SESLHDMG/127 - Medicine Guideline

Ferric Carboxymaltose (Ferinject®)

Areas where Protocol/Guideline applicable	SESLHD
Authorised Prescribers:	Medical Officers
Clinical condition	Iron deficiency anaemia
Indication for use	1. Supply obtained in the community via the PBS (General Schedule without restriction) for administration to non-admitted patients, including children > 9 months of age. 2. Adult inpatients for the treatment of iron deficiency, under the following conditions ONLY: • Patients for whom iron polymaltose is not appropriate due to fluid restriction status (e.g., congestive cardiac failure) • For treatment of iron deficiency anaemia in a perioperative peritonectomy patient • Pre-operative patients where rapid iron repletion is required and/or the anticipated post-operative Hb decrease is ≥ 30g/L • ED patients that are assessed as requiring IV iron replacement using Ferinject® • For inpatient postnatal women who fulfill the criteria for iron replacement based on Hb and ferritin parameters • Specific situations where a rapid IV iron infusion time is essential, as recommended by a specialist/consultant (e.g., patients with dementia)
Proposed Place in Therapy	First line unless contraindicated Refer to SESLHD/753 - Iron Infusion Procedure for decision algorithm
Contra-indications	• Anaemia not caused by simple iron deficiency (e.g., Haemolytic anaemia, megaloblastic anaemia caused by vitamin B12 deficiency, disturbances in erythropoiesis, hypoplasia of the marrow) • Hypersensitivity to iron hydroxide polymaltose complex • Iron overload (e.g., haemochromatosis, haemosiderosis) • Active infections • Administration via an AV fistula/graft

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Precautions

- Chronic polyarthritis
- Bronchial asthma
- Uncontrolled hyperparathyroidism
- Hypophosphataemia
- Hepatic disease including hepatic impairment and infection hepatitis
- High dose (i.e., > 1000 mg or 20 mg/kg)
- Pregnancy ≤ 14 weeks should only be administered if clinically necessary Osler-Rendu-Weber syndrome

Patients with the following conditions may be at higher risk of adverse reactions:

- Low iron binding capacity
- Folate deficiency
- History of allergic disorders (including drug allergies)
- Cardiovascular disease
- Autoimmune or inflammatory conditions may be at particular risk of delayed reactions, including fever and exacerbation or reactive joint pain (e.g., rheumatoid arthritis, inflammatory bowel disease, ankylosing spondylitis, and lupus erythematosus).
- Oral iron must be ceased 24 hours before IV iron and should not be given until 5 days after last parenteral administration.

Symptomatic hypophosphataemia is a known risk associated with use of ferric carboxymaltose and it is recommended that you routinely evaluate patient risk factors before commencing this medicine and follow up at-risk patients (i.e., those with lower baseline ferritin, gastrointestinal disorders, malnutrition or other causes of phosphate deficiency (low whole body phosphate).

Important Drug Interactions

The infusion should not be mixed with any other substances.

Dosage

Dose to be calculated by the treating Medical Officer.

Ferric Carboxymaltose (Ferinject®) recommended CUMULATIVE dose
*mg indicates elemental iron, not Ferric Carboxymaltose

Hb (g/L)	Bodyweight	
	35 to 70 kg	**> 70 kg**
< 100	1500 mg	2000 mg
≥ 100	1000 mg	1500 mg

*For patients with an Hb value ≥ 140, manufacturers recommend that an initial dose of 500mg be given and iron parameters checked prior to repeat dosing.

A single dose of ferric carboxymaltose (Ferinject®) must NOT exceed 20 mg /kg of body weight, capped at a maximum of 1000 mg.

Do NOT administer more than 1000 mg of iron per week.

The total cumulative dose may need to be administered as weekly infusions over a number of weeks.

Alternatively, the following formula can be used to calculate the dose:
Iron dose (mg) = [bodyweight (kg) x (target Hb* – actual Hb in g/L) x 0.24] + iron depot **
Patients > 34kg bodyweight: *Target Hb = 150g/L **Iron depot = 500mg
Patients ≤ 34kg bodyweight: *Target Hb = 130g/L **Iron depot = 15mg/kg
Example of calculation:
60 kg patient with actual Hb = 80g/L, target Hb of 150g/L and iron depot of 500mg
Required iron dose = [60 x (150 – 80) x 0.24] + 500mg
= 1008mg + 500mg
= 1508mg
This approximates to 1500mg iron

Renal patients
Haemodialysis Patients
A single maximum daily dose of 200 mg iron as Ferinject should not be exceeded in haemodialysis-dependent chronic kidney disease patients.

Peritoneal Dialysis Patients are infused:
- 500 – 1000 mg in a single infusion.

Paediatric patients:
Use Ganzoni formula to calculate dose according to iron deficit (haemoglobin) and body weight:

Iron dose (mg) = [bodyweight (kg) x (target Hb* – actual Hb in g/L) x 0.24] + iron depot **

For significantly overweight patients use ideal body weight for iron dose calculation (use 50th percentile weight for height age).

If the calculated dose required is more than 20 mg/kg or 1,000 mg then administer in divided doses separated by at least one week.
Use iron polymaltose if a full dose iron infusion is required in a single infusion.

*Target Haemoglobin in g/L			
6 months – 2 years	3 -5 years	6 – 12 years	> 12 years
100 – 110 g/L	110 – 120 g/L	120 – 130 g/L	130 – 150 g/L
CKD maintained on erythropoiesis stimulating agents			
6 months – 2 years		***> 2 years***	
110 g/L		*120 g/L*	

Patients > 34 kg bodyweight: **Iron depot = 500 mg
Patients ≤ 34 kg bodyweight: **Iron depot = 15 mg/kg

Dose Rounding:
Body weight ≤50 kg: round dose down to nearest 100 mg
Body weight >50 kg: round dose up to nearest 100 mg

Pregnant Woman:
Use Ganzoni formula to calculate dose according to iron deficit (haemoglobin) and pre-pregnancy body weight:

Iron dose (mg) = [bodyweight (kg) x (target Hb* – actual Hb in g/L) x 0.24] + iron depot **

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Prescribing Instructions

Calculate dose (Refer to Dosage)

Volume and Infusion Rate

Ferric Carboxymaltose (Ferinject®) * mg indicates elemental iron, not Ferric Carboxymaltose		
IV Injection		
Dose	**< 500 mg**	**500 – 1000 mg***
Volume	undiluted	undiluted
Rate	Max 100 mg/minute	Over 15 minutes

IV Infusion (Adults)		
Dose	**200 - 500 mg**	**500 – 1000 mg**
Volume Sodium chloride 0.9%	Up to 100 mL	Up to 250 mL
Rate	Over 6 minutes	Over 15 minutes

Paediatric Patients:
For children, Ferric carboxymaltose (Ferinject®) is usually diluted and infused over a longer period as a short infusion.

The suggested infusion times below are guidelines. They may need to be longer for some patients so that the rate does not exceed the allowed maximum tolerated for the individual (max. rate not exceeding maintenance).

IV Infusion (Paediatrics)			
Dose	**100 - 200 mg**	**201 – 500 mg**	**501 – 1000 mg**
Volume Sodium chloride 0.9%	50 mL	100 mL	250 mL
Rate	Over 15 – 20 minutes	Over 20 - 30 minutes	Over 30 -45 minutes
Please note that the infusion time can always be longer if patient is small or at risk of volume overload. In older, stable patients with a weight of >30 kg, the infusion time of a 250 mL bag may be shortened to 15-20 minutes if tolerated.			

Inpatient
Prescribing on the eMR via eFluids.

Outpatient
Prescribing on the Intravenous Adult Fluid Order Form or Community Medication Authorisation Record.
The infusion is ordered as elemental iron and should include dosage, diluent, and infusion rate.
e.g., “Iron (as ferric carboxymaltose) _x_mg in _x_mL sodium chloride 0.9%. Infuse at 40mL/hour for 15 minutes, then 250mL/hour if tolerated”

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Administration Instructions	• Ferric carboxymaltose (Ferinject®) must only ever be administered by the intravenous (IV) route and must only ever use sterile 0.9% sodium chloride as a diluent. • Check that the prescribed order does not exceed 20 mg/kg OR 1000 mg (whichever is lower) • Check that the patient will not have received greater than 1000 mg of iron within a one week period. • Ensure vial strengths are checked carefully – 500 mg and 100 mg vials have very similar packaging. • Infusion concentration should be no less than 2 mg/mL (for stability reasons), and the administration rate must not exceed 100 mg/min. Volume and administration rate recommendations are provided in the table above.

Adverse Effects	IV administration of iron and carbohydrate complexes may result in fatal anaphylactoid reactions, consequently it is only suitable for IV administration in a medically supervised setting.
	Anaphylactoid reactions, characterised by sudden onset of respiratory difficulties, tachycardia and hypotension, occur most frequently within the first minutes of administration.
	If any signs or symptoms of reaction develop, infusion is to be stopped immediately and medical assistance called for.
	Cardiovascular resuscitation equipment MUST be readily available
	
	Adverse effects may be delayed 1-2 days post infusion.
	Immediate Adverse Effects
	• Anaphylaxis
	  ○ Bronchospasm with dyspnoea
	  ○ Faintness, syncope, tachycardia, hypotension, circulatory collapse
	  ○ Loss of consciousness
	• Central nervous System
	  ○ Headache, dizziness
	• Gastrointestinal
	  ○ Nausea, vomiting (may indicate excessive infusion rate)
	• Musculoskeletal
	  ○ Joint and muscle pain
	• Dermatological
	  ○ Rash, urticarial
	  ○ Infiltration and extravasation (Staining of surrounding tissue) If this occurs STOP infusion immediately and seek a medical review
	• General
	  ○ Flushing, sweating
	Delayed Adverse Effects
	• Central Nervous System
	  ○ Dizziness
	  ○ Musculoskeletal
	  ○ Arthralgia, myalgia, sensation of stiffening of arms, legs or face
	• Haematological
	  ○ Generalised lymphadenopathy
	• Dermatological
	  ○ Angioneurotic oedema, rash, urticaria
	• General
	  ○ Chills, fevers, chest and back pain
	Maternity Specific
	• Fetal bradycardia may occur with parenteral iron preparations.
	• Kounis Syndrome (Acute Coronary Syndrome associated with hypersensitivity reactions) has been reported with parenteral iron preparations (Unknown frequency).

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Monitoring requirements	• Baseline observations are to be recorded pre-infusion, 5 minutes after commencement of infusion and at the end of the infusion. • Patient must be observed for any adverse reaction during the infusion and for 30 minutes after the completion of 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
	Maternity specific In pregnant women, fetal bradycardia may rarely occur with parenteral iron administration. Fetal heart monitoring for antenatal woman - intermittent auscultation at commencement and conclusion is adequate unless other risk factors For all pregnant and postnatal women, the eMR Standard Maternity Observation chart (SMOC) must be completed. Remain with woman at the commencement of the infusion and perform standard observations at baseline and every 30 minutes during iron infusion. Refer to site specific Workplace Instruction for further details.
	Paediatric Patients: Blood pressure, Pulse and Respiration Rate: • Prior to infusion • 5 minutes and 30 minutes after administration Injection site should be monitored within the first 5 minutes and every 15 – 30 minutes during the infusion for possible extravasation.

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Management of Complications	**Treatment of Anaphylaxis** 1. **STOP the infusion** 2. Call for help as per local clinical emergency response 3. Lie patient flat or left lateral if pregnant. If breathing is compromised allow patient to sit with legs outstretched 4. Medical Officer 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 5. Administer 100 % oxygen via mask via non rebreather mask 6. Obtain intravenous access in adults in the event of hypotension and give IV normal saline (20mL/kg) rapidly and consider large bore IV access 7. Commence CPR in the event of a cardiac arrest. **For mild reactions:** 1. **STOP the infusion** 2. Medical Officer 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 If extravasation is suspected: 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 The type of infusion related complication and action taken needs to be clearly documented in the patient's health care record and notified through ims+ for investigation.
Resources	• A General Guide to Iron and Iron Deficiency: Information for Patients, Families and Carers (CEC)

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Basis of Protocol/Guideline: (including sources of evidence, references)	1. MIMS Online 2023 Product Information Ferinject®. Vifor Pharma Pty Ltd. Revised 01 November 2021.<Accessed 23 February 2023> 2. Rossi, S. Australian Medicines Handbook. South Australia: Australian Medicines Handbook Pty Ltd, 2019. 3. Australian Injectable Drugs Handbook 8th Edition online 2022. The Society of Hospital Pharmacists. Revised 22 November 2022. Monograph: Ferric Carboxymaltose <Accessed 23 February 2023> 4. Meds4Kids Dosing Guide. The Children's Hospital at Westmead 2023. Monograph: Ferric Carboxymaltose < Accessed 23 February 2023> 5. Intravenous Iron Infusion: Iron Polymaltose (Ferrosig®) and Ferric carboxymaltose (Ferinject®) Practice Guideline. The Children's Hospital at Westmead 2020. <Accessed 23 February 2023> 6. Breymann, Christian, von Seefried, Bettina, Stahel, Michele, Geisser, Peter and Canclini, Camillo. "Milk iron content in breast-feeding mothers after administration of intravenous iron sucrose complex" , vol. 35, no. 2, 2007, pp. 115-118. 7. Qassim, A., Mol, B.W., Grivell, R.M. and Grzeskowiak, L.E. (2018), Safety and efficacy of intravenous iron polymaltose, iron sucrose and ferric carboxymaltose in pregnancy: A systematic review. Aust N Z J Obstet Gynaecol, 58: 22-39. 8. Woodward, T et al. "Fetal bradycardia following maternal administration of low-molecular-weight intravenous iron." *International journal of obstetric anesthesia* vol. 24,2 (2015): 196-7 9. Droney M, Scovell S, Hatfield J, Pender E. Case Findings: Sodium Ferric Gluconate Complex and Fetal Bradycardia. Maternal-Fetal Medicine. 2022:10-97. 10. Therapeutic Goods administration. Safety Updates. Ferric carboxymaltose and low blood phosphorous. 27 February 2020.
Groups consulted in development of this guideline	Haematology, Cardiology, Women's and Children's, Ambulatory Care Units, Obstetrics, Nephrology, Transfusion Medicine and Pharmacy.

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GOVERNANCE	
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