SESLHD PROCEDURE COVER SHEET

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SUMMARY	The purpose of this document is to provide SESLHD staff with information on the safe and appropriate use of iron infusions for the treatment of iron deficiency anaemia.

1. POLICY STATEMENT

This guideline provides recommendations regarding best practice for the safe prescribing, administration, and monitoring of iron infusions for the treatment of iron deficiency anaemia when treatment with oral supplementation is either inappropriate or ineffective.

2. BACKGROUND

Oral iron supplementation remains the first choice of treatment for iron deficiency anaemia due to its efficacy and low cost.

Oral supplementation is either inappropriate or ineffective in the following circumstances:

- Demonstrated intolerance, non-compliance, or lack of efficacy with oral iron despite modification of dose, timing and frequency,
- Intestinal malabsorption of oral medication,
- Ongoing iron (blood) losses that exceed absorptive capacity, and / or,
- A clinical need for a rapid iron supply.

In these situations, intravenous iron may be a suitable option.

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.

Intramuscular iron is poorly absorbed, and local reactions (particularly pain) and subcutaneous discolouration occur frequently at the injection site. Similar reactions can occur with intravenous administration if poor insertion technique is used.

3. RESPONSIBILITIES

3.1. Medical staff (or other authorised prescribers) will:

- Document in the patient's electronic record the indication for receiving an iron infusion
- Discuss with the patient the possible adverse reactions, risks and benefits associated with this medication and obtain informed consent
- Prescribe the iron infusion as specified in the relevant Medicine Guideline
- Review the patients following an adverse event as required
- Report any adverse events occurring to patients receiving iron infusions
- For inpatients document in the patient's discharge summary that the patient received an iron infusion during admission.

3.2. Registered Nursing / Midwifery staff will:

- Prepare the patient to receive the iron infusion
- Prepare and administer the iron infusion with reference to the relevant Medicine Guideline
- Monitor the patient receiving the iron infusion in accordance with the relevant Medicine Guideline
- Report any adverse events occurring to patients receiving iron infusions.

3.3. Enrolled nursing staff will:

- Check iron infusions for administration with a Registered Nurse / Midwife.

3.4. Pharmacy staff will:

- Review prescriptions for iron infusions where possible to ensure appropriateness
- Facilitate availability of iron preparations when appropriate
- Report any adverse events occurring to patients receiving iron infusions.

3.5. Nursing / Midwifery Unit Managers will:

- Ensure iron infusions are managed in accordance with the requirements of this procedure
- Review in detail any adverse clinical outcome associated with iron infusions.

4. PROCEDURE

4.1. Indications

4.1.1. Decision Algorithm

<table>
<tr><th colspan="3">Iron Deficiency Anaemia Management
When oral supplementation is either inappropriate or ineffective</th></tr>
<tr><td colspan="3">INPATIENT SETTING</td></tr>
<tr><td colspan="3">First Line</td></tr>
<tr><td colspan="3">SLOW dose STANDARD volume or LOW volume Iron Polymaltose (Ferrosig©)</td></tr>
<tr><td colspan="3">MUST be used in all cases when the required dose exceeds 2 g iron (as polymaltose)</td></tr>
<tr><td colspan="3">SLOW infusion preferred for patients who have a condition or previous adverse drug reaction that puts them at higher risk of reactions</td></tr>
<tr><td colspan="3">SLOW dose LOW volume may be considered for patients with renal impairment and patients with fluid restrictions. See Iron Polymaltose Medicine Guideline for administration instructions for patients who receive regular incremental doses of iron (i.e., on dialysis)</td></tr>
<tr><td colspan="3">Second Line</td></tr>
<tr><td>RAPID Iron Polymaltose (Ferrosig©)</td><td>Ferric Carboxymaltose (Ferinject©)</td><td>Iron Sucrose (Venofer©)</td></tr>
<tr><td>ONLY for doses less than 2 g iron (as polymaltose).</td><td>Approved for patients where LOW volume iron polymaltose is inappropriate due to fluid restriction (e.g., congestive cardiac failure).</td><td rowspan="8">Approved for use in patients unable to tolerate other parenteral iron products.</td></tr>
<tr><td>Suitable for patients who are haemodynamically stable.</td><td>Approved for iron deficiency anaemia in perioperative peritonectomy inpatients.</td></tr>
<tr><td>NOT to be used in patients with a condition that puts them at high risk of hypersensitivity reaction.</td><td>Approved for pre-operative patients where rapid iron repletion is required and/or anticipated postoperative Hb decrease is ≥ 30 g/L.</td></tr>
<tr><td rowspan="4">NOT to be used for patients with NYHA Class III or IV Heart Failure, patients with known LVEF ≤ 30%, patients with eGFR ≤ 15 mL/min or patients otherwise deemed at risk of fluid overload.</td><td>Approved for ED non-admitted patients requiring IV iron replacement.</td></tr>
<tr><td>For inpatient postnatal women who fulfill the criteria for iron replacement based on Hb and ferritin parameters</td></tr>
<tr><td>Approved for specific situations where a rapid IV iron infusion is essential as recommended by a specialist / consultant (e.g., patient with dementia).</td></tr>
<tr><td>Approved for use in subacute facilities (War Memorial & Calvary Hospital ONLY).</td></tr>
</table>

Iron Deficiency Anaemia Management *When oral supplementation is either inappropriate or ineffective*			
OUTPATIENT SETTING			
Iron Polymaltose (Ferrosig©)	Ferric Carboxymaltose (Ferinject©)	Iron Sucrose (Venofer©)	Ferric Derisomaltose (Monofer©)
Administration Protocol based on total dose. See Medicine Guideline for further details.	PBS supply obtained from community. Approved for patients aged 9 months or more.	PBS supply obtained from community.	PBS supply obtained from community.

4.2. Special Patient Populations

4.2.1. Paediatrics

Intravenous iron is not without risk and should primarily be used for children with proven severe iron deficiency anaemia unable to take or absorb oral iron. Whenever possible, oral iron should be used to treat iron depletion, iron deficiency or iron deficiency anaemia in children.

- There are two intravenous iron formulations approved for use in children in SESLHD: iron polymaltose (Ferrosig®) and ferric carboxymaltose (Ferinject®). They differ in formulation, administration, side effects, price and age limits. Please read carefully to choose the correct product for your patient.
- Iron polymaltose (Ferrosig®) is the only parenteral iron formulation suitable for total iron replacement in one single infusion. Ferric carboxymaltose (Ferinject®) is not suitable for total iron replacement in one single infusion if the patient requires a high dose (i.e., > 1000 mg or 20 mg/kg). If total iron replacement in one single dose is required, please use iron polymaltose (Ferrosig®).
- Ferric carboxymaltose (Ferinject®) is formally approved for treatment of severe iron deficiency anaemia in children 14 years and older. The SESLHD Drug and Therapeutics Committee has approved the use of ferric carboxymaltose (Ferinject®) from the age of 9 months.
- Ferric carboxymaltose (Ferinject®) is not approved for use in patients less than 9 months of age.

4.2.2. Maternity

The following reference ranges are recommended for diagnosing iron deficiency anaemia in pregnancy:

Pregnant Women < 20 weeks gestation	Pregnant Women ≥ 20 weeks gestation	Postpartum	Non-pregnant Female (adult)
Hb ≤ 110 g/L and Ferritin ≤ 30 ug/L	Hb ≤ 105 g/L and Ferritin ≤ 30 ug/L	Hb < 100 g/L and/or postpartum haemorrhage (PPH) > 2000 mL	Hb < 120 g/L

Investigate anaemia in pregnant woman according to facility Anaemia and Haemoglobinopathies in Pregnancy Local Operating Procedure or Clinical Business Rule.

Consider intravenous iron in the following circumstances:

- iron deficiency anaemia in a woman unresponsive to, or intolerant/non-compliant with oral iron, or where absorption of oral iron is likely to be impaired, e.g. inflammatory bowel disease

- Iron polymaltose (Ferrosig®) is suitable for a pregnant or postpartum inpatient with the following exceptions:
  - Requirement for fluid restriction (e.g., congestive cardiac failure)
  - Where rapid repletion is required and/or anticipated postoperative Hb decrease is ≥ 30 g/L
  - Specific situations where rapid intravenous iron infusion times is essential as recommended by a specialist/consultant (e.g., woman with dementia)
  - Recommended for a pregnant or postpartum woman unless fluid restriction or rapid correction of iron stores is indicated
- Ferric carboxymaltose (Ferinject®) is recommended for pregnant or postpartum women under the following circumstances:
  - total iron requirement ≤ 1000 mg
  - rapid administration is appropriate (i.e., outpatients or day only patients)
  - where recommended for specific indications by a consultant

4.2.3. Haemodialysis Dialysis

International consensus for both iron and haemoglobin targets and monitoring regimes differ for children with chronic kidney disease compared to the general population and reflect their specific clinical needs.

Absolute iron deficiency in children with CKD can be defined as:

- Ferritin < 100 microg/L for non-diaylsis and < 200 mg/L for dialysis patients
- Transferrin saturation (TSat) < 20 %

Target levels for patients with CKD stage 3-5

- Ferritin 200 – 500 microg/L
- Transferrin saturation 20 – 30%

If ferritin levels are > 500 microg/L discuss infusion with consultant

Intravenous iron is used to maintain adequate iron stores in patients on haemodialysis with the aim to keep Transferrin Saturation (TSat) > 20% and Ferritin > 200 microg/L.

Monitoring of iron studies:
Patients with chronic renal impairment not yet receiving an erythropoiesis stimulating agent should have their iron status checked 3 monthly.

Following commencement of erythropoiesis stimulating agent monitor every 4 weeks or whenever the dose is increased.

Once target haemoglobin has been reached monitor every 3 months.

Haemoglobin target for children with CKD maintained on erythropoiesis stimulating agents:

- *6 months to 2 years = 110 g/L*
- *Over 2 years = 120 g/L*

Iron indices should be collected on routine bloods:

- Monthly:
  - during initiation or adjustment of EPO therapy
  - after completion of course of IV iron
  - during periods of iron overload
- 2nd or 3rd monthly:
  - all patients with stable adequate iron stores at least every second or third month and the results reviewed by the renal registrar.

If the patient hasn't received an iron infusion within the last 12 months, it needs to be treated as a first dose.

4.2.4. Peritoneal Dialysis (PD)

Iron deficiency is one of the common causes of anaemia in PD patients. Routine monitoring of iron studies and iron supplementations are necessary measures in the prevention of iron deficiency anaemia.

Intravenous iron is used to maintain adequate iron stores in patients on haemodialysis with the aim to keep Transferrin Saturation (TSat) 20% - 50%, Ferritin 300 - 800 microg/L and Haemaglobin 100 – 120 g/L.

PD patients are to have iron studies every 3 months.

4.3. Medicine Guidelines

4.3.1. Iron Polymaltose (Ferrosig®)

4.3.2. Ferric Carboxymaltose (Ferinject®)

4.3.3. Iron Sucrose (Venofer®)

4.3.4. Ferric Derisomaltose (Monofer®)

4.4. Potential Adverse Reactions

Although rare, there have been reports of anaphylactic or anaphylactoid reactions associated with intravenous iron infusions. Patients most at risk of these types of reactions are those with bronchial asthma, low iron binding capacity, or folic acid deficiency. Caution is also recommended in patients with a history of allergic disorders, hepatic insufficiency, or cardiovascular disease. Reactions occur most frequently within the first few minutes of administration and are generally characterised by sudden onset of respiratory difficulties, tachycardia, and hypotension. Adrenaline and equipment for cardiopulmonary resuscitation must be available for the whole administration time.

4.4.1. Hypophosphatemia

Hypophosphatemia is a known adverse reaction from the administration of intravenous iron. The duration of this effect may be up to several months depending upon the specific formulation of intravenous iron used. Symptoms of hypophosphatemia include vertigo, nausea, general weakness, tingling in the hands and depression-like symptoms. Pre-existing vitamin D deficiency, low calcium levels, low phosphate levels or raised parathyroid hormone levels may be risk factors. These should be evaluated and corrected before administering intravenous iron.

4.4.2. Extravasation

Extravasation of intravenous iron may result in permanent skin staining (tattooing). Patients must be educated on the possibility of permanent skin staining as part of the informed consent process, prior to receiving intravenous iron. This education should include adequate discussion regarding the risks and benefits of intravenous iron therapy and provision of written information such as A general guide to iron and iron deficiency – Information for patients, families and carers. Prior to the administration of intravenous iron, patients should be advised to immediately notify clinical staff if any signs or symptoms of extravasation occur. All staff administering

intravenous iron must be educated on local policies and procedures, be aware of monitoring requirements and the signs and symptoms of potential adverse effects.

When intravenous iron therapies are clinically indicated, clinicians should employ infusion techniques to minimise the risk of staining, including:

- Insert an appropriate gauge peripheral cannula (20- to 24- gauge) via the distal veins of the forearm (preferred site). Cannulation at sites of flexion or on the back of the hand should be avoided (where possible).
- Ensure the cannula is secure and that an extension set is used to minimise cannula movement (avoid covering the site with a bandage that prevents visual inspection).
- Ensure that the patency of the vein is established with a flush prior to administration.
- Ensure the infusion duration is in accordance with the relevant Medicine Guideline (see section 4.3).
- Regular monitoring of the cannula site should be timed to correspond with the collection of other vital signs in accordance with the relevant Medicine Guideline (see section 4.3).

The risk of extravasation is increased if multiple venepunctures occur during attempts at cannulation. For patients who are difficult to cannulate or in the event of multiple attempts at cannulation, consider postponing the administration of intravenous iron therapy.

4.5. Premedication

Iron Infusions are generally well tolerated with exceedingly low risk of severe reaction. Use of premedication is unnecessary for most patients.

4.6. Patient Education

Prior to administration of iron, ensure the patient understands the importance of notifying staff of unexpected reactions, including systemic reactions such as breathlessness, chest tightness, chest pain, rash, itch, racing heart, nausea, or headache. **Signs of extravasation including pain, swelling, or tingling at the cannula site should be reported to clinical staff immediately.** Discolouration may also occur but could be a delayed symptom. Ensure the patient and carer knows to contact their general practitioner or present to emergency department if any delayed adverse events occur.

Counsel the patient/carer again at discharge. A patient information brochure on iron and iron deficiency may be provided to supplement counselling. Provision of patient education should be documented in the progress notes.

4.7. Prescribing

Intravenous iron must be prescribed by a Medical Officer (or other authorised prescriber). The infusion is ordered as elemental iron and should include dosage, diluent, and infusion rate. Ensure the rate is appropriate for the individual patient. For infusion rate refer to the specific Medicine Guideline for details.

Prescribers should prescribe (eMR or Intravenous Adult Fluid Order Form) as:

"Iron (as *iron polymaltose* or *iron sucrose* or *ferric carboxymaltose* or *ferric derisomaltose*) _x_ mg in _x_ mL 0.9% sodium chloride. Infuse at _x_ mL/hour for _x_ minutes, then _x_mL/hour if tolerated"

All doses MUST be expressed as milligrams of elemental iron.

4.8. Cannulation

Prevention of extravasation requires the cannula to be appropriately placed, avoiding the hand and sites of flexion. The veins of the distal forearms are optimal sites for insertion. Where there is difficulty with cannulation arrange for technology-assisted insertion. An existing cannula must be site appropriate, checked for patency and assessed for complication. If the cannula is compromised, remove it, and arrange for a new cannula. Frequent site monitoring including visual inspection, palpation and patient perspective is important. Document evidence of monitoring.

4.9. Administration

Iron infusions should only be administered during normal business hours and where direct nursing supervision is available. Adrenaline and equipment for cardiopulmonary resuscitation must be readily available during the entire administration period.

4.10. Monitoring

Record baseline observations including blood pressure, heart rate, oxygen saturations, respiratory rate, temperature, and cannula site appearance.
Ongoing monitoring and timing of observations during infusion are dependent on the formulation of iron. Refer to the specific Medicine Guideline for details.
Throughout the infusion, monitor patients for signs of extravasation during administration. Iron infusions may cause pain, inflammation, tissue necrosis, sterile abscess and permanent brown discolouration of the skin.

4.11. Managing Adverse Reactions

Treatment of Anaphylaxis

1. **STOP the infusion**
2. Call for help as per local clinical emergency response
3. Lie patient flat and raise their feet. If breathing is compromised sit patient up
4. Administer 100 % oxygen via mask via nonrebreather mask
5. Secure intravenous access in adults in the event of hypotension and give IV normal saline (20mL/kg) rapidly and consider large bore IV access
6. Medical Officer (or other authorised person) to give adrenaline (1:1000) immediately (0.01 mg/kg to a maximum dose of 0.5 mg) IM (repeat at 5-minute intervals if necessary).
7. Commence CPR in the event of a respiratory or cardiac arrest.

For mild reactions:

1. **STOP the infusion**
2. Medical Officer (or other authorised prescriber) review to consider prescribing promethazine, hydrocortisone and/or paracetamol. If deemed safe to restart the infusion following medical review, recommence infusion at a slower rate as instructed by the treating Medical Officer (or other authorised prescriber).

4.12. Tissue Extravasation with Iron

Tissue extravasation with parenteral iron carries a significant risk of permanent skin staining. Patients may experience a bruise-like stain extending from the cannulation site. The stain may or may not fade over an extended period (years). There may be some tissue (surround) swelling, depending on volume infused, and/or depth of vessel. Optimal placement of the cannula will reduce the likelihood of extravasation. The important early indicator of iron extravasation is pain. Consider the suitability of an iron infusion for patients who are sedated, confused, or have cognitive impairment.

In the event of extravasation, immediately:

1. **STOP the infusion**
2. Assess the site
3. Disconnect the giving set
4. Consider aspirating any fluid back from PIVC
5. Remove the cannula
6. Apply a cold compress and elevate the affected limb
7. Seek medical review
8. Document the volume of iron infused

Clinicians should seek expert guidance on the management of skin staining. Laser therapy can be considered as a treatment.

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6. VERSION AND APPROVAL HISTORY

Date	Version No.	Version and approval notes
8 August 2023	1	New document. Approved at SESLHD Drug and Therapeutics Committee and SESLHD Clinical and Quality Council.
24 July 2024	1.1	Hyperlink to medication guidelines (section 4.3) corrected by SESLHD Policy.
31 October 2024	1.2	Minor amendment to support safe and appropriate use of iron polymaltose as first line agent. Approved at SESLHD Drug and Therapeutics Committee meeting.
December 2024	1.3	Minor amendment to reflect AIDH and ensure consistency in relation to maximum dose able to be administered by rapid infusion. Approved at SESLHD Drug and Therapeutics Committee meeting.
6 March 2025	1.4	Minor amendment to ensure consistency with changes made in late 2024 to the iron polymaltose Medicine Guideline. Approved at SESLHD Drug and Therapeutics Committee meeting.