Managing anaemia – optimal Hb levels for children and young people

What is the efficacy and safety of different aspirational haemoglobin (Hb) targets for children and young people with CKD undergoing treatment for anaemia? **[2021]**

For a short explanation of why the committee made this recommendation see the rationale section on optimal Hb levels.

Full details of the evidence and the committee's discussion are in evidence review J: Aspirational haemoglobin target range for children and young people with CKD

### 5 Hyperphosphatemia in people with CKD stage 4 or 5

What are people with CKD and their family members and carers views and beliefs about taking oral phosphate binders? **[2021]**

For a short explanation of why the committee made this recommendation see the rationale section on hyperphosphataemia in people with CKD stage 4 or 5.

Full details of the evidence and the committee's discussion are in evidence review L: Use of phosphate binders.

## Other recommendations for research

### Cystatin-C equations

What is the diagnostic accuracy of cystatin-C equations in adults, young people and children in the UK? **[2021]**

### Investigations for proteinuria

In children and young people, what is the accuracy of reagent strips for detecting albumin in urine? **[2021]**

What is the effect of measuring proteinuria with albumin:creatinine ratio compared with protein:creatinine ratio on the timing of treatment changes in children and young people with CKD? **[2021]**

### Managing proteinuria

For adults, children and young people with suspected or diagnosed CKD and proteinuria or albuminuria, what is the clinical and cost effectiveness of angiotensin-converting enzyme (ACE) inhibitors compared with angiotensin-receptor blockers (ARBs) in lowering proteinuria? **[2021]**

### Risk assessment, referral criteria and shared care

What is the association between risk factors and CKD outcomes in children and young people? **[2021]**

What is the accuracy of the 4-variable Kidney Failure Risk Equation in children and young people living in the UK? **[2021]**

### Frequency of review

What is the most clinical and cost-effective frequency of review for children and young people with CKD? **[2021]**

### Managing anaemia

For adults, children and young people with CKD and anaemia, what is the diagnostic accuracy of eGFR thresholds of 60, 45, and 30 ml/min/1.73m$^2$ for determining whether the anaemia is due to CKD? **[2021]**

For adults, children and young people with CKD and anaemia who are on peritoneal dialysis, what amount of intravenous (IV) iron is most clinically and cost effective in managing anaemia and its associated outcomes? **[2021]**

### Phosphate binders

Which binders are the most clinically and cost effective in controlling serum phosphate in adults, children and young people with stage 4 or 5 CKD who are not on dialysis? **[2021]**

In adults with stage 4 or 5 CKD, including those on dialysis, what is the clinical and cost effectiveness and safety of long-term calcium acetate combined with magnesium carbonate for controlling serum phosphate? **[2021]**

### Self-management of CKD

Does the provision of educational and supportive interventions to people with CKD by healthcare professionals increase the person's skills and confidence in managing their conditions and improve clinical outcomes? **[2014]**

### Antiplatelet therapy

For people with CKD at the highest risk of cardiovascular disease, what is the clinical effectiveness of low-dose aspirin compared with placebo for primary prevention of cardiovascular disease? **[2014]**

### Renin–angiotensin–aldosterone system antagonists

For people aged over 75 years with CKD, what is the clinical effectiveness of renin–angiotensin–aldosterone system (RAAS) antagonists? **[2014]**

### Uric acid-lowering agents

In people with CKD who are at high risk of progression, what is the clinical and cost effectiveness of uric acid-lowering agents on the progression of CKD and on mortality? **[2014]**

### Vitamin D supplements in the management of CKD–mineral and bone disorders

In people with hyperparathyroidism secondary to CKD, does treatment with vitamin D or vitamin D analogues improve patient-related outcomes? **[2014]**

### Management of anaemia of CKD with concurrent illness

What is the optimal management (in terms of clinical and cost effectiveness) of anaemia of CKD in people who are receiving erythropoietic stimulating agents (ESAs) and have a significant concurrent acute infectious illness? **[2015]**

### Treatment of ESA resistance in people on haemodialysis

What is the most effective type of intervention to treat people on haemodialysis with ESA-resistant anaemia? **[2015]**

# Rationale and impact

These sections briefly explain why the committee made the recommendations and how they might affect practice.

## Creatinine-based estimate of GFR

Recommendation 1.1.3

### Why the committee made the recommendations

Evidence on the specific eGFR equations or ethnicity adjustments seen by the committee was not from UK studies so may not be applicable to UK black, Asian and minority ethnic groups. None of the studies included children and young people. The committee was also concerned about the value of P30 as a measure of accuracy (P30 is the probability that the measured value is within 30% of the true value), the broad range of P30 values found across equations and the relative value or accuracy of ethnicity adjustments to eGFR equations in different ethnic groups. Therefore, the committee was not able to make a new recommendation about ethnicity adjustments to eGFR equations, nor did they feel there was sufficient evidence to change the recommendation made in 2014. Instead, they agreed to make recommendations for research on appropriate eGFR equations for black, Asian and minority ethnic groups

(adults, children and young people) in the UK. They agreed that factors other than ethnicity should also be explored as biomarkers.

The committee agreed that in the absence of good evidence for their accuracy, the 2014 recommendations that cystatin-c equations should be considered during diagnosis in certain circumstances, should be removed. In particular, they noted that although using cystatin-c equations may reduce false-positive results, it will likely also increase false-negative results. This will avoid potentially misleading tests being conducted and the costs associated with these. They made a research recommendation for a large study using UK data to evaluate the accuracy of cystatin-c equations.

### Impact of the recommendations on practice

There will be no impact on practice, as no changes have been made to the adjustments that are recommended. Only a small number of centres in the UK currently use cystatin-c equations regularly, so most should not be affected by the removal of the cystatin-c recommendations.

Return to recommendations

## Investigations for proteinuria

Recommendations 1.1.11 to 1.1.14

### Why the committee made the recommendations

For children and young people with CKD, there was no evidence for the accuracy of measuring albumin:creatinine ratio (ACR) compared with protein:creatinine ratio (PCR) to quantify proteinuria. The committee discussed the recommendations for adults and agreed that, overall, these fit well with current practice and can be recommended for children and young people as well.

The committee discussed the eGFR threshold recommended for quantifying urinary albumin or urinary protein loss in adults without diabetes. They agreed that this threshold is not appropriate for children and young people because any reduction in GFR in this population would prompt measuring proteinuria. Therefore, for children

and young people they set the threshold for creatinine as above the upper limit of the age-appropriate reference range.

The committee agreed to make a research recommendation to identify the effect of measuring proteinuria with ACR compared with PCR on the timing of treatment changes in children and young people with CKD and the consequences of the delay in treatment changes on different levels of proteinuria.

**How the recommendations might affect practice**

The recommendations are in line with current practice, so no additional resources should be needed.

Return to recommendations

## Reagent strips for proteinuria and haematuria

Recommendations 1.1.15 to 1.1.16

**Why the committee made the recommendations**

The evidence showed that reagent strips were less useful to rule out than to rule in proteinuria. The committee highlighted that ruling out proteinuria with confidence was the main goal when using reagent strips. Therefore, they agreed that the recommendation not to use reagent strips to identify proteinuria, currently for adults, is also applicable to children and young people. The committee also highlighted that these tests are commonly used in clinical practice and agreed to make a further recommendation for further investigations in adults, children and young people with an incidental finding of unexplained proteinuria on reagent strips. Further testing is needed to confirm CKD by identifying other markers of kidney damage (such as ACR or glomerular filtration rate).

There was limited evidence on the accuracy of reagent strips for albuminuria, so the committee did not feel able to make recommendations. There were only 2 studies, and only 1 showed that reagent strips could be useful.

There was no evidence on the accuracy of reagent strips for haematuria in children and young people. The 2014 guideline (which did not cover children and young people) recommended reagent strips for detecting haematuria in adults. The

committee agreed to extend this recommendation to children and young people, because the evidence for adults is likely to be applicable to this population.

### How the recommendations might affect practice

The recommendations are in line with current practice, so no additional resources should be needed. The committee noted that if all dipstick tests are confirmed by laboratory testing anyway, there would be extra costs attached to using dipsticks as a first step, which were not justified by the benefits.

Return to recommendations

## Who should be tested for CKD

Recommendations 1.1.20 to 1.1.25

### Why the committee made the recommendations

For children and young people, the evidence showed that acute kidney injury and solitary functioning kidney were clinically significant risk factors for developing CKD. The committee highlighted that solitary functioning kidney was not due to kidney donation but to nephrectomy secondary to congenital anomalies of the kidney and urinary tract or to a lack of a kidney at birth or a non-functioning kidney.

The committee highlighted that there were other important risk factors for developing CKD in children and young people, but that no evidence was found for these. They agreed to add, based on their clinical knowledge and experience, the risk factors listed for adults and ‘low birth weight’ as additional risk factors in children and young people.

The committee agreed that more research on risk factors for developing CKD in children and young people would help to strengthen current guidance, so they made a research recommendation.

### How the recommendations might affect practice

The recommendations are in line with current practice, so no additional resources should be needed.

Return to recommendations

## Frequency of monitoring

Recommendations 1.3.1 to 1.3.2

### Why the committee made the recommendations

Most of the evidence showed that with eGFR decline, the risk of kidney disease progression and mortality increases, and this risk increases with the rate of eGFR decline. The committee agreed this is observed in clinical practice and any person presenting with an increase in eGFR decline would be monitored more frequently. The committee reviewed the recommendations and agreed that they are consistent with the evidence and clinical practice. They agreed to clarify monitoring by stating that repeat assessment is to be agreed with each person with or at risk of CKD.

The committee agreed that the frequency of monitoring they recommended was a minimum level and that more frequent monitoring would be appropriate for some patients. This should also be guided by rate of change in eGFR or ACR and specific comorbidities, including diabetes.

The committee discussed whether specific recommendations are needed for children and young people with CKD and decline in eGFR, but agreed that this population would be referred to specialist care.

### How the recommendations might affect practice

The committee noted that no changes had been made to the previous suggested monitoring schedule, and they believed it was relatively well implemented in clinical practice. Therefore, they were confident there should not be a substantial impact on practice from the new recommendations.

Return to recommendations

## Risk assessment, referral criteria and shared care

Recommendation 1.5.1 to 1.5.9

### Why the committee made the recommendations

New evidence found a UK validation of the 4-variable Kidney Failure Risk Equation for adults, which can be used as one of the referral criteria (5-year risk of needing

renal replacement therapy greater than 5%). The results of both the validation study and modelling undertaken for the guideline showed using this equation as a referral criteria (rather than an eGFR threshold) was likely to be both more sensitive and more specific than the criteria in the 2014 NICE guideline, meaning people who will progress to needing renal replacement therapy are identified earlier, and there are fewer unnecessary referrals to secondary care.

The benefits of this approach over using an eGFR threshold (as in the 2014 NICE guideline) were not large, but the committee agreed they were meaningful. They also agreed there were additional potential benefits of using the 4-variable Kidney Failure Risk Equation, including the ability to provide people with an individual risk assessment, which could help them to proactively manage their own risk, and inform the management plans in secondary care.

However, validation of the risk equation was only in adults, so the committee made a separate recommendation for children and young people. Black people were under-represented in the study and, although there was a sizeable proportion of people of Asian family origin, the location of the study suggests that people of east Asian family origin were likely to be under-represented. Therefore, the committee agreed to make a research recommendation for validation of the risk equation in adults, children and young people from black, Asian and other minority ethnic groups living in the UK.

The committee agreed that it is important to discuss with a person with CKD what risk means. They added additional recommendations on providing information about risk, using jargon-free language, allowing enough time for discussions and documenting any decisions made.

**How the recommendations might affect practice**

If the 4-variable Kidney Failure Risk Equation can be built into laboratory computer systems, as part of how eGFR and ACR results are returned to GPs, there should be no difficulty in implementing the recommendations. The referral criteria are predicted to slightly reduce monitoring costs but, excluding costs associated with dialysis, overall there should be no substantial impact on resource use.

Return to recommendations

## Pharmacotherapy for blood pressure control

Recommendations 1.6.1 to 1.6.3

### Why the committee made the recommendations

Evidence showed no meaningful difference between standard and more intensive blood pressure targets for adults with CKD. The 2015 guideline recommended maintaining systolic blood pressure below 140 mmHg and diastolic blood pressure below 90 mmHg. This is consistent with clinical practice. The committee noted that although there is a lack of evidence on blood pressure targets in people with CKD and proteinuria, it is important to maintain a systolic blood pressure below 130 mmHg and a diastolic pressure below 80 mmHg. They agreed that a useful target for blood pressure in children and young people with CKD and proteinuria is a systolic blood pressure below the 50th percentile for height.

The committee agreed that particular care had to be taken with people who were frail or who had multiple morbidities. For these people the committee agreed that the recommendations made in NICEs hypertension guideline were useful and they added a reference to this guideline.

### How the recommendations might affect practice

The recommendations for adults are consistent with current practice and should not have an impact on resources. The recommendation for blood pressure targets in children and young people may have some cost implications, although the committee did not think they would be significant.

Return to recommendations

## Pharmacotherapy for proteinuria and choice of antihypertensive agent

Recommendations 1.6.5 to 1.6.10

### Why the committee made the recommendations

There was evidence for adults, but not for children and young people. Paediatric experts on the committee agreed that the evidence for adults was also applicable to

children and young people. Therefore, the committee did not make separate recommendations for different age groups.

The evidence for adults covered people with proteinuria or albuminuria, and included people with diabetes. This allowed the committee to make separate recommendations for people with and without diabetes. In the committee's experience, many people with diabetes and CKD are frail, or are taking a lot of medicines, so they made a recommendation to address this.

**People without diabetes**

The evidence showed that, compared with placebo, ACE inhibitors reduced the risk of end-stage renal disease in people without diabetes. ARBs did not show the same effect. However, the committee did not believe the evidence was sufficiently robust to show that ACE inhibitors were better than ARBs. In addition, for people with type 2 diabetes, ARBs did reduce the risk of end-stage renal disease and heart failure. Based on the limitations of the evidence and the evidence available for people with type 2 diabetes, the committee recommended both ACE inhibitors and ARBs.

**People with type 2 diabetes**

For people with type 2 diabetes, ARBs reduced the risk of end-stage renal disease and heart failure. The committee also recommended ACE inhibitors because the evidence did not show a clear difference between ACE inhibitors and ARBs on the following outcomes:

- reduction of proteinuria
- end-stage renal disease
- all-cause mortality
- cardiovascular mortality
- non-fatal cardiovascular events
- adverse events (hypotension)
- hospitalisation.

There was no evidence comparing ACE inhibitors with placebo in people with type 2 diabetes. The evidence for people without diabetes did show that ACE inhibitors

reduced the risk of end-stage renal disease, compared with placebo. The committee used this evidence to make the recommendation for people with diabetes.

The committee also noted evidence that SGLT2 inhibitors reduced the risk of end-stage renal disease, mortality and hospitalisation in adults with type 2 diabetes, and made a recommendation for this. The committee agreed that this was probably a class effect rather than a single drug and noted that both canagliflozin and dapagliflozin were supported by the evidence. When making the recommendation, the committee discussed the different proteinuria thresholds used in the studies to recruit participants. They agreed that an ACR of 30 mg/mmol was appropriate and consistent with the inclusion criteria of all the studies they had considered. The committee cautioned that these drugs are not suitable for everyone and should only be used within their marketing authorisation. People taking them should also have monitoring.

The committee noted the high costs of these drugs and the lack of any cost-effectiveness evidence. However, they noted the drugs did have positive technology appraisal guidance for use in people with diabetes without CKD, and agreed that with the additional renal benefits in people with CKD, they were likely to be more cost-effective in this population.

Specifically, they noted technology appraisal guidance that SGLT2 inhibitors are cost effective as first-line treatment in people with diabetes for whom metformin, sulfonylurea and pioglitazone are not appropriate, or as part of dual and triple therapy when earlier lines of therapy are not sufficient. These technology appraisals were mostly conducted before the publication of recent large trials directly looking at cardiovascular events and mortality, and were therefore based on extrapolations from intermediate endpoints (in particular HbA1c). The committee noted that their recommendations would bring forward the use of these drugs for some people (those who develop CKD and proteinuria before they meet the criteria for an SGLT2 inhibitor based solely on their diabetes).

The committee noted that the doses of SGLT2 inhibitor used in people with diabetes and CKD were lower than in people without renal impairment. However, they were confident that these drugs would still be effective for blood glucose control in people

with diabetes and CKD, and would therefore provide similar benefits for diabetes control as in people without CKD. There would also be further benefits on proteinuria, as demonstrated in the trials included in this guideline, and therefore the overall clinical benefit in people with diabetic kidney disease would be larger than the benefit estimated in the technology appraisals for people with diabetes but not CKD. The committee were therefore confident that, with a larger benefit for a similar cost, it is appropriate that these drugs are available earlier for people with diabetes and CKD, and that this would represent a cost-effective use of NHS resources.

The committee agreed that this was a fast moving area and that studies were being done to assess the usefulness of SGLT2 inhibitors in people with CKD who do not have diabetes, but they agreed the evidence was not yet strong enough to make a recommendation, even though it looked promising.

**How the recommendations might affect practice**

The recommendations on ARBs and ACE inhibitors reflect current practice, so no additional resources should be needed.

The recommendation for SGLT2 inhibitors might result in a significant change in practice, since it will mean these drugs are prescribed more widely, and this would come with a substantial cost impact. The committee noted, however, that this was likely to represent a cost-effective use of resources, with these drugs providing additional benefits on renal outcomes, as well as the benefits they provide for diabetes management.

Return to recommendations

## Role of GFR in diagnosing anaemia

Recommendation 1.7.2

**Why the committee made the recommendation**

There was limited evidence showing that eGFR thresholds below 60 ml/min/1.73 $m^2$ could be used to identify anaemia as being due to CKD. The committee questioned the applicability of this evidence because the studies did not rule out other causes of anaemia (which is usually done in practice).

The limited evidence meant that the committee was unable to recommend specific thresholds or probabilities. Instead, they used the available evidence and their expertise to specify ranges of GFR indicating that anaemia is more or less likely to be caused by CKD.

When anaemia may have other causes (such as gastrointestinal bleeding and certain cancers), investigating further will increase the chance of the real cause being identified and treated.

Clinical judgement is needed on how extensively to look for other causes when eGFR is between 30 and 60 ml/min/1.73 $m^2$. Healthcare professionals will need to balance the risks of:

- putting people through extensive and unnecessary investigations when their anaemia is caused by CKD
- missing the real cause of their anaemia by assuming it is caused by CKD.

Only 1 study included people with diabetes, and no studies included children and young people. However, the recommendations still apply to these populations, because other causes of anaemia would be ruled out before attributing the anaemia to CKD.

The committee noted a need for further research on the diagnostic test accuracy of different eGFR thresholds, particularly for eGFR thresholds of 30 and 60 ml/min/1.73 $m^2$. They highlighted that in clinical practice, an eGFR threshold of 45 ml/min/1.73 $m^2$ can also trigger investigation into anaemia due to CKD, but limited evidence was identified for the diagnostic accuracy of this threshold. The committee made a research recommendation on the diagnostic accuracy of these specific eGFR thresholds for determining the likelihood of anaemia being CKD related.

**How the recommendations might affect practice**

These recommendations should not increase the cost to primary care, because they reflect current practice and act as cautions for healthcare professionals to explore the cause of anaemia. They may reduce costs by ensuring that the correct cause of anaemia is identified more quickly with appropriate investigations.

Return to recommendations

## Optimal Hb levels

Recommendation 1.9.11

### Why the committee made the recommendation

In the 2015 guideline, an aspirational Hb range between 100 and 120 g/litre was recommended for adults, young people and children aged 2 years and over. For children under 2 years, the Hb range was between 95 and 115 g/litre. These were based on evidence for adults. In 2020, the committee reviewed the evidence specifically for children and young people. The only evidence for this population came from a single small low-quality study, comparing the effects of a high and low Hb target on left ventricular mass index. No difference in effect was found. Given the lack of evidence, the committee agreed that the recommendations made in 2015 should not be changed.

The 2015 guideline recommended using the same target Hb range as adults for children and young people over 2 years, and a slightly lower level in children under 2. However, children and young people have different coagulation risks than adults, and are more prone to reductions in Hb from blood loss in haemodialysis circuits. In practice, higher Hb targets (up to 130 g/litre) are often used for children and young people. Because of the lack of evidence in this age group, the committee agreed that research is needed to inform future guidance and made a research recommendation.

Return to recommendations

## Correcting iron deficiency

Recommendation 1.9.18

### Why the committee made the recommendation

For people with stage 5 CKD who are on in-centre haemodialysis, the evidence showed that high-dose intravenous iron was better than a low-dose regimen at increasing levels of serum ferritin and haemoglobin as well as increasing the haematocrit. The committee agreed that the type of intravenous iron was not relevant and that there was no reason to recommend a specific preparation. An

example regimen for adults using iron sucrose was taken from the evidence to help guide practice, however the choice of preparation should be based on local availability and policies. The committee agreed that children and young people should be given a high dose as set out in the BNFc, although they noted that use of intravenous iron preparations in children under 14 years was off-label.

The committee was aware of a MHRA alert on intravenous iron and serious hypersensitivity reactions. The alert states that 'intravenous iron products should only be administered when staff trained to evaluate and manage anaphylactic or anaphylactoid reactions – as well as resuscitation facilities – are immediately available.' The committee agreed that intravenous iron should not be administered at home but recognised that this has a significant impact on people on home dialysis.

Most of the evidence was from studies with participants on haemodialysis. The committee agreed that more research would help to inform future guidance on intravenous iron for people with stage 5 CKD who are on peritoneal dialysis.

**How the recommendations might affect practice**

The recommendations are unlikely to lead to a substantial change in costs, as intravenous iron is relatively inexpensive, and there was evidence found in adults that use of high-dose iron leads to lower doses of erythropoiesis-stimulating agents being used, thereby offsetting any extra costs.

Return to recommendations

## Hyperphosphataemia in people with CKD stage 4 or 5

Recommendations 1.11.5 to 1.11.17

**Why the committee made the recommendations**

There was a significant amount of evidence (of varying quality) for adults with stage 5 CKD who are having dialysis. However, evidence was limited for adults not on dialysis, and for children and young people. The committee agreed to extrapolate from the evidence for adults with stage 5 CKD on dialysis, so they could make recommendations for the other groups.

### Which phosphate binders to use for children and young people

The committee reviewed the recommendations from the 2013 guideline in the light of limited new evidence. For children and young people with high serum calcium, they agreed to recommend sevelamer carbonate instead of sevelamer hydrochloride. This is because sevelamer carbonate offers a better balance of benefits and costs.

### Which phosphate binders to use for adults

The committee reviewed the evidence for phosphate binders both in adults on dialysis and adults not having dialysis. Although the evidence for those not on dialysis was limited, it did reflect the evidence for adults on dialysis in every area apart from sucroferric oxyhydroxide. As there was no evidence on sucroferric oxyhydroxide in adults not on dialysis, the committee did not recommend it for this group.

The evidence showed that the best treatment strategy is to start with calcium acetate, and switch to sevelamer carbonate if the person gets hypercalcaemia. This is because:

- calcium acetate as a first-line treatment provides the best balance of benefits, harms and costs
- calcium carbonate is cheaper than calcium acetate, but is more likely to cause high serum calcium levels and associated adverse outcomes
- sevelamer carbonate and sevelamer hydrochloride are more expensive than calcium acetate, and do not provide enough benefit as a first-line treatment to justify the extra expense
- when people have high serum calcium levels and cannot take calcium acetate, sevelamer carbonate is the best alternative; it is cheaper than sevelamer hydrochloride, and provides similar benefits, however, it still costs more than calcium acetate and, for first-line treatment, it does not provide enough benefit to justify this extra expense
- sucroferric oxyhydroxide is not cost effective as a first-line treatment, but is a reasonable choice for people who cannot take calcium acetate or sevelamer carbonate

- lanthanum carbonate is much more expensive than calcium acetate and sevelamer carbonate and may provide less benefit than other non-calcium-based phosphate binders.

Based on this evidence, the committee recommended a treatment sequence and alternatives for different situations.

Some oral phosphate binders are unpleasant to take, and this might affect adherence. It is important to involve people in the choice of phosphate binder as far as possible, to ensure they are prescribed one they are happy with and can take as recommended.

The committee also agreed that diet and dialysis (when appropriate) had a large impact on serum phosphate levels. Therefore, before offering phosphate binders it is important to provide dietary advice and ensure people are on the dialysis regime that works best for them.

The committee made a research recommendation to address the lack of evidence in adults not on dialysis.

**How the recommendations might affect practice**

Replacing sevelamer hydrochloride with sevelamer carbonate may result in lower resource use, because there is a cheap generic version of sevelamer carbonate available.

Using sucroferric oxyhydroxide may increase resource use. However, it is not currently used in practice, so any change in resource use will depend on how and when organisations use it. Any potential increase is unlikely to be substantial, as it is only recommended as a third-line option.

Return to recommendations

# Context

Chronic kidney disease (CKD) describes abnormal kidney function or structure. It is common and often occurs with other conditions (such as cardiovascular disease and diabetes). Moderate to severe CKD is also associated with an increased risk of acute

kidney injury, falls, frailty and mortality. The risk of developing CKD increases with age.

CKD is usually asymptomatic, but it is detectable, and tests for CKD are simple and available. There is evidence that treatment can prevent or delay the progression of CKD, reduce or prevent the development of complications, and reduce the risk of cardiovascular disease. However, CKD is often unrecognised or diagnosed at an advanced stage. Late presentation of people with kidney failure increases morbidity, mortality and associated healthcare costs.

As kidney disease progresses, some coexisting conditions become more common and increase in severity. Hyperphosphataemia is an example of this, occurring because of insufficient filtering of phosphate from the blood by poorly functioning kidneys. This means that a certain amount of the phosphate does not leave the body in the urine, instead remaining in the blood at abnormally high levels.

High serum phosphate levels can directly and indirectly increase parathyroid hormone secretion, leading to the development of secondary hyperparathyroidism. Left untreated, secondary hyperparathyroidism increases morbidity and mortality and may lead to renal bone disease, with people experiencing bone and muscular pain, fracture, bone and joint abnormalities, and vascular and soft tissue calcification.

Many people with CKD or established renal failure also develop associated anaemia. The prevalence of anaemia associated with CKD increases progressively with the stage of CKD, especially when the person reaches stage 4 or 5. Anaemia of CKD contributes significantly to the burden of CKD. However, it is potentially reversible and manageable with appropriate identification and treatment.

The Health Survey for England (2016) found that 13% of adults (16 years and over) had any CKD (stages 1 to 5). The prevalence of stages 3 to 5 was 5% for all adults, rising to 34% in people aged 75 and over. At the end of 2018 there were 826 children and young people and 66,612 adults receiving renal replacement therapy in the UK according to the UK Renal Registry annual report..

Since publication of the previous guidelines, new evidence was identified for several areas. The following areas of the guideline have been updated:

- investigations for CKD
- classification of CKD
- frequency of monitoring for CKD
- blood pressure control for people with CKD
- phosphate binders to manage mineral and bone disorder in CKD
- glomerular filtration rate for diagnosing anaemia associated with CKD
- intravenous iron for treating anaemia associated with CKD.

# Finding more information and committee details

To find NICE guidance on related topics, including guidance in development, see the NICE webpage on chronic kidney disease.

For details of the guideline committee see the committee member list.

# Update information

**June 2021**

This guideline is an update of NICE guideline CG182 (published July 2014), NICE guideline CG157 (published March 2013) and NICE guideline NG8 (published June 2015) and will replace them.

We have reviewed the evidence on the assessment and management of chronic kidney disease, management of hyperphophatemia in people with chronic kidney disease and the management of anaemia for people with chronic kidney disease.

Recommendations are marked **[2021]** if the evidence has been reviewed.

## Recommendations that have been deleted, or changed without an evidence review

We propose to delete some recommendations from the previous guidelines. Table 4 sets out these recommendations and includes details of replacement recommendations. Recommendations in table 4 marked [2013] are from NICE's guideline on hyperphosphatemia, those marked [2014] are from NICE's current guideline on chronic kidney disease in adults, those marked [2015] are from NICE's

guideline on anaemia; the original recommendation number from each guideline is given in brackets. If there is no replacement recommendation, an explanation for the proposed deletion is given.

In recommendations shaded in grey in the guideline and ending **[2006]**, **[2006, amended 2011]**, **[2006, amended 2015]**, **[2008]**, **[2008, amended 2014]**, or **[2014]**, we have not reviewed the evidence. In some cases minor changes have been made – for example, to update links, or bring the language and style up to date – without changing the intent of the recommendation. Minor changes are listed in table 5.

## Table 4 Recommendations that have been deleted

| Recommendation in previous guidelines | Comment |
|---|---|
| When to use a cystatin C-based estimate of GFR for diagnosis of CKD<br>Consider using eGFRcystatinC at initial diagnosis to confirm or rule out CKD in people with:<br>• an eGFRcreatinine of 45 to 59 ml/min/1.73 $m^2$, sustained for at least 90 days and<br>• no proteinuria (albumin:creatinine ratio [ACR] less than 3 mg/mmol) or other marker of kidney disease. [2014] (1.1.1)<br>Do not diagnose CKD in people with:<br>• an eGFRcreatinine of 45 to 59 ml/min/1.73 $m^2$ and<br>• an eGFRcystatinC of more than 60 ml/min/1.73 $m^2$ and<br>• no other marker of kidney disease. [2014] (1.1.2) | These recommendations were deleted and not replaced. |
| Apply a correction factor to GFR values estimated using the CKD EPI creatinine equation for people of African-Caribbean or African family origin (multiply eGFR by 1.159). [2014] (1.1.3) | Replaced by<br>For adults of African-Caribbean or African family origin, multiply eGFR by 1.159 if calculated using the CKD-EPI creatinine equation. (1.1.3) |
| Whenever a request for serum cystatin C measurement is made, clinical laboratories should report an estimate of glomerular filtration rate (eGFRcystatinC) using a prediction equation (see recommendation 1.1.7) in addition to reporting the serum cystatin C result. [2014] [1.1.6]<br>When an improved assessment of risk is needed (see recommendation 1.1.14), clinical laboratories should use the CKD EPI cystatin C equation to estimate GFRcystatinC. [2014] [1.1.7]<br>Clinical aboratories should use cystatin C assays calibrated to the international standard to measure serum cystatin C for cystatin C-based estimates of GFR. [2014] [1.1.8]<br>Interpret eGFRcystatinC with caution in adults with uncontrolled thyroid disease because eGFRcystatinC values may be falsely elevated in people with hypothyroidism and reduced in people with hyperthyroidism. [2014] [1.1.9] | These recommendations were deleted and not replaced. |

| Recommendation in previous guidelines | Comment |
|---|---|
| Monitor adults for the development or progression of CKD for at least 2 to 3 years after acute kidney injury, even if serum creatinine has returned to baseline. [2014] (1.3.9) | These recommendations were deleted and not replaced. |
| Advise people who have had acute kidney injury that they are at increased risk of CKD developing or progressing. [2014] (1.3.10) | These recommendations were deleted and not replaced. |
| In adults, children and young people with CKD aim to keep the systolic blood pressure below 140 mmHg (target range 120 to 139 mmHg) and the diastolic blood pressure below 90 mmHg [2008] )1.6.1)<br>In people with CKD and diabetes, and also in people with an ACR of 70 mg/mmol or more, aim to keep the systolic blood pressure below 130 mmHg (target range 120 to 129 mmHg) and the diastolic blood pressure below 80 mmHg. [2008] (1.6.2) | Replaced by:<br>In adults with CKD and an ACR under 70 mg/mmol, aim for a systolic blood pressure below 140 mmHg (target range 120 to 139 mmHg) and a diastolic blood pressure below 90 mmHg. (1.6.1)<br>In adults with CKD and an ACR of 70 mg/mmol or more, aim for a systolic blood pressure below 130 mmHg (target range 120 to 129 mmHg) and a diastolic blood pressure below 80 mmHg. (1.6.2)<br>In children and young people with CKD and an ACR of 70 mg/mol or more, aim for a systolic blood pressure below the 50th percentile for height. (1.6.3) |
| An estimated glomerular filtration rate (eGFR) of less than 60 ml/min/1.73 $m^2$ should trigger investigation into whether anaemia is due to CKD. When the eGFR is greater than or equal to 60 ml/min/1.73 $m^2$ the anaemia is more likely to be related to other causes. [2015] (1.7.2) | Replaced by:<br>In people with anaemia:<br>• If eGFR is above 60 ml/min/1.73 $m^2$, investigate other causes of anaemia as it is unlikely to be caused by chronic kidney disease.<br>• If eGFR is between 30 and 60 ml/min/1.73 $m^2$:<br>– think about/ look into? other causes of anaemia but<br>– use clinical judgement to decide how extensive this investigation should be, because the anaemia may be caused by chronic kidney disease.<br>• If eGFR is below 30 ml/min/1.73 $m^2$, think about other causes of anaemia but note that the anaemia is likely to be caused by chronic kidney disease. (1.7.2) |

| Recommendation in previous guidelines | Comment |
|---|---|
| For children and young people, offer a calcium-based phosphate binder as the first-line phosphate binder to control serum phosphate in addition to dietary management. [2013] (1.11.5) | Replaced by:<br>Before starting phosphate binders for adults, children and young people with CKD stage 4 or 5, optimise:<br>• diet (see recommendations 1.4.7 to 1.4.9 for adults)<br>• dialysis, for people who are having this (1.11.5)<br>Offer children and young people with CKD stage 4 or 5 and hyperphosphataemia, a calcium-based phosphate binder to control serum phosphate levels (1.11.8) |
| For children and young people, if a series of serum calcium measurements shows a trend towards the age-adjusted upper limit of normal, consider a calcium-based binder in combination with sevelamer hydrochloride, having taken into account other causes of rising calcium levels. [2013] (1.11.6) | Replaced by:<br>If serum calcium increases towards, or above, the age-adjusted upper normal limit:<br>• investigate possible causes other than the phosphate binder<br>• consider reducing the dose of the calcium-based phosphate binder and adding sevelamer carbonate or switching to sevelamer carbonate alone.<br>(1.11.9) |
| For children and young people who remain hyperphosphataemic despite adherence to a calcium-based phosphate binder, and whose serum calcium goes above the age-adjusted upper limit of normal, consider either combining with, or switching to, sevelamer hydrochloride having taken into account other causes of raised calcium. [2013] (1.11.7) | Replaced by:<br>If serum calcium increases towards, or above, the age-adjusted upper normal limit:<br>• investigate possible causes other than the phosphate binder<br>• consider reducing the dose of the calcium-based phosphate binder and adding sevelamer carbonate or switching to sevelamer carbonate alone.<br>(1.11.9) |

| | |
|---|---|
| For adults, offer calcium acetate as the first-line phosphate binder to control serum phosphate in addition to dietary management. [2013] (1.11.11)<br>For adults, consider calcium carbonate if calcium acetate is not tolerated or the person finds it unpalatable. [2013] (1.11.12)<br>For adults with stage 4 or 5 chronic kidney disease (CKD) who are not on dialysis and who are taking a calcium-based binder:<br>• consider switching to a non-calcium-based binder if calcium-based phosphate binders are not tolerated<br>• consider either combining with, or switching to, a non-calcium-based binder if hypercalcaemia develops (having taken into account other causes of raised calcium), or if serum parathyroid hormone levels are low. [2013] (1.11.13)<br>For adults with stage 5 CKD who are on dialysis and remain hyperphosphataemic despite adherence to the maximum recommended or tolerated dose of calcium-based phosphate binder, consider either combining with, or switching to, a non-calcium-based binder. [2013] (1.11.14)<br>For adults with stage 5 CKD who are on dialysis and who are taking a calcium-based binder, if serum phosphate is controlled by the current diet and phosphate binder regimen but:<br>• serum calcium goes above the upper limit of normal, or<br>• serum parathyroid hormone levels are low<br>consider either combining with, or switching to, sevelamer hydrochloride or lanthanum carbonate, having taken into account other causes of raised calcium. [2013] (1.11.15) | Replaced by:<br>Offer adults with CKD stage 4 or 5 and hyperphosphataemia, calcium acetate to control serum phosphate levels.<br>In June 2021, this was an off-label use of calcium acetate in people not on dialysis. See NICE's information on prescribing medicines. (1.11.11)<br>Offer sevelamer carbonate if calcium acetate is not indicated (for example, because of hypercalcaemia or low serum parathyroid hormone levels) or not tolerated.<br>In June 2021, this was an off-label use of sevelamer carbonate. See NICE's information on prescribing medicines. (1.11.12)<br>If calcium acetate and sevelamer carbonate cannot be used, consider:<br>• sucroferric oxyhydroxide, for adults on dialysis if a calcium-based phosphate binder is not needed or<br>• calcium carbonate, if a calcium-based phosphate binder is needed.<br>In June 2021, this was an off-label use of these phosphate binders in people not on dialysis. See NICE's information on prescribing medicines.( 1.1.13)<br>Only consider lanthanum carbonate for adults with CKD stage 4 or 5 if other phosphate binders cannot be used.<br>In June 2021, this was an off-label use of lanthanum carbonate phosphate binders in people not on dialysis and with serum phosphate levels less than 1.78 mmol/l. See NICE's information on prescribing medicines. (1.1.14)<br>If adults with CKD stage 4 or 5 remain hyperphosphataemic after taking the maximum dose recommended in the BNF (or the maximum dose they can tolerate if that is lower), of a calcium-based phosphate binder:<br>• check they are taking it as prescribed<br>• consider combining a calcium-based phosphate binder with a non-calcium-based phosphate binder. (1.11.15) |

| Recommendation in previous guidelines | Comment |
|---|---|
| If a combination of phosphate binders is used, titrate the dosage to achieve control of serum phosphate while taking into account the effect of any calcium-based binders used on serum calcium levels (also see recommendations 1.8.6, 1.8.71.1.6, 1.1.7 and 1.8.10 to 1.8.12, 1.1.10 to 1.1.12). [2013] (1.11.16) | Replaced by:<br>For all people who are taking more than one phosphate binder, titrate the dosage to achieve the best possible control of serum phosphate while keeping serum calcium levels below the upper normal limit. (1.11.16) |
| Take into account patient preference and the ease of administration, as well as the clinical circumstances, when offering a phosphate binder in line with recommendations 1.8.5 to 1.8.12, 1.1.5 to 1.1.12. [2013] (1.12.9)<br>Advise patients people with hyperphosphataemia (or, as appropriate,and their parents family and/or carers, if appropriate) that it is necessary to take phosphate binders with food to control serum phosphate. [2013] (1.12.10) | Replaced by:<br>Before starting phosphate binders, optimise:<br>• diet (see recommendations 1.4.7 to 1.4.9 for adults)<br>• dialysis, for people who are having this. (1.11.5)<br>When offering a phosphate binder, explain to people and their families or carers (as appropriate):<br>• the reason for offering phosphate binders<br>• the risks if they are not taken and<br>• that they need to take phosphate binders with food (including, for example, high-protein snacks).. (1.11.6) |
| At every routine clinical review, assess the person's serum phosphate control, taking into account:<br>• dietary phosphate management<br>• phosphate binder regimen<br>• adherence to diet and medication<br>• other factors that influence phosphate control, such as vitamin D or dialysis. [2013] (1.11.17) | Replaced by:<br>At every routine clinical review, assess the person's serum phosphate control, taking into account:<br>• diet<br>• whether they are taking the phosphate binders as recommended<br>• other relevant factors, such as vitamin D, serum parathyroid hormone levels or dialysis. (1.11.17) |

| Recommendation in previous guidelines | Comment |
|---|---|
| Agree the frequency of re (eGFRcreatinine and ACR) with the person with, or at risk of, CKD; bear in mind that CKD is not progressive in many people. [2014] (1.3.1)<br>Use table 2 to guide the frequency of GFR monitoring for people with, or at risk of, CKD, but tailor it to the person according to:<br>• the underlying cause of CKD<br>• past patterns of eGFR and ACR (but be aware that CKD progression is often non-linear)<br>• comorbidities, especially heart failure<br>• changes to their treatment (such as renin–angiotensin–aldosterone system [RAAS] antagonists, NSAIDs and diuretics)<br>• intercurrent illness<br>• whether they have chosen conservative management of CKD. [2014] (1.3.2) | Replaced by:<br>If a person has CKD, or is at risk of it, agree the frequency of monitoring (eGFRcreatinine and ACR) with them (and their family members or carers, as appropriate), bearing in mind that CKD is not progressive in many people (1.3.1)<br>Use table 2 to guide the minimum frequency of GFR monitoring, but tailor it according to:the underlying cause of CKD<br>• rate of change in eGFR or change in ACR (but be aware that CKD progression is often non-linear)<br>• other risk factors including heart failure; diabetes; hypertension<br>• changes to their treatment (such as renin–angiotensin–aldosterone system [RAAS] antagonists, NSAIDs and diuretics)<br>• intercurrent illness<br>• whether they have chosen conservative management of CKD. (1.3.2) |
| Offer a low cost renin–angiotensin system antagonist to people with CKD and:<br>• diabetes and an ACR of 3 mg/mmol or more (ACR category A2 or A3)<br>• hypertension and an ACR of 30 mg/mmol or more (ACR category A3)<br>• an ACR of 70 mg/mmol or more (irrespective of hypertension or cardiovascular disease)2. [2014] (1.6.3) | Replaced by:<br>Offer an angiotensin-receptor blocker (ARB) or an angiotensin-converting enzyme (ACE) inhibitor to adults, children and young people with CKD who have hypertension and an ACR over 30 mg/mmol (ACR category A3 or above). (1.6.5) |
| Monitor GFR at least annually in people prescribed drugs known to be nephrotoxic, such as calcineurin inhibitors (for example, cyclosporin or tacrolimus), lithium and non-steroidal anti-inflammatory drugs (NSAIDs). [2014](1.1.27) | Replaced by:<br>Monitor GFR at least annually in adults, children and young people prescribed drugs known to be nephrotoxic, such as calcineurin inhibitors (for example, cyclosporin or tacrolimus), lithium and non-steroidal anti-inflammatory drugs (NSAIDs). (1.1.27) |

| Recommendation in previous guidelines | Comment |
|---|---|
| To detect and identify proteinuria, use urine ACR in preference to protein:creatinine ratio (PCR), because it has greater sensitivity than PCR for low levels of proteinuria. For quantification and monitoring of levels of proteinuria of ACR 70 mg/mmol or more, PCR can be used as an alternative. ACR is the recommended method for people with diabetes. [2014] (1.1.18) | Replaced by<br>For the initial detection of proteinuria in adults, children and young people:<br>• use urine ACR rather than protein:creatinine ratio (PCR) because of the greater sensitivity for low levels of proteinuria<br>• confirm an ACR between 3 mg/mmol and 70 mg/mmol in a subsequent early morning sample.<br>A repeat sample is not needed if the initial ACR is 70 mg/mmol or more. (1.1.12) |
| Quantify urinary albumin or urinary protein loss as in recommendation 1.1.18 for:<br>• people with diabetes<br>• people without diabetes with a GFR of less than 60 ml/min/1.73 $m^2$. [2014] (1.1.21) | Replaced by<br>Measure proteinuria with urine ACR in the following groups:<br>• adults, children and young people with diabetes (type 1 or type 2)<br>• adults with a GFR less than 60 ml/min/1.73 m2<br>• adults with a GFR of 60 ml/min/1.73 m2 or more if there is a strong suspicion of CKD<br>• children and young people without diabetes and with creatinine above the upper limit of the age-appropriate reference range.<br>When ACR is 70 mg/mmol or more, PCR can be used as an alternative to ACR (1.1.14) |
| Do not use reagent strips to identify proteinuria unless they are capable of specifically measuring albumin at low concentrations and expressing the result as an ACR. [2014] (1.1.17) | Replaced by<br>Do not use reagent strips to identify proteinuria. (1.1.11) |
| When testing for the presence of haematuria, use reagent strips rather than urine microscopy.<br>• Evaluate further if there is a result of 1+ or more.<br>• Do not use urine microscopy to confirm a positive result. [2014] (1.1.23) | Replaced by:<br>Use reagent strips to test for haematuria in adults, children and young people.<br>• Evaluate further for results of 1+ or higher.<br>• Do not use urine microscopy to confirm a positive result. (1.1.16) |

| Recommendation in previous guidelines | Comment |
|---|---|
| People with CKD in the following groups should normally be referred for specialist assessment:<br>• GFR less than 30 ml/min/1.73 $m^2$ (GFR category G4 or G5), with or without diabetes<br>• ACR 70 mg/mmol or more, unless known to be caused by diabetes and already appropriately treated<br>• ACR 30 mg/mmol or more (ACR category A3), together with haematuria<br>• sustained decrease in GFR of 25% or more, and a change in GFR category or sustained decrease in GFR of 15 ml/min/1.73 $m^2$ or more within 12 months<br>• hypertension that remains poorly controlled despite the use of at least 4 antihypertensive drugs at therapeutic doses (see also NICE clinical guideline on hypertension in adults)<br>• known or suspected rare or genetic causes of CKD<br>• suspected renal artery stenosis. [2014] (1.5.2) | Replaced by:<br>Refer adults with CKD for specialist assessment (taking into account their wishes and comorbidities) if they have any of the following:<br>• a 5-year risk of needing renal replacement therapy of greater than 5% (measured using the 4-variable Kidney Failure Risk Equation)<br>• an ACR of 70 mg/mmol or more, unless known to be caused by diabetes and already treated<br>• an ACR of 30 mg/mmol or more (ACR category A3), together with haematuria<br>• a sustained decrease in GFR of 25% or more and a change in GFR category within 12 months<br>• a sustained decrease in GFR of 15 ml/min/1.73 m2 or more per year<br>• hypertension that remains poorly controlled (above the person's individual target) despite the use of at least 4 antihypertensive drugs at therapeutic doses (see also NICE's guideline on hypertension in adults)<br>• known or suspected rare or genetic causes of CKD<br>• suspected renal artery stenosis. (1.5.5) |

**Table 5 Minor changes to recommendation wording (no change to intent)**

| Recommendation numbers in current guideline | Comment |
|---|---|
| All recommendations except those labelled [2021] | Recommendations have been edited into the direct style (in line with current NICE style for recommendations in guidelines) where possible. Yellow highlighting has not been applied to these changes. |