Best practice guidelines for ferric carboxymaltose infusion (Ferinject®)

This procedure is ONLY for the administration of ferric carboxymaltose (Ferinject®).

Do NOT use for any other form of iron as the doses, rate of infusion and dilution are not interchangeable.

Ensure you have the correct product.

Maximum dose of Ferinject is 1000 mg in one week.

Ferinject is for intravenous use only and must not be administered subcutaneously or intramuscularly.

This guideline is for patients over the age of 14 years with confirmed iron deficiency and indications for intravenous iron.

Before prescribing, please review the full Product Information (PI) for Ferinject.

Scope

This guideline was developed after consultation with 3 medical professionals experienced in the establishment and routine practice of an iron infusion clinic. It can be used to support clinicians in the development of their own protocol, in delivering good medical care and providing a framework to guide professional judgement and due diligence.

The guideline is endorsed by Associate Professor Ralph Audehm, general practitioner, Dr Pradeep Jayasuriya, general practitioner, and Mrs Chriss McDonell, senior practice nurse, in accordance with best clinical practice.

The document addresses requirements to guide the administration of ferric carboxymaltose (Ferinject) for patients over the age of 14 years for the treatment of iron deficiency.

The best practice guideline intends for all patients to have ferric carboxymaltose (Ferinject) administered in a safe, appropriate and timely manner in accordance with standard precautions and medication administration guidelines. In line with the clinic's practice and policies, all clinical staff involved in the administration and prescribing of ferric carboxymaltose (Ferinject) should have access to this document or another similar document developed by the clinic.

Indication

Ferinject is indicated for the treatment of iron deficiency when:

- oral iron preparations are ineffective
- oral iron preparations cannot be used
- there is a clinical need to deliver iron rapidly.

The diagnosis must be based on laboratory tests.

Contents

Training and support requirements

Staff must be trained with the appropriate equipment including intravenous giving sets or volumetric infusion pumps (where applicable) and emergency equipment. Staff must be trained in the management of anaphylaxis. Staff must be familiar with the protocols and procedures for the management of the patient receiving the infusion including the patient consent procedure and patient information outlining follow-up arrangements. The staff must ensure that the patient is aware of all fees and costs before treatment.

Providing adequate training to all staff and having access to all appropriate equipment will assist in minimising the risk of adverse events and potential complications.

Training and ongoing upskilling of staff are essential.

It is recommended that all practice nurses have a Certificate of Competency to undertake cannulation in the general practice setting. Indemnity insurance for practice nurses who are cannulating must be up to date and should cover procedures such as intravenous cannulation.

The nurse's role in intravenous cannulation may be subject to state and territory legislation and the clinic's own policy. Competency should be demonstrated within the context of applicable legislation and organisation practice.

A number of organisations offer intravenous cannulation training in the skills and knowledge required to perform peripheral intravenous cannulation with varying degrees of face-to-face time and costs.

- Australian Government. Department of Education, Skills and Employment: https://training.gov.au/Training/Details/HLTHPS009

Iron infusion education

- Australian Red Cross Lifeblood: https://learn.transfusion.com.au/course/view.php?id=430
- BloodSafe eLearning: https://bloodsafelearning.org.au/iv-iron-tools/

Ongoing skill training requirements can be maintained by practical experience.

Preparation checklist

Suggested requirements

- Medical prescription for intravenous Ferinject, dose to be infused (mg) and rate of infusion (minutes)
- Ferinject vials (ferric carboxymaltose 1000 mg / 20 mL OR 500 mg / 10 mL OR 100 mg / 2 mL)
- Informed written consent form
- General observation chart
- A current patient weight (kg) recorded on medical record.

Equipment
- Intravenous administration set
- Volumetric infusion pump if available
- Additive label for the fluid bag (if required)
- Sterile dressing tray
- Patent IV access (wide cannula)
- Bung
- 70% isopropyl alcohol swabs
- 10 mL syringe for drawing up saline flush
- 10 mL normal saline (sodium chloride 0.9%) for injection
- 100 or 250 mL bag normal saline
- 10 mL syringe normal saline (to flush after completion of infusion)
- Tegaderm dressing
- Required ampoules and dose of Ferinject.

BloodSafe eLearning checklist: https://bloodsafelearning.org.au/wp-content/uploads/2019/07/administration_of_iron.pdf

Anaphylaxis kit (ASCIA and Aust Imm Handbook 2021)
- Adrenaline 1:1000 (at least 3 ampoules — check expiry dates; consider adrenaline injector availability for initial administration by nursing staff)
- At least 3 x 1 mL syringes, drawing-up needles and 25 mm needles (for intramuscular injection)
- Oxygen, airway equipment, including rebreather oxygen masks, nebuliser masks (not applicable during covid-19 pandemic) and suction
- Sphygmomanometer (blood pressure cuff)
- IV access equipment
- At least 3 litres of normal saline
- Cotton wool swabs
- A hands-free phone in procedure room, to allow staff in remote locations to receive instructions by phone while keeping hands free for resuscitation
- Pen and paper to record the time the adrenaline was administered
- Laminated copy of *Doses of intramuscular 1:1000 adrenaline for anaphylaxis*
- Laminated copy of *Recognition and treatment of anaphylaxis*.

Always keep an anaphylaxis response kit on hand in the procedure room. Check the contents regularly to ensure they are up to date and have not expired. For further information go to: Australian Immunisation Handbook. Preparing for vaccination. Equipment for vaccination. 27 September 2021. Available at: https://immunisationhandbook.health.gov.au/vaccination-procedures/preparing-for-vaccination

Procedure

Patient consent and education
- A thorough and detailed consent process is recommended
- Give patients clear information to understand the risks and benefits of treatment options in order to make an informed decision

- Fully inform patient about potential risks of IV iron infusions (including hypersensitivity reactions and permanent staining through extravasation) in a pre-consultation
- Make sure you have the patient's informed consent before the procedure (see sample Patient Consent Form)
- Ensure patient understands the complications that can arise from iron infusions and the alternative treatment options
- Make sure patient is aware of signs and symptoms when the cannula is out of position (pain and swelling) and the importance of notifying the supervising doctor or nurse immediately so the infusion can be stopped
- Provide education to patient regarding post-infusion care and ongoing follow-up
- Clearly document the discussion with the patient and their decision in the patient records
- Oral therapy should not be recommenced for at least 5 days after the last infusion of iron.

Procedure checklist

- Ensure the patient has ceased oral iron therapy one week before the infusion
- Document date of unprotected sexual intercourse since last menstrual cycle; discuss with GP if there is a chance of early pregnancy and perform a urine pregnancy test
- Determine previous reactions, sensitivities or allergic reactions to iron before the infusion to assess if clinically significant
- Weigh the patient
- Obtain a set of baseline observations: temperature, pulse, respirations and blood pressure, and oxygen saturation (finger oximetry)
- Inform the patient to notify staff if any of the following symptoms:
  - sudden gastrointestinal distress and anxiety
  - chest tightness
  - shortness of breath
  - racing heart
  - nausea
  - pain at the cannula site
- Set up emergency trolley and anaphylaxis kit
- Check the GP's notes for the dose, volume of fluid and rate of infusion (determined by the results of pathology and calculated using the patient's current weight, Hb levels and total iron deficit)
- Ensure a medical practitioner is in the vicinity and easily contactable for the duration of the iron infusion and for 30 minutes after the infusion
- Insert an intravenous cannula using a sterile technique, sited in the distal area of an upper extremity. Avoid intravenous iron administration via cannulation at site of flexion (e.g. antecubital fossa, wrist) or on the back of the hand
- Flush the cannula with 10 mL of normal saline 0.9% to ensure patency, prior to commencing the iron infusion
- Ensure the patient is comfortable and has no burning, swelling or pain at the site when flushed
- Document in the patient medical record the site and gauge of cannula inserted.

Contraindications

- Hypersensitivity to ferric carboxymaltose or to any of the excipients
- Anaemia not attributed to iron deficiency, e.g. other causes of microcytic anaemia
- Evidence of iron overload or disturbances in utilisation of iron

Special considerations and precautions

- Use with caution in patients with hepatic impairment
- Previous severe reaction to intravenous iron products e.g. circulatory collapse (shock), cardiac and respiratory arrest
- Children under the age of 14 years
- This preparation must not be used before the 16th week of pregnancy.

Dosage

Iron formulation

The adequate cumulative dose of Ferinject must be calculated for each patient individually and must not be exceeded. The dose of Ferinject is expressed in mg of elemental iron:

- 2 mL of solution contains 100 mg iron as ferric carboxymaltose
- currently available as iron (ferric carboxymaltose) in:
    - 100 mg/2 mL injection, 2 mL vial
    - 500 mg/10 mL injection, 10 mL vial
    - 1000 mg/20 mL injection, 20 mL vial.

Calculation of the total body iron deficit

- The cumulative dose of Ferinject for repletion of the total body iron deficit is based on patient weight (use ideal body weight if overweight) and haemoglobin (Hb) and must not be exceeded
- Some patients may require 2 infusions (at least 1 week apart) to cumulatively replace the total body iron deficit (because there is a maximum dose per infusion that must NOT be exceeded - see *Dosage per infusion* below)
- The total body iron deficit can be approximated using the table below
- Calculate the total body iron deficit in iron deficiency with a normal Hb as it generally only requires one infusion. See table below.

Dosage per infusion

- Maximum dose of Ferinject per infusion is 20 mg/kg to a maximum of 1000 mg/20 mL. Use ideal body weight in overweight patients
- The first dose of Ferinject is given at 20 mg/kg to a maximum of 1000 mg
- A second dose of Ferinject can be given over one week later to replace the remainder of the calculated total body iron deficit (see table), but not exceeding the maximum dose per infusion of 20 mg/kg.

Table. ADULT: determination of the iron need

Haemoglobin (Hb) (g/L)	Body weight 35 to < 70 kg	Body weight ≥ 70 kg
< 100	1500 mg	2000 mg
100 to < 140	1000 mg	1500 mg
≥ 140	500 mg	500 mg

Administration

Preparation of the infusion

Ferinject must only be mixed with 0.9% sodium chloride as there is potential for precipitation and/or interactions with other solutions and therapeutic agents.

Ferinject quantity	Iron dose	Maximum amount of sterile 0.9% sodium chloride solution	Minimum administration time
2-4 mL	100-200 mg	50 mL	3 minutes
> 4-10 mL	> 200 to 500 mg	100 mL	6 minutes
> 10-20 mL	> 500 to 1000 mg	250 mL*	15 minutes

* consider using smaller infusion volume in those with heart failure or any patients with fluid loading concerns

For stability reasons, dilutions to concentrations less than 2 mg/mL (not including the volume of the ferric carboxymaltose solution) are not permissible.

Cannulation and commencement of infusion

- Perform hand hygiene
- Prepare normal saline of chosen volume with the IV administration set and prime
- Repeat hand hygiene and, using an aseptic technique, cannulate patient
- Ensure that the cannula is patent by flushing with 10 mL normal saline for injection
- Apply a clear Tegaderm dressing over the cannulation site to provide stability and allow for monitoring of potential tissue infiltration
- Draw up the prescribed iron volume and add it to the infusion bag. Gently rotate the infusion bag to thoroughly mix the contents
- Allow a small amount of fluid to run through the line to definitively exclude any air bubbles. Connect the IV administration set to the cannula
- Commence the infusion at a slower rate to ensure patient is tolerating it, and increase the volume after the observations at the 5 minute mark
- The Ferinject infusion should run over at least a minimum 15-20 minutes
- Once completed, flush the IV with 10-20 mL normal saline.

Infusion
Intravenous infusion
- Maximum 20 mg/kg per single administration or 1000 mg maximum dose
- ≤ 1000 mg infused over at least 15 minutes
- Single doses above 1000 mg are not to be given.

Intravenous bolus injections
Ferinject can also be administered as a bolus injection. Please refer to the PI for details on administration.

Continuous monitoring
The GP or nurse must remain with the patient at all times.

Clinical observations
- Blood pressure
- Heart rate
- Respirations
- Temperature
- Oxygen saturations, documented at:
  - Pre-infusion (baseline)
  - 5 minutes after commencement of infusion
  - 10 minutes after commencement of infusion
  - Immediately at end of the infusion
  - 30 minutes post infusion.

Patients may be discharged 30 minutes post infusion if observations are satisfactory. Remove the intravenous cannula before discharge.

Adverse effects

Common	**Uncommon**	**Rare**
Headache	Hypersensitivity	Anaphylactoid reactions
Dizziness	Vomiting	
Hypertension		
Flushing		
Nausea		
Hypophosphataemia		
Infusion/injection site reactions		

The full list of potential adverse effects can be found in the Product Information (PI).

Management of reactions
- In the event of adverse effects, stop the infusion immediately and contact the medical practitioner on site
- If there is resolution, infusion may be recommenced 15 minutes after symptoms have resolved at 50% initial infusion rate
- Monitor every 15 minutes. If patient seems to be tolerating the infusion, consider gradually increasing the infusion to recommended infusion rate as before (Note: total infusion time will be longer than normal)

- If the patient complains of pain, cease the infusion immediately but do not disconnect the line from the patient. Contact the medical practitioner on site for assessment and treatment
- For mild reactions, promethazine (Phenergan), hydrocortisone or paracetamol may be ordered by the medical practitioner
- In the event of anaphylaxis, administer adrenaline 1:1000 as per the clinic's anaphylaxis management guidelines and it is recommended that affected patients are not exposed to further infusions of Ferinject.

Anaphylaxis

For severe/life-threatening hypersensitivity (anaphylaxis) with rapid worsening of symptoms (increasing wheeze due to bronchospasm, periorbital oedema, drop in blood pressure and oxygen saturation) contact the emergency response team and follow your local anaphylaxis management guidelines.

Anaphylactoid reactions occur most frequently within the first several minutes of administration and are characterised by sudden onset of respiratory difficulties, tachycardia and hypotension. Adrenaline and facilities for the cardio-pulmonary resuscitation must be available. Therefore, the infusions of Ferinject will only be completed in a clinic environment.

Tissue infiltration (extravasation)

Both patient and clinician must be alert to extravasation at all time. Skin staining due to extravasation is potentially long lasting. The patency of the IV cannula must be confirmed before commencing infusion.

- Check with patient that there is no pain or swelling with flushing. If there is pain or swelling, then the IV cannula may be incorrectly positioned. If you are not certain that the IV cannula is placed correctly, run normal saline only to infuse at least 10 mL and monitor patient's comfort. If it is still not certain that the IV cannula is placed correctly, do not use that cannula
- Instruct patient to notify staff immediately if any symptoms of pain, swelling or discomfort occur around the cannula site
- Stop infusion immediately if paravenous leakage is detected
- The important indicator of the severity of the extravasation is **PAIN** (no necrosis of the skin has ever been reported).

Hypophosphataemia

Patients who receive multiple higher doses for a long-term treatment and with underlying risk factors (such as vitamin D deficiency, calcium and phosphate malabsorption, secondary hyperparathyroidism, hereditary haemorrhagic telangiectasia, inflammatory bowel disease and osteoporosis) should be monitored for hypophosphataemic osteomalacia. In case of persisting hypophosphataemia, treatment with Ferinject should be re-evaluated.

Where a patient with underlying risk factors requires multiple iron infusions, seek specialist advice.

Sample: Ferinject infusion patient consent form

- I declare that none of the following conditions listed below are applicable:
    - Pregnancy in the first trimester
    - Allergy to ferric carboxymaltose
    - History of iron overload or haemochromatosis
    - Under the age of 14 years
    - Diagnosed with anaemia not caused by iron deficiency
    - Currently suffering from a fever, infection or acute illness.

- The doctor and nurse have explained to me what an iron infusion involves, including the risks, benefits and necessary follow-up of this treatment
- I have been provided with written information about an iron infusion, and I have had an opportunity to discuss and clarify any concerns with the doctor and nurse
- I understand that the results of the treatment procedure cannot be guaranteed
- I understand that the administration of Ferinject comes with the following risks including, but not limited to:

Common	**Uncommon**	**Rare**
Headache	Allergic reaction	Anaphylactoid reactions
Dizziness	Vomiting	
High blood pressure		
Flushing		
Nausea		
Low blood phosphate levels		
Infusion/injection site reactions		

The full list of potential adverse effects is found in the Consumer Medicines Information (CMI).

- If a staff member is exposed to my blood, I consent to a sample of my blood being collected and tested for infectious diseases. I understand that I will be given the results of the tests
- I agree for my medical record to be accessed by staff involved in my clinical care and for it to be used for approved quality assurances activities, including clinical research. I understand that my privacy will be preserved
- I understand that if immediate life-threatening events happen during the procedure, I will be treated accordingly
- I understand that I have the right to change my mind at any time before the treatment is undertaken, including after I have signed this form. I understand that I must inform my doctor or nurse if I change my mind.

Patient's full name: _____ DOB: _____

Patient's signature: _____ Date: _____

Doctor/Nurse: _____

Signature: _____ Date: _____

For clinical use only

IV cannula inserted (location) ……**Time:** ……

1. Observations before start of infusion

Time:	BP:	HR:	Temp:	SpO2:

2. Observations 5 minutes after the start of infusion

Time:	BP:	HR:	Temp:	SpO2:

3. Observations 10mins post commencement of infusion:

Time:	BP:	HR:	Temp:	SpO2:

4. Observations after infusion is finished

Time:	BP:	HR:	Temp:	SpO2:

Clinical notes

References

Vifor Pharma Pty Ltd. Ferinject (ferric carboxymaltose) Australian Approved Product Information. 13 September 2021. Available at: https://bit.ly/3nDPxvH (last accessed 2 February 2022).

Australian Government. Department of Health. Australian Immunisation Handbook. Last updated: September 2021. Available at: https://immunisationhandbook.health.gov.au/vaccination-procedures/preparing-for-vaccination (last accessed 19 January 2022).

Australasian Society of Clinical Immunology and Allergy (ASCIA). ASCIA Guidelines: acute management of anaphylaxis. 2021. Available at: https://www.allergy.org.au/hp/papers/acute-management-of-anaphylaxis-guidelines (last accessed 14 November 2021).

Suggested resources

Medical Council of New South Wales. Iron infusions – 5 things you can do to avoid a complaint. 2019. Available at: https://www.mcnsw.org.au/iron-infusions-–-5-things-you-can-do-avoid-complaint (last accessed 11 November 2021).

Informed consent: See the Medical Board of Australia's *Good Practice – A Code of Conduct for Doctors in Australia* [hyperlink] (*Working with Patients* section 3).

Iron infusion treatment information for practitioners – NPS Medicine Wise https://www.nps.org.au/radar/articles/ferric-carboxymaltose-ferinject-for-iron-deficiency-anaemia#safety-issues

Online eLearning: https://bloodsafelearning.org.au/

BloodSafe eLearning checklist: https://bloodsafelearning.org.au/wp-content/uploads/2019/07/administration_of_iron.pdf

IV iron tools including patient information, consent and protocol: https://bloodsafelearning.org.au/iv-iron-tools/

Administering IV iron (video): https://bloodsafelearning.org.au/resource-centre/videos

Australian Government. training.gov.au. Unit of competency details: HLTHPS009 - Perform peripheral intravenous cannulation (Release 1). https://training.gov.au/Training/Details/HLTHPS009

Government of South Australia. SA Health. IV iron preparations for treatment of iron deficiency anaemia (IDA) in Australia. April 2021. Available at: https://www.sahealth.sa.gov.au/wps/wcm/connect/4b7b89e1-bd2c-44a4-abd0-bd258e016b0e/FINAL+update+SA_IV_Iron_chart_TP-L3-811+v3.0+May+25th+2021.pdf?MOD=AJPERES&CACHEID=ROOTWORKSPACE-4b7b89e1-bd2c-44a4-abd0-bd258e016b0e-nKOM.w9 (last accessed 15 November 2021).

Disclaimer: The information set out in this document is current at the date of first publication and is intended for use as a guide for clinicians setting up an iron infusion service with Ferinject. The suggested resource list is not exhaustive of the subject matter. This information was developed after consultation with 3 medical professionals experienced in the establishment and routine practice of an iron infusion clinic. It can be used to support clinicians in the development of their own protocol, in delivering good medical care and providing a framework to guide professional judgement and due diligence.

PBS Information: Ferinject 10 mL (500 mg iron) and Ferinject 20 mL (1000 mg iron) is listed on the PBS as a parenteral iron preparation.

Please review Product Information before prescribing. To have a copy of the Product Information sent to you, telephone 1800 202 674.

Minimum Product Information: Ferinject® (ferric carboxymaltose) solution for intravenous (IV) use. **Indication**: Treatment of iron deficiency when oral iron preparations are ineffective, cannot be used, or when there is a clinical need to deliver iron rapidly. The diagnosis must be based on laboratory tests. **Contraindications**: Hypersensitivity to any of the ingredients; anaemia not attributed to iron deficiency; evidence of iron overload or disturbances in utilisation of iron. **Precautions**: Parenteral iron preparations can cause hypersensitivity reactions – monitor patients for at least 30 minutes after each administration; paravenous leakage can lead to skin discolouration and irritation; hypophosphataemia and hypophosphataemic osteomalacia; hepatic impairment; acute or chronic infections; iron overload; pregnancy category B3 treatment not recommended if <16 weeks gestation, monitor unborn baby; Not recommended in children < 14 years. **Adverse effects**: Common: headache, dizziness, hypertension, flushing, nausea, injection/infusion site reactions, hypophosphataemia, Uncommon: hypersensitivity. Rare: anaphylactoid reactions. **Dosage**: Dosage is calculated individually for each patient and must not be exceeded. Maximum single dose of 1000mg iron per week or 20 mg iron/kg body weight. IV injection: 500mg-1000mg iron over 15 minutes, 200-500mg iron at 100mg iron/min. IV infusion: 500mg-1000mg iron over 15 minutes; 200mg-500mg iron over 6 minutes; 100mg-200mg iron over 3 minutes. **Presentation**: 2mL, 10mL, and 20mL vials containing 100mg, 500mg, and 1000mg of iron, respectively. Full prescribing information available on request from Vifor Pharma Pty Ltd, Melbourne. Medical Information: 1800 202 674 (Australia). ®Registered Trademark. MPI-180521

Vifor Pharma Pty Ltd Melbourne VIC Website: www.viforpharma.com.au

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