Guideline on the Pre-operative Management of Adults for Elective and Scheduled Surgery Presenting with Anaemia

Key Document code:	WAHT-KD-017	
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Approved by:	Pre-op Directorate Governance Meeting	
Date of Approval:	4th January 2021	
Date of review: **This is the most current version and should be used until a revised document is in place**	12th November 2025	

Key Amendment

Date	Amendment	Approved by
21st January 2019	Inclusion of advice for edoxaban. Additional information for the management of medicines for diabetes	Medicines Safety Committee
25th June 2020	Document extended for 6 months during COVID-19 period.	QGC
4th January 2021	Pre-operative assessment Key Documents approved for 3 years	Pre-op Directorate Governance Meeting
27th December 2023	Extended document for 6 months whilst under review. Updated owner details.	Dr Harsha Mistry
12th November 2024	Document extended for 12 months whilst awaiting National Guidelines to inform if changes are required	Dr Harsha Mistry

Introduction

Anaemia is defined as haemoglobin below 13 g/dl in males and 12 g/dl in females (The Association of Anaesthetists of Great Britain and Ireland, 2010) and should be viewed as a serious and treatable medical condition (Kotze and Lavies, 2011). Pre-operative anaemia and allogeneic blood transfusion are independently associated with adverse outcomes (Kotze and Lavies, 2011).

Patients are more likely to be anaemic due to their age, presence of chronic diseases and the use of non-steroidal anti-inflammatory medication. Anaemia can be due to iron deficiency, B12/folate deficiency, anaemia of chronic disease including chronic kidney disease or a combination of these (Kotze and Lavies 2011).

Anaemia should be investigated and treated before planned surgery, using haematinics such as oral/intravenous iron rather than transfusion (The Association of Anaesthetists of Great Britain and Ireland, 2010). The urgency and nature of surgery, plus patient specific factors, will determine the balance between reversing anaemia and proceeding with surgery. The aim, to avoid perioperative blood transfusion, is best achieved when hospital pre-operative services work with other departments and primary care (The Association of Anaesthetists of Great Britain and Ireland 2010).

The aim of the guideline is to:

- Identify all patients whose Haemoglobin is reduced.

- Advise, arrange or institute treatment in identified patients
- Identify higher risk patients, such as patients with significant co-morbidities, patients with very low Haemoglobin levels and patients whose surgery may result in significant blood loss

Definition

Severity of anaemia:

- Mild- Hb 10-12g/dl
- Moderate- 8-10g/dl
- Severe below 8g/dl

Red blood cell size

- Normocytic MCV 76-96
- Microcytic MCV <76
- Macrocytic MCV>100

When deciding which category of anaemia applies in an individual patient, red cell count, mean cell haemoglobin, and mean cell haemoglobin concentration should be considered.

Screening

Patient blood management should start in primary care at the time of referral for surgery; working closely with the pre-operative assessment clinic at the hospital (Norfolk, 2013). Primary care can help optimise patients' fitness before surgery by optimising treatment of chronic conditions such as anaemia. This may help increase survival, decrease peri-operative morbidity and shorten the duration of hospital admission (The Association of Anaesthetists of Great Britain and Ireland 2010).

Anaemia needs to be identified as early as possible in the patient's pathway (Kotze and Lavies, 2011) therefore patients that fulfil the National Institute for Healthcare and Clinical Excellence (NICE, 2003) criteria (all adults over 60+, surgical severity 2 or more, all adults surgical severity 3 or more, several renal disease eGFR<45) require a full blood count (FBC) soon after the decision to treat is made.

Recommendations

The following guidance details the recommendations following review of the full blood count, for the investigation, treatment and management of anaemia. (BCSH)

Investigations

Investigations for all anaemic patients should include; urea, creatinine, liver function rests, CRP, ESR and TSH.

Red Cell Indicies:

These are performed as part of a routine FBC and the following are highly suggestive of iron deficiency anaemia:

- Microcytic RBC (MCV <76)
- Hypochromic RBC (MCH < 27)

- For microcytic patients investigations should include serum iron, ferritin and transferrin levels.
- For normocytic patients investigations should include, serum iron, ferritin, transferrin levels, serum folate and Vit B1

Low MCV and MCH are also seen in haemoglobinopathies. Ferritin should be used to complement the MCV/MCH results. Patients presenting with ferritin <100 and anaemia should be prescribed a trial with oral iron, if clinically appropriate.

Serum Ferritin

Serum ferritin is the best diagnostic test for iron deficiency and a serum ferritin of less than 12-15 ug/dl is proof of iron deficiency-Low levels indicate low iron stores. However, serum ferritin levels are difficult to interpret if infection or inflammation is present, as levels can be high even in the presence of iron deficiency (National Institute for Health and Care Excellence, 2014) - Serum ferritin may be raised if CRP is elevated or if the LFTs are elevated.

Iron therapy should initiated in patients with a Ferritin < 50ug/dl (mild anaemia) and with a Ferritin <100ug/dl (severe anaemia) and the response to therapy should be monitored.

Serum iron, total iron binding capacity and transferrin saturation (iron and iron binding capacity).

These should only be performed when ferritin levels are either normal or high and IDA is strongly suspected. See table below for differential diagnosis of anaemia (Author, 2015)

Diagnosis	**Ferritin**	**Serum iron**	**MCH/MCV**	**TIBC/Tf**	**sTfR**	**CRP**
IDA	Low	Low	Low	Raised	Raised	Normal
ACD	Normal or raised	Low	Normal/low	Low	Normal	Raised
IDA + Inflammation	Normal or raised (<100ug/dl)	Low	Low	Low	Raised	Raised
Beta Thalassaemia	Normal	Normal	Low	Normal	Normal	Normal

Total iron binding capacity (TIBC), Transferrin (Tf), Serum transferring receptor assay (sTfR)

However, true iron deficiency anaemia (IDA) can be confirmed by trial of oral iron therapy for duration of three weeks or parenteral iron if poor compliance, with measurable change in MCH being noted within seven days in true IDA.

Determining the cause of iron deficiency

Iron deficiency occurs when the body's iron demand is not met by iron absorption from the diet. Iron deficiency anaemia (IDA) occurs in the more severe stages of iron deficiency when the body is iron deficient to the degree that red blood cell production is reduced (National Institute for Health and Care Excellence, 2014).

The cause of IDA may already be known, if not the reason for IDA must be investigated in order to identify any other serious underlying causes such as colon cancer (Author, 2015). All men and post-menopausal women who present with no obvious cause for IDA should be investigated.

Treatment

It is important that as well as correcting the anaemia, iron stores are replenished. This is particularly important for patients undergoing surgery where blood loss is expected.

IDA can be treated in two ways:

- Oral iron therapy: this is the preferred treatment and should always be the first choice.
- Parenteral (IV iron)

Parental iron should only be used when oral iron is not tolerated, oral iron cannot be absorbed, the patient has continued blood loss or when rapid correction is needed pre-operatively in the event of scheduled or urgent surgery.

Oral iron

Therapeutic response the haemoglobin should rise by about 1-2 g/l per day. When the haemoglobin is normal, treatment should continue for a further 3 months to replenish stores (Author, 2015)

Recommended dose:

Please consult the British National Formulary for the recommended dose. NB: If iron is not tolerated at the recommended dose a lower dose could be considered, as clinically appropriate. Also consider oral suspensions which can be better tolerated than tablets

Parenteral Iron

Determination of the iron need

Hb		**Patient body weight**		
g/dL	**mmol/L**	**below 35 kg**	**35 kg to <70 kg**	**70 kg and over**
<10	<6.2	500 mg	1,500 mg	2,000 mg
10 to 14	6.2 to 8.7	500 mg	1,000 mg	1,500 mg
>14	>8.7	500 mg	500 mg	500 mg

Note: do not give more than 20mg/kg at any one time (given as infusion) or give more than 1,000mg of iron in a week. Doses above 1000mg must be split and given in a second dose a week later. I.e. give on day 1 and day 8
Use actual body to dose, even in patients with low or high BMI.

DRUG INTERACTION

- Ferinject injection should not be administered concomitantly with oral iron preparations as the absorption of oral iron will be reduced.
- Oral iron therapy should not be started earlier than 5 days after the last injection of Ferinject.

CONTRAINDICATIONS

- Non-iron deficiency anaemia (e.g. haemolytic anaemia)
- Drug hypersensitivity to the active substance, to Ferinject or any of its excipients such as Sodium hydroxide and Hydrochloric acid.
- Known serious hypersensitivity to other parenteral iron products.
- Immune or inflammatory conditions such as systemic lupus erythematous, rheumatoid arthritis where there is an increased risk of hypersensitivity reactions to parenteral iron complexes.
- Iron overload or disturbances in utilisation of iron. (e.g. haemochromatosis, haemosiderosis, decompensated liver cirrhosis, hepatitis and in particular Porphyria Cutanea Tarda)
- Parenteral iron must be used with caution in case of acute or chronic infection, asthma, eczema or atopic allergies

SPECIAL WARNINGS AND PRECAUTIONS FOR USE

- Ferinject can cause serious anaphylaxis or anaphylactoid reactions. Hypersensitivity reactions are known to have occurred with previous uneventful parenteral infusion of iron. Ferinject should be administered in a place where there is availability for immediate resuscitation. Equipment for resuscitation and drugs to treat serious anaphylaxis should be available including adrenaline, antihistamines and/or corticosteroids. Staff should stop the Ferinject infusion if hypersensitivity reaction is noted and seek medical review
- Paravenous leakage of Ferinject at the injection site may lead to irritation of the skin and potentially long lasting brown discolouration at the site of injection. In case of paravenous leakage, the administration of Ferinject must be stopped immediately.
- A single dose of Ferinject should not exceed 1000mg of iron as an infusion. The cumulative dose of Ferinject in one week should not exceed 1000mg.
- Patients with liver dysfunction should only be given Ferinject after careful risk/benefit assessment and should be avoided if iron overload is precipitating hepatic dysfunction.
- Patients who have haemodialysis-dependent chronic kidney disease should receive no more than 200mg iron per dose.

ADVERSE DRUG REACTION

- The most commonly reported adverse drug reaction is nausea (occurring in 3.1% of the patients), followed by headache, dizziness, and hypertension.
- The other uncommon reactions include Hypersensitivity, Paraesthesia, dysgeusia, Tachycardia, Hypotension, flushing, Dyspnoea, vomiting, dyspepsia, abdominal pain, constipation, diarrhoea,

pruritus, urticaria, erythema, rash, myalgia, back pain, arthralgia, muscle spasms, pyrexia, fatigue, chest pain and chills

- The rare reactions include Anaphylactoid reactions, bronchospasm and syncope.

CONSENT

- Explain the indication for Ferinject infusion, the potential risks and explain the procedure to the patient and gain informed verbal consent.

METHOD OF ADMINISTRATION

Dilution plan of Ferinject for intravenous infusion:

Ferinject	**Iron**	**Amount of sodium chloride 0.9%**	**Minimum administration time**
2mL-4mL	100mg to 200mg	50mL	2 minutes
>4mL-10 mL	>200mg to 500 mg	100 mL	6 minutes
>10mL -20 mL	>500mg to 1,000 mg	250 mL	15 minutes

- Ferinject must only be administered only by the intravenous route and given using an infusion pump.
- Intravenous infusion- maximum single dose -1,000 mg of iron (up to 20 mg/kg body weight).
- Sterile 0.9% sodium chloride solution should be used for the preparation and flushes
- One mL of solution contains 50 mg of iron as ferric carboxymaltose:
  Each 2 mL vial contains 100 mg of iron as ferric carboxymaltose. Each 10 mL vial contains 500 mg of iron as ferric carboxymaltose. Each 20 ml vial contains 1,000 mg of iron as ferric carboxymaltose.
- Do not dilute to concentrations less than 2mg of iron per ml.

MONITORING OF PATIENTS RECEIVING TOTAL DOSE FERINJECT INFUSION

- Record observations: BP, pulse and temperature and Oxygen Saturation at the beginning and end of the 15 minute infusion
- Observe the patient for one hour following the infusion.

CHECKING THERAPEUTIC RESPONSE

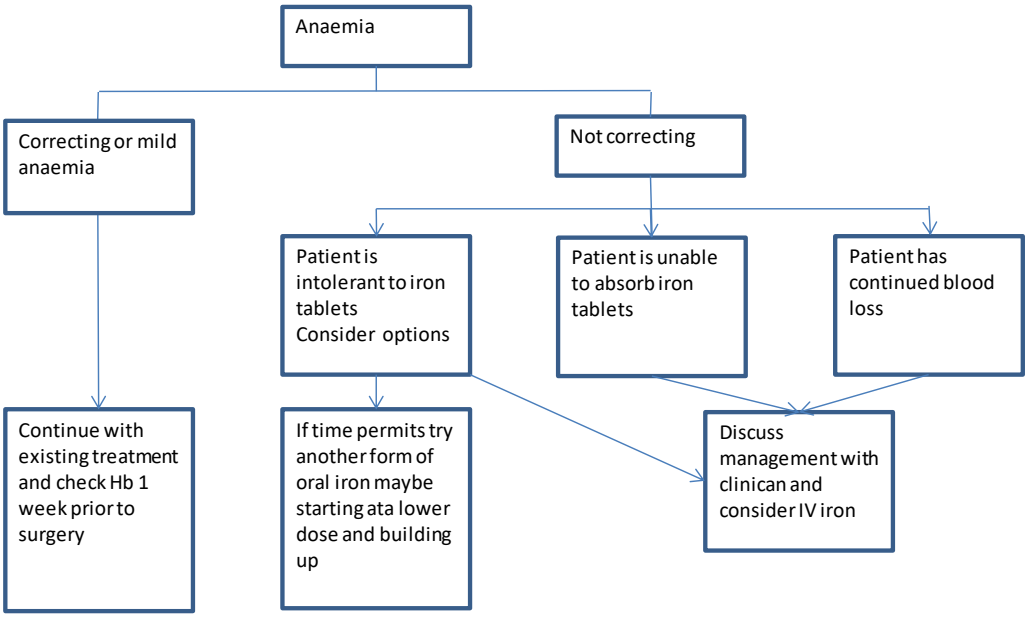
- The patient's Hb and ferritin should be measured 4 weeks after the last Ferinject infusion, to confirm the predicted response.

Management

Patient with existing anaemia:

- Confirm whether a diagnosis of anaemia has been made and review results.

- Confirm all baseline investigations have been arranged, if not arrange as detailed above
- Confirm current treatment and duration, if any.
- Evaluate the response to treatment
- Confirm date of surgery and severity of the proposed procedure
- Plan further management considering above information.



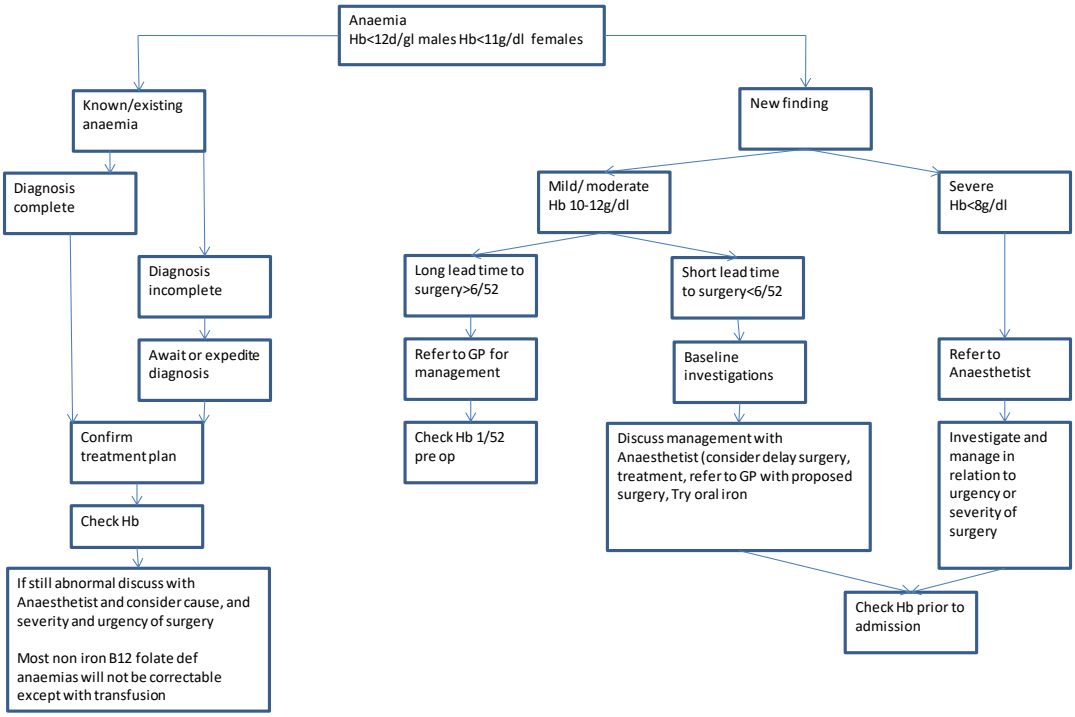
Patient recently found to be anaemic

- Review available blood test results
- Classify anaemia i.e. normocytic
- Ensure appropriate baseline investigations have been ordered and completed, if not arrange
- Confirm date if surgery
- If anaemia is mild/moderate and time allows refer to GP for treatment
- If anaemia is moderate/ severe or symptomatic, obtain clinicians opinion on management
- If peri-operative blood loss is associated with procedure, expedite diagnosis and management plan even if only mild anaemia

Anaemia that is not due to Iron/B12 or folate deficiency is unlikely to be correctable except with transfusion.

Appendix 1

Management of patients found to be anaemic pre-operatively



Local Pre-operative Management of Adults for Elective and Scheduled Surgery Presenting with Anaemia

At the time of listing for surgery, the Consultant Surgeon, Staff Grade or Registrar will detail the request for pre-operative Full Blood Count in the letter to the GP, advising of the proposed surgery. The referring clinician will notify the patient of the referral to the GP for assessment of anaemia. A standard template letter will be used for the referral.

Patients will generally be referred for pre-operative assessment (POA) three to four weeks prior to surgery. On attending for the POA clinic, the RN will ensure that a FBC was completed and note if any additional blood tests were completed by the GP (Ferritin and CRP). The RN will confirm the results, diagnosis and management plan from primary care.

In the event that a FBC was not completed by the GP at the time of listing, the RN will perform a FBC as per the National Institute for Healthcare and Clinical Excellence (NICE, 2003) criteria (all adults over 60+, surgical severity 2 or more, all adults surgical severity 3 or more, several renal disease eGFR<45). In the event that the FBC result is outside of the normal range, the RN will notify the Consultant Anaesthetist via

the e anaesthetic work list and the Consultant Surgeon to ascertain the further management of the patient and whether it is appropriate to proceed to surgery.

The RN will ensure that vital signs are recorded, including manual palpation of the pulse. An electrocardiogram (ECG) will be performed as clinically indicated.
In the event that the vital signs are outside of the normal range, the RN will manage the patient as clinically appropriate and make a referral to an additional service as required (GP, Anaesthetist). The RN will ensure appropriate 'safety netting' of the patient.
The RN will review the FBC result within 48 hours of the sample being taken. In the event that the result is abnormal the RN will notify the GP and the patient. The RN will further notify the Consultant Anaesthetist via the e anaesthetic work list and the Consultant Surgeon to ascertain the further management of the patient and whether it is appropriate to proceed to surgery.
The RN will inform the patient, Consultant Surgeon and Consultant Anaesthetist of the proposed management.
All patients presenting to pre-operative assessment for surgery which is likely to involve significant blood loss, will be provided with a copy of the patient information leaflet, 'Iron in the Diet'.
In the event that the patient is not fit to proceed to surgery, the RN will ensure that the patient, Consultant Surgeon, Anaesthetist, Secretary, ward and theatres have been notified of the cancellation.
The RN will ensure that the GP has been informed of the cancellation, in writing, and will notify the Consultant Surgeon in writing.