Administration of Intravenous Iron for Pre-Operative Patients

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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 2025	Document extended for 12 months whilst awaiting National Guidelines to inform if changes are required	Dr Harsha Mistry

Introduction

Pre-operative anaemia has been shown to be both common and also associated with increased length of stay and complications post-operatively. It is good practice to treat all surgical patients with pre-operative iron deficiency anaemia but there is particular emphasis on patients having major surgery.

Iron deficiency is the commonest cause of anaemia in the surgical population. NICE have recommended that IV iron should be considered before or after surgery for patients

- If they have iron deficiency anaemia (IDA) and they cannot tolerate / adhere or absorb oral iron therapy
- Are diagnosed with functional iron deficiency
- Are diagnosed with iron-deficiency anaemia and the interval before surgery is too short for oral iron to be effective.

This guideline is succinct guidance on:

- Who can be considered for IV Iron therapy
- How to refer for IV Iron
- The administration of IV Iron
- Managing IV Iron hypersensitivity reactions

This guideline is designed to be used in conjunction with WAHT TP 111 ‘Guideline on the Pre-operative Management of Adults for Elective and Scheduled Surgery Presenting with Anaemia’ which is a more complete guideline detailing investigation of pre-operative anaemia.

Details of Guideline

Intravenous Iron

- Intravenous Iron is highly efficacious at replenishing Iron stores and increasing Hb in anaemia due to Iron deficiency with or without inflammation

- There is often a rapid haemoglobin response with a maximum effect of haemoglobin seen at 2-3 weeks

- This helps reduce the transfusion requirement peri-operatively and may help reduce length of hospital stay

- Recent IV formulations are thought to be very safe with serious adverse events and mortality being reported in only 38 per 10^6 administrations. The benefits of IV Iron are stated to outweigh its risks where the oral route is insufficient or poorly tolerated.

- Screening for anaemia begins in primary care with GP referrals detailing the latest haemoglobin and treatment with haematinics commenced before surgery

- There is a group of patients who are at risk of pre-operative Iron deficiency anaemia (IDA). They include patients with:
    - GI or GU loss of blood (i.e. melena/haematemesis/haematuria)
    - A history of Iron deficiency anaemia
    - Menorrhagia
    - Coeliac Disease

In patients with anaemia the following investigations should be taken as a minimum:

- FBC
- Urea and Electrolytes
- CRP
- Serum Ferritin must always be ticked in the 'Pre-op' Panel on ICE (requires a gold top U/E bottle)

- Patients are regarded as anaemic if their Haemoglobin is below the local reference range (115g/L for women, 135g/L for men)

- In Iron Deficiency Anaemia (IDA) the Red Blood Cells will often be microcytic (i.e. their MCV will often be below 78 fl), although this is not always the case
- Ferritin is an Iron storage protein and the best marker for whether a patient is Iron deficient or not. Ferritin levels are also raised in the presence of inflammation.

- If the Ferritin is below 30 then this indicates Iron Deficiency
- If the Ferritin is below 100 and there is *co-existing inflammation* (i.e. CRP above 10) then this also indicates Iron Deficiency

- When assessing Ferritin it is essential to check for co-existing inflammation: a raised CRP (over 10 mg/L) indicates that there is co-existing inflammation. In the event of co-existing inflammation a Ferritin level of 100 or below indicates Iron Deficiency.

- Further diagnostic tests may be needed where IDA is suspected but Ferritin is found to be normal. These tests are guided after consulting with haematology.
    - The first test to consider after Ferritin is **Transferrin Saturation** (Serum Iron:Total Iron Binding Capacity). Transferrin Saturation describes how much serum Transferrin is bound with Iron. For example if the Transferrin Saturation is 20% this indicates that 20% of Transferrin is bound by Iron. In IDA the Transferrin Saturation is expected to be low (i.e. below 20%). If Ferritin is below 100 and transferrin saturation is below 20% this is indicative of Iron Deficiency Anaemia.

  If the Ferritin is raised and the Transferrin Saturation is above 20% then further tests may be considered after consultation with haematology. These may include:
    - **Serum Iron** – reflects the amount of circulating Iron, although this level demonstrates considerable diurnal variation and is not reliable as a sole test
    - **Soluble Transferrin Receptor** (sTFR) and sTFR-Ferritin Index

Functional Iron Deficiency

- Functional Iron Deficiency describes the state when there is apparently adequate Iron stores, but problems with mobilisation and utilisation of Iron, often due to increased Hepcidin levels. Raised Hepcidin, a key Iron regulator, increases Iron trapping in macrophages and reduces GI Iron absorption
- Functional Iron Deficiency is common in chronic inflammatory states and chronic renal failure
- Generally it is considered to be present when the Ferritin is normal (i.e. below 100) but the Transferrin Saturation is low (i.e. below 20%)
- There is evidence to suggest that IV Ferric Carboxymaltose is an effective treatment for Functional Iron Deficiency (Khalafallah et al 2016).

Actions to take when Iron Deficiency Anaemia is identified in Pre-op

Identifying Iron Deficiency in Surgical Outpatients

IV Iron takes approximately 2 – 4 weeks to maximise increase in haemoglobin level. The earlier it is identified then the more effective IV Iron can be in increasing haemoglobin. When a patient who has a history of IDA, or who is at high risk of ODA is reviewed in surgical outpatients the consultant surgeon should:

- Perform an FBC, U&E, CRP and Ferritin level
- Refer the patient to Pre-Operative Assessment for consideration of IV Iron
- Please send an email referral to the IV Iron service for consideration of IV Iron. **Please email wah-tr.iviron@nhs.net** with referrals for IV Iron consideration.
- This referral will then be put onto the worklist enabling the pre-op anaesthetists to review the case and decide if IV Iron is appropriate and if the patient should be booked

Identifying Iron Deficiency in Pre-operative Assessment Clinic

When IDA is identified the Pre-operative assessment nurse should:

- Inform the GP using the template letter (appendix 2) on the shared drive/ BlueSpier/ the POA intranet site
- Inform the surgeon via e-mail or telephone
- Put onto the Preoperative worklist for attention of anaesthetic consultant
- Ensure the patient has a CRP / U+E / Ferritin / Folate and B12 checked (Yellow top bottle)

- Record the patients vital observations and if observations are outside expected range then make a referral to an additional service (i.e. GP/Anaesthetic consultant)
- Ensure the patient has a copy of the NHS leaflet 'Iron in the Diet' (will also be made available on Pre-op internet site)

The pre-op anaesthetic consultant should use haemoglobin, MCV, Ferritin, CRP, clinical history and any other tests (i.e. transferrin saturation) to decide whether the patient has a likely Iron deficiency anaemia and therefore would benefit from IV Iron therapy (instructions on how to book given below).
International guidelines have identified the indications for IV Iron as:

1. Iron deficiency anaemia with Haemoglobin levels below the reference ranges
2. Surgery planned for less than 6 weeks after diagnosis of Iron Deficiency Anaemia
3. Patient cannot tolerate oral iron replacement therapy
4. Patient has previously not shown a response to oral Iron therapy (this will usually include patients with ongoing blood loss)
5. Functional Iron Deficiency is suspected (see above)

Guidance on delaying surgery in the presence of Iron Deficiency Anaemia
After identifying Iron Deficiency Anaemia the decision about whether to delay surgery or proceed will be on a case by case basis. The following will need to be considered:

- Whether the surgery is for a benign or malignant process.

  Surgery for malignant disease
  Where the surgery is for a malignant disease (i.e. cancer) then on a risk : benefit basis it will usually be appropriate to continue with surgery using IV Iron to replenish Iron stores and reduce transfusion requirements. The surgery planned will often address the cause of the IDA (i.e. surgery for colorectal cancer). The GP should still be informed of the diagnosis of anaemia in case further investigation is required.
  Surgery for benign disease which is longer than 6 weeks away
  Where the surgery is for a "benign" condition (i.e. elective joint replacement) and there is longer than 6 weeks until surgery the patient should be seen by the GP:
    - IDA without a known underlying cause needs urgent GP investigation to exclude underlying cancer
    - While being investigated the patient should be started on oral Iron as first line. If this cannot be tolerated then IV Iron may be given
    - A template letter should be used (Appendix 2) to send to the GP in these cases

  Surgery for benign disease which is within 6 weeks
  Where the surgery is for a "benign" condition, as above, and there is less than 6 weeks until surgery it could be appropriate to give IV Iron and continue with the planned surgery. Whenever possible this should be a shared decision between the pre-op anaesthetist, the surgeon and the patient. The following factors will need to be considered and would favour continuing with surgery:
    - If the IDA is longstanding and has been investigated previously (i.e. there is a low chance of underlying undiagnosed cancer)
    - If the patient has waited for a significant period for the operation and there is a time pressure to optimise the patient rapidly

- If the patient is in pain/discomfort which the surgery will address
- If the IDA is mild (i.e. Hb above 100)
- If the patient cannot tolerate oral Iron or has not had a response to oral Iron

Factors which disfavour continuing with surgery:

- IDA which has no known underlying cause should be investigated prior to surgery and this may require delaying surgery. IV Iron could be appropriate during investigation to replenish Iron stores for when surgery does occur.

It is important to note that there are important contra-indications to IV Iron therapy

1. Non iron deficiency anaemia
2. Drug hypersensitivity to Ferric Carboxymaltose or any of the excipient ingredients, such a Sodium Hydroxide and Hydrochloric Acid.
3. Known serious hypersensitivity to other parenteral iron products.
4. Iron overload or disturbances in utliisation of Iron (i.e. haemachromatosis, haemosiderosis, decompensated liver cirrhosis, hepatitis or Porphyria Cutanea Tarda)
5. Active infection being treated by antibiotics

Logistical aspects of IV Iron Infusion

Booking a patient for IV Iron therapy

When a patient is thought to be suitable for IV Iron they can be booked onto a slot on Medical Day Case Unit at Worcester for a dose of Ferric Carboxymaltose.

Actions to take:

1. The booking anaesthetist should telephone the patient and inform the patient they will be booked for IV Iron which will require cannulation, a hospital visit for 1-2 hours and administration of an IV drug. Anaesthetist should also enquire about allergies and other contra-indications to IV Iron (as above).
2. Booking anaesthetist should email the patient details to wah-tr.iviron@nhs.net or Laura.Moore14@nhs.net.
3. Booking anaesthetist should ensure the patient is added onto the IV Iron Worklist on EZ notes.
4. Booking anaesthetist should complete prescription of IV Iron on a Trust infusion prescription which can be found in Anaesthetic Dept, Pre-op Office, 1st floor, Worcester Royal Hospital. Generally 1000mg Ferric Carboxymaltose will be appropriate for most patients. If the patient weighs less than 35KGS then a reduced dose may be needed. The Iron need is given in the table below.

Hb		**Patient body weight**		
g/dL	**mmol/L**	**below 35 kg**	**35 kg to <70 kg**	**70 kg and above**
<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

- A dose up to 500mg should be diluted in 100mls 0.9% Saline
- A dose up to 1000mg should be diluted in 250mls 0.9% Saline

5. The Pre-op secretary will liaise with patient and the Medical Day Case Unit to arrange a date and time suitable for IV Iron. Ideally this would be 4-6 weeks prior to the surgery date. IV Iron should not be booked within 24 hours of the surgery date.
6. The Pre-op secretary will send out a letter to the patient informing them of the time and place for the IV Iron (see Appendix 3). The Pre-op secretary will also send out a letter to the patients GP informing them that the patient has received an IV Iron infusion for optimisation (see Appendix 2).
7. The pre-op secretary will send out a template email to the patients surgical consultant informing them that an IV Iron infusion is planned, including the date and time (see Appendix 4).

Administration of IV Iron on Medical Day Case Unit

Pre Infusion

- Patient will attend at appointment time as per booking procedure above
- Patient will be given Ferrinject information leaflet and risks of procedure leaflet to read
- Patient will be cannulated as per Trust policy
- A set of observations (pulse, BP, SpO2, RR) must be done and recorded on a NEWS 2 chart before the IV Iron infusion is commenced
- The prescription should be checked to ensure it is legible and fully completed
- 10mls of 0.9% saline must be used to flush the line to ensure it is patent
- Pre-infusion checklist must be completed with the patient. Certain factors will identify patients at increased risk of hypersenstitivity and the decision about whether to proceed will be made by the pre-op anaesthetist on a risk/benefit basis . Factors which indicate hypersensitivity risk include:
    - Any current acute/chronic infection
    - Any atopic allergy (asthma or eczema)
    - Systemic inflammatory condition i.e. SLE or Rheumatoid Arthiritis
    - Treated on beta blocker or ACE inhibitor may exacerbate reaction severity

During Infusion

- Ferric Carboxymaltose is given as an IV Infusion
- Ferric Carboxymaltose is given in line with manufacturers recommendations which is available on TAU. At the time of writing this states that:
    - A dose up to 500mg should be diluted in 100mls 0.9% Saline
    - A dose up to 1000mg should be diluted in 250mls 0.9% Saline
- The bag of saline with Ferric Carboxymaltose must be clearly labelled as per Trust Policy
- The administration record must be clearly completed, with a counter signature for the staff member who checked the drug
- The maximum dose to be given at one time is 1000mg. More than 1000mg of IV Iron should not be administered in one week
- The cannula phlebitis score should be noted before and after the infusion (*0=no pain or signs, 1=pain/redness around site, 2= pain redness and palpable venous cord, 3=pain, swelling, induration, palpable venous cord and pus, 4=all of above plus tissue damage)*
- **The infusion of Ferric Carboxymaltose should be given over 30 minutes** a fast infusion rate is a risk factor for developing IV Iron related Hypersensitivity (see below)
- The cannula must be checked throughout the infusion for signs of extra-vasation. If there is redness or extra-vasation at the site the infusion must be stopped immediately, cannula removed

and a cold compress applied to the site. The cannula site should be elevated and medical assistance requested. It may be necessary to site a further IV cannula in another site and continue if there is a significant fraction of the infusion left.

- It is extremely important to monitor the cannula site very closely, particularly at the start of the infusion, to ensure there is no extra-vasation

After the IV Iron Infusion

- A set of observations (pulse, BP, SpO2, RR) must be done and recorded on a NEWS 2 chart at the end of the IV Iron infusion
- The patient must be observed for 30 minutes after the end of the IV Iron infusion for any signs of hypersensitivity reaction
- A set of observations (pulse, BP, SpO2, RR) must be done and recorded on a NEWS 2 chart at the end of the 30 minutes observation
- If observations are within normal parameters for the patient and the patient feels well then they can be discharged home
- Please ensure the patient has a copy of the NHS leaflet 'Iron in the Diet' and 'Ferrinject' patient information
- Please ensure a letter to the GP is completed to inform them that an IV Iron infusion has been given
- Please ensure the patient knows who to contact in case of problems later (details in Ferinject patient information leaflet)

Ferric Carboxymaltose and Hypersensitivity

Procedural requirements

- Ferric Carboxymaltose must only be given in an area which has immediate access to facilities and equipment to carry out basic life support including:
    - IM Adrenaline (1:1000 formulation)
    - IV Chlorphenamine (10mg)
    - IV Hydrocortisone (100mg)
    - IV fluid (0.9% Saline or Hartmanns 1000mls)
- Staff should have received BLS training within the last 12 months
- The patient must be monitored closely during the Ferric Carboxymaltose for signs of hypersensitivity
- Factors which indicate hypersensitivity risk include:
    - Any current acute/chronic infection
    - Any atopic allergy (asthma or eczema)
    - Systemic inflammatory condition i.e. SLE or Rheumatoid Arthiritis
    - Treated on beta blocker or ACE inhibitor may exacerbate reaction severity

Classification of hypersensitivity

- Hypersensitivity reactions may be mild, moderate or severe
- True IgE mediated hypersensitivity is rare but patients may develop a severe reaction via CARPA (complement activation related pseudo allergy)

- In those patients identified as high risk for hypersensitivity:
  - The infusion should be started slowly (speed of infusion is a risk factor for developing hypersensitivity) and may be given over 60 rather than 30 minutes
  - Medical personnel should be in close proximity and aware while IV Iron infusion is given
  - Signs of hypersensitivity must be carefully watched for during and after infusion

Management of Hypersensitivity reaction to IV Iron

See appendix 5

Mild reactions:

In mild reactions the features of hypersensitivity tend to be more subjective than objective. They include: feeling anxious, itchy, hot, flushed, back pain, slight chest tightness.

If these features are present:

- Stop the IV Iron infusion for at least 15 minutes
- Monitor pulse, BP, respiratory rate, oxygen saturations
- Reassure patient
- If symptoms do not resolve or deteriorate then manage as for moderate reaction
- If symptoms resolve consider restarting infusion at 50% of original rate
- If symptoms recur stop Iron infusion and manage as above

Moderate reactions:

In moderate reactions, patients may develop sudden hypersensitivity or this may be preceded by a mild prodrome as above. Features are more pronounced than in mild reactions. They include: cough, flushing, more pronounced chest tightness, urticaria, hypotension and tachycardia.

If these features are present:

- Stop IV Iron infusion
- Inform the patients parent team (usually surgical team)
- Lie patient flat
- Consider IV Volume load (i.e. 0.9% Saline 500mls)
- Consider IV Hydrocortisone 100-500mg
- Observe patient for 1-4 hours
- If patient deteriorates manage as for severe reaction as below

Severe/life threatening reactions:

In severe reactions, symptoms might be of sudden onset, or may develop on the background of a moderate reaction. Features include: increasing wheeze, stridor associated with laryngeal oedema, tiredness, periorbital oedema, hypoxia, marked tachycardia and hypotension.

If these features are present:

- This is a major medical emergency
- Stop IV Iron infusion
- Call the cardiac arrest team immediately using 2222
- Use an ABC approach to diagnosis and treatment
- Support patients airway using basic adjuncts as required
- Give facial oxygen at a high rate (i.e. over 10L/min), consider IV Salbutamol if wheeze is predominant feature
- Lie patient flat

- Elevate patients legs and give IV fluid (1Litre 0.9% Saline or similar isotonic fluid)
- If reaction is severe give Adrenaline IV, 50 mcg – 100mcg aliquots. Several doses may be required. If multiple doses required consider IV adrenaline infusion
- Establish continuous ECG, SpO2 and regular NIBP monitoring
- Arrange review and transport to critical care for ongoing management

APPENDICES
Appendix 1. Letter to be sent to GP informing them of Iron Deficiency Anaemia

Patient Casenote Number: <Patient: Hospital Number>
Patient NHS Number: <Patient: NHS Number>
CONFIDENTIAL
To: <GP: Name>
<GP: Address>

Re: <Patient: Name>, DOB : <Patient: Date of Birth>
<Patient: Address Line>
<Todays Date>

Urgent **For Information** **Please Action** **Response required**

This above patient has been identified as anaemic prior to surgery.

Operation planned:

Proposed date of surgery:

Surgical Consultant:

DELETE AS APPROPRIATE

******* Clinically it has been decided to continue with the planned operation on a risk/benefit basis. Your assistance with prescribing appropriate haematinics when necessary is appreciated. Please repeat the FBC after 2-4 weeks of haematinics to assess response.

- If the anaemia is related to the surgical condition then further investigations are not required.
- If the anaemia is an unexpected finding unrelated to the surgical condition you may need to institute further investigation and referral (i.e. endoscopy for iron deficiency anaemia of unknown cause
- If the patient is given IV Iron in hospital as part of their optmisiation we will send a letter to confirm this. Usually a patient will not need oral and IV Iron. ******

******Clinically it has been decided to delay the planned operation until the anaemia is investigated and treated. This is because there is a chance that the anaemia is related to an underlying pathology such as colorectal cancer. Please investigate as you usually do and contact:

when you are satisfied that anaemia has been investigated and managed. Usually we aim for a Hb above 130g/L before elective surgery.**********

Appendix 2. Letter to be sent to GP informing them of IV IRON INFUSION

Confidential

SAFE HAVEN FAX

To: <GP: Name> **Fax No: <GP: Fax>**

From: The Pre Assessment Clinic **Date: <Todays Date>**

Re: <Patient: Name> **Pages: (including cover sheet)**

Date of Birth:<Patient: Date of Birth> **NHS number: <Patient: NHS Number>**

Hospital Casenote number: <Patient: Hospital Number>

Urgent *For Information* *Please Action* *Response required*

This above patient has been identified as anaemic prior to surgery and an IV Iron infusion has been arranged as optimisation before surgery.

We have arranged this as a day case procedure for: ____/____/____

Thank you for your co-operation with the ongoing pre-operative optimisation.

- **Please note that this is only an optimization of haemoglobin for upcoming surgery.**
- **If the anaemia is related to the patients surgical condition, further investigations are not required.**
- **If the anaemia is an unexpected finding unrelated to the surgical condition, you may need to institute further investigations and referral (i.e. endoscopy for iron deficiency anaemia of unknown cause)**

Usually we will advise patients to stop their oral Iron immediately after an injection of IV Iron.

We will usually arrange for a repeat FBC 2-3 weeks after IV Iron or immediately before their surgery (whichever is sooner).

Many thanks for your help in this matter.

Yours sincerely

Many thanks for your help with this matter,

Appendix 3. Letter to be sent to patient informing them of IV IRON INFUSION

Patient Casenote Number: <Patient: Hospital Number>
Patient NHS Number: <Patient: NHS Number>
CONFIDENTIAL
To: <Patient: Name>
<Patient: Address>

To <Patient: Name>, DOB : <Patient: Date of Birth>
<Patient: Address Line>
<Todays Date>

It has been identified that you may benefit from an infusion of intravenous Iron. This will help boost your haemoglobin before your upcoming surgery.

This has been arranged for: (DATE AND TIME OF IV IRON INFUSION)

Please report to: Medical Day Case Unit, Level 0, Worcestershire Royal Hospital

The procedure will involve an IV cannula being inserted and an Iron infusion being given to you over about 30 minutes. You will be ready to go home after 60 minutes.

A full information leaflet is enclosed, but in summary:

You should **not** receive IV Iron if you have the following:

- If you are allergic to a drug called Ferric Carboxymaltose ("Ferrinject")
- If you have experienced serious allergic reactions to other injectable Iron preparations
- If you have too much Iron in your body (i.e. haemochromatosis)

Please tell us if any of the above apply to you before having IV Iron.

Common side effects (may affect up to 1:10 people): Dizziness, headache, feeling hot (flushing), high blood pressure, nausea or injection site reactions

Uncommon side effects (may affect up to 1:100 people): numbness, tingling, low blood pressure, high heart rate, difficulty breathing, vomiting, indigestion, diarrhoea, feeling faint, itching, hives, redness of skin, muscle, joint and / or back pain, muscle pain, swelling of hands or feet

Rare side effects (may affect up to 1:1000 people):inflammation of a vein, loss of consciousness, anxiety, fainting, feeling faint, wheeze, fall in blood pressure, rapid swelling of face and tongue which may cause problems with breathing, paleness, headache, feeling ill (influenza like illness)

Please contact us if you have any concerns,

Dr James Hutchinson, Consultant Anaesthetist
On behalf of the pre-operative anaesthetist group

Appendix 4: Template for email to Surgeon informing them of IV Iron arrangements

Patient name
Patient NHS
Patient DOB

The above patient has been booked for a pre-operative IV Infusion in an attempt to optimise their haemoglobin and reduce their transfusion requirements during surgery.

They will have the IV Infusion on Medical Day Case, Worcestershire Royal Hospital.

Reactions to IV Iron are very rare, but in the event that there is an adverse reaction to the IV Iron your team will be contacted to facilitate on-going management.

Your assistance with this would be much appreciated.

Kind regards

James Hutchinson, on behalf of the pre-operative anaesthetist group.

Appendix 5. Algorithm 1 Grading and management of acute hypersensitivity reaction to IV Iron Infusions. *Taken from Rampton et al: Hypersensitivity reactions to intravenous iron: guidance for risk minimization and management. Haematologica 2014; 99(11)*