MONOGRAPH

IRON

Scope (Staff):	Medical, Pharmacy, Nursing
Scope (Area):	All Clinical Areas

Child Safe Organisation Statement of Commitment

CAHS commits to being a child safe organisation by applying the National Principles for Child Safe Organisations. This is a commitment to a strong culture supported by robust policies and procedures to reduce the likelihood of harm to children and young people.

This document should be read in conjunction with this DISCLAIMER

QUICKLINKS

Dosage/Dosage Adjustments | Administration | Compatibility | Monitoring

DRUG CLASS

Drugs for anaemias.[1]

Iron is an essential element required for the formation of haemoglobin and myoglobin.[1]

INDICATIONS AND RESTRICTIONS

- Prevention and treatment of iron deficiency[2]
  - Treating the cause of iron deficiency is the treatment of choice. Consider dietary intake, especially if cow's milk is a major part of the diet.[3]
  - First line treatment of iron deficiency is correction of deficiency with diet and/or oral supplements.[4]
  - Second line treatment of iron deficiency ,is parenteral therapy when oral therapy is unsuccessful, inappropriate or not tolerated.[2]
  - Parenteral iron must be used in haemodialysis (HD) patients receiving erythropoiesis stimulating agents.[1]

At Perth Children's Hospital (PCH) there are THREE types of parenteral iron preparations available, and the following indications apply:

- Iron sucrose:
  - Inpatients who require small doses of intravenous iron (up to 300 mg).

- Treatment of iron deficiency in haemodialysis patients receiving erythropoietin.

- Ferric carboxymaltose
  - For initiation in day patients or outpatients when oral preparations are ineffective or not appropriate. Prescriber should write a PBS prescription to be processed in pharmacy.
  - For use in theatre or inpatient wards to expedite discharge when oral preparations are ineffective or not appropriate.

- Iron polymaltose: When intramuscular (IM) administration of iron is required. IM use may be more painful and there is a risk of permanent skin staining.[1]

CONTRAINDICATIONS

- Hypersensitivity to iron or any component of the formulation[1]
- Anaemia not due to iron deficiency[1]
- Iron overload e.g. haemochromatosis, haemosiderosis[1]

PRECAUTIONS

- Acute or chronic infections – withhold parenteral iron whilst patients have active, serious, systemic infection.[5]
- History of asthma, eczema or atopic allergies – increased risk of allergic reaction.[6]
- Hypophosphataemia – may lead to hypophosphataemic osteomalacia and fractures, especially with ferric carboxymaltose. Correct pre-existing hypophosphataemia prior to initiating treatment and monitor serum phosphate concentrations in at risk patients.[6, 7]
- Hepatic impairment – where iron overload is a precipitating factor.[5]
- Sodium controlled diet - Ferric carboxymaltose injection contains 0.24 mmol/mL sodium.[5]
- Pregnancy (especially first trimester) – avoid parenteral administration if possible.[1]

FORMULATIONS

Listed below are products available at PCH, other formulations may be available, check with pharmacy if required:

<u>Oral</u>

- Elemental iron 6 mg/mL (as ferrous sulfate 30 mg/mL) solution (Ferro-Liquid®)
- Elemental iron 105 mg (as ferrous sulfate 325 mg) MR tablet (Ferro-Grad®)
- Elemental iron 105 mg (as ferrous sulfate 325 mg)/Sodium ascorbate 562.4 mg MR tablet (Ferro-Grad C®)
- Elemental iron 87.4 mg (ferrous sulfate 270 mg)/Folic acid 300 microg MR capsule (Fefol®)

<u>Parenteral</u>

- Elemental iron (as iron sucrose) 100 mg/5 mL ampoule (Venofer®)

- Elemental iron (as ferric carboxymaltose) 500 mg/10 mL vial (Ferinject®)
- Elemental iron (as iron polymaltose) 100 mg/2 mL ampoule (Ferrosig®)

Imprest location: Formulary One

DOSAGE & DOSAGE ADJUSTMENTS

Neonates: Refer to Neonatal Medication Protocols

Dosing in Overweight and Obese Children: Use ideal body weight to calculate total iron deficit for parenteral dosing.[8]

Note: Prescribed as ELEMENTAL iron (doses below are expressed as ELEMENTAL iron)

ORAL

Prevention of iron deficiency[2]

4–12 months (exclusively breast-fed and a delay in starting iron-rich solids): 1 mg/kg daily.

>12 months (with poor or restricted diet, malabsorptive states): 1-2 mg/kg (maximum 30 mg) daily.

Treatment of iron deficiency

4 weeks –18 years: 3–6 mg/kg (maximum 200 mg) daily for at least 3 months.[10, 11]

- Whilst studies in paediatrics are limited, alternate day dosing may provide improved iron absorption with reduced side effects, and may be considered in patients with mild-moderate iron deficiency who do not tolerate once daily dosing.[12]

PARENTERAL

Total iron deficit is calculated using the Ganzoni equation.[5]

Iron deficit [mg] = [body weight* *[kg]* **x (**target Hb **–** actual Hb**)** *[g/L]* **x** 0.24**] +** depot iron *[mg]*
* Use ideal body weight in overweight patients. If underweight, use actual body weight.[8]

- *< 35 kg:* Target Hb = 130 g/L and depot iron = 15 mg/kg
- ≥*35 kg:* Target Hb = 150 g/L and depot iron = 500 mg

The total iron deficit is NOT the same as the allowable iron dose per infusion and varies with each product (see individual products below for details).

IRON SUCROSE[13]

≥4 weeks to ≤ 18 years

Calculate total iron deficit using Ganzoni equation (see above)

- *Initial dose:* 2.5–7 mg/kg (maximum 100 mg) IV.

- *Subsequent dose(s):* 2.5–7 mg/kg (maximum 300 mg) IV every 3 to 7 days until replacement of total deficit is achieved.

FERRIC CARBOXYMALTOSE

Calculate total iron deficit using Ganzoni equation (see above)

- Maximum single dose:[9, 14]
    - 1-13 years: 15 mg/kg (max 750 mg)
    - ≥ 14 years: 20 mg/kg (max 1000 mg)
- Repeat dose(s) after at least 7 days up to maximum 1500 mg per course.[9]

IRON POLYMALTOSE

Calculate total iron deficit using Ganzoni equation (see above)

- Maximum single daily dose by intramuscular injection:[15]

Infants up to 5 kg	0.5 mL
5-10 kg	1 mL
>10 kg to 45 kg	2 mL
>45 kg	4 mL

- If more than one dose is required to replace iron deficit then further intramuscular injections can be administered every second day until total dose is attained.[15]

HAEMODIALYSIS

IRON SUCROSE[16, 17]

- Initial REPLETION therapy (ferritin <100 microg/L and/or TSAT< 20%): 0.5 - 1 mg/kg/dose (max 100 mg) IV with each dialysis session until TSAT and ferritin are satisfactory (measured on a weekly basis) then continue with maintenance therapy.[18]
- MAINTENANCE therapy (ferritin >100 microg/L & <700 microg/L and TSAT >20% & <40%): 0.5 - 2 mg/kg/dose (maximum 100 mg) IV every 2 weeks for 12 weeks. Repeat therapy if necessary.[19]
- More frequent doses (than every 2 weeks) can be given when approved by Consultant Nephrologist.
- Withhold if ferritin >700 microg/L or TSAT >40%.

DOSAGE ADJUSTMENT

Renal impairment:

- No dosage adjustment required.[7, 9]

Hepatic impairment:

No dosage adjustment required but use caution in patients with chronic liver disease where iron overload is a precipitating factor.[5]

ADMINISTRATION

ORAL

- Ferrous salts are best absorbed on an empty stomach. If gastrointestinal upset occurs, take with food.[2] Absorption of iron may be increased by administration with ascorbic acid, either in a combination product or with orange juice. Do not mix with milk or other dairy products (breast milk/formula suitable).[7]
- Gastrointestinal adverse effects may be minimised by starting at a low dose and gradually increasing after 2-4 weeks, or by dividing the daily dose.[2]
- Dilute oral liquid in water and drink through a straw to prevent teeth discolouration.[2]
- Oral iron therapy should not be started for at least 5 days after the last parenteral iron injection.[20]

PARENTERAL

Serious hypersensitivity reactions can occur with parenteral iron, even when previous administration has been tolerated. Facilities for cardiopulmonary resuscitation must be immediately available and patients must be closely monitored (see monitoring section).

IRON SUCROSE

IV only. Not suitable for IM use due to high pH.[13]

IV infusion:

- Flush infusion line with 10 mL of sodium chloride 0.9% before commencing infusion to minimise risk of extravasation.
- Dilute to 1 mg/mL with sodium chloride 0.9%. (Do not dilute to concentrations less than 1 mg/mL).[7, 21] Infuse at the following rates[13]:

Iron dose	Infusion time
1-100 mg	≥30 minutes
101 mg to 200 mg	≥60 minutes
201 mg to 300 mg	≥90 minutes

- Flush with 30mL of sodium chloride 0.9% following the infusion to minimise extravasation.

Haemodialysis patients: Administered undiluted into the venous limb of the dialysis line at a rate of no more than 20 mg/minute during haemodialysis.[20]

Iron sucrose infusions have a higher risk of extravasation due to high pH (10.5-11).[7] Extravasation may cause pain, inflammation, tissue necrosis, sterile abscess and brown discolouration of the skin. If extravasation occurs, stop the infusion and apply ice to cause local vasoconstriction and decrease fluid absorption. Do not massage the area.[20] Refer to the Peripheral Intravenous Cannula (PIVC) Insertion and Maintenance Guideline.

FERRIC CARBOXYMALTOSE

Intravenous only

- Flush infusion line with 10 mL of sodium chloride 0.9% before commencing infusion to minimise risk of extravasation.
- Dilute to 2-5 mg/mL with sodium chloride 0.9% and administer over at least 15 minutes (max 60 minutes). Solutions less than 2 mg/mL are not recommended due to stability reasons.[5, 21]

Iron dose	Maximum volume	Minimum Infusion time
100 mg to 200 mg	50 mL	At least 15 minutes
>200 mg to 500 mg	100 mL	
>500 mg to 1000 mg	250 mL	

- Avoid leakage at the injection site as permanent discolouration and skin irritation may occur. Preferred site of administration is the distal veins of the forearm.[21]
- Flush with 30 mL of sodium chloride 0.9% following the infusion to minimise extravasation.

IRON POLYMALTOSE

Intramuscular: The technique of IM injection is crucial. Ventrogluteal* injection using the Z-track technique must be used. (Refer to IM injection procedures or product information for details.)

- Do not inject into the arm or other exposed areas as pain and persistent discolouration of the skin may occur.[15]
- After injecting, withdraw the needle slowly and apply pressure beside the puncture site with a finger for about 1 minute. The patient should move around after the injection.[15]

*Caution: Not recommended injection site for children < 7 months or with poorly developed gluteal muscle.[22]

COMPATIBILITY *(LIST IS NOT EXHAUSTIVE)*

Compatible fluids: Sodium chloride 0.9%[21]

Compatible at Y-site: No data

Compatibilities of IV drugs must be checked when two or more drugs are given concurrently.

MONITORING

IV INFUSION

- Temperature, heart rate, respiratory rate, oxygen saturation and blood pressure should be documented[9, 13]
    - At baseline
    - At 5 minutes from commencement of infusion
    - At 15 minutes from commencement of infusion
    - Then every 30 minutes during and for at least 30 minutes after the infusion.
- Anaphylactoid/hypersensitivity reactions are rare but are a medical emergency[21]
    - Characterised by sudden onset of respiratory difficulties (bronchospasm with dyspnoea), tachycardia, significant hypotension, fainting, syncope, chest pain, circulatory collapse
    - Most likely within the first minutes of administration. Can occur even when a previous administration has been tolerated[6]
    - Cease the infusion immediately and initiate a **Code Blue** call.
- If other acute symptoms occur including flushing, sweating, chills, fever, pruritis, urticaria, headache, joint/back pain the infusion should be stopped, and medical review called. In some circumstances the infusion may be restarted at a slower rate once symptoms abate.[23]
- Extravasation may cause irreversible skin staining, tissue necrosis and ulceration.[5, 21]
    - Symptoms include pain, burning, stinging, swelling, redness, brown staining.
    - Monitor vascular site during and after infusion for sign of phlebitis/extravasation.
    - If extravasation occurs, stop the infusion immediately and seek medical review.
- Monitor iron status – haematocrit, haemoglobin, serum ferritin, transferrin, percent transferrin saturation – ≥ 48 hours (iron sucrose), ≥4 weeks (ferric carboxymaltose), ≥ 3 weeks (iron polymaltose) after IV iron infusion.[5, 13, 15]
- Monitor serum phosphate in patients at risk for hypophosphataemia who require repeat treatment.[5, 6]

ADVERSE EFFECTS[5-7]

Common: Constipation, diarrhoea, headache, hypotension, hypertension, dizziness, infection, injection site reactions, nausea, stool discolouration, flushing, transient metallic taste, temporary black discolouration of teeth (oral).

Infrequent: Abdominal pain, arthralgia, arrhythmias, back pain, chest pain, chills, dysgeusia, dyspnoea, fever, hyperhidrosis, muscle cramps, myalgia, pruritis, vomiting, tachycardia, altered LFT's, bronchospasm, peripheral oedema, paraesthesia, rash.

Rare: Angioedema, anaphylactoid reactions, confusion, heart failure, seizures, syncope, pallor, palpitations, tremor, influenza-like illness.

STORAGE

- Oral solution (Ferro-Liquid®): store below 25°C (as per product packaging)
- MR tablet (Ferro-grad®): store below 30°C (as per product packaging)
- MR tablet (Ferro-grad C®): store below 25°C (as per product packaging)
- MR capsule (Fefol®): store below 30°C, protect from light and moisture (as per product packaging)
- Ampoule (Venofer®): store below 25°C[20]
- Vial (Ferinject®): store below 30°C, do not freeze, do not refrigerate[5]
- Ampoule (Ferrosig®): store below 25°C, do not freeze, protect from light[15]

INTERACTIONS

This medication may interact with other medications; consult PCH approved references (e.g. Clinical Pharmacology), a clinical pharmacist or PCH Medicines Information Service on extension 63546 for more information.

Please note: The information contained in this guideline is to assist with the preparation and administration of **Iron**. Any variations to the doses recommended should be clarified with the prescriber prior to administration

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