UKMi North West

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A summary of prescribing recommendations from NICE guidance

Anaemia management in people with CKD

NICE NG8; 2015

This guideline covers the management of anaemia associated with CKD in adults, children and young people.

Definition of terms

CKD	chronic kidney disease
eGFR	estimated glomerular filtration rate
Hb	haemoglobin
%HRC	percentage hypochromic red blood cells
TSAT	transferrin saturation
ESA	erythropoietic stimulating agent
IV	intravenous
SC	subcutaneous
ACEI	angiotensin converting enzyme inhibitor
ARB	angiotensin receptor blocker
U	unlicensed

Assessment and diagnosis

eGFR

- If eGFR is:
  - < 60 ml/min/1.73m^2 - investigate if anaemia is due to CKD,
  - ≥ 60 ml/min/1.73m^2 - consider other causes of anaemia.

Hb

- Consider treating anaemia in people with CKD if:
  - their Hb level falls to ≤110 g/l (≤105 g/l in children <2 years old), **OR**
  - they develop symptoms of anaemia e.g. tiredness, shortness of breath, lethargy and palpitations.

Other diagnostic tests

- 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 receiving haemodialysis).
- Use %HRC > 6%, but only if blood sample can be processed within 6 hours.
- If unable to use %HRC use reticulocyte Hb content (<29 pg) or equivalent tests e.g. reticulocyte Hb equivalent.
- If these tests are not available or the person has thalassaemia or thalassaemia trait, use a combination of transferrin saturation (<20%) and serum ferritin measurement (<100 micrograms/litre).
- **Do NOT** request transferrin saturation or serum ferritin measurement alone to assess iron deficiency status in people with anaemia of CKD.
- **Do NOT** use age alone as a determinant for treatment of anaemia of CKD.
- **Do NOT** use erythropoietin levels for diagnosing or managing anaemia of CKD.

Treatment and management

- Treat clinically relevant hyperparathyroidism to improve the management of anaemia.

Iron therapy

- Offer iron therapy to people who are iron deficient and **not receiving** ESA therapy, before discussing ESA therapy.
- Discuss the risks and benefits of treatment options. Take into account the person's choice.
- In people treated with iron, serum ferritin levels should not rise above 800 micrograms/litre. To prevent this, review dose of iron when serum ferritin levels reach 500 micrograms/litre.
- Discuss results of iron therapy with the person or family/carers as appropriate and offer ESA therapy if needed.

People not on haemodialysis

- Consider a trial of oral iron before offering IV iron therapy.
- Offer IV iron therapy if intolerant of oral iron or target Hb levels are not reached within 3 months.
- When offering IV iron therapy consider **high-dose low-frequency** as treatment of choice for adults and young people when trying to achieve iron repletion. Take into account all of the following:
  - preferences of person or family/carers as appropriate,
  - nursing and administration costs,
  - cost of local drug supply,
  - provision of resuscitation facilities.

People on haemodialysis,

- Offer IV iron therapy.
- Offer oral iron therapy only if:
  - IV iron therapy is contraindicated, **OR**
  - the person chooses not to have IV iron therapy after discussing relative efficacy and side effects of both.
- IV iron at a **low-dose high-frequency** may be more appropriate for all children**U** and for adults who are receiving in-centre haemodialysis.

Erythropoietic Stimulating Agent (ESA) therapy

- Give ESAs to people who are likely to benefit from treatment in terms of quality of life and physical function.
- **Do NOT** initiate ESAs without managing any pre-existing iron deficiency.
- ESAs need not be given if comorbidities or prognosis is likely to negate the benefits of correcting the anaemia.
- Discuss advantages and disadvantages of anaemia management with patient, family/carers.
- Initiate a trial of anaemia correction when there is uncertainty over whether the presence of comorbidities, or the prognosis, would negate benefit from correcting the anaemia with ESAs.
- Give GPs and patients information about why ESA therapy is required, how it works and what benefits and side effects may be experienced.
- There is no evidence to distinguish between ESAs in terms of efficacy.
- Discuss choice of ESA with the patient when starting treatment and at subsequent reviews. Consider the:
  - patient's dialysis status, lifestyle and preferences,
  - route and frequency of administration e.g. SC vs. IV, long-acting vs. short-acting preparations, pain of injection, cost and local availability of ESAs.
- When prescribing ESAs, take into account patient preferences about supervised- or self-administration, dose frequency, pain on injection, method of supplying ESA and storage.
- If appropriate make arrangements to provide ready, reasonable and uninterrupted access to supplies so that people can self-administer ESA in a way that is clinically effective and safe.

See NICE pathway: Anaemia management in people with CKD

NHS

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Anaemia management in people with CKD……continued

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Adjusting ESA dose and frequency

- Optimise iron status before or at initiation of ESA administration and during maintenance treatment.
- Use of ACEIs or ARBs is not precluded, but if used, consider an increase in ESA therapy.
- Dose and frequency of ESA should be:
  - determined by the duration of action and route of administration of ESA,
  - adjusted to keep the rate of Hb increase between 10 and 20 g/litre/month.
- Take into account:
  - when using short-acting ESAs, SC injection allows use of lower doses than IV administration,
  - Hb measurements when determining dose and frequency of ESA administration
- Investigate cause of an unexpected change in Hb level (e.g. intercurrent illness, bleeding) to enable intervention and optimise iron status.
- Increase or decrease ESA dose and/or frequency when Hb measurements fall outside action thresholds (usually <105 g/litre or >115 g/litre), or for example, when rate of change of Hb suggests an established trend (e.g.>10 g/litre/month).

Optimising and monitoring Hb status

People receiving iron therapy

- When determining an individual's aspirational Hb range take into account symptoms and comorbidities, required treatment and patient preference.

People receiving ESA therapy

- Correction to normal levels of Hb with ESAs is not usually recommended.
- Typically* maintain aspirational Hb range:
  - between 100 and 120 g/litre for adults, young people and children aged ≥2 years,
  - between 95 and 115 g/litre for children < 2 years of age, reflecting the lower normal range in that age group.
- To keep Hb level within aspirational range, do not wait until levels are outside this range before adjusting treatment e.g. take action when levels are within 5 g/litre of range limits.
- Consider accepting Hb levels below aspirational range if:
  - high doses** of ESAs are required to achieve the aspirational range, **OR**
  - aspirational range is not achieved despite escalating ESA doses.
- Monitor Hb:
  - every 2 to 4 weeks in induction phase of ESA therapy,
  - every 1 to 3 months in maintenance phase of ESA therapy,
  - more actively after an ESA dose adjustment,
  - in a clinical setting chosen in discussion with the patient, taking into consideration convenience and local healthcare systems.

Correcting iron status in people on ESA therapy

- Offer IV iron therapy for:
  - adults and young peopleU,
  - childrenU who are receiving haemodialysis.
- Consider oral iron for children who are not receiving haemodialysis. If intolerant of oral iron or target Hb levels are not reached within 3 months offer IV iron therapy.
- Offer oral iron therapy to adults and young peopleU receiving ESA therapy only if:
  - IV iron therapy is contraindicated, **OR**
  - the person chooses not to have IV iron therapy after discussing relative efficacy and side effects.
- Offer people who are receiving ESAs iron therapy to achieve:
  - %HRC <6%***
  - reticulocyte Hb count or equivalent tests >29 pg***
- If the above tests are not available or the person has thalassaemia or thalassaemia trait, iron therapy should maintain transferrin saturation > 20% and serum ferritin level >100 micrograms/litre***
- Most patients will need 500–1000 mg of iron for adults or equivalent doses for children (see BNFC), in a single or divided dose depending on the preparation.
- IV iron should be administered in a setting with facilities for resuscitation.

Maintaining iron status

- Once %HRC is <6%, reticulocyte Hb count or equivalent tests >29 pg, or transferrin saturation is >20% and serum ferritin level is >100 micrograms/litre, offer maintenance iron.
- The dosing regimen will depend on modality e.g. haemodialysis patients will need the equivalent of 50 to 60 mg/week IV iron (or an equivalent dose in childrenU of 1 mg/kg/week).
- Offer iron therapy to people receiving ESA maintenance therapy to keep their:
  - %HRC<6%***
  - reticulocyte Hb count or equivalent tests >29 pg*** transferrin saturation level >20% and serum ferritin level >100 micrograms/litre***
- The marker of iron status should be monitored every 1 to 3 months in people receiving 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.

Reviewing ESA therapy

- Review all people started on ESA therapy after an agreed interval and assess effectiveness in order to decide whether or not to continue using ESAs. This should be a mutual decision between clinician, the person with anaemia of CKD and their families/carers.

Monitoring iron status

- People with anaemia of CKD should not have iron levels checked earlier than one week after receiving IV iron. The length of time to monitoring of iron status is dependent on product used and amount of iron given.
- Routine monitoring of iron stores to prevent iron overload using serum ferritin should be at intervals of 1 to 3 months.

ESA resistance – see NICE pathway

- After other causes of anaemia have been excluded, people should be considered resistant to ESAs when:
  - an aspirational Hb range is not achieved despite treatment with ≥300 IU/kg/week of SC epoetin or ≥450 IU/kg/week of IV epoetin or 1.5 micrograms/kg/week of darbepoetin, **OR**
  - there is a continued need for administration of high doses of ESAs to maintain aspirational Hb range.

Red cell transfusion – see NICE pathway

- **Do NOT** use androgens to treat anaemia of CKD.
- **Do NOT** give supplements of vitamin C, folic acid or carnitine as adjuvants for treatment of anaemia of CKD.

*See MHRA guidance

**>175 international units (IU)/kg/week for haemodialysis population; >125 IU/kg/week for peritoneal dialysis population; >100 IU/kg/week for non-dialysis population

*** unless serum ferritin is >800 micrograms/litre

Recommendations – wording used such as 'offer' and 'consider' denote the strength of the recommendation.

Drug recommendations – the guideline assumes that prescribers will use a drug's Summary of Product Characteristics (SPC) to inform treatment decisions