IRON INFUSION IN PREGNANCY

SCOPE: This guideline applies to all medical, midwifery and nursing practitioners within Tairawhiti District Health (TDH).

AUTHOR: HOD Obstetrics and Midwifery Educator

PURPOSE: The purpose of this guideline is to provide guidance for prescribing iron in pregnancy, and the safe and effective use of intravenous ferric carboxymaltose (Ferinject®) where indicated for the pregnant woman.

Once prescribed, in accordance with the TDH ‘Medications – Prescribing’ policy, this medication should be administered and documented in accordance with the TDH ‘Medications – Administration’ policy (see associated TDH documents section).

GUIDELINE:

BACKGROUND
Serum ferritin should be performed to establish the diagnosis of iron deficiency before treatment with parenteral iron. Oral iron supplementation is the first line treatment. IV iron infusion is the preferred method for administration of parenteral iron. Caution should be exercised with any form of parenteral iron. As gestation advances the need to replenish iron stores becomes more urgent and an early diagnosis of iron deficiency enables its treatment through the use of oral iron supplementation. To that end, a serum ferritin is recommended with the “booking bloods” for the pregnant woman, and at 26 - 28 weeks gestation.

If iron deficiency anaemia (Hb < 100 g/L) is detected at booking, this is an urgent indication to start oral iron supplementation and refer for consideration of parenteral iron.

Ferric carboxymaltose is indicated in iron deficiency anaemia which is unresponsive or intolerant to oral iron, or when the woman is unable to ingest an adequate dose (eg ongoing bleeding).

After parenteral administration, iron is cleared by the reticuloendothelial cells and processed. The iron is then released back into the plasma and bone marrow. Because the rate of iron incorporation into haemoglobin does not exceed that achieved by oral iron therapy, the Hb can be expected to increase at a rate of 15 to 22g/L/week during the first 2 weeks and by 7 to 16g/L/week thereafter until normal values are attained.
PRESCRIBING

If, after following the pathway for iron supplementation in pregnant women (see appendix one for 26-28 weeks gestation, appendix two for ≥ 30 weeks gestation) parenteral iron is indicated, then the obstetrician should:

- Coordinate with the maternity unit and schedule an appropriate time on the “maty schedule”
- Complete an “Application for Subsidy by Special Authority” which needs to be faxed to the number indicated on the form itself (see appendix one).
- Complete an outpatient prescription to be sent to pharmacy to obtain the medication
- Complete an inpatient prescription chart so the administration of the infusion can be recorded

If Hb < 70 then iron infusion is indicated.

Otherwise, please follow the pathway according to Hb and ferritin levels and assess response to oral iron after 4 weeks of therapy.

If the rise in Hb is not more than 15 g/L with anaemia (Hb < = 100 g/L), iron infusion is recommended.

Determination of the cumulative iron dose

The cumulative dose for repletion of iron using FERINJECT is determined based on the patient's body weight and Hb level and must not be exceeded. There are two methods for determining the cumulative dose, the Ganzoni Method and the Simplified Method. Caution is recommended with the Simplified Method since it is based on experience in a single trial in adults with median Hb 104 g/L (range 61-146 g/L) and body weight ≥35 kg.

Ganzoni Method

Cumulative Iron Dose = Body Weight kg x (Target Hb – Actual Hb g/L) x 0.24 + Iron Stores mg

where

- Target Hb = 130 g/L for body weight <35 kg and 150 g/L for body weight ≥35 kg
- Iron Stores = 15 mg/kg body weight for body weight <35 kg and 500 mg for body weight ≥35 kg.

Round down to nearest 100 mg if body weight ≤ 66 kg and round up to nearest 100 mg if body weight > 66 kg.
Simplified Method (for patients of body weight ≥ 35 kg)
The cumulative iron dose is determined according to the following table:

<table>
<thead>
<tr>
<th>Hb g/L</th>
<th>Body weight 35 to &lt; 70 kg</th>
<th>Body weight ≥70 kg</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;100</td>
<td>1500 mg</td>
<td>2000 mg</td>
</tr>
<tr>
<td>≥100</td>
<td>1000 mg</td>
<td>1500 mg</td>
</tr>
</tbody>
</table>

**PRESENTATION OF FERRIC CARBOXYMALTOSE FOR INFUSION**
- 2 mL of solution in a vial. Each 2 mL vial contains 100 mg of iron as ferric carboxymaltose.
- 10 mL of solution in a vial. Each 10 mL vial contains 500 mg of iron as ferric carboxymaltose.

Trade name: FERINJECT.

**MEDICATION ADMINISTRATION OF FERRIC CARBOXYMALTOSE INFUSION**

**Intravenous infusion:**
FERINJECT may be administered by intravenous infusion up to a maximum single dose of 1,000 mg iron (up to a maximum of 20 mg iron/kg body weight). Do not administer more than 1,000 mg iron per week.

Medical staff members should be advised of commencement of infusion, and it is recommended a doctor is present at the start of the infusion in case of an adverse reaction.

**Dilution plan of FERINJECT for intravenous infusion**

<table>
<thead>
<tr>
<th>FERINJECT</th>
<th>Iron</th>
<th>Maximum amount of sterile 0.9% m/V sodium chloride solution</th>
<th>Maximum administration time</th>
</tr>
</thead>
<tbody>
<tr>
<td>2 to 4 mL</td>
<td>100 to 200 mg</td>
<td>Up to 50 mL</td>
<td>3 minutes</td>
</tr>
<tr>
<td>&gt;4 to 10 mL</td>
<td>&gt;200 to 500 mg</td>
<td>Up to 100 mL</td>
<td>6 minutes</td>
</tr>
<tr>
<td>&gt;10 to 20 mL</td>
<td>&gt;500 to 1000 mg</td>
<td>Up to 250 mL – safe to administer diluted in 100 mL</td>
<td>15 minutes</td>
</tr>
</tbody>
</table>

**IMPORTANT:** FERINJECT must be mixed and administered within the above time frames as the solution will degrade if administered more slowly and the risk of adverse reactions will increase.

**MONITORING DURING AN INFUSION**

**Maternal**
Iron infusions should be scheduled on the Maternity online scheduler and coordinated with the maternity unit.
Baseline observations of pulse, temperature, respiration rate and blood pressure should be documented in MEWS within MCIS prior to commencement of infusion. Monitor for adverse effects.

After commencement of infusion repeat observations every 5 minutes until infusion completed.

Woman to remain in facility for 30 minutes following infusion completion.

Arrange follow up full/complete blood count (FBC/CBC) test 2 weeks after infusion.

**Fetal**

For pregnancies beyond 28 weeks gestation, record baseline CTG immediately prior to infusion commencing (normal as defined by RANZCOG) while preparing securing IV access and preparing solution and continue this until infusion is completed.

**CONTRA-INDICATIONS, WARNINGS AND PRECAUTIONS IN PREGNANCY FOR FERRIC CARBOXYMALTOSE INFUSION**

**Use in pregnancy**

Intravenous iron should not be administered in the first trimester of pregnancy. Intravenous iron should not be used in pregnancy unless clearly necessary.

**Pregnancy category**

Ferric carboxymaltose is ADEC category B3 – There are no adequate and well-controlled studies in pregnant woman. A careful risk/benefit evaluation is required before use during pregnancy and FERINJECT should not be used during pregnancy unless clearly necessary.

Iron deficiency occurring in the first trimester of pregnancy can in many cases be treated with oral iron. If the benefit of FERINJECT treatment is judged to outweigh the potential risk to the fetus, it is recommended that treatment should be confined to the second and third trimester.

**Contra-indications**

Consult “contraindications, warnings, and precautions” in manufacturer’s datasheet for details (see supporting evidence section).

- Hypersensitivity to ferric carboxymaltose complex, to FERINJECT or to any of its excipients
- Anaemia not attributed to iron deficiency, e.g. other microcytic anaemia
- Evidence of iron overload (e.g. haemochromatosis or thalassaemia)
- Disturbances in utilisation of iron (e.g. Osler-Rendu-Weber syndrome)
- Acute infection or ongoing bacteraemia

**Adverse reactions and effects**

The most common reported adverse effects are headache, dizziness, nausea, gastrointestinal symptoms and rash (1-3%).
The reactions may be classified as ‘mild’, ‘moderate’ or ‘severe’ based on the definitions below. If there is a rash, swelling, wheeze and/or abnormal vital signs, consider anaphylaxis and manage as per ‘severe reaction’ (below).

Severe reactions are very rare, if anaphylaxis is suspected/diagnosed treat according to the TDH/NZ Resuscitation Council Anaphylaxis guideline (see associated TDH documents section). Please note all adverse reactions to iron infusions should be reported to the Centre for Adverse Reactions Monitoring (CARM). Reporting will allow a “Danger” to be entered against the woman’s NHI on the Medical Warning System to alert other health professionals. To report a reaction, go to the CARM website (see supporting evidence section). Also record in adverse reactions in the woman’s MCIS records.

**Mild reaction**

Definition: “symptoms but no observable patient discomfort”

Management:
- Stop the infusion immediately
- Reassure the woman – most symptoms resolve in 10 minutes
- Check vital signs (BP, pulse, respiratory rate, CTG)
- Wait and observe for 15 mins

If symptoms resolve, the infusion may be restarted.

If symptoms persist beyond 15 minutes consult medical staff members.

**Moderate reaction**

Definition: “symptoms and observable patient discomfort”

Management:
- Stop the infusion immediately
- Reassure the woman
- Check vital signs (BP, pulse, respiratory rate, CTG)
- Consult medical staff members
- Give 1g PO paracetamol for arthralgia and 10 mg PO loratidine for allergic symptoms such as itching
- Wait and observe for 15 mins (30 mins if medication given)

If symptoms resolve, the infusion may be restarted at 40 mL/hr and then increased to 250 mL/hr as tolerated after 15mins as per the rapid infusion protocol.

If symptoms recur, consult medical staff members again.

**Severe reaction**

Definition: “severe distress or cardiorespiratory compromise”

Management:
Stop the infusion immediately and disconnect the giving set
Check vital signs (BP, pulse, respiratory rate, CTG)
Call for emergency medical assistance (dial ‘777’ declare an ‘Obstetric Emergency’, request crash team, obstetrician and anaesthetist and give the operator the location)
Initiate maternal and fetal resuscitation as necessary
Check CTG as soon as possible

Further management
As per the arriving medical team. If anaphylaxis is not suspected and no cardiorespiratory compromise has occurred then the options are:

a) Give paracetamol/loratidine and proceed as above;

b) Consider whether the woman could continue with oral iron therapy with advice around management of side effects and retesting of Hb/ferritin in two weeks;

c) Consider IV iron sucrose therapy;

If anaphylaxis is suspected/diagnosed treat according to the TDH/NZ Resuscitation Council Anaphylaxis guideline (see associated TDH documents section). Please note all adverse reactions to iron infusions should be reported to CARM.

Interactions
As with all parenteral iron preparations the absorption of oral iron is reduced when administered concomitantly. Therefore, if required, oral iron therapy should not be started for at least 5 days after the last injection of FERINJECT.

REFERENCES:
Centre for Adverse Reactions Monitoring (CARM). Reporting on the Medical Warning System
Journal of pregnancy 2012
Medsafe Ferinject Datasheet for contraindications, warnings, and precautions
Medsafe Prescriber Update – March 2014
ASSOCIATED DOCUMENTS:

- Anaphylaxis Policy
- Medications – Safe Use of Medicines
- Medications - Allergies & Adverse Drug Reactions (ADRs) Identification, Documentation & Recording
- Intravenous and Related Therapies Policy

EVALUATION: By audit.

Date of Approval: 12/04/2018
Next Review Date: 13/04/2021
APPLICATION FOR SUBSIDY
BY SPECIAL AUTHORITY

Applicant: PATIENT NH: ___________________________ REFERRER Reg No: ___________________________

Name: ___________________________ Surname: ___________________________

Address: ___________________________ Address: ___________________________

Fax Number: ___________________________ Fax Number: ___________________________

Ferric carboxymaltose

INITIAL APPLICATION - serum ferritin less than or equal to 20 mg/L

Applications from any medical practitioner. Approvals valid for 3 months.

Prerequisites (tick boxes where appropriate)

☐ Patient has been diagnosed with iron-deficiency anaemia with a serum ferritin level of less than or equal to 20 mg/L.

☐ Patient has been compliant with oral iron treatment and treatment has proven ineffective

☐ Treatment with oral iron has resulted in dose-limiting intolerance

☐ Rapid correction of anaemia is required

RENEWAL - serum ferritin less than or equal to 20 mg/L

Current approval Number: (If known): ___________________________

Applications from any medical practitioner. Approvals valid for 3 months.

Prerequisites (tick boxes where appropriate)

☐ Patient continues to have iron-deficiency anaemia with a serum ferritin level of less than or equal to 20 mg/L.

☐ A re-take with oral iron is clinically inappropriate

INITIAL APPLICATION - iron deficiency anaemia

Applications only from an internal medicine physician, obstetrician, gynaecologist, anaesthetist or any other medical practitioner or the recommendation of a internist medicine physician, obstetrician, gynaecologist or anaesthetist. Approvals valid for 3 months.

Prerequisites (tick boxes where appropriate)

☐ Patient has been diagnosed with iron-deficiency anaemia

☐ Patient has been compliant with oral iron treatment and treatment has proven ineffective

☐ Treatment with oral iron has resulted in dose-limiting intolerance

☐ Patient has symptomatic heart failure, chronic kidney disease stage 3 or more or active inflammatory bowel disease and a trial of oral iron is unlikely to be effective

☐ Rapid correction of anaemia is required

See also: RENEWAL - iron deficiency anaemia p2

I confirm the above details are correct and that in signing this form I understand I may be audited.

Signed: ___________________________ Date: ___________________________

Post application to Ministry of Health, Private Bag 3813, Wanganui – Fax: 0800 190 131

Author: Obstetric HOD Date of first approval: March 2015
Authorised By: HOD Obstetrics Date last review completed: May 2018
Clinical Care Manager, Woman, Child & Youth Page: 8 of 10
Version 2
APPENDIX TWO

Pathway for Iron Supplementation in pregnant women 26-28 weeks gestation

- Ferritin >50 Hb >100 g/L
  - No iron tablets likely to be necessary
- Ferritin <50 but >15 Hb >100 g/L
  - Iron tablets required later in pregnancy
- Ferritin <15 Hb >100 g/L
  - Low dose iron tablets (1 Ferrotab/day)
    - Hb >70 g/L
      - Yes
        - High dose iron tablets (2 Ferrotabs/day)
    - No
      - Yes
        - Assess response after 4 weeks therapy: Ferritin and Hb
          - Hb <100g/L and Ferritin < 15 umol/l
            - No
              - Continue
            - Yes
              - IV Iron Recommended
          - Hb rise >15g/L
            - Yes
              - IV Iron Recommended
            - No
              - Continue
- IDA* No need for earlier delivery
- IDA* early delivery possible (e.g. IUGR)

*Iron deficiency anaemia (IDA)
Hb <100g/L and Ferritin < 15 umol/l

** Ferrotabs: 65mg elemental iron / 200mg tablet
**Fergradumet: 105 mg elemental iron / 325 mg tablet
(a funded alternative)
Pathway for Iron Supplementation in pregnant women ≥30 weeks gestation

IDA* in late gestation

30-34 weeks gestation

- Hb >70g/L
  - High dose Iron 2 FerroTabs/day
  - Assess response after 3 weeks therapy
    - Hb rise >10g/L
      - Yes: Continue
    - No: IV Iron recommended

- Hb <70g/L
  - *Iron deficiency anaemia (IDA)
    - Hb <100g/L and Ferritin < 15 umol/l

>34 weeks gestation

- Hb 90-99g/L
- Hb <90g/L
  - IV Iron recommended

**FerroTabs:
- 65mg elemental iron / 200mg tablet
**Ferogradumet:
- 105 mg elemental iron / 325 mg tablet
(a funded alternative)