1 Key Points

- Hb < 110g/L and ferritin < 30 microgram/L should be used for the purpose of diagnosing anaemia.
- Treatment should be according to:
  - Appendix 1 – Management of Iron Deficiency in Pregnancy
  - Appendix 2 – Management of Iron Deficiency in PPH/postnatal anaemia
  - Appendix 3 – Management of Iron Deficiency in the Gynaecology and Preoperative Settings
- If iron infusion is required, iron carboxymaltose is the preferred treatment option.
- For iron infusions, the patient information leaflet Iron Infusions should be provided.
- For iron infusions, a new 20g IV cannula is to be inserted into the best viable vein and a clear dressing applied to allow monitoring of the IV site and detect signs of extravasation. Avoid the back of the hand.

2 Purpose

This clinical guideline describes the diagnosis and management of iron deficiency in maternity and gynaecology patients. Anaemia is independently associated with morbidity, increased mortality and adverse perinatal outcomes.

3 Definitions

Iron deficiency: low iron stores (ferritin < 15 microgram/L) and reduced mean red corpuscular volume (MCV) < 80fL) but normal haemoglobin (Hb) concentration; or serum ferritin 15-30 microgram/L, plus two of the following: serum iron < 10 micromol/L; total iron binding capacity > 68 micromol/L; serum transferrin > 3.5g/L or transferrin saturation < 15% \(^1\)

Iron deficiency anaemia: low iron stores, reduced MCV and reduced Hb level.

Abbreviations

FBE – Full blood examination
Hb – Haemoglobin
HMB – Heavy menstrual bleeding
IDA – Iron deficiency anaemia
IBD – Inflammatory bowel disease
PPH – Postpartum haemorrhage
PRBC – Packed red blood cells

4 Responsibilities

All staff involved with the prescribing, dispensing and administration must be familiar with this guideline to ensure the safe and appropriate use of iron.

5 Guideline

4.1 Diagnosis of iron deficiency anaemia

There is no agreed normal range for haemoglobin (Hb) measurements in pregnant women in Australia. The Hb level associated with optimal maternal and perinatal outcomes is not known, however it is known that anaemia is associated with increased maternal morbidity and poor perinatal outcomes \(^5\).

Hb < 110g/L and ferritin < 30 microgram/L should be used for the purpose of diagnosing anaemia, please note this is different to the RWH laboratory ranges: first trimester 110-143g/L; second trimester 100-137g/L; third
Management of Iron Deficiency in Maternity and Gynaecology Patients

Guideline

trimester 98-137g/L and non-pregnant women 120-160g/L.

Ferritin

- The serum ferritin is the most readily available and useful measure of iron deficiency.
- Ferritin is an acute phase protein and is elevated in inflammation, infection, liver disease and malignancy. In these patients, iron deficiency may be present despite an elevated ferritin.
- Ferritin < 15micrograms/L indicates iron depletion in all stages of pregnancy.
- Treatment should be considered before iron deficiency develops when ferritin between 15-30micrograms/L.

4.2 *Indications for testing/screening*

**Pregnancy-screening**

All pregnant women have a full blood examination (FBE) in early pregnancy. Women with risk factors for iron deficiency should also have serum ferritin measured.

Risk factors for iron deficiency in pregnancy:

- Aboriginal and Torres Strait Islander women, adolescents, recent immigrants
- Women with past history of anaemia
- Multiparity ≥ P3; particularly if consecutive pregnancy < 1 year following delivery or last birth was complicated by PPH
- Vegetarian, vegan
- Low socioeconomic status.
- High risk of bleeding
- Women who will refuse transfusion or unable to access transfusion e.g. Jehovah’s Witness

All pregnant women have Hb (or FBE) measured at 28 weeks gestation. Those with anaemia or risk factors for iron deficiency should also have serum ferritin measured.

Check Vitamin B12 levels in the following patient groups:

- Life-long vegetarian/vegan diet
- Inflammatory bowel disease.
- Macrocytosis (elevated MCV)

In the majority of maternity patients, the cause of iron deficiency anaemia is inadequate dietary iron intake combined with iron demands of pregnancy and menstruation. If the woman has a history of rectal blood loss or gastrointestinal symptoms, referral to a gastroenterologist may be appropriate.

**Gynaecology-screening**

All women presenting with excessive menstrual bleeding or abnormal bleeding should be screened for IDA with FBE and serum ferritin.

When iron deficiency anaemia is diagnosed in post-menopausal women, evaluation for benign and malignant gastrointestinal lesions, inflammatory conditions (e.g. inflammatory bowel disease) and peptic ulceration is indicated. Results and need for further follow-up should be communicated to the woman and her General Practitioner.

**Surgical patients-screening**

In patients undergoing surgery, preoperative anaemia should be identified, evaluated and managed to minimize red cell transfusion.
4.3 Management of iron deficiency

Iron deficiency/ Iron deficiency anaemia in pregnancy

Dietary changes alone are insufficient to manage iron deficiency anaemia in pregnancy and iron therapy is necessary. Referral to a dietitian for advice to optimise dietary iron intake and absorption should also be considered.

The approach to iron therapy including selection of oral or intravenous therapy is outlined in Appendix 1.

Management of PPH/postnatal anaemia

FBE should be checked within 48 hours of delivery in all women with an estimated blood loss >500mL and in women with uncorrected anaemia in the antenatal period or symptoms suggestive of postpartum anaemia. Women with Hb < 100g/L, who are haemodynamically stable, asymptomatic, or mildly symptomatic, should be offered oral iron supplementation (100-200mg elemental iron daily) for at least 3 months and a repeat FBE and ferritin to ensure Hb and iron stores are replete⁴.

The approach to iron therapy including selection of oral or intravenous therapy is outlined in Appendix 1.

Management of excessive menstrual bleeding and preoperative settings

Menstrual loss and heavy menstrual bleeding increase the risk of iron deficiency and iron deficiency anaemia³. IDA should be treated along with measures to manage the excessive menstrual bleeding.

Preoperative iron deficiency anaemia may place a patient at increased risk of blood transfusion during surgery and adverse postoperative sequelae.

For treatment of iron deficiency in the gynaecology and preoperative settings⁷, refer to Appendix 3.

Blood transfusion

Blood transfusion for iron deficiency anaemia is only appropriate in severe anaemia where there are signs of cardiovascular compromise. Blood transfusion does not correct the iron deficit, hence, treatment with iron is also required. Refer to Blood transfusion administration guideline (adult)

4.4 Oral iron preparations

Oral iron supplementation is effective and safe option to replace iron. Multivitamins should not be used for the treatment of iron deficiency as they contain insufficient amounts of elemental iron. Oral iron supplements containing 100-200mg elemental iron daily should be recommended⁴, see Appendix 4.

GI upset may be reduced by taking the medicine with food, or at night, and by increasing the dose gradually. When a rapid rise in Hb is not required, intermittent dosing (1 tablet alternate days), or lower doses may reduce GI side-effects.

Commonly reported side effects of iron tablets include constipation, black stools, abdominal discomfort, nausea and vomiting. For nausea and epigastric discomfort, iron supplements with lower iron content should be recommended. Slow release and enteric coated forms should be avoided⁴.

Response to oral iron

Following administration of oral iron, haemoglobin level typically increase by 20g/L every 3-4 weeks or 1-2g/L per day³.

In women with established anaemia, the response to oral iron should be assessed within a few weeks after commencing treatment by measuring the Hb. Once the Hb level is in the normal range, replacement should continue for 3 months and until at least 6 weeks postpartum to replenish iron stores⁴.
In non-anaemic women repeat Hb and serum ferritin after 8 weeks of treatment to confirm response[4].

4.5 Parenteral iron therapy

Intramuscular iron injections tend to be painful and there is significant risk of permanent skin staining and is no longer recommended.

Intravenous iron therapy should be avoided in the first trimester of pregnancy due to uncertain fetal effect, but if IV iron is required in the first trimester, then iron sucrose is recommended.

Intravenous iron can be considered in the following circumstances:

- Demonstrated intolerance, non-compliance or lack of efficacy with oral iron
- Severe anaemia, to avoid imminent decompensation/transfusion
- Ongoing blood loss that exceeds the capacity of oral iron to meet needs e.g. heavy uterine bleeding
- Women with anticipated significant surgical blood loss likely to require transfusion, e.g. placental adhesive disorders in the maternity setting, resection of major endometriosis or myomectomy in the gynaecology setting
- Moderate-severe postpartum anaemia, where rapid restoration of Hb is required
- Where absorption of oral iron is likely to be impaired
  - Surgery: bariatric
  - Medicines: calcium
  - Concurrent illness: inflammatory states, IBD, renal disease, helicobacter pylori infection

IV iron results in more rapid restoration of Hb and iron stores than oral iron, however levels of Hb are equivalent at 3 months (3).

4.6 Treatment choice

- Iron carboxymaltose is the preferred intravenous iron infusion at the Women’s.
- All iron infusions administered on the day of discharge or in the outpatient settings (including administration in PDC) are required to be accompanied by a discharge/outpatient prescription as well as a record of administration documented in EPIC.

4.7 Intravenous iron dose

All dosages should be prescribed in milligram (mg) of elemental iron. There are several methods for calculating the dose of iron required to replete the patient’s total body iron deficit. The simplified method is preferred.

**Total body iron deficit:**

<table>
<thead>
<tr>
<th>Hb(g/L)</th>
<th>Body weight 35 kg to &lt; 70 kg*</th>
<th>Body weight ≥ 70 kg*</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥ 100</td>
<td>1,000 mg of elemental iron</td>
<td>1,000 mg of elemental iron</td>
</tr>
<tr>
<td>&lt; 100</td>
<td>1,500 mg of elemental iron</td>
<td>2,000 mg of elemental iron</td>
</tr>
</tbody>
</table>


**Maximum dose for iron carboxymaltose is 1000mg per infusion.** A second dose the following week is required if the total body iron deficit exceeds 1000 mg.

**Maximum dose for iron sucrose is 500mg per infusion.** Give multiple weekly dose until the total iron deficit is reached.
4.8 Pre-Administration Preparation

- A patient information leaflet should be provided to the patient
- Take care with placement of the IV cannula and avoid the back of the hand. Use the best viable vein
- Ensure a new 20 gauge cannula is inserted for the infusion and check for draw back
- Ensure the IV site remains visible so early signs of extravasation can be identified
- Use a clear dressing over IV insertion site

4.9 Administration

<table>
<thead>
<tr>
<th></th>
<th>Iron carboxymaltose</th>
<th>Iron sucrose</th>
<th>Iron polymaltose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Elemental iron concentration</td>
<td>50mg/mL</td>
<td>20mg/mL</td>
<td>50mg/mL</td>
</tr>
<tr>
<td>Maximum dose in a single administration</td>
<td>Do not exceed 1000mg once a week</td>
<td>Given weekly in divided (500mg) doses until the total iron deficit is reached</td>
<td>2000mg</td>
</tr>
<tr>
<td>Preparation of dose</td>
<td>Dilute 500-1000mg to in 100mL of 0.9% sodium chloride</td>
<td>Dilute 500mg in 500mL of 0.9% sodium chloride</td>
<td>Dilute the calculated dose (up to 2000mg) in 500mL of 0.9% sodium chloride</td>
</tr>
<tr>
<td>Rate of administration</td>
<td>Infuse dose over 15 minutes</td>
<td>First 20mg of iron sucrose (20mL of diluted solution) should be infused over 15 minutes. If tolerated, increase to a rate of not more than 50mL/15 minutes</td>
<td>Infuse at an initial rate of 40mL/hour for 15 minutes, if tolerated, increase rate to 100mL/hour</td>
</tr>
<tr>
<td>Common adverse reactions</td>
<td>Flushing, sweating, chills and fever; chest and back pain</td>
<td>Transient taste perversion, hypotension, fever and shivering, injection site reactions and nausea</td>
<td>Headache, dizziness, hypertension, flushing, nausea, injection/infusion site reactions</td>
</tr>
</tbody>
</table>

4.9.1 Extravasation

Flush IV cannula with 50mL of 0.9% sodium chloride before and after iron infusion to minimise the risk of extravasations

- **Extravasation** - Alert to extravasation at all times and monitor IV site throughout infusion. Paravenous leakage of IV iron products should be avoided. Patients should be instructed to report pain at the IV site during infusion, and the site should be inspected if pain is reported. Leakage may cause long lasting brown discolouration, pain, inflammation, tissue necrosis and sterile abscess. Ice may be applied to cause local vasoconstriction and decrease fluid absorption. Massage of the area should be avoided.

- **Figure below of permanent stained skin post iron infusion**
Patients with multiple drug allergies may be at higher risk of developing adverse reactions. Premedications should be prescribed for patients who have had a previous reaction to iron. The recommended premedications are:

- Hydrocortisone 100mg IV and
- Loratadine 10mg orally

- If any adverse reaction occurs, the infusion must be stopped and the duty registrar called for assessment. Consider a MET call/Code Blue as determined by the severity of the adverse reaction
- *Anaphylaxis should be managed as per the procedure: Anaphylaxis Management of and Adrenaline Standing Orders Procedure.

4.10 Monitoring

- Take baseline vital signs – heart rate (HR), respiratory rate (RR), blood pressure (BP), temperature and oxygen saturation
- Iron carboxymaltose: Repeat observations at the completion of infusion and monitor patient for 30 minutes afterwards
- Iron sucrose: after initial test dose and then every 30 minutes until completion of the infusion and monitor patient for 30 minutes afterwards
- Iron polymaltose: during IV infusion monitor the baseline vital signs every 5 minutes during the initial rate and then every 15 minutes during infusion and monitor patient for 30 minutes afterwards
- If no side effects observed then no further monitoring is required.
- If side effects observed, contact treating doctor and monitor patient accordingly

4.11 Precautions

Iron therapy should not be used in the setting of iron overload conditions. Recurrent IV infusions are not generally recommended as the risk of iron toxicity is increased. In patients with recurrent iron deficiency, the cause of iron deficiency anaemia should be addressed.

Oral iron after an iron infusion is not generally required if the total iron deficit has been calculated and adequate IV iron prescribed.
4.12 Follow-up Testing and referral

- The response to iron preparation should be assessed with follow-up testing (FBE).

<table>
<thead>
<tr>
<th>Preparations</th>
<th>Anticipated effects</th>
<th>Follow-up testing</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oral iron</td>
<td>3-4 weeks after starting oral iron Hb increase by 10g/L or more suggests adequate absorption</td>
<td>FBE in 4 weeks after the commencement of oral treatment</td>
</tr>
<tr>
<td>IV iron</td>
<td>Hb should rise within 2-3 weeks</td>
<td>FBE in 2-3 weeks after the commencement of IV treatment</td>
</tr>
</tbody>
</table>

- In circumstances where serum ferritin level greater than 100microgram/L, possible anaemia of chronic disease or inflammation, or other cause, seek advice from haematologist (7).

5 Evaluation, monitoring and reporting of compliance to this guideline

Compliance to this guideline will be evaluated and reported through monitoring and reporting the following incidents to the Medicine Safety Committee on a monthly basis:

- Number, severity and outcome of incidents involving medicines
- Number, severity and outcome of side effects, allergic and anaphylactic reactions.

6 References


7 Legislation/Regulations related to this guideline

Not applicable.
8 Appendices

Appendix 1 – Management of Iron Deficiency in Pregnancy
Appendix 2 – Management of Iron Deficiency in PPH/postnatal anaemia
Appendix 3 – Management of Iron Deficiency in the Gynaecology and Preoperative Settings
Appendix 4 - Oral iron supplements available in Australia

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Management of Iron Deficiency in Pregnancy

Hb ≤ 110g/L

Is ferritin level <30microgram/L?

Suspect cause other than isolated iron deficiency

First trimester
Second trimester
Third trimester

Oral iron supplements

Able to tolerate oral iron supplement? Hb increase ≥ 10g/L

If > 34 weeks gestation with severe anaemia and need for rapid restoration of iron stores

IV iron

If no significant change or drop in Hb

Continue oral iron

Recheck FBE and ferritin
### Management of PPH/postpartum anaemia

<table>
<thead>
<tr>
<th>Hb &lt; 70 g/L</th>
<th>1-2 units of PRBC + IV iron</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hb 70-90 g/L</td>
<td>IV iron, consider 1 unit of PRBC for significant symptomatic anaemia – consult haematologist</td>
</tr>
<tr>
<td>Hb &gt; 90 g/L</td>
<td>Oral iron supplements</td>
</tr>
</tbody>
</table>

IV iron should be given on the day of discharge if clinically appropriate.
Appendix 3

Management of iron deficiency in the gynaecology and preoperative settings

Hb ≤ 110g/L

yes

Ferritin > 30microg/L
Low risk
- Minor procedure (expected blood loss unlikely to lead to transfusion)
- Time to procedure > 30 days
- No significant ongoing blood loss

Ferritin < 30microg/L
High risk
- Major procedure (expected blood loss likely to lead to transfusion)
- Time to procedure < 30 days
- Blood refusal
- Significant ongoing blood loss

Oral iron supplementation

Able to tolerate oral iron supplement?

yes

Continue oral iron

Recheck Hb and ferritin

no

Consider iron studies if concerns of active inflammation/malignancies

IV iron (outpatient setting or upon discharge if clinically appropriate)
# Appendix 4

## Oral iron supplements available in Australia

<table>
<thead>
<tr>
<th>BRAND NAME</th>
<th>FORMULATION</th>
<th>ELEMENTAL IRON CONTENT</th>
<th>OTHER ACTIVE INGREDIENTS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ferro-Grad®</td>
<td>325mg ferrous sulfate controlled release tablet</td>
<td>105 mg</td>
<td>Nil</td>
</tr>
<tr>
<td>Ferrograd C®</td>
<td>325mg ferrous sulfate controlled release tablet</td>
<td>105 mg</td>
<td>Ascorbic acid 500mg</td>
</tr>
<tr>
<td>Ferro-f-tab®</td>
<td>310mg ferrous fumarate Tablet</td>
<td>100 mg</td>
<td>Folic acid 350micrograms</td>
</tr>
<tr>
<td>Fefol®</td>
<td>270mg ferrous sulfate controlled release capsule</td>
<td>87.4 mg</td>
<td>Folic acid 300micrograms</td>
</tr>
<tr>
<td>Ferro-grad F®</td>
<td>250mg ferrous sulfate controlled release tablet</td>
<td>80 mg</td>
<td>Folic acid 300micrograms</td>
</tr>
<tr>
<td>Ferro-tab®</td>
<td>200mg ferrous fumarate Tablet</td>
<td>65.7 mg</td>
<td>Nil</td>
</tr>
<tr>
<td>Ferro-liquid®</td>
<td>30mg/mL Ferrous sulfate oral liquid</td>
<td>6mg/mL</td>
<td>Nil</td>
</tr>
<tr>
<td>Maltofer Syrup®</td>
<td>37mg/mL Iron polymaltose complex syrup</td>
<td>10mg/mL</td>
<td>Ethanol 3.25mg/mL</td>
</tr>
<tr>
<td>Maltofer tablet®</td>
<td>370mg Iron polymaltose complex tablet</td>
<td>100mg</td>
<td>Nil</td>
</tr>
</tbody>
</table>

Ferro-Grad®, Ferro-f-tab® and Ferro-liquid® are the oral iron preparations available at the Women’s.