INTRAVENTOUS IRON POLYMALTOSE THERAPY (FERROSIG®)

AIM

To provide best practice requirements for the administration and management of intravenous iron (IV) polymaltose therapy.

BACKGROUND

IV iron infusion may be used to augment haemoglobin levels in patients with identified iron deficiency anaemia who have failed to respond sufficiently to oral iron; or in patients whom a rapid repletion of iron stores is required as a result of a large blood loss or impending blood loss.\(^1,2,3\)

Anaemia is defined as $\text{Hb} < 110\,\text{g/L}$ in first and third trimester, $<105\,\text{g/L}$ in 2nd trimester of pregnancy and $<100\,\text{g/L}$ in the postpartum period. In non-pregnant adult women anaemia would be classified as $\text{Hb} < 120\,\text{g/L}$ as per World Health Organisation categories.\(^4\) A serum ferritin level of less than $30\,\text{ug/L}$ for an adult is diagnostic of iron deficiency. Other markers of iron function including serum iron and % transferrin saturation are not a reliable measure of iron status as they are affected by diurnal patterns or have limited reference ranges for pregnancy and a lack of standardisation.\(^1,2,4\)

While safe in experienced hands, there is still an incidence of significant reactions and complications, both immediate and delayed, which includes the potential of an increased risk to infection.\(^6, 7, 8, 9\) The use of IV iron is associated with a transient decrease in plasma phosphate and increase in fibroblast growth factor-23,\(^10, 11\) which has been linked to an increased risk of cardiovascular events in long term use of IV iron in patients with chronic kidney disease.\(^12\) The impact of hypophosphatemia in pregnancy or non-pregnant women has not been formally evaluated, thus it is important to balance the risks versus the benefits of treatment with IV iron.

Intravenous 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 production.\(^14\)

There are a number of medications whose efficacy is reduced or toxicity is increased (increasing the risk of adverse reactions) with the use of iron polymaltose (IP) therapy as indicated in table 1. This should be factored in the decision to use IV iron, particularly in women with hypertension, hypothyroidism, infection and metabolic bone disorders.
### Table 2 Drug interactions

<table>
<thead>
<tr>
<th>Drug</th>
<th>Interaction effect</th>
</tr>
</thead>
<tbody>
<tr>
<td>Methyldopa, Levodopa</td>
<td>IP ↓ effect of Methyldopa and Levodopa</td>
</tr>
<tr>
<td>Thyroxine sodium, Liothyronine sodium</td>
<td>IP ↓ effect of Thyroxine sodium</td>
</tr>
<tr>
<td>Doxycycline monohydrate</td>
<td>IP has its effect ↓ by, and ↓ the effect of Doxycycline monohydrate</td>
</tr>
<tr>
<td>Doxycycline</td>
<td>IP has its effect ↓ by, and ↓ the effect of Doxycycline</td>
</tr>
<tr>
<td>Tetracycline hydrochloride</td>
<td>IP has its effect ↓ by, and ↓ the effect of Tetracycline hydrochloride</td>
</tr>
<tr>
<td>Doxycycline hydrochloride</td>
<td>IP has its effect ↓ by, and ↓ the effect of Doxycycline hydrochloride</td>
</tr>
<tr>
<td>Minocycline hydrochloride</td>
<td>IP has its effect ↓ by, and ↓ the effect of Minocycline hydrochloride</td>
</tr>
<tr>
<td>Penicillamine</td>
<td>IP may ↓ the absorption of Penicillamine</td>
</tr>
<tr>
<td>Ofloxacin, Moxifloxacin</td>
<td>IP ↓ effect of Ofloxacin, Moxifloxacin and Ciprofloxacin</td>
</tr>
<tr>
<td>Chloramphenicol</td>
<td>IP has its effect ↓ by Chloramphenicol</td>
</tr>
<tr>
<td>ACE inhibitors i.e. Ramipril, Captopril etc*</td>
<td>IP has its toxicity ↑ by ACE inhibitors</td>
</tr>
<tr>
<td>Agents affecting calcium &amp; bone metabolism i.e. Alendronic acid*</td>
<td>IP may ↓ absorption of a Agents affecting calcium &amp; bone metabolism</td>
</tr>
<tr>
<td>Hypolipidaemic agents i.e. Cholestyramine*</td>
<td>IP may have its serum concentration ↓ by hypolipidaemic agents</td>
</tr>
</tbody>
</table>

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

### INDICATIONS

Intravenous iron may be appropriate in:

- Iron deficiency anaemia (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.\(^1,2,3\)

- Functional iron deficiency when stored iron cannot be released for erythropoiesis.\(^1,6\) 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 intravenous 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.

- Contact the Haematologist if there are any doubts concerning the indications for intravenous iron infusion.

- Patients with haemoglobinopathy disease frequently present with moderate to severe anaemia, which may be related to iron deficiency and may benefit from treatment. However some patients present with hyperferritinaemia and...
intravenous iron would be contraindicated. Interpretation of laboratory tests and management is complex and these patients should be discussed with a Haematologist if there are any concerns.

**CONTRAINDICATIONS**

- Anaemia not due to iron deficiency (i.e. B12 deficiency, haemolytic anaemia, bone marrow disease or disturbances in erythropoiesis)  
- First trimester of pregnancy
- Hypersensitivity to iron polymaltose
- Chronic poly arthritis
- Acute renal infection
- Uncontrolled hyperparathyroidism
- Infectious hepatitis
- Less than 14 years of age
- Iron overload (i.e. haemochromatosis)
- Asthma

**PRECAUTIONS**

- Allergy
- Previous adverse reaction to other forms of parenteral iron
- Current bacterial infection
- Concomitant administration of angiotensin converting enzymes (ACE) inhibitors may increase the incidence of adverse effects of intravenous iron including erythema, abdominal cramps, nausea, vomiting and hypotension
- Patients with rheumatoid arthritis and other inflammatory diseases may be at particular risk of delayed reaction including fever and reactivation of joint pain

**DOSAGE**

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%  

\[ \text{Dose} = \text{Current weight} \times (1 - 0.1) \]

i.e. If current weight is 50k, then the dose weight calculation would be 50 – 5 = 45k (See table 2).
Table 2 Dosage Table

Each ampoule contains elemental iron 100mg in 2 mL, (in the form of iron polymaltose 318mg/2mL).
The infusion is to be ordered as elemental iron, not iron polymaltose.

<table>
<thead>
<tr>
<th>Body Weight</th>
<th>Hb 60g/L</th>
<th>Hb 75g/L</th>
<th>Hb 90g/L</th>
<th>Hb 105g/L</th>
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</thead>
<tbody>
<tr>
<td>kg</td>
<td>*mg</td>
<td>mL</td>
<td>amps</td>
<td>*mg</td>
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<td>22</td>
<td>11</td>
<td>1000</td>
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</tr>
<tr>
<td>90+</td>
<td>1800</td>
<td>36</td>
<td>18</td>
<td>1500</td>
</tr>
</tbody>
</table>

*mg indicates elemental iron, not iron polymaltose
amps = number of ampoules

DURING PREGNANCY THE MAXIMUM DOSE IS 1000MG ELEMENTAL IRON

- IV iron polymaltose shall not be mixed with other drugs or with solutions other than 0.9% sodium chloride
- Hand hygiene shall be performed prior to and after contact with the patient or equipment
- The iron shall not be injected into the tubing of the IV giving set
- Regardless of the dose to be administered, the iron shall be added to 500mL 0.9% Sodium Chloride
- Do not administer IV iron if the patient is receiving intravenous antibiotics in treatment of acute bacterial infection, it can be considered following cessation of intravenous antibiotics and is dependent upon the patient’s condition.

TEST DOSE AND INFUSION RATES

All patients require a test dose of iron polymaltose, as anaphylactoid reactions are most likely to occur in the first few minutes of the infusion\(^5\). In order for this to be administered, prime the infusion line with IV polymaltose to the cannula and administer at a rate of 50mL an hour for 5 minutes.
Test dose & infusion rate (Iron added to 500mL 0.9% normal saline)

| Infusion rates in pregnancy | Commence at 50mL/hour for first 5 minutes **IF NO REACTION OCCURS**
|                           | Increase rate to 250mL/hour for the remainder of the infusion
|                           | (Total infusion time approximately 125min) |

| Infusion rates (non-pregnant) | Commence at 50mL/hour for first 5 minutes **IF NO REACTION OCCURS**
|                              | Increase rate to 375mL/hour for the remainder of the infusion
|                              | (Total infusion time approximately 85min) |

If the woman experiences an adverse reaction, cease the infusion for a while and see below adverse reaction.

**ADMINISTRATION PROCEDURE**

1. The iron polymaltose infusion should be prescribed on the woman’s Intravenous Fluid and Additive Order Sheet by a Medical Officer.

2. If there is 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 intravenously.

3. 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 iron infusion.

4. Educate the woman about the possible adverse reactions both immediate and delayed.

5. The initial 5 minutes of any iron polymaltose infusion shall be given at a slow rate as a test dose to exclude adverse reactions (see above).

Adverse reactions may include
- Itch and Urticaria
- Bronchospasm/ dyspnoea
- Back, joint or muscle pain
- Nausea, indigestion, abdominal pain
- Headache
- Hypotension
- Tachycardia
- Syncope
- Circulatory collapse

Adverse reactions may be more likely in women with a history of asthma and/or other allergic conditions.

6. The woman 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:

- Respiratory rate
- Oxygen saturation
- Heart rate
- Blood pressure
- Temperature
- Conscious state
- Pregnant women should have a foetal heart rate recorded before the start of the infusion and if any adverse event occurs should have a CTG undertaken. The foetal heart rate should be recorded at the end of the infusion, prior to discharge home.

8. The observations shall be performed

- Prior to commencement of the infusion
- Repeated at 15 minutes (on completion of the test dose), then
- Every 60 minutes

Notify the Medical Officer if any of the vital signs change significantly.

9. On completion of the iron infusion, flush the giving set with 50mL sodium chloride. This should be given at the same rate as the iron infusion.

10. At the end of the infusion the woman shall remain on the unit for a further 30 minutes. If no adverse symptoms occur, the woman may be discharged. If symptoms do occur, notify the medical officer immediately to review the woman.

11. On discharge the woman 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).

**ADVERSE REACTION**

1. STOP the infusion.

2. Perform and record observations as indicated by the woman’s clinical condition including

   - Respiratory rate
   - Oxygen saturations
Heart rate
Blood pressure
Temperature
Conscious state
Foetal 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 intravenous iron.

5. Hypotension in the pregnant woman: The patient should be placed in the full left lateral position to relieve any aortocaval compression and foetal 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: http://wnhs.hdwa.health.wa.gov.au/__data/assets/pdf_file/0013/101515/0562_BS_with_Disclaimer.pdf

They should be instructed not to take any oral iron for 7 days post iron infusion. Pregnant and post-natal women should be encouraged to continue with oral iron supplements until breastfeeding is complete.

It is important that a follow-up full blood picture and iron studies are obtained one month post-IV iron infusion 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 intravenous iron 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.

**REFERENCES (STANDARDS)**

1. Pasricha S-R et al. Diagnosis and management of iron deficiency anaemia: a clinical update. MJA 2010 Nov; 193(9):525-532
7. Ferrosig Injection MIMS Full Prescribing Information 2006

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

**RESPONSIBILITY**

<table>
<thead>
<tr>
<th>Policy Sponsor</th>
<th>HoD Haematology</th>
</tr>
</thead>
<tbody>
<tr>
<td>Initial Endorsement</td>
<td>May 2009</td>
</tr>
<tr>
<td>Last Reviewed</td>
<td>July 2015</td>
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<tr>
<td>Last Amended</td>
<td>July 2016</td>
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