Worcestershire Acute Hospitals NHS Trust

Clinical Guideline for the Use of Intravenous Iron (Ferric Carboxymaltose, Ferinject®)

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.	
Lead Clinician/s Dr Thomas Skibbe	Consultant haematologist
Approved by Trust Transfusion Committee on:	20th August 2017
Approved by Medicines Safety Committee on:	31st October 2017
This guideline should not be used after end of:	4th March 2021

Guidelines written Dr Susanne Morton; Consultant in haematology and transfusion medicine, University Hospitals, Birmingham.

Key amendments to this document

Date	Amendment	Approved by:
June 2018	No changes to document	Gill Godding
July 2020	Document extended for 6 months whilst review and approval process takes place	Gill Godding

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Introduction

Iron deficiency is a common cause of anaemia. In the majority of patients treatment is with oral iron and treatment of the underlying cause; this is often managed in the community by general practitioners. A significant minority however are seen in the emergency department or outpatient clinics. These may primarily present with iron deficiency anaemia or may be found to have iron deficiency during investigation for other conditions.

Patients presenting to hospitals with iron deficiency may be very symptomatic of anaemia, have a very low haemoglobin level or may be intolerant of oral iron. Patients are frequently diagnosed with iron deficiency anaemia in pre-operative assessment clinics where rapid normalisation of haemoglobin is required to avoid delays to surgery. National and local audits have shown a significant rate of inappropriate blood transfusion among such patients.

In addition patients with chronic diseases may be anaemic due to functional iron deficiency; total body iron stores are sufficient but the iron is not available for erythropoiesis in the bone marrow. These patients may require intravenous iron to aid erythropoiesis.

Best practice in iron deficiency is to replace iron rather than undertake transfusion unless there is significant clinical compromise. Serious adverse events occur in approximately 1 in 22,000 blood transfusions as compared to 1 in 200,000 iron infusions. Transfusion associated circulatory overload (TACO) and haemolytic transfusion reactions (HTR) are significant risks following transfusion particularly in patients with risk factors. Other risks of transfusion, including immune modulation, are more difficult to quantify.

Investigation of anaemia

There are multiple causes of anaemia, which are beyond the scope of this guideline. Further information can be found in the Blood Transfusion Treatment pathway Anaemia Policy and from the on call haematology registrar when required.

Patients meeting the following parameters may benefit from iron replacement (which will be oral in the first instance unless meeting the criteria described below). This list is not exhaustive and patients with chronic inflammatory disease such as inflammatory bowel disease, rheumatoid arthritis and chronic renal failure may also benefit from intravenous iron. In these cases the decision to give intravenous iron lies with the consultant in charge of the patient's care.

The following suggest a diagnosis of iron deficiency

• Ferritin <30 micrograms/L (some sources indicate a normal range of >15 mcg/L for women but in women who are anaemic with a ferritin 15-30 mcg/L and no other clear cause for anaemia, a trial of iron therapy should be given)

• Transferrin saturation <20% with serum iron <12 mcg/L and TIBC (total iron binding capacity) >60 micromoles/L

The following suggest a diagnosis of functional iron deficiency (see below for criteria in renal patients)

• Ferritin <100 mcg/L with CRP >30 mg/L or clinical evidence of active inflammation/chronic disease

• Fe saturation <20%, serum iron <12 mcg/L AND CRP >30 mg/L or clinical evidence of active inflammation/chronic disease

NB if anaemia of chronic disease is diagnosed, consideration must be given to the disease driving this process. Malignancy must be suspected and a thorough history and examination performed with appropriate investigations particularly where no other clear cause is apparent.

Details of Guideline

Method of Iron replacement

• This may be with oral iron, IV iron or (rarely) blood transfusion, or a combination of these treatments. NB the preferred method of replacement is a clinical decision based on symptoms of anaemia, cause of iron deficiency, and success of previous treatment.

• Haemoglobin can be anticipated to begin to increase within 1-2 weeks of IV iron treatment. If the patient is symptomatic but not compromised, and able to tolerate symptoms over a few weeks, blood transfusion is **not** indicated. Many patients' symptoms will improve even before a rise in haemoglobin is seen.

Indications for IV iron

IV iron should be considered in patients with demonstrated iron deficiency in **any** of the following situations**:**

• Patient intolerant of or unresponsive to oral iron
• Patient due surgery in next 6 weeks or pregnant with gestation more than 34 weeks
• Haemoglobin <80 g/L (if the anaemia is chronic and oral iron has not been given, a trial
• of oral iron is also an option)
• Patients with active inflammatory bowel disease where oral iron is likely to cause
• unacceptable side effects

IV iron can also be used in pre-dialysis renal patients with renal anaemia **once per month** if:

- Haemoglobin <120 g/L in those on erythropoiesis-stimulating agents (ESAs)
- Haemoglobin <110 g/L in those not on ESAs
- Functional iron deficiency with ferritin <200 mcg/L or ferritin <500 mcg/L AND transferrin saturation <20%

Contraindications for use of intravenous iron

The following relate to use of **Ferric Carboxymaltose only (Ferinject®, FCM).**

Absolute contraindications to FCM administration

• Anaphylaxis or other significant hypersensitivity reaction to any IV iron preparation
• Current confirmed bacteraemia
• 1st trimester of pregnancy
• Iron overload

FCM should not be administered to patients with an absolute contraindication.

Cautions for use of FCM

In patients with the following conditions a clinical decision weighing the risks and benefits must be made. This will depend on the availability of other treatment, the chronicity, severity and impact of the anaemia and the expected duration of the relative contraindication.

Due to concern of exacerbating the condition:

• Decompensated liver cirrhosis or hepatitis

Significant active bacterial infection

Due to increased risk of hypersensitivity reaction:

• History of atopy and/or anaphylaxis (e.g. drugs, bee stings)
• History of immune or inflammatory conditions e.g. rheumatoid arthritis

Reference should be made to the summary of product characteristics for full details of relative contraindications.

Patient information

If a decision is made to give IV iron, the patient's clinical team should discuss the decision with the patient, including side effects of IV iron. The most common reported side effect is nausea (3.1%). Less than 1% of patients can be expected to experience a hypersensitivity reaction which is mild in the majority; between 0.01 and 0.1% patients will experience an anaphylactoid reaction. Patients may also experience myalgia and should be alerted to the risk of extravasation which can cause pain and tissue discolouration.
Reference should be made to the summary of product characteristics for FCM for full details of side effects.
Alternative strategies for treatment of anaemia and the risks and benefits associated with these should also be discussed with the patient.

Prescription of FCM

For doses up to 15mg/kg the drug can be given as a slow injection over 6 minutes and requires no further dilution.
For doses up to 20mg/kg and in patients at risk of hypersensitivity (as described above, or with a history of previous reaction), an infusion (dose diluted in 250ml 0.9% saline) over 15 minutes is required.

The dose should be calculated as below. Weight 35-70kg		Weight >70kg
Hb <100 g/L	1500mg	2000mg
Hb >100 g/L	1000mg	1500mg

Patients should be closely monitored for signs of hypersensitivity during and for at least 30 minutes after every administration of an IV iron product, see https://www.gov.uk/drug-safety-update/intravenous-iron-and-serious-hypersensitivity-reactions-strengthened-recommendations
The cannula should be flushed with 10 mls 0.9% saline following administration.

Adverse reactions

Procedure for management of anaphylaxis

In the event of anaphylactic reaction follow the Anaphylaxis Policy see Resuscitation Policy Pathway(Treatment pathway).

Hypersensitivity reactions

If the patient experiences any of the following signs, the infusion should be stopped immediately and a full set of observations performed.
• Breathlessness
• Dizziness
• Wheezing
• Cough
• Urticaria
• Back, chest and/or joint pains
•If there is **no evidence** of
• hypo/hypertension
• tachycardia

• wheeze
• chest pain

the infusion may be restarted at a slower rate. If symptoms are persistent or any of these features are present the patient should be assessed medically and treated with intravenous hydrocortisone 100mg and 10 mg intravenous chlorphenamine. If the symptoms are mild and settle quickly, the infusion can be restarted at half the previous rate. If symptoms recur, no further FCM should be given and this must be recorded as an allergy on the patient's record. Progressive symptoms or anaphylaxis must be treated as per the Trust anaphylaxis guideline as above.
If extravasation occurs the infusion should be stopped, the cannula aspirated and cold packs applied to the site. Extravasation does not usually cause tissue injury but there will be discolouration of the skin at the affected site which may be long-lasting. This is due to iron deposition in the skin and subcutaneous tissues

MONITORING AND COMPLIANCE				
This section should identify how the Trusts plan to monitor compliance with and the effectiveness of these documents. It should include auditable standards and/or key performance indicators (KPIs) and details on the methods for monitoring compliance				
What	**How**	**Who**	**Where**	**When**
These are the 'key' parts of the process that we are relying on to manage risk.	*What are we going to do to make sure the key parts of the process we have identified are being followed?*	*Who is responsible for the check?*	*Who will receive the monitoring results?*	*Set achievable frequencies.*
The key parts of the transfusion processes are: • The decision to transfuse • Patient information and consent • Appropriate prescribing of blood • The request for transfusion • Collection and delivery of blood components • The administration of blood • Monitoring the patient throughout the process • Completion and documentation of the event • Management of transfusion reactions	An Audit will be completed to establish if the key parts of the process are being followed	Transfusion practitioners	Trust Transfusion committee	yearly

CONSULTATION	
This Treatment pathway has been circulated to the following individuals for consultation	
Name	**Designation**
Dr Thomas Skibbe	Consultant Haematologist
Dr Alyson McClung	Consultant physician
Dr Nick Turley	Consultant A&E
Dr Shiju Mathew	Consultant anesthetist
Dr Baylon Kamalarajan	Consultant paediatrician
Mr Steve Goodyear	Consultant surgeon - vascular
Catherine Hilman-Cooper	Consultant Obstetrics
Manon Van Setters	Consultant gynaecologist
Jane Brown	Clinical Governance facilitator
Cathy Lim	National blood service liaison
Rebecca Thompson	Community IV therapy lead
Camran Khan	Transfusion Laboratory manager
Juliette Stone	Senior Sister Theatres
Debra Clinton	Assistant Transfusion practitioner
Jon Dickens	Charge Hand A&E
This Treatment pathway has been circulated to the chair(s) of the following committee's / groups;	
Trust Transfusion Committee	
Safe Patient group	

IMPLEMENTATION
Plan for implementation
How are you going to implement and ensure all relevant staff are aware of this pathway?
The individual members of the transfusion committee will be responsible for informing their relevant clinical directorate
The updated pathway will be presented at the link nurse day. The link nurses will cascade the information to the ward teams

DISSEMINATION
A link of the blood transfusion treatment pathway will be forward to all matrons, and ward managers once the pathway has been ratified

TRAINING AND AWARENESS
This section should refer to training as identified in the Trusts Training Needs Analysis Appendix A of the Trusts Mandatory Training Policy
All staff involved in the transfusion process should be trained and competent in the process they are taking part in. The training is described in the Trusts Training Needs Analysis Appendix A of the Trusts Mandatory Training Policy

SUPPORTING DOCUMENT ONE – EQUALITY IMPACT ASSESSMENT TOOL		
To be completed by the Treatment pathway owner and submitted to the appropriate committee for consideration and approval.		
		Yes/No
1.	Does the treatment pathway affect one group less or more favourably than another on the basis of:	**no**
	Race	**no**
	Ethnic origins (including gypsies and travellers)	**no**
	Nationality	**no**
	Gender	**no**
	Culture	**no**
	Religion or belief	**no**
	Sexual Orientation	**no**
	Age	**no**
2.	Is there any evidence that some groups are affected differently?	**no**
3.	If you have identified potential discrimination, are any exceptions valid, legal and/or justifiable?	**no**
4.	Is the impact of the policy/guidance likely to be negative? If so can the impact be avoided?	**no**
5.	What alternatives are there to achieving the policy/guidance without the impact?	**no**
6.	Can we reduce the impact by taking different action?	**no**
7.	Other comments	**none**

If you have identified a potential discriminatory impact of this key document, please refer it to Human Resources, together with any suggestions as to the action required to avoid/reduce this impact.

For advice in respect of answering the above questions, please contact Human Resources.

SUPPORTING DOCUMENT TWO – FINANCIAL IMPACT ASSESSMENT		
To be completed by the Treatment pathway owner and submitted to the appropriate committee for consideration and approval.		
		Yes/No
1.	Does the implementation of this document require any additional Capital resources	**no**
2.	Does the implementation of this document require additional revenue	**no**
3.	Does the implementation of this document require additional manpower	**no**
4.	Does the implementation of this document release any manpower costs through a change in practice	**no**
5.	Are there additional staff training costs associated with implementing this document which cannot be delivered through current training programmes or allocated training times for staff	**no**
6.	Other comments	**none**

If the response to any of the above is yes, please complete a business case and which is signed by your Finance Manager and Directorate Manager for consideration by the Accountable Director before progressing to the relevant committee for approval