INTRA-VENOUS FERRIC CARBOXYMALTOSE THERAPY (FERINJECT®)

AIM
To provide best practice requirements for the administration and management of intravenous (IV) ferric carboxymaltose (FC) therapy.

BACKGROUND

The use of FC is restricted to use in the Infusion Unit only, where its use and impact upon our patient group is being closely monitored. Ferric carboxymaltose is listed on the PBS as a drug for iron deficiency anaemia (IDA) only.

IV FC may be used to augment haemoglobin levels in patients with identified IDA who have failed to respond sufficiently to oral iron1,2,3,4

World Health Organisation4,5 defines anaemia as identified below (Table 1).

Table 1 Classification of anaemia in adult women

<table>
<thead>
<tr>
<th>Haemoglobin (g/L)</th>
<th>Categories</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;110</td>
<td>1st and 3rd trimester of pregnancy</td>
</tr>
<tr>
<td>&lt;105</td>
<td>2nd trimester of pregnancy</td>
</tr>
<tr>
<td>&lt;100</td>
<td>Postpartum period</td>
</tr>
<tr>
<td>&lt;120</td>
<td>Non-pregnant adult women</td>
</tr>
</tbody>
</table>

A serum ferritin level of < 30 microgram/L for an adult is diagnostic of iron deficiency5.

Other markers of iron function including serum iron and transferrin saturation (%) are not reliable measures of iron status as they are affected by diurnal patterns or have limited reference ranges for pregnancy and a lack of standardisation1,2,6.

The use of IV iron is commonplace1,2,3, however there is still an incidence of significant reactions and complications, both immediate and delayed, including the potential increased risk to infection8, 10, 11.

The use of IV iron is associated with a transient decrease in plasma phosphate to a greater degree with FC than iron polymaltose; in particular in women with known phosphate metabolism dysregulation12,13,14,15,16. Thus FC should not be used in patients with known/suspected vitamin D deficiency16, hyperparathyroidism or pre-existing hypophosphataemia.

IV iron is not licenced for use as an acute treatment in the management of major haemorrhage. Management of these patients is complicated by red cell loss, acute dilutional anaemia and the inflammatory processes which supress red cell production17.

FC is a relatively new medication and as such there are a small number of known medications whose efficacy is reduced or toxicity is increased (increasing the risk of adverse reactions) with the use of FC therapy as indicated in Table 2. This should be factored in the decision to use FC.
Table 2 Drug interactions

<table>
<thead>
<tr>
<th>Drug</th>
<th>Interaction effect</th>
</tr>
</thead>
<tbody>
<tr>
<td>ACE inhibitors e.g. ramipril, captopril etc*</td>
<td>FC has its toxicity ↑ by ACE inhibitors</td>
</tr>
<tr>
<td>Iron polymaltose / Iron sucrose</td>
<td>FC causes additive toxicity with Iron polymaltose complex</td>
</tr>
<tr>
<td>Oral iron supplements*</td>
<td>FC causes additive toxicity with oral iron supplements; oral iron therapy should not be started for at least 5 days after the last injection of Ferinject®</td>
</tr>
</tbody>
</table>

* See MIMS for further information with wide number of medications within this group

INDICATIONS

The use of IV FC may be appropriate in:

- **IDA** where oral iron therapy may not be sufficient due to intolerance, non compliance, malabsorption/ gastric surgery or in situations where a rapid repletion of ferritin is required i.e. planned surgery when a significant blood loss is anticipated. Functional iron deficiency associated with failure of the release of stored iron for erythropoiesis. This may be seen in patients with renal disease, inflammatory disease or cancer. Ferritin can be raised in these conditions as it is an acute phase protein and some patients with a ‘normal’ range ferritin may still benefit from IV iron. Interpretation of the results in patients with co-existing inflammatory disease or cancer is complicated and advice should be sought from a Consultant Haematologist, particularly as FC is PBS listed for the treatment of IDA only

- Contact the Haematologist if there are any doubts concerning the indications for IV FC infusion

- Patients with haemoglobinopathy/thalassaemia frequently present with moderate to severe anaemia, may be iron deficient and may benefit from treatment. However some patients present with hyperferritinaemia rather than iron deficiency. IV FC would be unhelpful in this situation. Interpretation of laboratory tests and management is complex and these patients should be discussed with a Haematologist if there are any concerns

CONTRAINDICATIONS

- First trimester of pregnancy (Safety not tested in early pregnancy, animal studies have demonstrated increased fetal skeletal abnormalities and spontaneous abortions at maternally toxic doses during organogenesis. The level of drug crossing the placenta is unknown.

- Hypersensitivity to FC

- Vitamin D deficiency (due to hypophosphatemia)

- Uncontrolled hyperparathyroidism (due to hypophosphatemia)

- Liver dysfunction (elevated liver enzymes including lactate dehydrogenase occurs following administration)

- Less than 14 years of age (FC has not been studied in children and therefore is not recommended)

- Iron overload (i.e. haemochromatosis)

- Anaemia not due to iron deficiency (i.e. B12 deficiency, haemolytic anaemia, bone marrow disease or disturbances in erythropoiesis)

- Current bacterial infection
PRECAUTIONS

- Allergy\(^8\)
- Previous adverse reaction to other forms of parenteral iron \(^8,9\)

DOSAGE

The maximum dosage of FC is 1000mg per week, thus if a larger dose is required then consideration should be given to the use of iron polymaltose which allows a greater dose to be administered as a single infusion. The dose should be calculated on current weight in non pregnant women. In pregnant women, the pre-pregnancy weight should be used. If this is not known then the dose should be based on current weight less 10\(^\%\)\(^2,8,18\). For example, if current weight is 50kg, then the dose weight calculation would be 50 – 5 = 45kg (See table 3).

DURING PREGNANCY AND BREASTFEEDING PERIOD THE MAXIMUM DOSE IS A SINGLE INFUSION OF 1000MG ELEMENTAL IRON AS FERRIC CARBOXYMALTOSE

Table 3 Dosage table

<table>
<thead>
<tr>
<th>Body Weight</th>
<th>Hb &lt;100g/L</th>
<th>Hb &gt;100g/L</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Total dose mg</td>
<td>Total volume mL</td>
</tr>
<tr>
<td>35 - 70kg</td>
<td>1500*(^a)</td>
<td>30</td>
</tr>
<tr>
<td>&gt;70kg</td>
<td>2000*(^a)</td>
<td>40</td>
</tr>
</tbody>
</table>

\(^*\)Refer to iron polymaltose guidelines and single dose infusion if greater than 1000mgs dose required and patient not currently pregnant or breastfeeding

\(^a\)mg indicates elemental iron
- Do not administer IV FC if the patient is receiving IV antibiotics in treatment of acute bacterial infection, it can be considered following cessation of IV antibiotics and is dependent upon the patient’s condition
- Hand hygiene shall be performed prior to and after contact with the patient or equipment
- Regardless of the dose to be administered, FC shall be added to 250mL 0.9% Sodium Chloride
- FC shall not be mixed with other drugs or with solutions other than 0.9% sodium chloride
- FC shall not be injected into the tubing of the IV giving set
- Maximum daily dose of FC should not be more than 200mg elemental iron in haemodialysis dependent chronic renal disease

INFUSION RATES

As injection site reactions are common and paravenous leakage is common\(^8\) and associated staining a hazard, all FC will be administered as an infusion in 250mL of 0.9% sodium chloride (as opposed to an IV injection of the undiluted solution). See table 4.

The maximum dose is 1000mg per week.
Table 4 Infusion rate table

<table>
<thead>
<tr>
<th>Dose</th>
<th>Volume ferric carboxymaltose mL</th>
<th>Infusion rate and administration time</th>
</tr>
</thead>
<tbody>
<tr>
<td>500 - 1000mg</td>
<td>10 – 20</td>
<td>Commence at 500mL/hour rate for 30 minutes</td>
</tr>
</tbody>
</table>

If the patient experiences an adverse reaction, cease the infusion and see adverse reaction below.

ADMINISTRATION PROCEDURE

1. The infusion should be prescribed on the patient’s Intravenous Fluid and Additive Order Sheet (MR740) by the Medical Officer; in addition a separate PBS prescription will be completed by the Medical Officer.

2. If the patient has a history of a previous adverse reaction, the Medical Officer must be informed and be present prior to the commencement of the infusion. Consider prophylaxis with Loratadine 10mg orally and hydrocortisone 100mg IV.

3. Explain the procedure and educate the patient about the possible adverse reactions both immediate and delayed.

4. The patency of the IV cannula must be confirmed before commencing any infusion to ensure there is no extravasation of iron, which can cause a permanent stain. Connect a 50mL 0.9% sodium chloride flush and allow this to infuse by gravity. If the saline does not infuse freely, there is swelling or discomfort this cannula must not be used for the IV FC.

5. All women should be observed for signs of adverse reaction which may be acute or delayed (see below).

Common adverse reactions to FC include\(^8\):
- Headache, dizziness
- Injection site reactions
- Hypertension
- Elevated liver enzymes
- Hypophosphataemia

Less common reactions include\(^8\):
- Nausea, abdominal pain, constipation, diarrhoea
- Hypersensitivity including anaphylaxis
- Paraesthesia and dysguesia
- Hypotension
- Tachycardia
- Flushing
- Back, joint or muscle pain
- Pruritis and urticaria
- Pyrexia, fatigue and malaise
- Dyspnoea and bronchospasm
- Syncope

6. The patient must be able to reach her call bell at all times and must be instructed to use it if she becomes aware of any adverse reaction.

7. Monitoring and recording of vital signs shall include:
8. The observations shall be performed
   - Prior to commencement of the infusion
   - 5 minutes after commencement of the infusion
   - If the patient complains of feeling unwell/reports any potential adverse effects
   - At the end of the infusion
   Notify the Medical Officer if any of the vital signs change significantly.

9. On completion of the infusion, flush the administration set with 50mL 0.9% sodium chloride. This should be given at the same rate as the IV FC.

10. At the end of the infusion the patient shall remain on the unit for 30 minutes. If no adverse symptoms occur, the patient may be discharged. If symptoms do occur, notify the Medical Officer immediately to review the patient.

11. On discharge the patient should be given the Intravenous Iron Information Sheet and advised to report any delayed adverse reactions to the KEMH staff (inpatient) or her GP (outpatient) and CNC Haematology (whose contact details are provided on the discharge information sheet). Patients will be provided with a form to have FBP and iron studies 1 month post iron infusion, to ensure that they have responded to treatment and exclude iron overload.

12. The Iron Infusion Audit form is completed and followed up by the Infusion Unit staff.

ADVERSE REACTION

1. STOP the infusion.

2. Perform and record observations as indicated by the patient’s clinical condition including
   - Respiratory rate
   - Oxygen saturations
   - Heart rate
   - Blood pressure
   - Temperature
   - Conscious state
   - Fetal heart rate and CTG (if pregnant)
   Consider ECG and cardiac monitoring

3. Mild Adverse reactions: The vast majority of adverse reactions are not hypersensitivity reactions and respond to simple measures. These include headache, nausea, rash, myalgias and cannula site discomfort. Options may include ceasing the infusion for 10-15 minutes, oral loratadine 10mg (itch, rash), IV hydrocortisone 100mg or paracetamol 1g orally (headache or discomfort). It may be appropriate to reduce the rate or dose. Usually the infusion can be recommenced once the symptoms have resolved.

4. More severe reactions: Inform the Medical Officer and request urgent review. Cease the infusion immediately and seek advice from a Medical Officer experienced with IV iron.

5. Hypotension in the pregnant patient: The patient should be placed in the full left lateral position to relieve any aortocaval compression and fetal heart rate monitoring instituted.
6. Call a “Code Blue Medical” if any of the following occur

- Stridor, facial or neck swelling
- Respiratory rate > 30 or oxygen saturations < 90%
- Heart rate > 130bpm or < 40 bpm, or systolic blood pressure < 80mmHg
- Altered conscious state
- Any serious concerns

7. If a true anaphylactoid reaction occurs treat accordingly and the infusion must be abandoned and the patient transferred to ASCU for observation and management.

**POST INFUSION MANAGEMENT**

The patient should be provided post iron infusion discharge information available at:

They should be instructed not to take any oral iron for 5 days post iron infusion. Pregnant and post-natal women should be encouraged to continue with oral iron supplements until breastfeeding is complete. Women with menorrhagia or continued bleeding should be encouraged to continue on oral iron until resolution of underlying bleeding.

It is important that a follow-up full blood picture and iron studies are obtained one month post-IV FC to ensure the results have normalised. The patient should be provided with a completed request form with clear instructions to have this undertaken within a PathWest Collection Centre, with a copy of the results forwarded to Debbie Pinchon, Clinical Nurse Consultant, Haematology Department, KEMH.

**DOCUMENTATION**

The administration of IV FC should be clearly documented (to reduce the risk of duplicate administration, as iron infusions are carried out in Theatre, ASCU and the Infusion Unit), Self-adhesive brown coloured stickers designed to identify the dose and date of iron infusion should be annotated and placed in the patient’s medical record, in addition to placement on the special instructions sheet at the front of the patient’s medical records (MR004/005) and, the handheld Pregnancy Health Record (MR220) if the patient is pregnant.

**REFERENCES**

1. Pasricha S-R et al. Diagnosis and management of iron deficiency anaemia: a clinical update. MJA 2010 Nov; 193(9):525-532


8. Ferinject Injection MIMS Full Prescribing Information 2013


Myers B, Myers O, Moore J. Comparative efficacy and safety of intravenous ferric carboxymaltose (Ferinject) and iron (III) hydroxide dextran (Cosmofer) in pregnancy Obstetric Medicine 2012; 5: 105 – 107.


The Women’s Pregnancy and Breastfeeding Medicines Guide, Royal Women’s Hospital, Melbourne 2014

REFERENCES (STANDARDS)
As Above

National Standards – 4 Medication Safety
Legislation - NIL
Related Policies - Nil
Other related documents – Parenteral Therapy : Iron Therapy

RESPONSIBILITY
Policy Sponsor Transfusion Medicine Committee
Initial Endorsement December 2015
Last Reviewed
Last Amended
Review date December 2018