Iron in Pregnancy and Post-Partum

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• Directorate(s)	Women's Health
• Department(s)	Maternity (including outliers)
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• Used by which staff?	All clinicians in maternity, including Access Holder Lead Maternity Carers (LMCs)
• Excluded	
Keywords	
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1. Purpose of guideline

The purpose of this guideline is to provide guidance for prescribing iron in pregnancy and post-partum, wherever indicated. This applies to all clinicians, midwifery and nursing practitioners within Te Toka Tumai Auckland. Oral iron is the first line of therapy in the majority of circumstances and a clinical pathway is included to guide the most appropriate management.

A New Zealand study by Calje and Skinner concluded that in the population studied, a high percentage of women approached birth with a low or unknown iron status, and this continued into the post-partum period. Our aim is to address any variations occurring within our District, to support LMC's to achieve consistency for women birthing and post-partum.

2. Background

2.1 Prevalence

Pregnant women are particularly vulnerable. Risk factors also include a vegetarian diet, multiple pregnancies, adolescent pregnancies, low socioeconomic status and short pregnancy intervals. The World Health Organisation is working to reduce anaemia in women of reproductive age by 50% in 2025 as part of the Comprehensive Implementation Plan on maternal, infant and young child nutrition - endorsed by the Sixty-fifth World Health Assembly.

A report titled "The Global Prevalence of Anaemia in 2011" estimated the prevalence of anaemia in ***pregnant women*** was 38.2% and for ***all women*** of reproductive age was 29.4%. In the same report, meta-analyses suggest that iron supplementation would increase the mean blood haemoglobin (Hb) concentration by 10.2 g/L (95% CI: 6.1—14.2) in pregnant women and applying these shifts to estimated blood Hb concentrations indicates that about 50% of anaemia in women ***could be eliminated by iron supplementation***.

2.2 Impact

Iron deficiency anaemia (IDA) in pregnancy may be associated with low birth weight and increased risk of maternal and perinatal mortality. Iron is essential for foetal brain development. Maternal iron status may affect birth stores in the infant, and infants born to anaemic mothers are more vulnerable to anaemia during their first year of life. There are correlations between maternal and infant measures of iron status near the time of birth – all providing evidence that in utero factors influence infant iron status. However, based on current evidence it is uncertain what impact maternal postpartum Hb and iron status have on infant parameters after birth.

Maternal iron deficiency (ID) / IDA can also affect work productivity, cognition, including post-natal depression and effects on bonding, poor wound healing, as well as fatigue.

Correction of anaemia prior to birth will reduce the risks associated with blood transfusion.

3. Investigations

3.1 Investigations to establish iron status in pregnancy

Assay FBC and serum ferritin to establish the diagnosis of ID/IDA before any treatment with oral or IV iron.

Ferritin is an acute phase protein that can be raised in inflammatory conditions and ID may still be present with ferritin values up to 100 microgram/L. Occasionally, it will be necessary to assay CRP and other iron indices (such as transferrin, total iron binding capacity (TIBC), transferrin saturation

(TSAT), soluble transferrin receptor, serum iron, and reticulocyte Hb content) in interpretation of iron status. Seek advice from a haematologist or physician if unsure how to proceed.

3.2 When to do iron status investigations in pregnancy

RANZCOG do not currently recommend routine antenatal ferritin screening, but do advise FBC at the first antenatal visit and at 28 weeks. This may lead to a missed opportunity to identify and correct ID before anaemia develops.

At Te Toka Tumai we suggest ferritin testing at booking, around 28 weeks or at other points in the pregnancy, if there are additional risk factors. Risk factors would include refusal of blood transfusion, RBC antibodies or prior evidence or suspicion of ID/IDA that could occur with vegetarian diet, multiple pregnancies, adolescent pregnancies, low socioeconomic status and short pregnancy intervals.

4. Initial therapy with oral iron

4.1 Initial Treatment of ID/IDA

Oral iron supplementation is the first line treatment in most situations; refer to the flowcharts for guidance.

As the gestation advances, the need to replenish iron stores becomes more urgent, and an early diagnosis of ID enables early treatment. We encourage consideration of investigation in the second trimester, and treatment if clinically indicated. For treatment in the second trimester follow the 26-29 weeks flow chart.

4.2 When to give oral iron

If iron deficiency anaemia exists, this is an indication to start oral iron supplementation.
An Hb level of less than 110 g/L in pregnancy is considered to represent anaemia and a ferritin <15ug/L is considered to represent depleted iron stores.

4.2.1 What oral formulation to use

It is worth noting that once an individual has ID or IDA, increasing the intake of foods rich in iron will not be adequate to replace the deficit. Iron supplements will be required.

Recommended iron supplements:

- Ferro-Tab (ferrous fumarate 200 mg = 65 mg of elemental iron)

OR

- Ferrograd/Ferrogradumet (ferrous sulphate 325 mg = 105 mg of elemental iron)

are the recommended oral treatment. Both are available over the counter or on prescription.

5. Parenteral iron (iron infusion)

Intravenous (IV) iron infusion is the preferred method for administration of parenteral iron. Exercise caution with any form of IV iron and be aware of potentials risks of extravasation and permanent skin discolouration (see later).

Intramuscular administration is not recommended.

5.1 When to give IV Iron

Refer to the guidance on the flow charts but generally, IV iron infusion is indicated in iron deficiency anaemia (IDA) when:

- There is inadequate response or intolerance to oral iron
- The time frame for response is too short for oral iron to be effective e.g. too late in the pregnancy/close to delivery
- Severe anaemia or other risk factors exist
- PPH/APH has occurred
- There is inability to ingest an adequate oral dose (e.g. ongoing bleeding or in the first few weeks post operatively where absorption is reduced)
- There is anaemia with impaired iron utilization (e.g. severe renal failure).

There is currently no safety data regarding the use of IV iron during the first trimester. In most cases, IDA in the first trimester can be treated with oral iron.

5.2 What IV formulation to use

Ferric carboxymaltose (Ferinject®) is the preferred IV iron infusion formulation at Te Toka Tumai for pregnancy and postpartum.

Iron polymaltose may be considered postpartum where larger doses of parenteral iron are required (for example, major obstetric haemorrhage).

6. Post-partum considerations

Post-partum, iron stores are more rapidly replaced with IV iron. This is particularly relevant if there is pre-existing ID/IDA or if there has been a post-partum haemorrhage (PPH). It is also worth noting that post surgery the inflammatory response affects oral absorption of iron for two to three weeks whereas IV iron is still effective.

Refer to section 13 for details regarding total dosage of parenteral iron.

7. Follow up

A follow up Hb and ferritin should be done 2 – 3 weeks after starting oral iron therapy. See flowcharts 4 and 5.

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

A follow up FBC should be taken 2 weeks after last IV iron dose. If, after the follow up blood test, the woman requires further iron treatment, or if otherwise unsure how to proceed at any time, consult with an Obstetrician or Obstetric Physician.

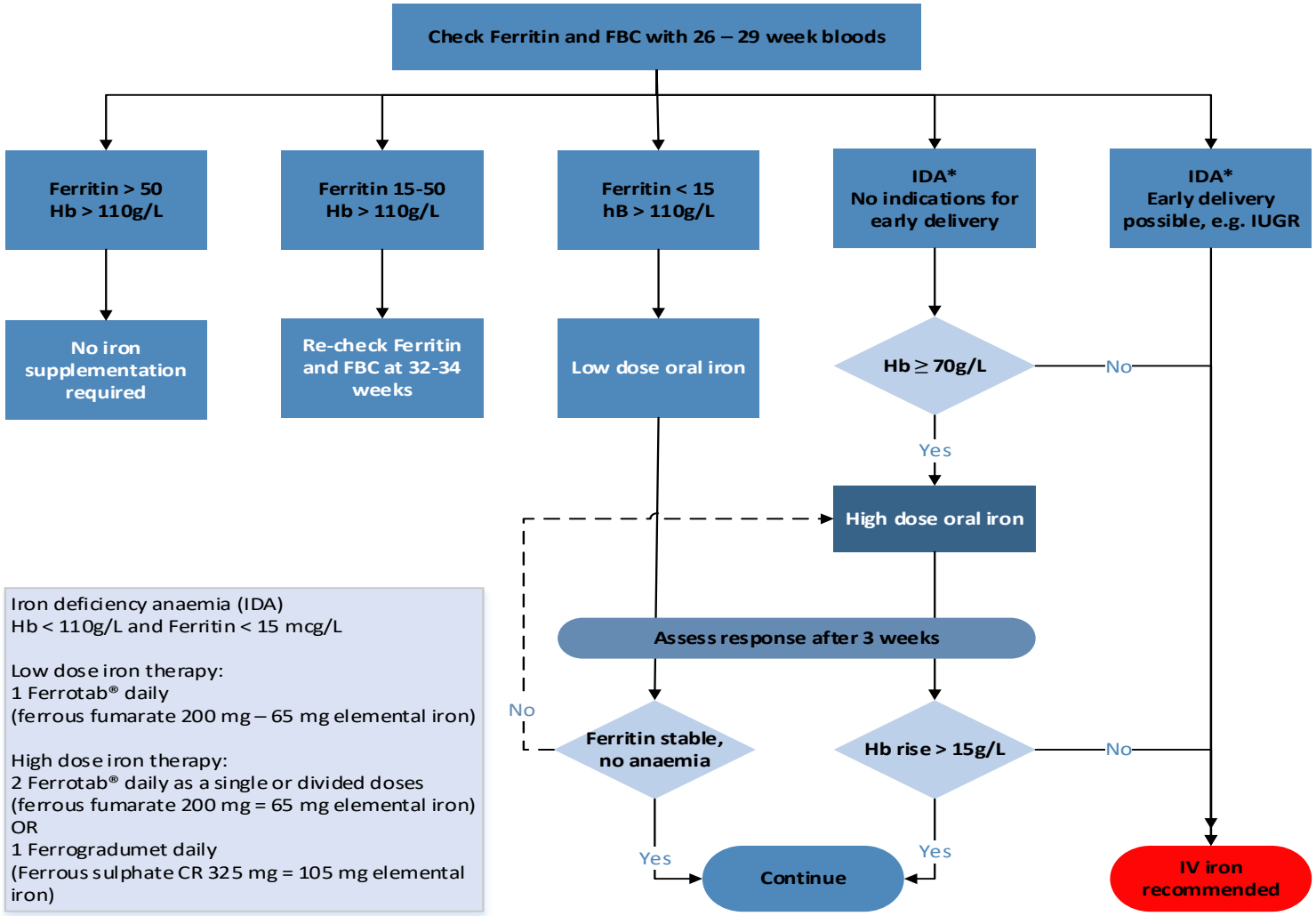
8. Prescribing in Pregnancy

A CR9048: IV Iron Prescribing Checklist must be completed before prescribing intravenous iron in pregnancy (see Associated documents). Please ensure that the latest version of the checklist is used.

The Prescribing Checklist should be completed by the referring clinician if a virtual consultation is planned. Otherwise it should be completed by the reviewing doctor at the time of face to face consultation.

Once prescribed, in accordance with the Te Toka Tumai Auckland 'Medications–Prescribing' policy, this medication should be administered and documented in accordance with the Te Toka Tumai Auckland 'Medications – Administration' policy (see Associated documents section).

9. Flowchart: Pathway for iron supplementation in pregnancy starting at 26 – 29 weeks



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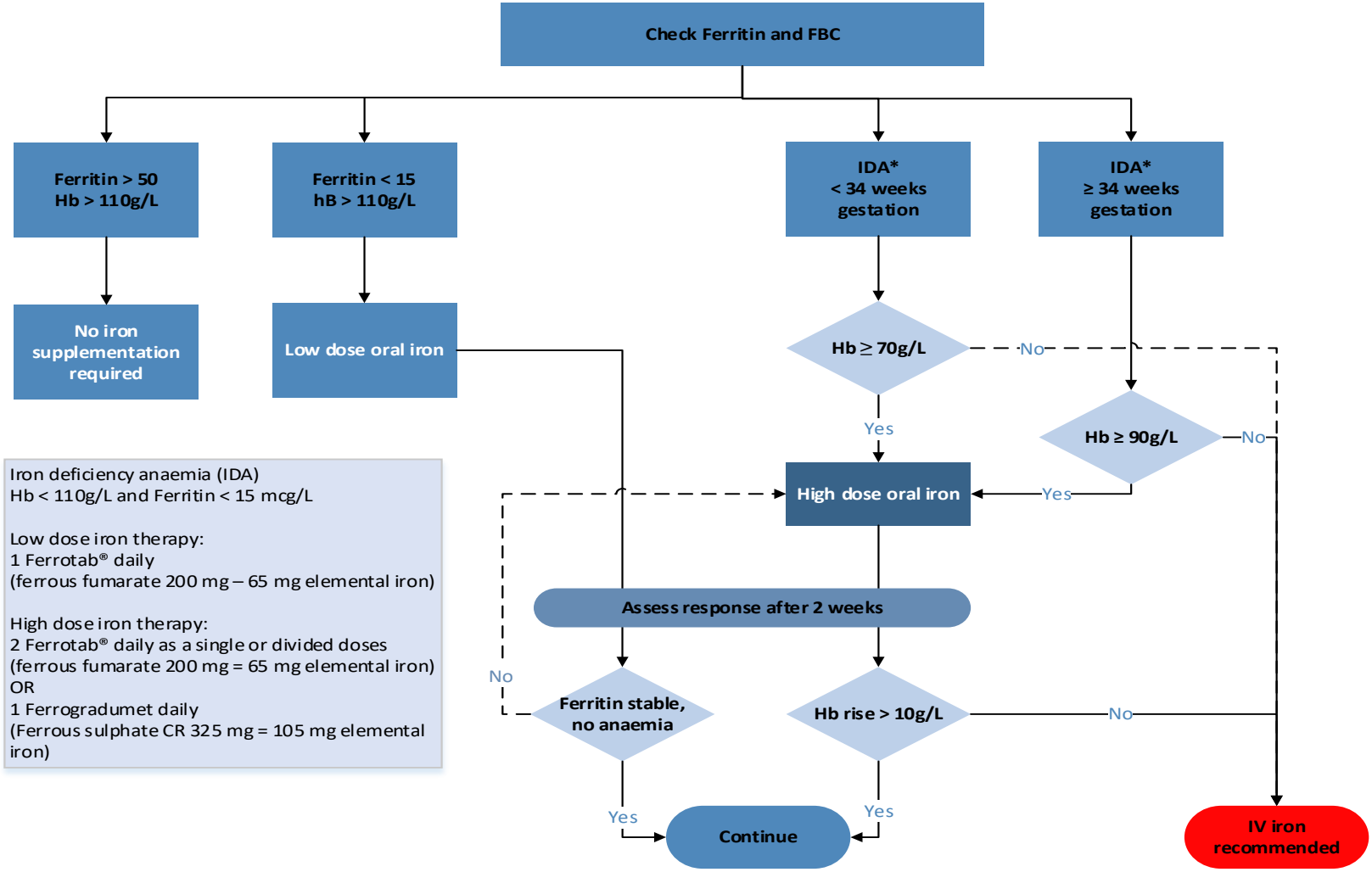
10. Flowchart: Pathway for iron supplementation in pregnancy starting at ≥ 30 weeks

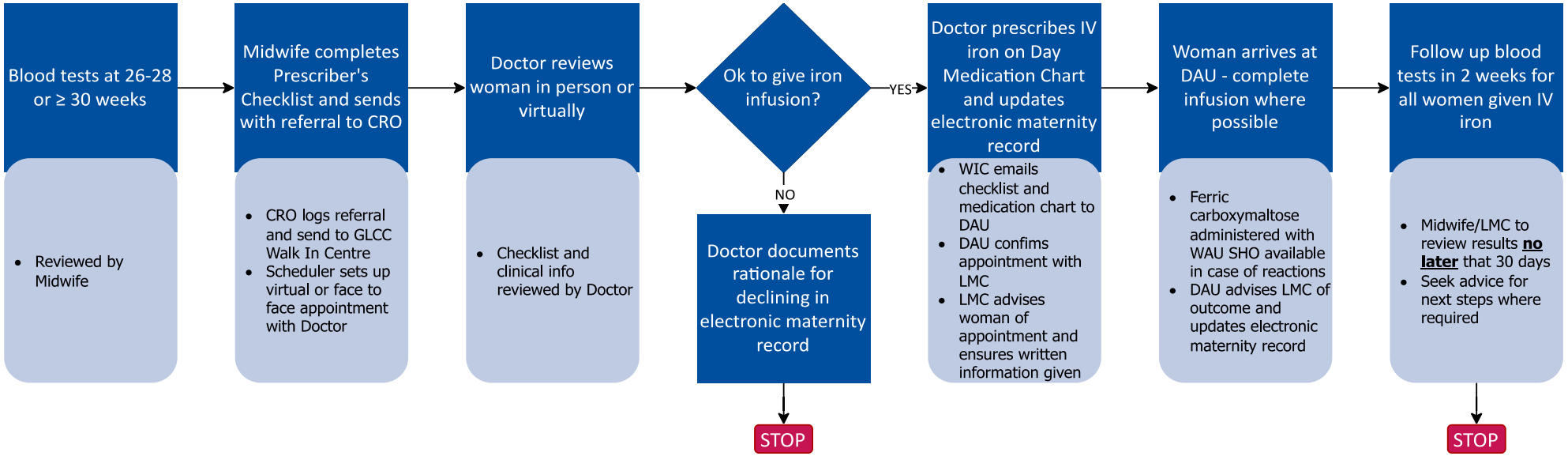


11. Summary statements

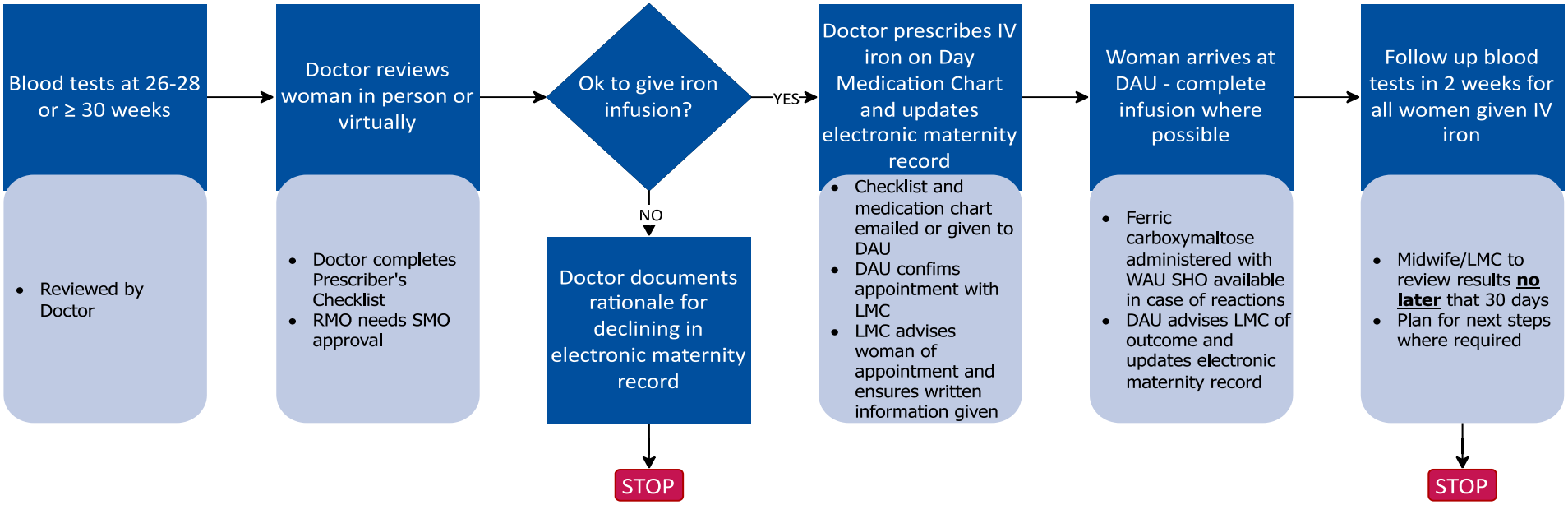
- Oral iron therapy is usually the most appropriate iron therapy to start initially.
- For second trimester iron supplementation for ID/IDA follow the 26-29 week flowchart – the aim is to recognise and treat early.
- Alternate day oral iron may be better tolerated in some women compared to daily supplementation and may be sufficient to avoid iron infusion.
- If Hb < 70g/L this indicates severe anaemia and iron infusion is indicated. Otherwise, follow the pathway according to Hb and ferritin levels and assess response to oral iron as indicated by the flow charts.
- If the rise in Hb is not adequate after 2-3 weeks of oral iron, iron infusion is recommended.
- IV iron takes 10-14 days to make any meaningful Hb rise – late referral and treatment should be avoided.
- Some pregnant women will require closer monitoring of Hb and iron stores than indicated in the flow charts. Examples would be those women who refuse a blood transfusion, women who have pathologically adherent placentas or placenta praevia, women with repeated APH, and women with RBC antibodies. This list is not exhaustive and individual situations are best discussed with a clinician.
- The post-partum period is included in this guideline to more effectively and appropriately manage ID/IDA and aid recovery from pregnancy and support breast feeding.
- In all situations when oral or IV iron is given, appropriate and timely follow up is recommended so the treatment effectiveness can be assessed, and management plan reviewed. Other causes (other than pregnancy) of ID/IDA should be considered.

12. Flowchart: Processes for referral in pregnancy for an infusion in Day Assessment

12.1 Process for Midwives



12.2 Process for LMC Obstetricians, Obstetric SMOs and RMOs, Obstetric Physicians



13. Dose and administration of ferric carboxymaltose for infusion

13.1 Antenatal dose of ferric carboxymaltose

	Hb ≥ 90 g/L	Hb < 90 g/L
Cumulative dose required	1000 mg	1500 mg

IMPORTANT: The maximum weekly dose of ferric carboxymaltose is 1000 mg.
Do NOT exceed this weekly dose.

Oral iron is contraindicated for 1 week after a dose of IV iron.

If the woman's required cumulative dose is > 1000 mg, a second dose of 500 mg can be planned for at least 1 week after the first dose. This can be arranged from DAU at the time of giving the first dose.

13.2 Postnatal dose of ferric carboxymaltose

The obstetric doctor responsible should ensure that the iron is charted as soon as possible after birth.

- In the event of a PPH, 0.5 mg of iron is required to replace each 1 mL of blood loss, e.g. if 1000 mL blood loss, woman requires extra 500 mg iron.
- If the required dose is 1000 mg, give this as IV ferric carboxymaltose in PACU, LBS or on the postnatal ward before discharge.
- If the woman's required dose is > 1000 mg, preferably give 1500 mg of IV Iron Polymaltose as soon as possible after birth. Follow the Te Toka Tumai Medication Administration Guide for IV Iron Polymaltose in a monitored environment (e.g. PACU, MCCA or DCCM.)
- If the woman's required dose is > 1000 mg AND it is not possible to give IV Iron Polymaltose before postnatal discharge, instead give 1000 mg IV ferric carboxymaltose in PACU, MCCA, DCCM or the postnatal ward, then arrange a further dose as an outpatient at least 1 week later.

IMPORTANT: The maximum weekly dose of ferric carboxymaltose is 1000 mg.
Do NOT exceed this weekly dose.

Oral iron is contraindicated for 1 week after a dose of IV iron.

A follow up FBC should be taken 2 weeks after last IV iron dose. If, after the follow up blood test, the woman requires further iron treatment, or if otherwise unsure how to proceed at any time, consult with an Obstetrician or Obstetric Physician.

13.3 Preparation and administration

Explain the purpose of the iron infusion to the woman including potential risks/side effects including the risks of permanent skin discolouration with extravasation (see below), and obtain and document verbal consent.

An IV iron patient information sheet is available via the Women's Health external website.

- Add the required dose of Ferinject® to 250 mL sodium chloride 0.9%
- Sodium chloride 0.9% is the only diluent to be used
- Do not dilute to concentrations less than 2 mg/mL of iron
- Infuse over 15 minutes
- Intravenous infusion only

- Ferinject® can be given undiluted over 15 minutes. If using a syringe driver then 20mls of iron carboxymaltose (1 g) given at 80 mL/hr will deliver the medication over 15 minutes, in accordance with manufacturer's instructions.
- Person administering the medication should be familiar with its use and potential adverse effects.
- Because of concerns with permanent skin discolouration with unrecognized tissued IV lines, a new IV line (<12 hours) must be in situ and flushed immediately before and after the infusion. For the same reason, a butterfly should not be used. If the woman suffers ANY discomfort from the infusion STOP the infusion immediately and ask the WAU SHO or registrar to check the site and place another IV line as necessary. The IV site should be followed up for any concerns by the DAU midwife.

14. Monitoring during an Iron infusion

14.1 Maternal

- Baseline observations should be documented on a MEWS chart. The WAU SHO or registrar should be consulted prior to commencing the infusion if the MEWS score is > 0.
- After commencement of the infusion repeat observations at 5 minutes, and at the end of the infusion.
- A nurse or midwife must remain at the bedside for the first 5 minutes of administration to observe for any immediate adverse reactions.
- The woman should continue to be monitored for adverse reactions for the remainder of the infusion, and for 30 minutes afterwards.
- Prior to discharge after the final IV iron infusion, the woman should be provided with a form for the follow up of full blood count (FBC).

14.2 Fetal

- Listen to the fetal heart before and after the infusion.
- More frequent monitoring should occur if there is any concern e.g. a maternal adverse reaction (consider a CTG). Refer to the latest Medsafe datasheet for any further monitoring advice.

15. Adverse reactions

Adverse reactions to IV iron infusion should be managed as per the flowchart in Section 11.

Adverse reactions can be immediate or delayed. They may include:

- Headache
- Dizziness
- Hypertension
- Flushing
- Nausea
- Injection site reactions

Less common adverse reactions are hypersensitivity including anaphylactoid reactions, paraesthesia, tachycardia, dyspnoea, vomiting, abdominal pain, diarrhoea, rash, myalgia, arthralgia, muscle spasms, itch, pyrexia, and chills.

16. Contraindications, warnings & precautions for ferric carboxymaltose infusion in pregnancy

16.1 Use in pregnancy

Due to lack of safety and efficacy data, intravenous iron should not be administered in the first trimester of pregnancy.

Intravenous iron should not be used in a pregnancy unless clearly necessary.

Ferric carboxymaltose is ADEC category B3 – medicine which has been taken by only a limited number of pregnant women, without any increase in the frequency of malformation, or other direct or indirect harmful effects on the human fetus having been observed. Studies in animals have shown evidence of an increased occurrence of fetal damage, the significance of which is uncertain in humans.

16.2 Contraindications

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

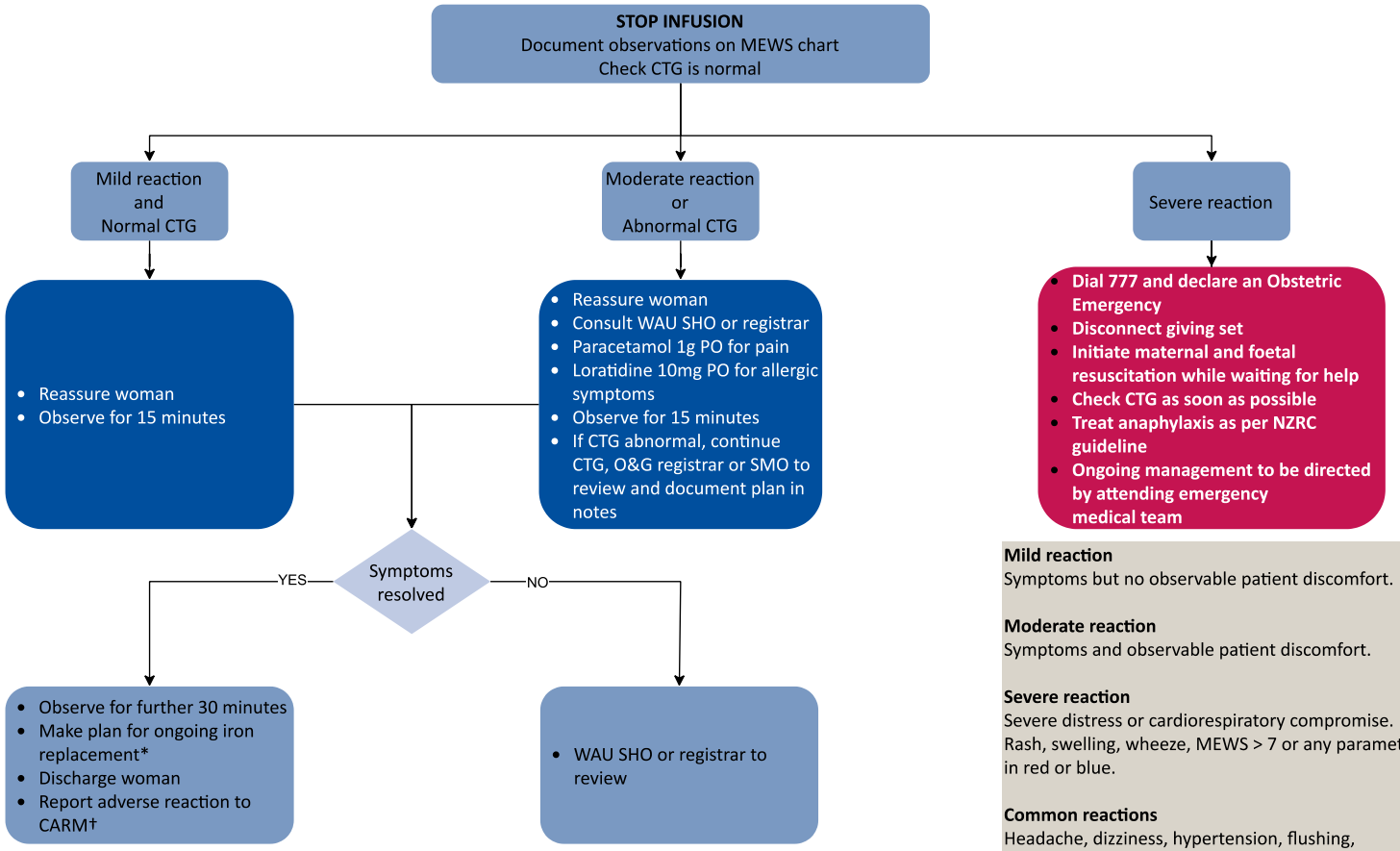
Contra-indications for ferric carboxymaltose (Ferinject®)

- Hypersensitivity to ferric carboxymaltose complex, Ferinject®, or to any of its excipients
- Anaemia not caused by iron deficiency (e.g. other microcytic anaemia)
- Evidence of iron overload, or disturbances in the utilisation of iron

16.3 Precautions

- Avoid administering to a woman with a liver dysfunction, where iron overload is the precipitating factor
- Acute infections e.g. sepsis, pneumonia. Consider giving if needed once ready for discharge home (plan in advance).
- Avoid administering iron in a woman with severe asthma, eczema or atopic allergies
- Hypersensitivity reactions are reported, including anaphylactic reactions, which may be potentially fatal. A woman must be observed for adverse effects both during the infusion and for 15 minutes following the Ferinject® injection.

17. Flowchart: Management of adverse reaction to ferric carboxymaltose



*Options for ongoing iron replacement after an adverse reaction include oral iron, repeat attempt at Ferinject infusion, or use of an alternative agent e.g. iron sucrose. In the event of uncertainty around how to proceed, consult Obstetrician or Obstetric Physician.
†All adverse reaction to Ferinject should be reported to the Centre for Adverse Reactions Monitoring (CARM) - https://nzphvc.otago.ac.nz/report/

Mild reaction
Symptoms but no observable patient discomfort.

Moderate reaction
Symptoms and observable patient discomfort.

Severe reaction
Severe distress or cardiorespiratory compromise. Rash, swelling, wheeze, MEWS > 7 or any parameter in red or blue.

Common reactions
Headache, dizziness, hypertension, flushing, nausea, infusion site reactions.

Uncommon reactions
Hypersensitivity, anaphylactoid reactions, paraesthesia, tachycardia, dyspnoea, vomiting, abdominal pain, diarrhoea, rash, myalgia, arthralgia, muscle spasms, itch, pyrexia, chills.

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18. Interactions

Ferric carboxymaltose infusion should not be administered concomitantly with oral iron preparations, as the absorption of oral preparations is impaired. Oral iron therapy should not commence until at least 7 days after the last infusion of ferric carboxymaltose. Oral iron should be taken at different times of day from antacids or calcium.

19. Supporting evidence

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20. Associated documents

- Anaphylaxis Management – Perioperative
- Intravenous Fluid Prescription – Adult
- Iron Infusion in Adult Chronic Kidney Disease (CKD) & Dialysis Patients
- Iron Polymaltose Infusion Adult MAG
- Ferric carboxymaltose Infusion Adult MAG
- Medications – Administration
- Medications – Allergies & Adverse Drug Reactions (ADRs) Identification, Documentation & Reporting
- Medications – Intravenous & Infusions Administration
- Medications – Prescribing

Clinical forms
- CR9048: IV Iron Prescribing Checklist

Patient information
- Intravenous (IV) Iron Infusions
- Oral (IV) Iron

21. Disclaimer

No guideline can cover all variations required for specific circumstances. It is the responsibility of the health care practitioners using this Te Toka Tumai Auckland guideline to adapt it for safe use within their own institution, recognise the need for specialist help, and call for it without delay, when an individual patient falls outside of the boundaries of this guideline.

22. Corrections and amendments

The next scheduled review of this document is as per the document classification table (page 1). However, if the reader notices any errors or believes that the document should be reviewed ***before*** the scheduled date, they should contact the owner or Document Control without delay.