Specialised Medication – Adult Intravenous Iron Therapy Guideline

1. Guiding Principles

Oral iron supplementation remains the first choice of treatment due to its efficacy and low cost. For some conditions oral supplementation is not possible due to gastrointestinal side effects and time required to treat anaemia and replace iron stores.

The original intravenous iron product, Iron Dextran, was associated with an elevated risk of anaphylaxis. Current formulations available in Australia are dextran free and have improved safety profiles enabling higher doses to be given as more rapid infusions.

Obstetric Considerations

Iron deficiency anaemia in pregnancy carries risks of adverse pregnancy outcome including increased maternal susceptibility to severe infections and increased risk of blood transfusion associated with haemorrhagic complications of pregnancy.

Infants of iron deficient mothers are at increased risk of iron deficiency and consequences thereof. Iron deficiency anaemia in pregnancy is associated with increased risk of preterm labour, low birth weight, placental abruption and post-partum haemorrhage.

In general, for pregnant or breastfeeding women, Iron Polymaltose is the recommended treatment as a TGA Category A medicine (no proven harmful effects on the foetus). Refer to the King Edward Memorial Hospital (KEMH) O&G Clinical Guidelines – Iron Therapy: Intravenous

Where use of iron polymaltose infusions for treatment in pregnancy is likely to be confounded by compliance issues, usually relating to extreme social and/or geographic situations, often in association with multiple risk factors for adverse pregnancy outcome, the option of offering ferric carboxymaltose infusion may be considered on a regional basis by WA Country Health Service (WACHS) Regional Drug and Therapeutic committees or equivalent.

Decisions to prescribe ferric carboxymaltose infusions for the treatment of iron deficiency anaemia in the second and third trimesters of pregnancy are to include consultation with an obstetrician/ GPO and a risk / benefit evaluation taking into account both the client and the foetus. Ferric carboxymaltose is a Category B3 medication.

Haemodialysis Considerations
The use of intravenous iron supplementation is common in haemodialysis patients. The use in these patients is outside the scope of this document – refer to local dialysis guidelines for dose and administration information.

Paediatric use
The use in paediatric patient is outside the scope of this document. Consult the Perth Childrens Hospital Iron Monograph for more information.

2. Guideline

2.1 Indication

- Absolute* or Functional ** iron deficiency where
  - Patient is unable to tolerate oral iron
  - Patient is non-compliant to oral iron
  - Oral iron is ineffective due to malabsorption or other pre-existing medical condition.
- Perioperative Management of anaemia or iron deficiency as recommended by the National Blood Authority guidelines
- Management of iron deficiency anaemia in pregnancy during the second and third trimester and post-partum anaemia due to PPH.
- Management of anaemia of Chronic Kidney Disease

*Absolute iron deficiency is defined as ferritin <15-30 microg/L or ferritin <100microg/L with a transferrin saturation <20%
** Functional iron deficiency exists when stored iron cannot be released for erythropoiesis.

2.2 Contraindications

Absolute Contraindications
- Previous severe reaction to IM or IV iron
- Iron overload (transferrin saturation >45%, haemochromatosis and ferritin >1000microg/L)
- De-compensated hepatic cirrhosis or infectious hepatitis

Relative Contraindications
- First trimester of pregnancy (no safety data below 16 weeks gestation, abnormalities reported with high doses in animal studies)
- Anaemia not due to iron deficiency
- Severe active infection or inflammation including inflammatory arthritis
- Polycythaemia vera

Precautions:
- Severe asthma or eczema increased the risk of adverse reaction.
- Treatment with beta-blockers and ACE inhibitors is associated with increased risk of hypersensitivity reactions.
- Vitamin D deficiency due to risk of hypophosphataemia (particularly with Ferric Carboxymaltose)

2.3 Safety recommendations

Administration must only occur where there is a medical officer either on site or able to attend the hospital quickly in the case of a reaction. The medical officer must be aware the procedure is taking place.

The infusion must take place where there is easy access to resuscitation equipment and staff must be trained in the management of anaphylaxis.

When possible, the patient should cease oral iron therapy one week prior to infusion and oral therapy should not be recommenced until one week after last injection/infusion of iron.

Skin staining as a result of extravasation is irreversible.

- Patient consent and education should include the risk of staining from extravasation.
- Ensure the cannula is in the largest vein possible and secured.
- Renal patients (dialysis and non-dialysis): preferably no cannulation or blood sampling above the wrist.
- Flush with 50mL sodium chloride before and after iron to minimise the risk of skin staining.

Recommendations for safe administration are:

- An infusion pump must be used to administer iron infusions
- Do not add any other medications to infusion or mix in the same line.
- Resuscitation equipment, including oxygen, adrenaline, hydrocortisone and promethazine must be readily available in the clinical area

In case of a hypersensitivity reaction, treatment should be stopped immediately and appropriate management initiated. ACE inhibitors may increase the incidence of adverse effects like erythema, hypotension, nausea and vomiting.

Prophylaxis against allergic reactions is unnecessary, except where there is a history of severe asthma/allergy or previous adverse reaction to parenteral iron. Consider a premedication prior to commencing infusion for these patients or using an alternative iron formulation.

2.4 Prescribing

The decision to prescribe intravenous iron should by a senior medical officer. Where a senior medical officer is not available on site a junior medical officer or nurse practitioner (working within scope of practice) can prescribe in consultation with a senior medical officer.

Intravenous iron is to be prescribed on the MR173C WACHS Intravenous Iron Consent and Prescription Chart including:

- Formulation of iron to be prescribed
- Dose of elemental iron
- Rate of administration

2.5 Presentation

- Iron Polymaltose (Ferrum H®, Ferrosig®)
  - Complex of iron (III) hydroxide and polymaltose
  - Each 2mL contains 100mg elemental iron
  - Only Ferrosig® is licensed for IV use and is the preferred brand, however, use of Ferrum H® represents a clinically acceptable alternative if necessary.
  - Unrestricted on formulary

- Ferric Carboxymaltose (Ferinject®)
  - Each **10mL** contains **500mg elemental iron**
  - Formulary restrictions limit use to day infusion and outpatients or patients who have a documented hypersensitivity to iron polymaltose.
  - A PBS prescription may be required for supply by the hospital to a day patient or outpatient.

- Iron Sucrose (Venofer®)
  - For use in renal patient who are unable to tolerate iron polymaltose.
  - May be used as an alternative agent in patients with hypersensitivity to other iron products.
  - Administration direction not included in WACHS policy. For administration instructions consult the product information.
  - Each **5ml** contains **100mg elemental iron**

- Ferric derisomaltose (Monofer®)
  - For use in outpatients and day patients who require doses above 1000mg elemental iron or who are unable to tolerate ferric carboxymaltose.
  - Maximum dose per administration is 20mg/kg or 1500mg.
  - Doses below 1000mg are diluted in 100 to 500ml normal saline 0.9% and administered over 20 minutes.
  - Doses between 1000mg and 1500mg are administered over 30 minutes.
  - PBS prescription is required for the hospital to supply to a day patient or outpatient.

2.6 Consent

Consent is to be obtained by a medical officer and is to specify risks of adverse reactions.

Provide the patient with the intravenous iron patient information from the intravenous Iron consent and prescription form.

2.7 Dosage and Administration

Iron Polymaltose	Ferric Carboxymaltose
Dose	
≤70kg body weight = 1000mg iron >70kg body weight = 1500mg iron Replacement of iron stores = 500mg iron Maximum dose 2500mg iron	Single dose should not exceed 1000mg iron or 15mg/kg ≤70kg = 500mg iron >70kg = 1000mg iron Higher doses may be required for severe iron deficiency anaemia For doses >1000mg, give remainder of calculated dose after 7 days
Preparation	
Use a filtered needle and protect bag from light after preparation. For doses up to 1500mg add to 250ml sodium chloride 0.9%. For doses greater than 1500mg add to 500ml Sodium Chloride 0.9%.	For 500mg dilute in 100ml Sodium Chloride 0.9% For 1000mg dilute in 250ml Sodium Chloride Inspect vials visually for sediment and damage before use. Only use those containing sediment-free, homogeneous solutions.
Administration	
Flush with 50ml sodium chloride 0.9% before infusion For patients who are receiving doses above 2g, haemodynamically unstable, inflammatory disease state or cardiac failure use the slow infusion. **Rapid infusion (80 minutes)** Infuse 40ml/hr for the first 15 minutes then increase to 250ml/hr **Slow infusion (2.5 hours)** Infuse 40ml/hr for 15 minutes then increase to 125ml/hr Slower infusions over 5 hours may be appropriate for some patients particularly if they have experienced reactions in the past. Test dose are no longer required.	Flush with 50ml sodium chloride 0.9% before infusion Infuse over 15 minutes using an infusion pump. Flush with 50ml sodium chloride 0.9% after infusion.

Patients may be commenced on the full dose but should still be monitored closely for the first 15 minutes. Flush with 50ml sodium chloride 0.9% after infusion.	
Monitoring	
For all infusions Monitor temperature, pulse, respiratory rate, oxygen saturation and blood pressure on the Adult Observation and Response Chart Record observations at baseline then repeat every 5 minutes for the first 15 minutes then every 15 minutes during the rapid infusion and every 30 minutes for the slow infusion. Observe for signs of extravasation Repeat observations 30 minutes post infusion.	Monitor temperature, pulse, respiratory rate, oxygen saturation and blood pressure. Record observations at baseline then repeat every 5 minutes until completion of the infusion Observe for signs of extravasation. Repeat observations 30 minutes post infusion

For administration of iron sucrose (Venofer®) or Ferric Derisomaltose (Monofer®) refer to product information or Australian Injectable Drug Handbook.

2.8 Adverse effects / Infusion reactions

Discuss the Patient information brochure with the patient and possibility of delayed adverse reactions to IV Iron infusions which may include fatigue, myalgia, arthralgia, chest or back pain, rash or headache.

Advise the patient to contact the hospital if they become unwell. Complete the contact details on the patient information brochure.

Patient and nurse/midwife should be alert to side effects or extravasation at all times during the infusion. Anaphylaxis and hypersensitivity reactions are uncommon.

Mild reactions

- Flushing, sweating, chills, fever, headache, dizziness
- Nausea and vomiting
- Rash and urticaria
- Musculoskeletal pain/ stiffness
- Lymphadenopathy
- Phlebitis where extravasation is not suspected.
- Slowing the infusion rate or administering an antihistamine may be beneficial.

Severe hypersensitivity / anaphylactic reactions

Syncope, tachycardia, hypotension, circulatory collapse
Angioedema
Bronchospasm with dyspnoea
+/- the symptoms experienced in 'mild' reactions.

Stop the infusion immediately, and consult the prescriber or treating team. The administration of hydrocortisone, adrenaline and/or oxygen may be necessary depending on clinical symptoms.

Patient management should be escalated according to the appropriate local Medical Emergency Response chart (see WACHS Clinical Escalation Including Code Blue Medical Emergency Response (MER) Policy). For guidance on the management of anaphylaxis, refer to the Medication Administration Policy: Anaphylaxis Flowchart (Appendix 7).

Extravasation

Paravenous leak / extravasation of IV iron therapy may cause irreversible skin staining, blistering, tissue necrosis and ulceration. Some symptoms may be delayed up to eight days post infusion.

Symptoms include pain, burning, stinging, swelling, redness or brown staining.

If extravasation is suspected, the initial steps include 'SLAP'.

STOP the injection or intravenous infusion immediately.

LEAVE the venous access device (VAD) in place.

ASPIRATE any residual drug from the VAD using a sterile syringe.

PLAN

- **CALL for assistance** notify medical officer, pharmacist and/or a senior nurse.
- **ASSESS** the affected area for the presence of symptoms e.g. erythema, swelling, burning, pain and **TRACE** the affected area with a marker pen.
- **PHOTOGRAPH** the area.
- **REMOVE** IV device – do not apply pressure.
- **APPLY** a cold pack and elevate affected limb.
- **ADMINISTER** pain relief if indicated.
- **REFER patient for further follow up to** authorised prescriber within 3 days, who may arrange review by senior medical officer for long term management (according to individual case if clinically indicated).
- Laser therapy has been successful in reducing the skin staining long term.

3. Definitions

Nil

4. Roles and Responsibilities

The **Medical Officer** is responsible for:

- completing orders for the medication on the appropriate chart and any PBS prescription requirements for an outpatient
- patient consent (following clear explanation of possible reactions) and provide written information about potential adverse events.
- ensuring the appropriate venous access is inserted if required
- reviewing recorded observations regularly and alter treatment where required
- completing all treatment and duties within scope of practice.

The **Registered Nurse/Midwife** is responsible for:

- ensure the patient understands the procedure and has consented to it
- recording observations as directed and notify the medical officer of any abnormal reading
- preparing the medication in readiness for treatment including checking with another registered nurse/midwife, enrolled nurse or medical officer
- completing all nursing duties for the patient within scope of practice
- completing all required documentation
- confirming the patient has been provided with the WACHS Intravenous Iron Patient Leaflet with education of the patient on the signs and symptoms of infusion reactions that may occur up to eight days post infusion

5. Compliance

Failure to comply with this policy document may constitute a breach of the WA Health Code of Conduct (Code). The Code is part of the Integrity Policy Framework issued pursuant to section 26 of the *Health Services Act 2016* (WA) and is binding on all WACHS staff which for this purpose includes trainees, students, volunteers, researchers, contractors for service (including all visiting health professionals and agency staff) and persons delivering training or education within WACHS.

WACHS staff are reminded that compliance with all policies is mandatory.

6. Records Management

All WACHS clinical records must be managed in accordance with Health Record Management Policy.

7. Evaluation

A Datix Clinical Incident Management System (Datix CIMS) form must be completed for all extravasations.

Patients who experience an adverse reaction during the infusion must have the details of the reaction documented in the notes and the reaction reported in accordance with local reporting processes.

Any issues reported to the local Regional Drug and Therapeutics committee are to be referred to the WACHS Blood and Blood Products Committee for consideration in review of the guideline.

An annual report is to be tabled at the WACHS Blood and Blood Products Committee to assess compliance to the policy.

8. Standards

National Safety and Quality Health Service Standards
Medication safety Standard: 4.3, 4.7, 4.13 and 4.15
Blood Management Standard: 7.4

9. Legislation

Medicines and Poisons Regulation 2016 (WA)

10. References

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6. High Risk Medication Guideline – Iron – Intravenous Administration. SCGH. 2017
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8. MHRA. Intravenous iron and serious hypersensitivity reactions: new strengthened recommendations to manage and minimise risk. Drug Safety Update Vol 7, issue 1 August 2013.
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10. Garg, M, Morrison, G, Friedman, A, Lau, A, Lau, D and Gibson PR. (2011). A rapid infusion protocol is safe for total dose iron Polymaltose: time for a change
11. EVIQ – supporting Document – Extravasation Management [internet]. Sydney, Cancer Institute NSW. April 2019 (cited 9th October 2019) available from https://www.eviq.org.au/clinical-resources/extravasation/157-extravasation-management##management.

11. Related Forms

MR173C WACHS Intravenous Iron Consent and Prescription Form
MR140A Adult Observation and Response Chart (A-ORC)

12. Related Policy Documents

WACHS Clinical Escalation of Acute Physiological Deterioration including Medical Emergency Response Policy

WACHS Medication Administration Policy

13. Related WA Health System Policies

OD 0657/16 WA Health Consent to Treatment Policy

14. Policy Framework

Clinical Governance, Safety and Quality

This document can be made available in alternative formats on request for a person with a disability

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