TREATMENT AND MANAGEMENT OF ANAEMIA ASSOCIATED WITH CHRONIC KIDNEY DISEASE

This guidance does not override the individual responsibility of health professionals to make appropriate decision according to the circumstances of the individual patient in consultation with the patient and /or carer. Health care professionals must be prepared to justify any deviation from this guidance.

INTRODUCTION

The nature and continuing care of patients with renal anaemia requires a collaborative approach between clinicians, specialist nurses, allied health care professionals and patients. A system of shared care; encompassing specialist and primary care optimises care delivery and the continuing management of renal anaemia.

This guideline offers best practice advice on the diagnostic evaluation and assessment of renal anaemia, along with the management and maintenance using erythropoietin stimulating drugs and oral/IV iron.

The patients covered by this guideline are renal patients under the care of renal consultants at Worcestershire Royal Hospital.

THIS GUIDELINE IS FOR USE BY THE FOLLOWING STAFF GROUPS:

Renal Consultants and Renal Anaemia Team (Specialist Nurse and Pharmacist)

Lead Clinician(s)

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This is the most current document and should be used until a revised version is in place

Key amendments to this guideline

Date	Amendment	By:
27.03.12	Extended for 6 months without amendment to allow for further review.	Dr M Ferring
29.05.12	Extended for two years without amendment.	Dr M Ferring
05.08.15	Document extended for 12 months as per TMC paper approved on 22nd July 2015	TMC
10/7/18	Patient pathway updated	Dr M Ferring

TREATMENT AND MANAGEMENT OF ANAEMIA ASSOCIATED WITH CHRONIC KIDNEY DISEASE

INTRODUCTION

The care of patients with renal anaemia requires a system of shared care between primary and secondary care. The delivery of care is detailed in the following guideline, which applies the principles set out in the NICE guidance NG8 (2015) to the clinical care of Worcestershire patients. Specifically, the guideline addresses the three components of renal anaemia management:

1. Diagnostic evaluation of renal anaemia
2. Anaemia correction using erythropoetin stimulating agents (ESAs) and / or iron, and
3. Maintenance of target haemoglobin (Hb).

Disease Background

Anaemia in patients with Chronic Kidney Disease (CKD) may develop in response to a variety of causes.

Healthy kidneys produce a hormone called erythropoietin that stimulates the bone marrow to produce red blood cells. Moderate to severe CKD may affect the ability of the kidneys to stimulate red blood cell production, resulting in insufficient erythropoietin production leading to the development of anaemia. Erythropoietin deficiency is the primary cause of anaemia associated with CKD and becomes more common as Glomerular Filtration Rate (GFR) declines, it is almost universal in end stage kidney disease.

Other causes of renal anaemia include functional or absolute iron deficiency, blood loss (either occult or overt) and deficiency of folate and or vitamin B12.

Possible adverse effects of anaemia include risk of cardiovascular complications (eg left ventricular hypertrophy), exacerbation of symptoms such as tiredness, lethargy, shortness of breath, reduced cognition and concentration, sleep disturbances and reduced immune response. This can lead to an increase in hospital admissions and impaired quality of life.

If patients with CKD are found to be anaemic (Hb 110 g/litre or less), NICE guidance NG8 (2015) recommends that these patients are fully evaluated to identify whether any other factors other than erythropoietin deficiency are the cause of anaemia. In particular, iron deficiency is common and should be corrected prior to commencement of ESA therapy.

Anaemia treatment should be offered to all patients with CKD “who are likely to benefit in terms of quality of life and physical function”. Therefore, NICE guidance NG8 suggests aspirational Hb range between 100 and 120 g/litre, do not wait until Hb levels are outside the aspirational range before adjusting treatment. (eg take action when Hb levels are within 5 g/litre of the range’s limits)

However full correction of anaemia to the adult Hb reference range is associated with higher mortality, which seems counterintuitive, but has level one evidence.

PROTOCOL

Please see algorithms 1 – 5 below.

A) Initial assessment (Algorithm 1)
The likely cause of anaemia needs to be established and confirmed as being due to CKD. Anaemia in CKD is typically normochromic, normocytic, hypoproliferative in the context of a GFR of < 60 ml/min, with a normal white cell and platelet count. Thus, anaemia should be routinely investigated in patients with Hb 110g/l or less of if the patient develops symptoms attributable to anaemia.

B) Correction of anaemia in CKD (Algorithm 2, 3, 4)
The aim of treatment is to maintain the aspirational Hb range between 100 and 120g/ litre. Prior to starting ESA, the need for iron therapy needs to be assessed. Iron should be given if iron deficiency is confirmed. Iron status should be monitored to achieve a target ferritin of greater than 100mcg/litre and transferrin saturations greater than 20%. A trial of oral iron should be offered in the first instance. If after 3 months the aspirational Hb is not achieved Intravenous Iron should then be offered. In people treated with iron, serum ferritin levels should not rise above 800mcg/litre. Review the dose of iron when serum ferritin levels reach 500mcg/litre to prevent this from happening.

ESA treatment is given if anaemia without iron deficiency is confirmed. Neo-Recormon (Epoetin-Beta) is the drug of choice. The required dose is calculated at 60 units/per kg weekly in the first instance. The ESA dose should be adjusted according to the response, i.e. rise of Hb (target 10-20 g/l) achieved by 4 weeks. In order to keep Hb levels within the aspirational range, do not wait until Hb levels are outside the aspirational range before adjusting treatment. (ie take action when Hb levels are within 5g/litre of the range's limits). Further monitoring of Hb every 2- 4 weeks is needed until an Hb of 110g/l is reached.
Poor response to ESA, despite increasing doses, requires further medical assessment of the patient.

C) Maintenance of stable Hb target in CKD (algorithm 5)
Once target range Hb (100–120g/l) is achieved, the ESA dose is maintained unless there is a further rise in Hb, or reduced if Hb continues to rise. In order to keep Hb levels within the aspirational range, do not wait until Hb levels are outside the aspirational range before adjusting treatment. (ie take action when Hb levels are within 5g/litre of the range's limits). Four-weekly Hb measurements are recommended until Hb stable (i.e. when Hb remains within target range). Thereafter, Hb can be monitored every 3 months, unless there are clinical symptoms of anaemia, angina, heart failure, or there is blood loss. Ferritin, transferrin saturations and BP should be monitored every 3 months if stable.

D) Blood pressure guideline (BP):
ESA treatment can increase blood pressure and result in uncontrolled hypertension. This may result in accelerated hypertension and hence requires careful monitoring.

- ESA therapy should not be started if blood pressure (BP) is > 160/100mmHg
- In principle BP is best controlled at 140/80mmHg or better by the time ESA therapy is started
- If BP rises > 180/105mmHg during ESA treatment and is still raised after three consecutive readings (within a 1 month time frame) or if the patient is symptomatic with hypertension, further ESA injections should be withheld until BP is adequately controlled. Antihypertensive medications should be reviewed in order to achieve this.

In general, BP should be monitored for the first 2 months at weekly intervals. Thereafter, BP check should be at least once every 2 months. Depending on individual patients' needs, more frequent or less frequent monitoring may be appropriate.

E) Delivery of care and responsibilities

Aim of the renal anaemia clinic:
The renal anaemia clinic aims to provide clinically effective, consistent and safe management of patients with renal anaemia. Patients will be encouraged to participate within their care where possible.

Patient pathway:
All patients will be under the care of a nephrologist at Worcester Royal Hospital (WRH). Patients with a GFR <60 and Hb level of 110g/l or less will be referred to the renal anaemia service.

All patients will have preliminary investigations performed, and appropriate treatment pathway commenced (Iron therapy or ESA therapy).

For patients requiring ESA therapy they will be invited to attend the renal anaemia clinic for ESA therapy to be initiated. (Correction phase) During this time where possible patients/carers will be taught how to administer their own injections. At clinic visit 5 patients will have repeat blood tests taken to appraise their response to ESA therapy. Future dose of ESA therapy will then be established (Maintenance phase). At clinic visit 6 patients will be issued with a further 6 ESA injections that will be supplied by pharmacy at WRH and instructions for further administration in the community. Arrangements will be made with the patient to have repeat blood tests taken 4 weeks later. This will allow for further monitoring and dose changes as required. Patients will have on going monitoring of blood tests will be undertaken by the Renal Anaemia Team and direct liaison with the patient by telephone regarding their future doses and administration will be made. GP's will be informed by letter. All patients will continue to be seen by the nephrologists during their scheduled renal clinic appointments.

Modifications to this pathway may be considered in exceptional cases to accommodate individual patients' needs (for example patient is too frail to attend anaemia clinic frequently).

Duties of care in the renal anaemia clinic:

In the renal anaemia clinic, the assessment, commencement of appropriate treatment pathway and correction of renal anaemia is carried out by the Renal Anaemia Team, who are supported by nephrologists at WRH. Initial ESA therapy is administered by the Renal Anaemia Team in the clinic setting. Where possible patients/carers are taught how to administer their own injections. Intravenous Iron therapy is administered in our medical day case department at WRH or the AEC clinic at AH and arrangements for this are made by the Renal Anaemia Team. Practice is guided by trust protocols and algorithms within this protocol which are approved by WAHT Medicines Safety Committee. The nephrologists will be asked to assess patients, in particular if there is suspicion about a non-renal cause for anaemia, if there is poor ESA response, or if there are problems with blood pressure and / or fluid retention.

Advice:

Advice on renal anaemia management is given to primary care at each clinic visit in the form of the clinic letter, and the specialist nurse or the nephrologists may be contacted if there are queries outside of clinic visits.

ESA treatment requires regular monitoring of blood pressure, Hb, ferritin and transferrin saturations. It is desirable to share this monitoring with primary care whenever possible for patient convenience.

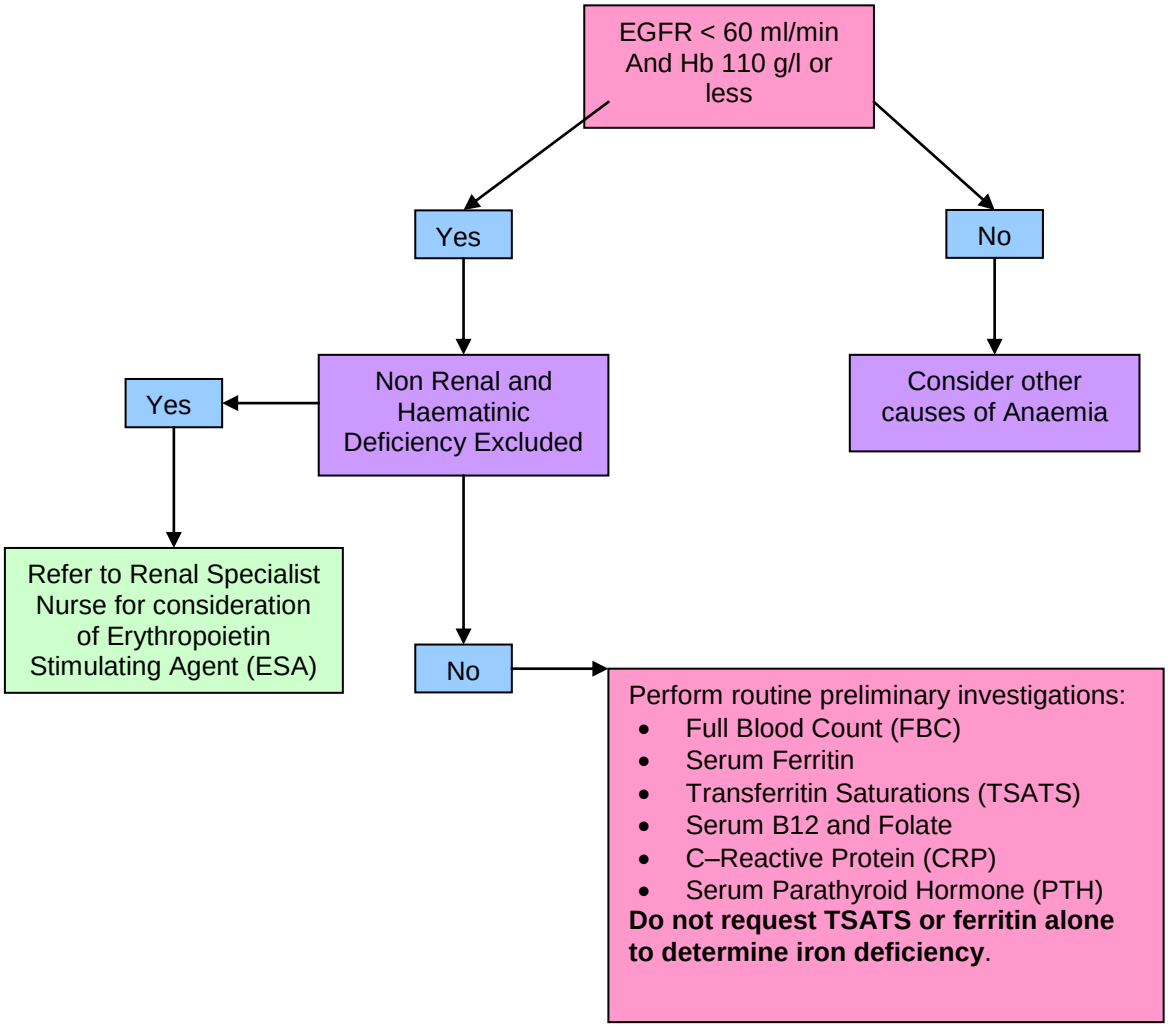
For patients who are not able to self-administer their own injections, it may be necessary for these ESA injections to be administered by the practice nurse based within local GP surgery's or district nurses for housebound patients.

Supply of ESA:

ESA is currently prescribed via the renal anaemia clinic, and supplied from WRH pharmacy.

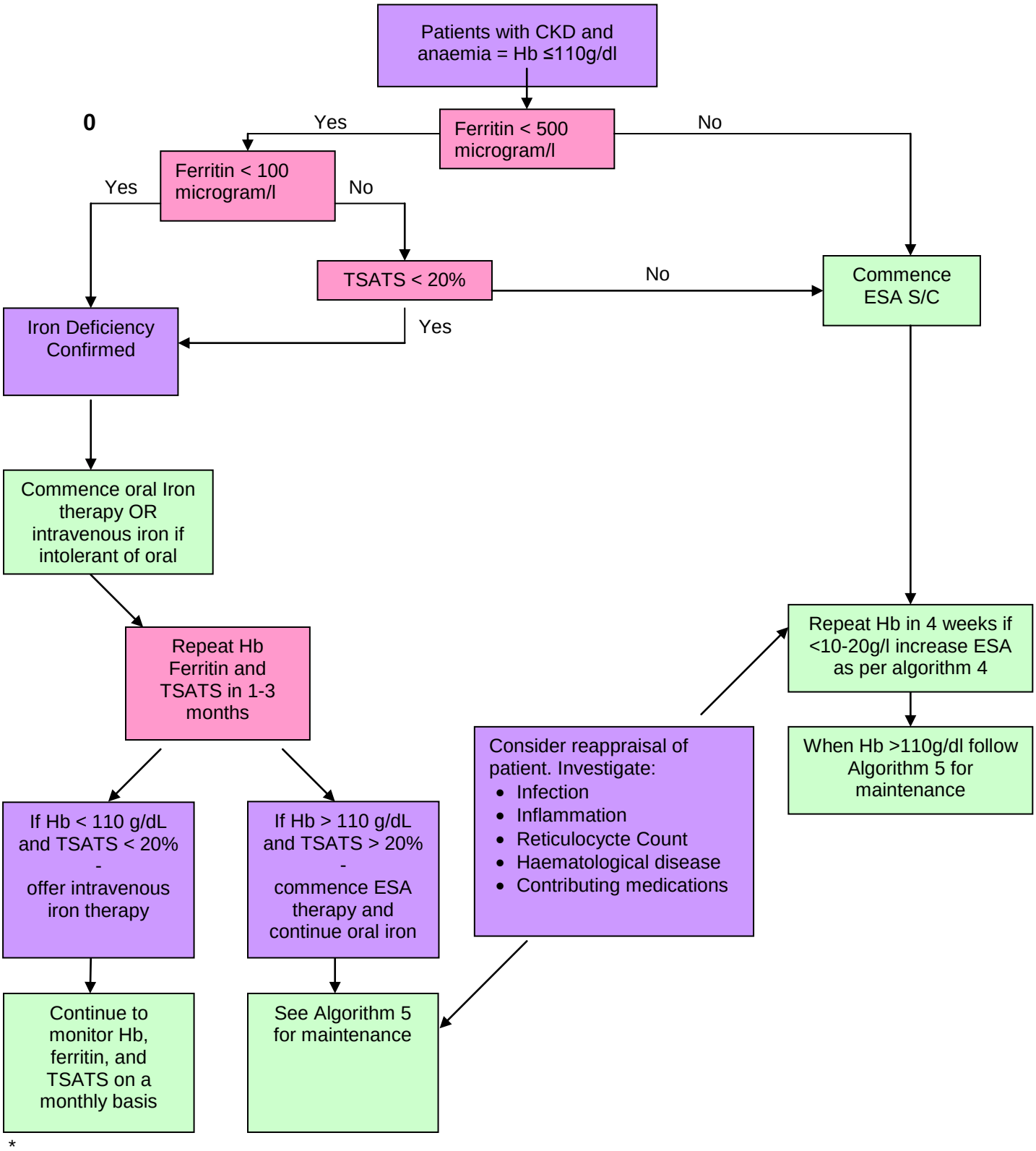
ALGORITHM 1

Algorithm for Diagnosis of Anaemia in CKD Adults



ALGORITHM 2

Algorithm for correction of anaemia in CKD (overview)



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ALGORITHM 3

Algorithm for the administration of IV Ferinject (Ferric Carboxymaltose) in CKD patients with confirmed iron deficiency anaemia

Intravenous Iron is to be administered in patients with
Hb<110g/dl
Ferritin <100mcg or
TSATS <20%.

Who have not responded to a 3 month trial of oral iron or in patients who are intolerant of oral iron.

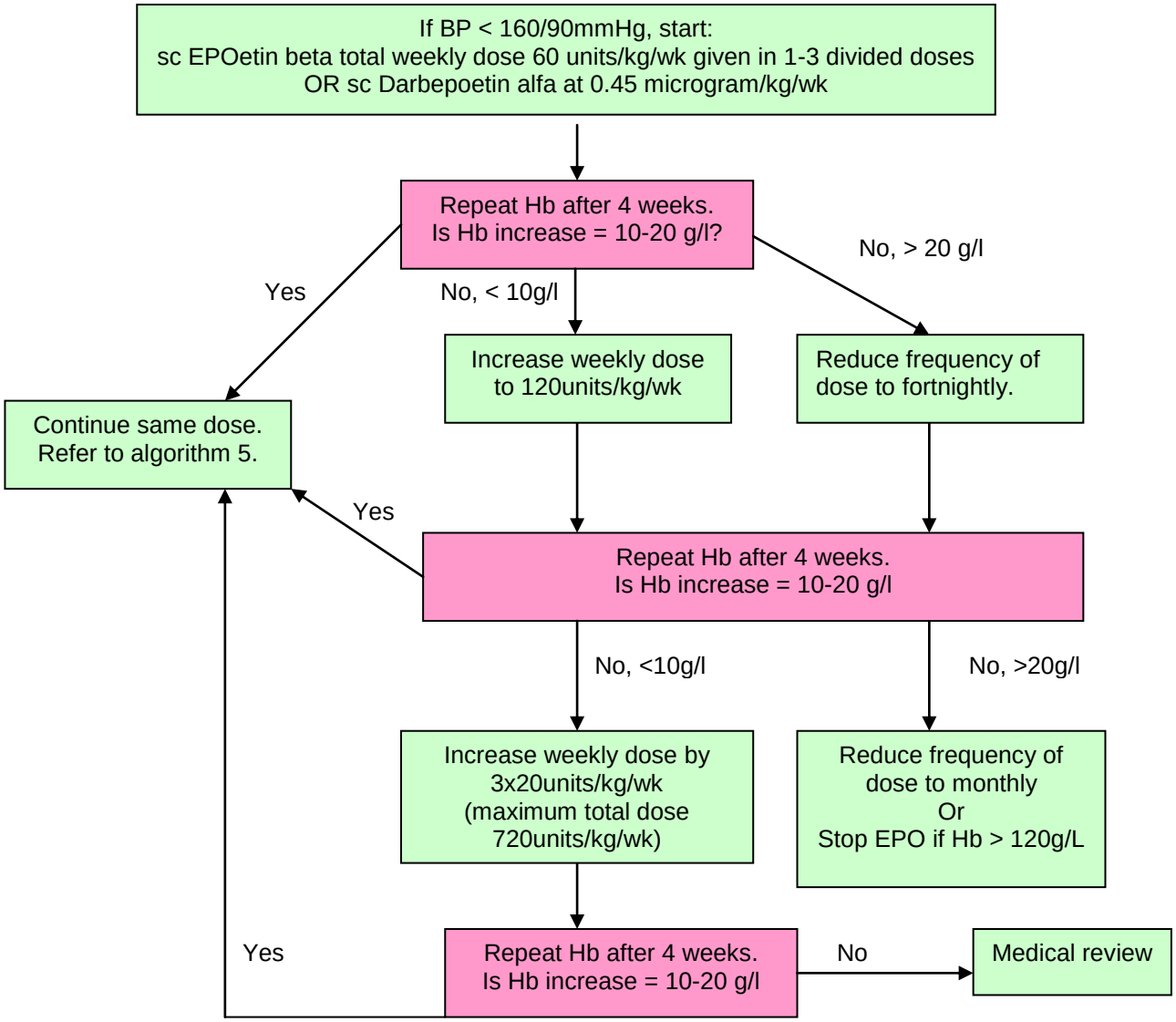
Each injection to be administered **once only within a month**

Hb, Ferritin and TSATS to be checked 1month post treatment and 1-3 months thereafter.

Body Weight	Maximum single dose / month
≤ 50 kg	**500 mg** in 250 mls 0.9% NaCl over 30 minutes
> 50 kg	**1000 mg** in 250 mls 0.9% NaCl over 30 minutes

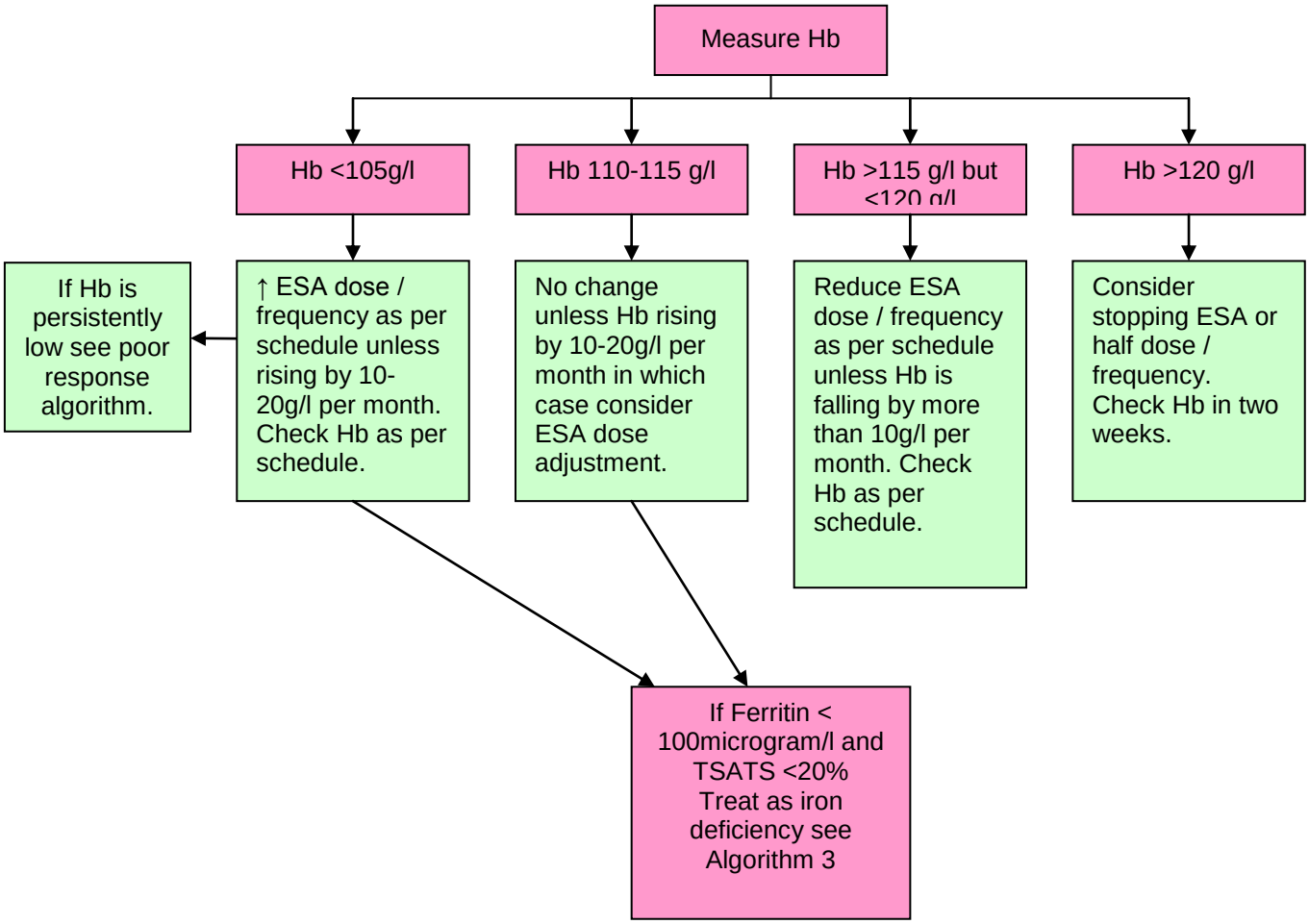
ALGORITHM 4

Algorithm for ESA prescribing for correction of anaemia



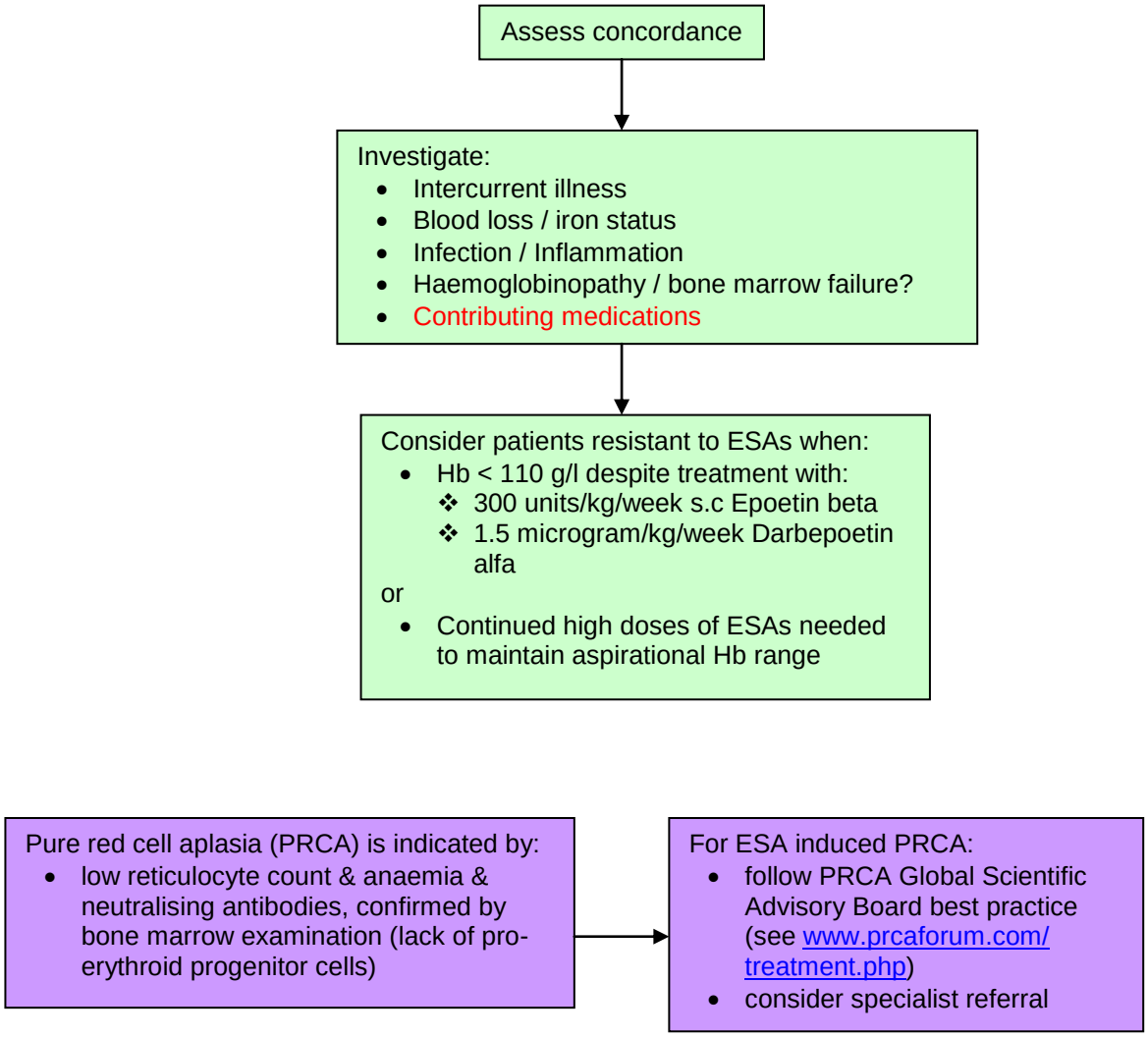
ALGORITHM 5

Algorithm for Hb Maintenance



ALGORITHM 6

Algorithm for poor response to ESA



MONITORING TOOL

How will monitoring be carried out?
The Renal Anaemia Team monitors patients after initiation of anaemia treatment through appropriate blood tests and adjusts treatment by algorithms.
Also patients treated through the renal anaemia nurse continue to attend the renal clinic where they see the renal consultant who reviews all renal aspects including anaemia.

Who will monitor compliance with the guideline?
Renal nurse specialist / renal team to audit renal anaemia practice

STANDARDS	%	CLINICAL EXCEPTIONS
Full renal anaemia work-up blood tests on all new patients	100	Patient declines
Blood test monitoring after initiation of anaemia treatment	100	Patient declines
Administration of iv iron treatment if oral iron fails / not tolerated	100	Iv iron contra-indicated eg asthma or acute infection
EPO dose reviewed after 4 weeks and again within 3 months of initiation	100	Patient declines blood test

REFERENCES

1. National Institute for Clinical Excellence (2015) Anaemia Management in Chronic Kidney Disease. (NG8) London.

2. Roche (2006) Information for patients with anaemia and kidney disease. Welwyn Garden City.

3. WAHT Patient Group Directions for the Administration of Epoetin beta, Darbepoetin alfa.

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