Policy Category	BC - Best Care		
Best Care Goals	☒ Safe ☐ Personal ☐ Connected ☐ Effective		
Applies To	National		
Version	**Approval Authority**	**Effective from**	**Review by date**
1	National Medical Director, WA	10/09/2021	23/09/2024

Contents

1. Rationale

The purpose of this Clinical Protocol is to provide Medical Practitioners and clinical staff a guiding framework for the administration of iron infusions either in the home or in a clinic.

2. Scope

The Clinical Protocol applies to Nationally for the administration of Iron Carboxymaltose infusion

3. Acceptance Criteria and Pathway

RED Unacceptable for community admission to HATH Refer to ED/ Inpatient management. (May become suitable for HATH after ED or inpatient stabilisation)	Absolute Exclusion • Previous hypersensitivity reaction to any intravenous iron. • 1st trimester of pregnancy. • Anaemia not attributed to iron deficiency. • Iron overload • Haemochromatosis
ORANGE Requires discussion with Medical Governance prior to acceptance.	Relative Exclusion • Acute or chronic infection • Asthma, eczema or atopic allergies • Hepatic dysfunction • In home administration. Nursing teams need to feel confident to determine difference between anaphylactic and other forms of hypersensitivity/allergic reactions and manage accordingly
GREEN Accepted for HATH	There are five required inclusion criteria: • Meet criteria for iron depletion/iron deficient erythropoiesis/IDA as defined below AND • Demonstrated intolerance, non-compliance or lack of efficacy with oral iron, despite modification of form of oral iron dose, timing and frequency AND • The patient's medical condition has been assessed as stable; • The patient has a clear diagnosis for the cause of the iron deficiency, clear prognosis and is at a low risk of deterioration AND • The referrer has discussed the risks and benefits of intravenous iron treatment.

Note:

- All referrals can be provisionally accepted upon confirmation that the pathology requirement is or will be available prior to infusion occurring, and the referrer should be informed that the governing doctor will assess the pathology results and

clinical information and will make contact should any further information be required prior or should the referral be declined.

- Please check if there is a history of drug hypersensitivity, asthma, or other co morbidities. While clients may still be considered suitable for iron infusions, the information is required for the governing doctor to make an assessment of the safety of proceeding and/or the need for a slower infusion or more frequent monitoring.
- Please advise the referrer to cease oral iron to allow at least 1 week of no oral iron prior to the infusion as the presence of oral iron may reduce the effectiveness of the infusion.

4. Pathology Work Up

- U&E FBP, Full fasting iron studies
- Coeliac serology result if not done previously

5. General Management

Practice Points/Risks

Absolute iron deficiency is defined as Ferritin <15-30 microgram/L or Ferritin <100 microgram/L and Transferrin saturation <20%. Functional iron deficiency exists, when stored iron cannot be released for erythropoiesis. This is commonly seen in patients with kidney disease, inflammatory states or cancer

Spectrum of Iron Deficiency

Example of laboratory profile	Normal	Iron depletion	Iron deficient erythropoiesis	Iron deficiency anaemia
Serum ferritin (µg/L)	60	***<15***	***<15***	***<15***
Transferrin saturation (%)	35	35	***<15***	***<15***
Haemoglobin (g/L) female	>120	>120	>120	***<120***
Haemoglobin (g/L) male	>130	>130	>130	***<130***

- Deficiency of iron may lead to fatigue, shortness of breath, decreased physical performance, impaired and concentration, altered body temperature, and altered immune function.
- The cause of iron deficiency states must always be determined, as it may relate to a serious underlying condition such as occult malignancy

- IM iron administration is not recommended as it can lead to permanent skin discolouration
- Intravenous iron supplementation is well tolerated, though a small proportion of people develop influenza-like symptoms for a few days after the infusion. Transient hypophosphataemia has been reported after iron infusion (especially ferric carboxymaltose), but the clinical significance of this is uncertain
- Anaphylactic reactions occur most frequently within the first several minutes of administration and are characterised by sudden onset of respiratory difficulties, tachycardia and hypotension. Adrenaline and facilities for the cardio-pulmonary resuscitation must be available. Therefore, infusions of iron carboxymaltose will only be completed in a home environment if management of anaphylaxis can be safely assured
- Anaphylaxis can occur with any infusion-not just the first. A previous hypersensitivity reaction to IV iron increases the risk of an adverse response to a subsequent iron infusion.
- Extravasation: Both patient and nurse must be alert to extravasation at all time. Skin staining due to extravasation is irreversible. Ensure cannula is in the largest vein possible and secured and an extension is used. Flush with 50mls Normal saline 0.9% prior to and following infusion to minimise risk.
- Drug interactions: Oral iron therapy – if possible, cease one week prior to and at least one week after infusion. Oral and parenteral iron should not be used together. Oral iron may block iron binding sites so that intravenous iron is less well absorbed and there is a greater likelihood of adverse effects.

6. Medical Management / Treatment Plan

6.1. Dosage

- Iron Carboxymaltose (Ferinject®)
- Classification: Iron supplementation
- Presentation: Ferric carboxymaltose.
- 500mg elemental iron /10mL (Ferinject®)

There are two components to the dosage calculation. The first is the total dose to be given and this is calculated based on weight and haemoglobin. Since more than one infusion may be required, the second is the dose to be given on each occasion.

Total Dosage Calculation Based on Weight and Haemoglobin

Total Ferric carboxymaltose dose required based on haemoglobin and body weight	Body Weight 35kg - <70 kg	Body Weight ≥ 70kg

Haemoglobin (g/L)		
< 100	1500mg	2000mg
≥ 100	1000mg	1500mg

Maximum Dose

The maximum dose is 1000mg (not exceeding 20mg/kg) in a week. (Maximum PBS quantity is 2 vials per prescription)

Dose per Infusion

The following doses are suggested per infusion based on body weight:

- ≤55kg – 500mg elemental iron (as ferric carboxymaltose)
- >55kg – 1000mg elemental iron (as ferric carboxymaltose)

6.2. Administration

Preparation

- Ensure resuscitation equipment is readily available (including oxygen, adrenaline, hydrocortisone and promethazine).
- Dilute:
  - 500mg ferric carboxymaltose in 100mL sodium chloride 0.9%.
  - 1000mg ferric carboxymaltose in 250mL sodium chloride 0.9%.

Infusion

- Secure IV access should be established, bearing in mind when selecting the site that there could be irreversible staining with extravasation.
- Flush with 50mL sodium chloride 0.9% before and after iron infusion to minimise risk of extravasation.
- Infuse over 15 minutes. No test dose required.

Observations

- Temperature, pulse, respiratory rate, blood pressure and oxygen saturation prior to commencement of the infusion (baseline), 5 minutes into the infusion, as required through out the infusion, if the patient reports feeling unwell/any potential adverse effects, and at the end of the infusion.

- Patients must be observed for 30 mins following the infusion.

6.3. Potential Adverse Reactions

- Phlebitis
- Flushing, sweating, chills, fever, headache, dizziness
- Nausea and vomiting
- Rash, urticaria, angioedema (more likely to be delayed 1-2 days)
- Anaphylaxis (Incidence 1:250,000, less likely with infusion vs IV push)
- Syncope, tachycardia, hypotension,
- Bronchospasm, dyspnoea
- Musculoskeletal pain/stiffness
- Urticaria/rash

Note: Some adverse reactions may be delayed by 1-2 days following infusion

6.4. Factors increasing risk and or severity of hypersensitivity reactions in patients

- Previous reactions to IV iron
- Fast iron infusion rates
- History of other drug allergy or allergies
- Mastocytosis
- Severe respiratory or cardiac disease
- Old age
- Treatment with B blockers, ACE inhibiters
- Pregnancy-first trimester
- Systemic Inflammatory disease eg rheumatoid arthritis, SLE
- Anxiety-patient or staff

6.5. Management of adverse reactions

Note most adverse symptoms resolve without treatment. They are more common with ‘total dose’ infusions of iron polymaltose but can occur with iron carboxymaltose.

In the event of a significant adverse reaction, the very first response must be cessation of the infusion and assessment for symptoms and signs of anaphylaxis

- Anaphylaxis must be managed as per the anaphylaxis protocol with adrenaline and NOT with antihistamines or hydrocortisone.

- Antihistamines are first line treatment for drug induced urticaria and angio oedema (noting that these reactions are more likely to occur 1-2 days after the infusion)

- First line treatment of urticaria and angio oedema is with non sedating anti histamines such as cetritizine, or desloratidine. Sedating antihistamines can be used at night eg promethazine. These can be given in standard oral dosages.
- Although oral corticosteroids can temporarily relieve acute urticaria, high doses are needed and often the condition recurs when treatment stops so they are not routinely recommended.

6.6. Following Infusion

- One or more infusions will be arranged as required using the calculations above.
- If more than one infusion is required, arrange the next infusion at least 7 days later, and inform the patient's GP after each time that the infusion has occurred and when the next infusion will occur.
- Following the last infusion, the patient's GP should be advised to recheck iron level between 21 and 28 days following the final infusion to ensure iron levels have improved.
- Recurrent need for infusion should be investigated. The risks of iron toxicity are increased with recurrent infusions.

6.7. Standing Drug Order

In the event of an adverse reaction associated with Carboxymaltose infusion, please refer to: *Anaphylaxis Emergency Management in the Community BC-PRO-0031.*

7. Monitoring

- Standard monitoring procedure-administer infusion over 15-30 mins, monitor throughout and for 30 minutes afterwards
- Observation/monitoring should occur every 5-15 min and for 30 min after the infusion finishes or as per local Medical Governance requirements.
- In clients identified as being of potential increased risk of hypersensitivity reactions it is recommended that the iron infusion should be initiated at less than 50% of the rate recommended by the manufacturer and not increased to the recommended rate until it is clear that it is being well-tolerated (usually 10–15 min).

8. Medical Governance

- Primary medical oversight can be held by referring medical specialists, credentialed referring GPs or by Silver Chain medical staff.

- The client must have access to medical governance support for 24 hours per day, 7 days per week
- When governance/oversight is retained by a Silver Chain medical officer, the client will have a medical review within 48 hours of admission and the medical officer will determine when scheduled follow up and anticipated discharge will occur. It is expected there will be regular medical reviews
- Where the primary medical governor is unavailable the Silver Chain medical officer will provide the medical oversight
- Care delivery is planned and provided in consultation with the client, medical officer/specialist holding medical governance and nursing staff.
- In the instance when a client's condition deteriorates the Silver Chain medical officer or nursing staff will escalate back to the referrer. ED is not considered an appropriate escalation point except in the case of an emergency
- A summary of the episode of care is sent to the referrer or the client's GP at discharge

9. Discharge Planning

- Ensure the client has an appointment arranged with own General Practitioner (GP) prior to discharge to ensure continuity of care.
- Ensure discharge summary has highlighted the key clinical concerns/risks you wish to hand over
- Fax client discharge summary to GP.

10. Supporting Documents

Silver Chain Group documents that directly relate to and inform this Clinical Protocol are available with this document in the Policy Document Management System (PDMS).

Other documents that directly relate to and inform this Clinical Protocol are as follows:

- National Blood Authority. Iron product choice and dose calculation for adults. Guidance for Australian Health Providers 2016; https://www.blood.gov.au/system/files/documents/Iron%20product%20choice%20and%20dose%20calculation20052016.pdf.
- Therapeutic Goods Administration. Consumer Medicine Information Ferinject™. 2016; https://www.ebs.tga.gov.au/ebs/picmi/picmirepository.nsf/pdf?OpenAgent&id=CP-2011-CMI-02558-3&d=20180227161146224483.

- King Edward Memorial Hospital. Intravenous Ferric Carboxymaltose Therapy (FERINJECT®). 2015; http://www.kemh.health.wa.gov.au/development/manuals/O&G_guidelines/sectiona/4/IronCarboxymaltoseTherapy.pdf.
- Northern Territory Government Department of Health. Iron Infusion (Ferric Carboxymaltose) PHC Remote Clinical Guideline. 2015; http://remotehealthatlas.nt.gov.au/iron_infusion_protocol.pdf.
- European Medicines Agency. New recommendations to manage risk of allergic reactions with intravenous iron-containing medicines. 2013; http://www.ema.europa.eu/docs/en_GB/document_library/Press_release/2013/06/WC500144874.pdf.
- Government of South Australia SA Health. Ferric Carboxymaltose (Ferinject®) Infusion for ADULTS with confirmed iron deficiency and indications for IV iron. Version 1.0. 2017; http://www.sahealth.sa.gov.au/wps/wcm/connect/56c9728042c5cd328b00ff8cd21c605e/Generic+ferric+carboxymaltose+infusion+protocol+for+adults.pdf?MOD=AJPERES&CACHEID=ROOTWORKSPACE-56c9728042c5cd328b00ff8cd21c605e-lX5RWSG. Accessed 18/8/2021
- Hypersensitivity reactions to intravenous iron: guidance for risk minimization and management. Haematologica. 2014 Nov; 99(11): 1671-1676 https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4222472/

11. Document Details

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