Medicine Guideline

Iron Polymaltose (Ferrosig®)

Areas where Protocol/Guideline applicable	SESLHD
Authorised Prescribers:	Medical Officers
Clinical condition	Iron deficiency anaemia

Indication for use	• Oral therapy is contraindicated
	• Enteric absorption of iron is defective
	• Patient non-compliance or persistent gastrointestinal intolerance makes oral therapy impractical.
	• Chronic Kidney Disease or End Stage Kidney Disease
	  ○ Peritoneal dialysis patients with Hb < 100 g/L and Ferritin < 300 ug/L and/or transferrin saturation < 20%
	  ○ Worsening of iron deficiency or suboptimal response to erythropoietin replacement therapy despite oral iron supplementation
	• **Maternity Specific Indications**
	  ○ where there is inadequate time for oral replacement e.g., birth expected within three weeks, and/or severe anaemia - Hb < 80g/L
	  ○ symptomatic blood loss, or at high risk of significant blood loss in the antenatal or postnatal period where iron deficiency is diagnosed, with or without a reduction in Hb (Hb < 100 g/L postnatally)
	  ○ woman at high risk of intrapartum/intraoperative blood loss, where iron deficiency or iron deficiency anaemia is diagnosed, and woman is unable to achieve target ferritin > 100 µg/L with oral supplementation or women is unwilling/unable to accept blood products

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 • Decompensated hepatic cirrhosis • Administration via an AV fistula/graft

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Precautions	• Chronic polyarthritis • Bronchial asthma • Uncontrolled hyperparathyroidism • Hyperphosphataemia • Hepatic disease including hepatic impairment and infection hepatitis • Excess dose • 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).
Important Drug Interactions	The infusion should not be mixed with any other substances.
Dosage	Dose to be calculated by the treating Medical Officer.

Iron Polymaltose (Ferrosig®)
*mg indicates elemental iron, not Iron Polymaltose

Bodyweight	Hb 60 g/L			Hb 75 g/L			Hb 90 g/L			Hb 105 g/L		
kg	mg	mL	Amps	mg	mL	Amps	mg	mL	Amps	mg	mL	Amps
5	150	3	1.5	150	3	1.5	150	3	1.5	100	2	1
10	300	6	3	300	6	3	250	5	2.5	200	4	2
15	500	10	5	450	9	4.5	350	7	3.5	300	6	3
20	650	13	6.5	550	11	5.5	500	10	5	400	8	4
25	800	16	8	700	14	7	600	12	6	550	11	5.5
30	950	19	9.5	850	17	8.5	750	15	7.5	650	13	6.5
35	1250	25	12.5	1150	23	11.5	1000	20	10	900	18	9
40	1350	27	13.5	1200	24	12	1100	22	11	950	19	9.5
45	1500	30	15	1300	26	13	1150	23	11.5	1000	20	10
50	1600	32	16	1400	28	14	1200	24	12	1050	21	10.5
55	1700	34	17	1500	30	15	1300	26	13	1100	22	11
60	1800	36	18	1600	32	16	1350	27	13.5	1150	23	11.5
65	1900	38	19	1650	33	16.5	1450	29	14.5	1200	24	12
70	2000	40	20	1750	35	17.5	1500	30	15	1250	25	12.5
75	2100	42	21	1850	37	18.5	1600	32	16	1300	26	13
80	2250	45	22.5	1950	39	19.5	1650	33	16.5	1350	27	13.5
85	2350	47	23.5	2050	41	20.5	1700	34	17	1400	28	14
90	2450	49	24.5	2150	43	21.5	1800	36	18	1450	29	14.5

Note: Each 2 mL ampoule of Ferrosig® Injection contains the equivalent of 100 mg of iron

	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 = 15 ampoules Iron (as Polymaltose) (Ferrosig®) 100mg/2mL

Haemodialysis Patients at POWH

If the patient hasn't received iron within the last 6 months and the Ferritin is less than 200 microg/L and / or transferrin saturation < 20% a loading dose of iron should be administered:

Loading dose: 500 mg (iron as iron polymaltose) as a single infusion

For patients who have had a loading dose, or are currently receiving intravenous iron replacement, the dose and frequency of iron adjusted by the renal registrar based on the algorithm below.

Subsequent doses:

TSat	Ferritin (microg/L)			
	< 200	**200 - 500**	**501 – 800**	**> 800**
< 20%	100 mg IV weekly	100 mg IV fortnightly	100 mg IV monthly	Review with Nephrologist
20 – 29%	100 mg IV fortnightly	100 mg IV fortnightly	Review with Nephrologist	Withhold
30 – 39%	100 mg IV monthly	100 mg IV monthly	Withhold	Withhold
40 – 49%	100 mg IV 2nd monthly	Withhold	Withhold	Withhold
≥ 50%	Withhold	Withhold	Withhold	Withhold

Haemodialysis Patients at SGH

If the patient has absolute iron deficiency (ferrin < 200 ug/mL and TSat < 50%) or functional iron deficiency (normal ferritin 200 – 800 ug/mL and TSat < 20%) iron should be administered:

- 100 mg each dialysis session for 10 consecutive sessions unless contraindicated
- Check iron studies 1 month after completion of course
- Once optimal iron parameters are achieved, titrate to a monthly dose of iron
- If, after 2 courses of iron, ferritin 200 – 800 ug/mL and TSat < 20% revert to monthly maintenance dose & monitor iron studies monthly until review by Nephrologist .

TSat	Ferritin (microg/L)		
	< 200	**200 - 800**	**> 800**
< 20%	100 mg IV for 10 sessions (max 2 courses) Retest Iron Studies 1 month post course	100 mg IV for 10 sessions (max 2 courses) Retest Iron Studies 1 month post course	Withhold
20 – 50%		100 mg IV monthly	Withhold
≥ 50%	Withhold	Withhold	D. Withhold

If Hb > 120 g/L, ferritin 100 – 200 ug/mL and TSat > 20%: revert to monthly maintence dose & monitor iron studies monthly until review by Nephrologist.

Peritoneal Dialysis Patients:

- 500 – 1000 mg in a single infusion

Paediatric patients:
Rarely used in infants < 6 months. Recommend Haematology consult.

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).

Usual Dose Limit: 2500 mg. Higher doses may be prescribing by Haematology as per clinical requirements.

*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

Iron polymaltose is the only parenteral iron product suitable for total iron replacement in one infusion.

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 **

Prescribing Instructions	The intramuscular (IM) route is discouraged. It is no safer than the IV route. IM iron injections tend to be painful and there is significant risk of permanent skin staining. **Calculate dose** (Refer to Dosage) **Volume and Infusion Rate** - Refer to Administration Instructions SLOW or RAPID or Haemodialysis or Peritoneal or Paediatric Protocol The rapid protocol should only be utilised for: • Patients receiving subsequent infusions where iron Ferrosig® has previously been well tolerated. Please note - Anaphylactoid reactions have been reported in those who have tolerated a previous dose. • Patients who are haemodynamically stable • The total dose is ≤1500mg iron (as polymaltose) • Patients who do not have a condition that puts them at higher risk of reactions (Refer to Precautions). • Rapid protocol has **not** been trialled in patients with class III/IV heart failure, known left ventricular ejection fraction < 30%, known kidney disease with an eGFR < 15mL/min, or otherwise at risk of fluid overload. **Inpatient** Prescribing on the eMR via eFluids. **Outpatient** Prescribing on the Intravenous Adult Fluid Order Form. The infusion is ordered as elemental iron and should include dosage, diluent, and infusion rate. e.g., "Iron (as polymaltose) _x_mg in _x_mL sodium chloride 0.9%. Infuse at 40mL/hour for 15 minutes, then 250mL/hour if tolerated"
Administration Instructions	• Iron polymaltose must be administered by the intravenous route only and must be diluted in sterile sodium chloride 0.9% solution and administered as an infusion through a standard intravenous line with 200 micron filter. • Check IV cannula for patency by administering 10 mL sodium chloride 0.9% prior to infusion. If there is any pressure, stop immediately If there are any concerns, re-site cannula • Instruct patient to avoid movement of arm to prevent extravasation • Protect the infusion bag from light once prepared and during administration • For peritoneal dialysis use a peripheral cannula: **DO NOT** use arm containing AV fistula/graft.
	SLOW dose Protocol • Dilute dose of Iron Polymaltose (up to 2.5 g) into 500 mL 0.9% sodium chloride (**maximum concentration 5 mg/mL**) • Commence slow infusion rate of 40 mL/hr, for the first 15 minutes via an infusion control device ○ set rate to 40 and volume 10 • If vital signs are within normal limits and in the absence of any adverse reaction, increase the rate to 120 mL/hr for remainder of infusion Time required for infusion = approximately 5 hours

	RAPID dose Protocol
	• Dilute dose of Iron Polymaltose (up to 2 g) into 250 mL 0.9% sodium chloride (**maximum concentration 8 mg/mL**)
	• Commence a test dose of 40mL/hr, for the first 15 minutes via an infusion control device
	  ○ set rate to 40 and volume to 10
	• If vital signs are within normal limits and in the absence of any adverse reaction, increase rate to:
	  ○ 250 mL/hr for doses ≤ 1.5 g,
	  ○ 166 mL/hr for doses > 1.5 g
	Time required for a rapid dose protocol infusion varies dependant on dose.
	• For example
	  ○ 1.5 g (280 mL) = 1 hr and 40 mins
	  ○ 2 g (290 mL) = 2 hrs and 15 min

Haemodialysis Protocol:

LOADING DOSE (POWH):

- Dilute dose of Iron Polymaltose (500mg elemental iron) into 100 mL 0.9% sodium chloride
- Commence a test dose of 40mL/hr, for the first 15 minutes via an infusion control device
  - set rate to 40 and volume to 10
- If vital signs are within normal limits and in the absence of any adverse reaction, increase rate to:
  - 120 mL/hr for 45 minutes

INITIAL INFUSION (SGH):

- Dilute dose of Iron Polymaltose (100 mg elemental iron) into 100 mL 0.9% sodium chloride
- Commence a test dose of 15 mL/hr, for the first 30 minutes via an infusion control device
  - Set rate 15 and volume 7.5
- If vital signs are within normal limits and in the absence of any adverse reaction, increase the rate to 120 mL/hr for remainder of infusion

SUBSEQUENT DOSES:

- Dilute dose of Iron Polymaltose (100 mg elemental iron) with 8 mL 0.9% sodium chloride
- Administer via heparin syringe driver on the haemodialysis machine
- Administer over last hour of haemodialysis

Alternatively, dilute dose of Iron Polymaltose (100 mg elemental iron) with 3 mL 0.9% sodium chloride and bolus over 5 minutes.

SUBSEQUENT DOSES: *Home Haemodialysis ONLY*

- Dilute dose of Iron Polymaltose (100 mg elemental iron) into a 20 mL syringe with 18 mL 0.9% sodium chloride
- Turn down the blood flow rate to 200 mL per minute
- Swab arterial port and administer as a bolus slowly over 2 – 5 minutes toward the end of dialysis

Peritoneal Protocol:

Use a peripheral cannula: **DO NOT** use arm containing AV fistula/graft.

INITIAL DOSE:

- Dilute dose of Iron Polymaltose into 500 mL 0.9% sodium chloride
- Commence a test dose of 15 mL/hr, for the first 30 minutes via an infusion control device
  - set rate to 15 and volume to 7.5
- If vital signs are within normal limits and in the absence of any adverse reaction, increase the rate to 120 mL/hr for remainder of infusion

SUBSEQUENT DOSES:

- Dilute dose of Iron Polymaltose into 500 mL 0.9% sodium chloride and infuse over 4 hours

Paediatric Protocol:

Ensure that the volume of 0.9% sodium chloride and maximum rate of infusion are appropriate for the age and size of patient, clinical situation and do not exceed maintenance fluid rates. Please note that both infusions can be run slower if required in small children or children at risk of fluid overload

- Dilute to a **maximum concentration of 5 mg/mL** in sodium chloride 0.9%.

Iron Polymaltose Dose	**Suggest volume of sodium chloride 0.9%**
100 – 500 mg	100 mL
501 – 1000 mg	250 mL
1001 – 2500 mg	500 mL

- Commence infusion

Infusion Time (minutes)	**Total final volume**		
	100 mL	**250 mL**	**500 mL**
0 - 30	3 mL/hr	7.5 mL/hr	15 mL/hr
31 – 60	6 mL/hr	15 mL/hr	30 mL/hr MAX rate: patient < 15 kg
61 – 90	12 mL/hr	30 mL/hr MAX rate: patient < 15 kg	60 mL/hr MAX rate: patient 15 – 40 kg
91 – 120	18 mL/hr MAX rate: patient < 5 kg	45 mL/hr	90 mL/hr MAX rate: patient 40 - 75 kg
Final rate until finished	24 mL/hr	60 mL/hr	120 mL/hr

The rate may need to be further reduced if the child is at risk of fluid overload. An iron polymaltose infusion can always be run slower if required.

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).

Monitoring requirements	• Baseline observations are to be recorded pre-infusion • Slow dose protocol- observations must be completed at 15 min and prior to rate increase. Remain with patient for 5 minutes to observe for reaction or extravasation • Rapid dose protocol- observations must be completed at 15 min and prior to rate increase • Hourly observations until the completion of infusion • Perform observations 30 minutes after completion of the infusion. • Monitor patients for signs of extravasation during administration. Iron polymaltose complex 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 women, the eMR Standard Maternity Observation chart (SMOC) must be completed. Refer to site specific Workplace Instruction for further details.
	Haemodialysis Patients: Initial dose: Perform a full set of vital signs: • Every 5 minutes for the first 15 minutes • Every 30 minutes until infusion complete • 30 minutes following completion of the infusion Subsequent doses: A full set of vital signs recorded every 15 minutes during the infusion
	Paediatric Patients: Blood pressure, Pulse and Respiration Rate: • Prior to infusion • Every 15 minutes for 75 minutes • Every 30 minutes until the end of the infusion • 30 minutes after the end of the infusion Injection site should be monitored within the first 5 minutes and every 15 – 30 minutes during the infusion for possible extravasation.

Management of Complications	**Treatment of Anaphylaxis** 1. **STOP the infusion** 2. Call for help as per local clinical emergency response 3. Lie patient flat, if breathing is compromised sit with legs extended 4. Medical Officer to give adrenaline (1:1000) immediately (0.01 mg/kg to a maximum dose of 0.5 mg) 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. (repeat at 5 minute intervals if necessary) followed by hydrocortisone (4 mg/kg to a maximum of 100 mg if < 12 years or 300 mg if > 12 years) IV and promethazine (0.5 mg/kg to a maximum 50 mg) IV if required. 8. 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 of 60mL/hr or 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. Clinical Excellence Commission (CEC). 2018.

Basis of Protocol/Guideline: (including sources of evidence, references)	1. Intravenous Iron Infusion: Iron Polymaltose (Ferrosig®) and Ferric carboxymaltose (Ferinject®) Practice Guideline. The Children's Hospital at Westmead 2020. <Accessed 23 February 2023> 2. MIMS online 2021 Product Information Ferrosig® Injection. Sigma Pharmaceuticals Pty Ltd. Revised 27 July 2021.<Accessed 30 March 2022> 3. Rossi, S. Australian Medicines Handbook. South Australia: Australian Medicines Handbook Pty Ltd, 2019. 4. Australian Injectable Drugs Handbook 8th Edition online 2022. The Society of Hospital Pharmacists. Revised 15 March 2022. Monograph: Iron Polymaltose Complex. <Accessed 30 March 2022> 5. Garg M, Morrison G, Friedman A, Lau A, Lau D, Gibson PR. A rapid infusion protocol is safe for total dose iron polymaltose: time for a change. Intern Med J 2011; 41: 548-54. 6. Ganzoni AM. Intravenous iron-dextran: therapeutic and experimental possibilities. Schweiz Med Wochenschr. 1970; 100:301–303. Available at: http://www.ncbi.nlm.nih.gov/pubmed/5413918 7. Banakh I, et al. Ultrarapid Iron Polymaltose Infusions Are Safe for Management of Iron Deficiency. Portuguese Journal of Gastroenterology. 2023, January 19. Available at: https://repository.monashhealth.org/monashhealthjspui/handle/1/49431 8. Qassim A, et al. Safety and efficacy of intravenous iron polymaltose, iron sucrose and ferric carboxymaltose in pregnancy: A systematic review. ANZJOG. 2017, September 18. Available at: https://obgyn.onlinelibrary.wiley.com/doi/full/10.1111/ajo.12695 9. Kidney Disease: Improving Global Outcomes (KDIGO). Clinical Practice Guidelines for Anemia in Chronic Kidney Disease. Kidney International. 2012;2(4). Available at: https://kdigo.org/guidelines/anemia-in-ckd/ 10. 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. 11. MacGinley R, et al. Use of iron in chronic kidney disease patients. CARI Guidelines. Kidney Health Australia. 2012, Aug. Available at: https://www.cariguidelines.org/guidelines/dialysis/biochemical-and-haematological-targets/iron/ 12. https://www.nps.org.au/assets/AP/pdf/Anaphylaxis-Wallchart-2022.pdf 13. https://resus.org.au/the-arc-guidelines/ First Aid Management of Anaphylaxis 14. 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 15. Droney M, Scovell S, Hatfield J, Pender E. Case Findings: Sodium Ferric Gluconate Complex and Fetal Bradycardia. Maternal-Fetal Medicine. 2022:10-97.
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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