Southern Health and Social Care Trust

TITLE	**Management of Iron Deficiency in Heart Failure (HF) using Ferric Carboxymaltose (Ferinject)**
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SPECIALITY	**Heart Failure**
DIRECTORATE	**Acute**
DATE	**22/11/23**
REVIEW DATE	**22/11/23**
Clinical Guidelines ID:	**CG0796b[1]**

Management of Iron Deficiency in Heart Failure (HF) using

These guidelines have been informed by the 2021 ESC Guidelines for the Diagnosis and Treatment of Acute and Chronic Heart Failure (*European Heart Journal*, Volume 42, Issue 36, 21 September 2021, Pages 3599–3726).

Available at: https://doi.org/10.1093/eurheartj/ehab368

Context

Iron deficiency (ID) is common in patients with heart failure (HF) and is independently associated with reduced exercise capacity, recurrent HF hospitalizations, and high cardiovascular and all-cause mortality.

ID, which can be present independently of anaemia, is present in up to 55% of chronic HF patients and in up to 80% of those with acute. Although the exact cause of iron deficiency in HF remains unknown, it may be caused by increased loss, reduced intake or absorption (i.e. malnutrition, gut congestion) and/or impaired iron metabolism caused by the chronic inflammatory activation of HF.

Oral iron therapy is not effective in iron repletion in HF and is not recommended for the treatment of iron deficiency in patients with HF. Intravenous iron supplementation using is recommended (ESC 2023).

Recommendation Table 5 — Recommendations for the management of iron deficiency in patients with heart failure

Recommendations	Class[a]	Level[b]
Intravenous iron supplementation is recommended in symptomatic patients with HFrEF and HFmrEF, and iron deficiency, to alleviate HF symptoms and improve quality of life.[c] [12,41,47–49]	I	A
Intravenous iron supplementation with ferric carboxymaltose or ferric derisomaltose should be considered in symptomatic patients with HFrEF and HFmrEF, and iron deficiency, to reduce the risk of HF hospitalization.[c] [12,41,43–46]	IIa	A

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This document outlines the use of Ferric Carboxymaltose for the treatment of ID in HF.

Definition of Iron Deficiency:

Ferritin <100 ug/L (absolute iron deficiency)
OR
Ferritin 100 – 299 ug/L with Transferrin Saturation (TSAT) <20%

Screening

All patients with a diagnosis of HF should be regularly screened (at first assessment and at least six monthly intervals for anaemia and ID with full blood count, serum ferritin concentration, and TSAT.

The detection of anaemia and/or ferritin <30 ug/L should prompt appropriate investigation to define their cause. The primary physician / GP should be notified so that prompt investigation can take place under their care.

Patients to consider for IV iron replacement with Ferric Carboxymaltose

1. Patients with **LVEF <45%** and iron deficiency, defined as serum ferritin <100 ug/L OR serum ferritin 100 - 299 ug/L with TSAT <20%.
2. Patients with **LVEF <50% who have recently been hospitalized for HF** and have iron deficiency, defined as serum ferritin <100 ug/L or serum ferritin 100-299 ug/L with TSAT <20%.
3. Any patient with a diagnosis of heart failure who falls outside indications 1 and 2, but who may benefit from treatment on the recommendations of a HF consultant.

Exclusion Criteria/ Contraindications:

- Hypersensitivity to active substance (Ferric Carboxymaltose) or any of its excipients.
- Hypersensitivity to other parenteral iron products.
- Non-iron deficiency anaemia (e.g. haemolytic anaemia).
- Iron overload or disturbances in utilisation of iron.
- Decompensated liver cirrhosis.
- Active ongoing bacteraemia
- First trimester pregnancy
- Second and third trimester pregnancy (can consider if benefit outweighs risk and following discussion with HF Consultant).

Ferric Carboxymaltose Prescribing Considerations

Summary of product characteristics for Ferric Carboxymaltose are available at: www.medicines.org.uk/emc

Dosing of Ferric Carboxymaltose is determined based on the patient's body weight and haemoglobin (Hb) level. The following baseline bloods / measurements should be reserved before prescribing:

- Full blood count
- Ferritin
- Iron profile
- Weight (in kg)
- Bone Profile (for pre infusion check of phosphate, if same low, discuss with consultant before proceeding).
- B12 and folate.

Ferric Carboxymaltose Dosing Schedule

Hb	Patient body weight		
g/L	below 35 kg	35 kg to <70 kg	70 kg and above
<100	500 mg	1,500 mg	2,000 mg
100 to <140	500 mg	1,000 mg	1,500 mg
≥140	500 mg	500 mg	500 mg

- Do not exceed maximum single dose of 1000mg of Ferric Carboxymaltose at any one administration.
- Do not administer 1000mg of Ferric Carboxymaltose more than once a week.
- For doses greater than 1000mg of iron, give initial dose of 1000mg (up to maximum of 20mg/kg) and give remainder after at least one week.

IV Ferric Carboxymaltose should be prescribed as a 'stat' dose on the patient's drug kardex and should also be prescribed on a fluid balance chart.

Preparation

Ferric Carboxymaltose is administered via an intravenous infusion. No test dose is required.
It must only be diluted in sodium chloride 0.9% as below:

Dose	Sodium chloride 0.9%	Infusion time
Up to 1000mg	100ml	Administer over 30 minutes

Pre-Administration

Patients should be provided with written information about the reason for their infusion and the associated risks. A record of this should be kept in their notes. A copy of this can be found in Appendix 1.

A set of observations (including blood pressure, pulse rate and temperature) and the NEWS score should be measured and recorded before administration.

If the patient has any signs or symptoms of infection alert the appropriate doctor. They must decide whether or not is appropriate to delay giving the dose until any infection has resolved.

During and Post Administration

Observations should be recorded after 5 minutes and 10 minutes following commencement of the infusion.

A set of observations should also be checked on completion of the infusion and on discharge (minimum 30 minutes post-completion of infusion).

The patient must be visible to nursing staff for the duration of the infusion.

As with all IV preparations, acute anaphylaxis may occur with Ferric Carboxymaltose. Ensure adrenaline (epinephrine) is available prior to administration.

Parenterally administered iron preparations such as Ferric Carboxymaltose can cause hypersensitivity reactions including anaphylactoid reactions, which may be potentially fatal. The risk is enhanced for patients with known allergies including drug allergies, including patients with a history of severe asthma, eczema or other atopic allergy. There is also an increased risk of hypersensitivity reactions to parenteral iron complexes in patients with immune or inflammatory conditions (e.g. systemic lupus erythematosus, rheumatoid arthritis).

If hypersensitivity reactions or signs of intolerance occur during administration, the infusion must be stopped immediately.

Patients should be monitored for signs of hypersensitivity during and for at least 30 minutes following each injection. Caution is needed with every dose of intravenous iron that is given, even if previous administrations have been well tolerated.

Iron deposition in the tissues can be irreversible and cause skin staining. The infusion site must be monitored to ensure that the cannula is correctly positioned for the duration of the infusion.

Ferric Carboxymaltose should only be administered in areas where staff are trained to evaluate and manage anaphylactic or anaphylactoid reactions and where facilities for cardio-pulmonary resuscitation and equipment for handling acute anaphylactic/anaphylactoid reactions are available.

Post Infusion Phosphate Monitoring

There is a potential risk of phosphate drop after administration of Ferric Carboxymaltose, and this may persist for up to 3 months following the last dose. The implications of low phosphate for myocardial and systemic function are typically underestimated. Symptoms are more common at lower levels, and may include myopathy, rhabdomyolysis, weakness, respiratory failure, arrhythmias, cardiomyopathy, irritability, confusion, hallucinations, somnolence, convulsions and coma.

Phosphate levels must be checked at baseline and then again 2 weeks post completion of treatment.

Hypophosphataemia should be managed in line with the SHSCT guideline CG0088(3) Treatment of Hypophosphataemia in Adults. A summary of the guidance is given below, however it is recommended that the most up to date SHSCT Clinical Guideline is reviewed prior to initiating treatment. It is available to view at:

https://southernguidelines.hscni.net/?page_id=0&limit=&q=hypophosphataemia

1. Mild hypophosphataemia (0.6-0.8mmol/l) is of little clinical consequence and rarely requires treatment.

2. Moderate hypophosphataemia (0.3-0.6mmol/l) should be treated if symptomatic e.g. muscular weakness. Consideration should also be given to treatment of hypophosphataemia in 'sick' patients as phosphate is essential for red cell oxygen carriage, white cell chemotaxis and phagocytosis, myocardial contractility and diaphragmatic function.

   Treatment of moderate hypophosphataemia: Phosphate Sandoz® tablets (16.1 mmol phosphate per tablet) 1 - 2 tablets three times a day. Phosphate should be rechecked no later than one week post replacement.

3. **Severe hypophosphataemia (<0.3mmol/l) is life-threatening and should be treated without delay.**

   Treatment of severe hypophosphataemia: Total of 20 mmol Phosphate infused over 24 hours in the following manner:

   A ready-made infusion bag containing 10mmol phosphate and 20mmol potassium in 500ml sodium chloride 0.9% is infused intravenously over 12 hours.

   A second identical infusion bag is infused intravenously over the next 12 hours.
   The infusion time must not be exceeded as this carries a real risk of causing metastatic calcification with hypocalcaemia.

Onwards Monitoring

Phosphate must be checked two weeks post infusion. Hb, ferritin and iron studies should be measured 4 – 6 weeks after the last infusion. If the patient remains iron deplete, further dosing should be discussed with the HF Consultant.

If IV iron is given at a day clinical centre site, the day clinical centre must complete the post infusion details on the referral form and email a copy of this along with the discharge letter to heart.failureservices@southerntrust.hscni.net

On recepit, the heart failure nurses must arrange appopriately timed bloods. The GP should not be asked to check post iron infusion bloods.

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Appendix 1:

Information for Patients Receiving Intravenous Iron Preparations

Your medical team have recommended intravenous iron to treat your anaemia / low blood count. This will be given as an infusion/drip over 15 or 30 minutes. Please read the following information prior to your treatment and if you have any questions let the nurse caring for you know.

1. Intravenous iron is used to treat a low blood count due to a low amount of iron in your body. This may have occurred due to low amounts of iron in your diet, a problem with your body's ability to absorb and use iron or be as a result of blood loss.
2. Intravenous iron is a highly effective method to replenish your body's stores of iron and hopefully allow you to increase your blood count over the coming days and weeks.
3. Intravenous iron allows a much larger dose of iron to be given than iron in tablet form.
4. All medication carries a risk of side effects and reaction. Prior to receiving your treatment it is important you are aware of the side effects / risks of intravenous iron. The nurse caring for you will ask if you understand the information below and are content to proceed prior to you treatment.

Side Effects of Intravenous Iron Therapy

1. Intravenous iron has a good safety profile and is an effective therapy for treatment of iron deficiency anaemia. Common side effects include headache, dizziness, flushing, nausea and a reaction at the site of injection/infusion. You will be monitored while intravenous iron is being administered and for 30 minutes after your treatment has been completed.
2. Staining – If your cannula was to displace from your vein during treatment the drug could be deposited in your skin rather than into your bloodstream. This could result in a permanent brown stain to the skin. If you notice pain at the injection site during your treatment please inform the nurse caring for you immediately. This will minimise any such risk.
3. Change in total body skin colour – This is an extremely rare occurrence. It has been reported that some patients noted their skin to become darker (like a sun tan) for a period of weeks after treatment with intravenous iron. This was not permanent and resolved after a number of weeks.
4. Allergy – Historically intravenous iron preparations carried a risk of allergy (ranging from a mild reaction like itchy skin through to anaphylaxis that could be life threatening). With today's modern iron preparation anaphylaxis is rare (1 in a 1000 to 1 in a 10,000 risk). Please inform the nurse caring for you immediately if you experience any of the following during your treatment (swelling of lips, tongue, face or throat, shortness of breath, itching, a feeling of all over body heat, heart racing heat or faint like symptoms)
5. Delayed reaction – Although uncommon, some patients may experience muscle or joint pains and fever in the days after treatment. This usually lasts two to four days and can be managed with simple painkillers like paracetamol.

I confirm that the above information has been given to/explained to the patient prior to treatment	PRINT NAME SIGNATURE DATE

REFERENCES

ESC 2023 https://doi.org/10.1093/eurheartj/ehad195