1. Introduction

Anaemia is a common consequence of chronic kidney disease with a significant impact on patient morbidity and probably mortality. Anaemia is known to contribute to long term health issues including cardiomyopathy(1) and left ventricular hypertrophy(2). There is now good evidence that correction of anaemia with erythropoesis-stimulating agents (ESAs) reduces morbidity and probably improves survival in dialysis patients. Similar data are emerging for the use of ESAs in pre-dialysis patients. Current targets for anaemia management follow the Renal Association (3), and NICE guidelines (4).

2. Scope

This guideline is for use by the nephrology MDT team to aid in the management of anaemia in patients with established renal failure.

3. Recommendations, Standards and Procedural Statements

3.1 Aims and Objectives

- To maintain haemoglobin between 100 and 120g/L in patients with ERF.
- To administer drug safely, minimising the risk of infection and optimising effectiveness of the drug

3.2 Indications for ESA therapy

- Haemoglobin consistently lower than 11g/dL i.e. at least two recordings more than two weeks apart
- Other causes of anaemia excluded
- Adequate iron stores - ferritin >100µg/L, transferrin saturation (TSAT) >20%, reticulocyte haemoglobin content (CHr) > 29pg.

3.3 Contraindications to ESA therapy

- Uncontrolled blood pressure
- Inadequate iron stores

3.4 Prior to starting ESA therapy

- Exclude other treatable cause of anaemia eg blood loss, occult infection, chronic inflammation.
- Check iron status (see below).
- Check vitamin B12 and folate levels.

The decision to prescribe ESAs will only be made by a consultant or specialist registrar (Consultant only for pre-dialysis patients).

3.5 Assessing iron status

Iron deficiency is the single most important reason for a failed response to ESAs.
For patients being considered for ESA treatment:

- If Ferritin >100ug/L but <500ug/L start oral iron (all patients receiving ESAs should take oral iron unless not tolerated)
- If Ferritin < 100ug/l or TSAT <20% start oral iron and arrange IV iron sucrose as separate guidance. Start ESA with last iron infusion.

- Iron-deficient unit-based haemodialysis patients will receive an intravenous course of replacement iron and then maintenance intravenous iron (see “Iron therapy for anemia of chronic disease” guideline).

3.6 Dosing and route of administration

Pre-dialysis, peritoneal dialysis and home haemodialysis patients.

- ESAs are administered via the sub-cutaneous route in these patients.
- Eprex (Epoetin alpha) start on low dose (50-60unit/kg/week in 2 doses).
- Aranesp (Darbepoetin alpha) start on 0.45micrograms/kg/week as single weekly dose.
- If dose needs to be changed, either change frequency of injection or alter individual injection dose in increments of 1000units or 10micrograms for Epoetin alpha and Darbepoetin alpha respectively to avoid waste.
- Use lowest possible maintenance dose to achieve target Hb.

Unit-based Maintenance Haemodialysis patients.

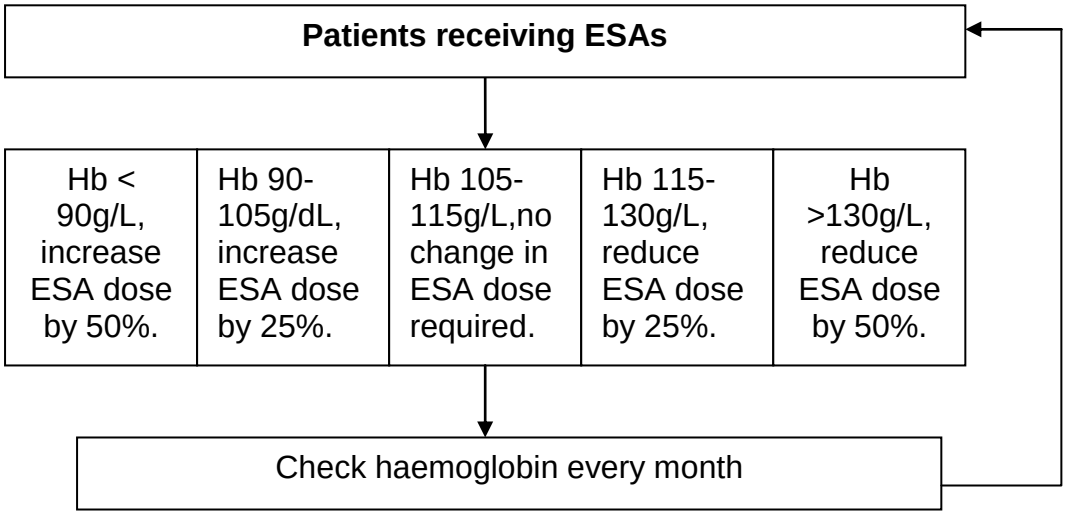
- ESAs are administered via intravenous route while on dialysis (once, twice or three times weekly). Epoetin alpha, and Darbepoetin alpha are licensed for this route and used locally. Use same total weekly dose as for subcutaneous administration and modify dose in the same way.
- The vast majority of established patients on HD, and new patients expecting to remain on HD should be given Epoetin alpha IV. If a patient prefers to continue with SC self-administration of Darbepoetin alpha then this should be allowed. In particular patients who are receiving temporary unit HD, with the expectation of a definitive community based treatment do not need to be changed to IV ESAs.

3.7 Correction phase of treatment with ESAs

- Target Haemoglobin: 10 - 12 g/dl.
- Correction rate: 10 to 20 g/L/ month

A suggested algorithm for the adjustment of ESA dose is given in figure 1.

Figure 1: Algorithm for adjusting ESA dose



3.8 Epo resistance

Failure to reach the target Hb or the need for doses greater than 300iu/kg/week of sc epoetin, 450iu/kg/week iv epoetin or 1.5µg/kg/week or darbapoetin to maintain the target Hb defines ESA resistance.

Possible causes include:

- Iron Deficiency (most common)
- B12 and folate deficiency
- Infection (common)
- Blood loss/destruction (check reticulocyte response to EPO).
- Insufficient dialysis
- Severe hyperparathyroidism
- Malignancy
- Aluminium toxicity
- Pure red cell aplasia (anti-erythropoietin antibodies)

3.9 Rapid response to ESA therapy

If Hb rises at >10g/L/month but <20g/L/month, monitor blood pressure very carefully. If blood pressure rises, treat blood pressure and lower the ESA dose to 1/3 - 1/2 of current dose.

If Hb rises at >20g/L/month, these patients are at risk of accelerated hypertension. Stop ESA for two weeks, monitor blood pressure and adjust therapy accordingly. Re-start ESA after two weeks at 1/2 previous dose.

3.10 Blood pressure

If blood pressure rises on ESA treatment, this should be controlled aggressively with anti-hypertensives. A rapid rise in, and very high absolute level of blood pressure can occur on ESAs. This could result in hypertensive encephalopathy. Under these circumstances ESAs should be discontinued and the blood pressure stabilised before the ESA is restarted.

3.11 Procedure for the administration of intravenous ESAs.

- IV drugs may be administered by a registered practitioner who has completed competencies set by UHL and thereby holds an 'I.V. certificate' (policy 10877, 2002).
- Intravenous ESA can be given at any time during haemodialysis treatment. There is no known interaction with other drugs.
- The prescription for ESA should be clearly written in patients drug chart using Generic name (epoetin alfa, or darbepoetin) and signed by a member of the medical staff (or Nurse Prescriber within the agreed Clinical Management Plan). The dose will be inputted into the 'New Epo Screen' on PROTON and will be updated if any dose change is made.
- The nurse who will administer the drug will wash hands using soap and water or alcohol rub.
- Two qualified nurses should ensure that the prescription corresponds to the patient, and confirmed by use of photographic ID card or patient identity bracelet if locally agreed.
- The drug, dose, frequency, route and expiry date should be checked against the prescription. The patient should be informed of the procedure and will have given consent to continue with administration.
- Administration of the drug should be recorded on the patient's drug sheet and signed for by both nurses.
- The empty syringe will be disposed of in a sharps bin.

3.12 Procedure for the administration of subcutaneous ESAs

- Administration should be by a Registered Nurse with the appropriate training and competency. (UKCC 2000 revised NMC 2002), or an appropriately supervised student nurse, patient or carer.
- ESAs should be prescribed clearly on the patient's drug sheet using the Generic name (Epoetin alfa, or Darbepoetin) and signed by a member of medical staff (or nurse prescriber within the agreed Clinical Management Plan). The dose will be inputted into the 'EPO Screen' on PROTON and will be updated if any dose change is made.
- Two qualified nurses should ensure that the prescription corresponds to the patient, and confirmed by use of photographic ID card or patient identity bracelet if locally agreed.
- The drug, dose, frequency, route and expiry date should then be checked against the prescription. The patient should be informed of the procedure and will have given consent to continue with administration.
- The injections should be divided equally over the week, sites should be rotated at each injection and the injection given at a 90° angle, subcutaneously, the preferred sites are the lateral aspect of the upper arm and thighs and the abdomen (not recommenced where a Peritoneal Catheter is in situ).
- Administration of the drug should be recorded on the patient's drug sheet and signed for by both nurses.
- The empty syringe will be disposed of in a sharps bin.

4. Education and Training

Nil specific

5. Monitoring and Audit Criteria

Key Performance Indicator	Method of Assessment	Frequency	Lead
Number of ERF patients with Hb in target range	Audit / Renal Registry data	Annual	P Topham

6. Legal Liability Guideline Statement

See section 6.4 of the UHL Policy for Policies for details of the Trust Legal Liability statement for Guidance documents

7. Supporting Documents and Key References

NICE guideline NG8. Chronic kidney disease: managing anaemia
https://www.nice.org.uk/guidance/ng8/resources/chronic-kidney-disease-managing-anaemia-51046844101

Renal Association Clinical Guideline. Anaemia in CKD.

https://renal.org/wp-content/uploads/2017/06/anaemia-of-chronic-kidney-disease5d84a231181561659443ff000014d4d8.pdf

8. Key Words

Anaemia, ESA, epo, renal failure

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This table is used to track the development and approval and dissemination of the document and any changes made on revised / reviewed versions

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