Frimley Health
NHS Foundation Trust

Treatment of iron deficiency anaemia in pregnancy and postpartum including use of Ferinject®

Key Points

- Anaemia is the most common medical disorder in pregnancy. Pregnancy causes 2-3 fold increase in requirement of iron and 10-20 fold increase in folate requirement.
- Iron deficiency anaemia is associated with increased maternal morbidity e.g. susceptibility of infection, PPH and perinatal morbidity such as preterm labour, low birth weight babies.
- Ferritin is the first laboratory test to become abnormal as iron stores decrease and it is not affected by recent iron ingestion.
- Oral iron should be the preferred first-line treatment for iron deficiency.
- Parenteral iron is indicated when oral iron is not tolerated or absorbed, patient compliance is in doubt or if the woman is approaching term and there is insufficient time for oral supplementation to be effective.

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Abbreviations

BP	Blood Pressure
FBC	Full Blood Count
Hb	Haemoglobin
MCH	Mean Cell Haemoglobin
MCHC	Mean Cell Haemoglobin Concentration
MCV	Mean Cell Volume
P	Pulse
PPH	Postpartum Haemorrhage
R	Respiration
T	Temperature

Contents

1. INTRODUCTION

- Anaemia is the most common medical disorder in pregnancy. Pregnancy causes 2-3 fold increase in requirement of iron and 10-20 fold increase in folate requirement. In the UK, the prevalence of anaemia was found to be 24% in a multicentre national study. Healthcare workers should be aware that iron deficiency is the most common cause of anaemia in pregnancy and the risk of iron deficiency should be considered in all pregnant women.

- Iron deficiency causes maternal morbidity due to increased susceptibility to infections, physical weakness, preterm labour, increased risk of postpartum haemorrhage, and postnatal depression. Maternal iron depletion also increases the risk of iron deficiency in the neonate and is associated with increased perinatal morbidity and mortality including potential implications for the future neurodevelopment of the infant.

- Early detection and appropriate management of iron deficiency anaemia may prevent otherwise young and healthy patients from receiving an unnecessary blood transfusion and thereby avoiding associated risks. Treatment of iron deficiency should be oral iron +/- parenteral iron, together with patient education on the risks and benefits of treating iron deficiency anaemia in pregnancy to best ensure compliance.

However, iron supplementation should not be offered routinely to all pregnant women.

2. DEFINITION OF IRON DEFICIENCY ANAEMIA IN PREGNANCY

The definition of anaemia in pregnancy is Hb levels of:

- <110g/l in the first trimester
- <105 g/l in the second and third trimesters
- <100 g/l in the postpartum period.

(Pavord, 2020)

3. DIAGNOSIS OF IRON DEFICIENCY ANAEMIA

3.1 Clinical signs and symptoms

These are usually non specific in pregnancy, unless anaemia is severe. Fatigue is the most common symptom. Other complaints include pallor, weakness, headache, palpitations, dizziness, dyspnoea and irritability. Iron deficiency anaemia may also impair temperature regulation and cause pregnant women to feel colder than normal. Rarely, pica may develop (craving for non food items).

3.2 Laboratory tests

Haemoglobin (Hb) concentration should be routinely measured at booking and at around 28 weeks' gestation.

Full blood count and red cell indices

A low Hb, MCV (Mean Cell Volume), MCH (Mean Cell Haemoglobin) and MCHC (Mean Cell Haemoglobin Concentration) are suggestive of iron deficiency but need to be interpreted with caution in view of the physiological increase of MCV in pregnancy.

However, microcytic, hypochromic indices may also occur in haemoglobinopathies, even when not pregnant and fully iron replete. Women who are haemoglobinopathy carriers should have serum ferritin testing prior to iron administration to confirm concomitant iron deficiency and exclude iron overload. Co-existing thal trait and iron deficiency is common in the local population in East Berkshire.

Serum Ferritin

It is the first laboratory test to become abnormal as iron stores decrease and it is not affected by recent iron ingestion. **It is generally considered the best test to assess iron-deficiency in pregnancy**. Treatment should be considered when serum ferritin levels fall below 30 µg/l, as this indicates early iron depletion which will worsen unless treated.

N.B. Serum ferritin accurately reflects iron stores in the absence of inflammatory change. Ferritin is an acute phase reactant and should rise physiologically in 2nd and 3rd trimester and a normal ferritin level does not exclude iron deficiency. So a Ferritin <50ug/L should be regarded as suspicious for iron deficiency in late pregnancy.

Serum Iron (Fe) and total iron binding capacity (TIBC)

These are unreliable indicators of availability of iron to the tissues.

4. MANAGEMENT OF IRON DEFICIENCY ANAEMIA

4.1 Dietary advice

- Haem iron from meat, fish and poultry is absorbed 2- to 3-times more readily than non-haem iron. Meat also promotes absorption of iron from other less bioavailable non-haem iron sources. However, approximately 95% of dietary iron intake is from non-haem iron sources.
- Vitamin C (ascorbic acid) significantly enhances iron absorption from non-haem foods.
- Tannins in tea and coffee inhibit iron absorption when consumed with a meal or shortly after.
- Milk, eggs and wholegrain also inhibit the absorption of iron.
- Once women become iron-deficient in pregnancy it is not possible to ensure repletion through diet alone and a trial of therapeutic iron replacement should be considered.

4.2 Oral iron supplements

- Women should be counselled as to how to take oral iron supplements correctly. This should be on an empty stomach with a source of vitamin C (ascorbic acid) such as orange juice to maximise absorption. However, women who do not tolerate on empty stomach should be advised to try with a meal. Other medications or antacids should not be taken at the same time.
- For nausea and epigastric discomfort, alternate day dosing or preparations with lower iron content should be tried. Slow release and enteric-coated forms should be avoided. Most patients can tolerate oral iron when encouraged and given concomitant laxatives if needed.
- The optimal dose of elemental oral iron, 40–80 mg every morning is suggested, checking Hb at 2–3 weeks to ensure an adequate response to assess compliance, correct administration, and response to treatment.
- The Hb concentrations should rise by 20g/L over 3-4 weeks.
- Once Hb is in the normal range, treatment should be continued for a further 3 months and at least until 6 weeks postpartum with a repeat FBC and Ferritin at the end of therapy to replenish iron stores.
- If anaemia without an obvious other cause is detected, a diagnostic trial of oral iron should be given without delay, with a repeat full blood count in 4 weeks.
- If response to oral iron replacement is poor, concomitant causes that may be contributing to the anaemia considered, such as folate deficiency, anaemia of chronic disease, or malabsorption.
- Escalation to specialist medical care is required if anaemia is severe (Hb <70 g/l) and/or associated with significant symptoms or advanced gestation (>34 weeks) or if the Hb is failing to respond after 4 weeks of oral iron correctly taken.

In WPH and FPH, Ferrous sulphate 200mg is prescribed once a day for iron deficiency anaemia in pregnancy. This can be reduced to every other day if not tolerated. If alternate days not tolerated, then prescribe Ferrous Fumarate once a day or alternate days.

5. NON-ANAEMIC WOMEN AT RISK OF IRON DEFICIENCY ANAEMIA IN PREGNANCY

Many iron-depleted women are not yet anaemic when they first present in pregnancy until the advanced stages of iron deficiency. Therefore, these non-anaemic women identified to be at increased risk of iron deficiency should have a serum ferritin checked early in pregnancy and be offered oral supplement if ferritin is <30µg/l.

See Appendix 1 - list of non-anaemic women at risk of iron deficiency anaemia.

Intravenous iron infusion: should be considered from the 2nd trimester onwards and postpartum period.

5.1 Indications

1. Persistent iron deficiency anaemia <85g/L due to oral iron intolerance/ non-compliance/ treatment failure/proven malabsorption or active inflammatory bowel disease, the woman is approaching term **(Hb<100 g/l after 34 weeks)** and there is insufficient time for oral supplementation to be effective. (N.B. Non-compliance should be challenged with appropriate counselling)

2. Symptomatic postpartum anaemia <80g/L and haemodynamically stable

3. Haemodynamically unstable patients should be transfused to a stable state (approx 80g/L) and then offered intravenous iron in addition. This is achieved by a single unit transfusion ***followed by*** intravenous iron to treat severe iron deficiency in selected cases

5.2 Contraindications

- Non iron deficiency anaemia (e.g., Low vitamin B12, low folic acid, haemolytic anaemia)
- First trimester of pregnancy
- Patients with haemoglobinopathies, e.g., sickle cell and thalassaemia ***without*** evidence of concomitant iron deficiency
- Iron overload or disturbances in the utilisation of iron, e.g., haemochromatosis
- History of hypersenstivity to parenteral iron
- History of severe asthma, eczema or anaphylatic reactions
- Decompensated hepatic cirrhosis or hepatitis
- Acute or chronic bacteraemia
- Acute kidney injury
- Rheumatoid arthritis with signs or symptoms of active inflammation

5.3 Special warnings

- **Parenteral iron can cause allergic or anaphylactic reactions (≥1 in 10,000 to <1,000):**
    - Anaphylaxis box should be kept in close vicinity
    - Anaphylactic reaction will ususally occur within the first few minutes
    - If this occurs stop the infusion, administer IM adrenaline and initiate resuscitation measures

- Mild reactions (e.g., urticaria, rashes, itching, nausea and shivering) should be managed by stopping the infusion and administering antihistamines (chlorphenamine 10mg slowly IV)

- Hypotensive episodes may occur if IV iron is administered too rapidly, therefore decrease infusion rate as indicated.

- Delayed reactions (e.g. arthralgia, myalgia and sometimes fever) may also occur, from several hours up to 4 days, advise patient of this possibility. Symptoms usually last 2-4 days and settle spontaneously or following the use of simple analgesics such as paracetamol.

5.4 Procedure

- Patient must be seen by a obstetrician; should be informed of potential side effects and written information should be provided
- Decision for iron infusion made
- Documentation in notes from obstetrician about discussion regarding need for iron infusion

Frimley Park Hospital

- Iron infusion prescribed by obstetrician
- If outpatient: all pregnant and postnatal women will go to IVAS and Ferinject will be prescribed in Epic orders. IVAS staff will then contact the women directly to arrange an appointment.
- If inpatient: Infusion will be completed on current ward. Ferinject is kept as stock on antenatal and postnatal ward.

Wexham Park Hospital

- Iron infusion prescribed by obstetrician and prescription chart along with the completed proforma to be sent to Pharmacy.

Day of infusion

- Cannulate
- Make up infusion
- Record baseline observations
- Observe throughout
- Stay for 1 hour post infusion

5.5 Patient Monitoring

- Pulse and Blood pressure should be checked prior to infusion, at the end of infusion, 30 minutes and 60 minutes after the infusion.
- Patients should stay for at least 1 hour after the infusion has been completed.

5.6 Follow Up

- FBC, reticulocyte count and ferritin should be checked 3-4 weeks post infusion.
- Oral iron should not be started earlier than 5 days after last iron infusion

5.7 Doses and administration of parenteral iron (Ferinject®)

The parenteral iron preparation of choice throughout Frimley Health is ferric Carboxymaltose (Ferinject®). The dose of parenteral iron should be calculated on the basis of pre-pregnancy weight, aiming for a target Hb of 110 g/l.

Dose

Haemoglobin	patient body weight		
(g/L)	under 35 kg	35-70 kg	70 kg and over
less than 100	30mg/kg	1500mg	2000mg
100 – 140	30mg/kg	1000mg	1500mg

The maximum dose per single infusion is 20 mg iron/kg body weight or 1000 mg of iron. If further infusions are required to complete the dose these should be at least a week apart.
Risk of anaphylactoid reaction >1/10,000 to <1/1,000.

5.8 Administration

- Dilute 500mg in 100mL sodium chloride 0.9% and infuse over a minimum of 15 minutes
- Dilute 1000mg in 250mL sodium chloride 0.9% and infuse over a minimum of 15 minutes
- Ferinject should not be diluted to concentrations less than 2 mg iron/mL
- The infusion should be used immediately after preparation.
- The dose of Ferinject® is expressed in mg of elemental iron. One ml of solution contains 50 mg of iron as Ferric Carboxymaltose.

6. MANAGEMENT OF LABOUR IN WOMEN WITH IRON DEFICIENCY ANAEMIA

- The intended place of birth for women with iron deficiency anaemia may be influenced by pre-labour Hb, as anaemic women may have both a higher likelihood of PPH and lower iron stores for coping with haemorrhage.

- Other risk factors should also be taken into consideration, including previous PPH, grandmultiparity, fibroid uterus, multiple pregnancy, severity of anaemia and whether blood components will be accepted or not.

- Women with Hb <100g/l approaching labour should have an individualised plan discussed and documented clearly in the birth plan or maternity notes. This should include the availability of intravenous access, blood group and save, active management of the third stage of labour and birth in an obstetrician-led unit.

7. MANAGEMENT OF POSTPARTUM IRON DEFICIENCY ANAEMIA

- Women with PPH >500 ml, those with uncorrected anaemia in antenatal period or who are symptomatic of anaemia postnatally - should have their Hb checked within 48 hrs of delivery.

- Women with Hb <100 g/l within 48 h of delivery, who are haemodynamically stable, asymptomatic/mildly symptomatic - should be offered oral elemental iron 40–80 mg daily for at least 3 months.

- Use of IV iron postpartum should be considered in women who are previously intolerant of or did not respond to oral iron and/or where the severity of symptoms of anaemia warrants prompt management. Breastfeeding- unlikely to be significant as <1% iron passed into milk.

- Blood transfusion should be reserved for those with risk of further bleeding, imminent cardiac compromise or symptoms requiring immediate attention. Please refer to 'Blood Transfusion Policy for Adult Patients' and Postpartum Haemorrhage Guidelines.

8. REFERENCES

Auerbach, M. and Ballard, H. (2010) 'Clinical use of intravenous iron: administration, efficacy and safety',*Hematology. American Society ofHematology Education Programme,*2010(1), pp. 338-347. Available at: https://ashpublications.org/hematology/article/2010/1/338/96129/Clinical-Use-of-Intravenous-Iron-Administration (Accessed: 4 March 2024).

Barroso, F.*et al.* (2011) 'Prevalence of maternal anaemia and its predictors: a multi-centre study', *European Journal of Obstetrics, Gynecology and Reproductive Biology*,159(1), pp. 99–105.

Joint Formulary Committee (2023) 'Ferric carboxymaltose', in *British National Formulary*. Available at: https://bnf.nice.org.uk/drugs/ferric-carboxymaltose/ (Accessed: 27 March 2023).

National Institute for Health and Care Excellence (2021) *Antenatal care*. NG201. Available at: https://www.nice.org.uk/guidance/ng201 (Accessed: 4 March 2024).

Pavord, S. *et al*.(2020) 'UK guidelines on the management of iron deficiency in pregnancy', *British Journal of Haematology,*188(6), pp. 819-830. Available at: https://onlinelibrary.wiley.com/doi/full/10.1111/bjh.16221 (Accessed: 4 March 2024).

Vifor Pharma UK Limited (2024) *Ferinject 50 mg iron/mL dispersion for injection/infusion SmPC*. Available at: https://www.medicines.org.uk/emc/product/5910/smpc#gref (Accessed: 4 March 2024).

APPENDIX 1 – LIST OF WOMEN WITH HIGH RISK OF IRON DEPLETION

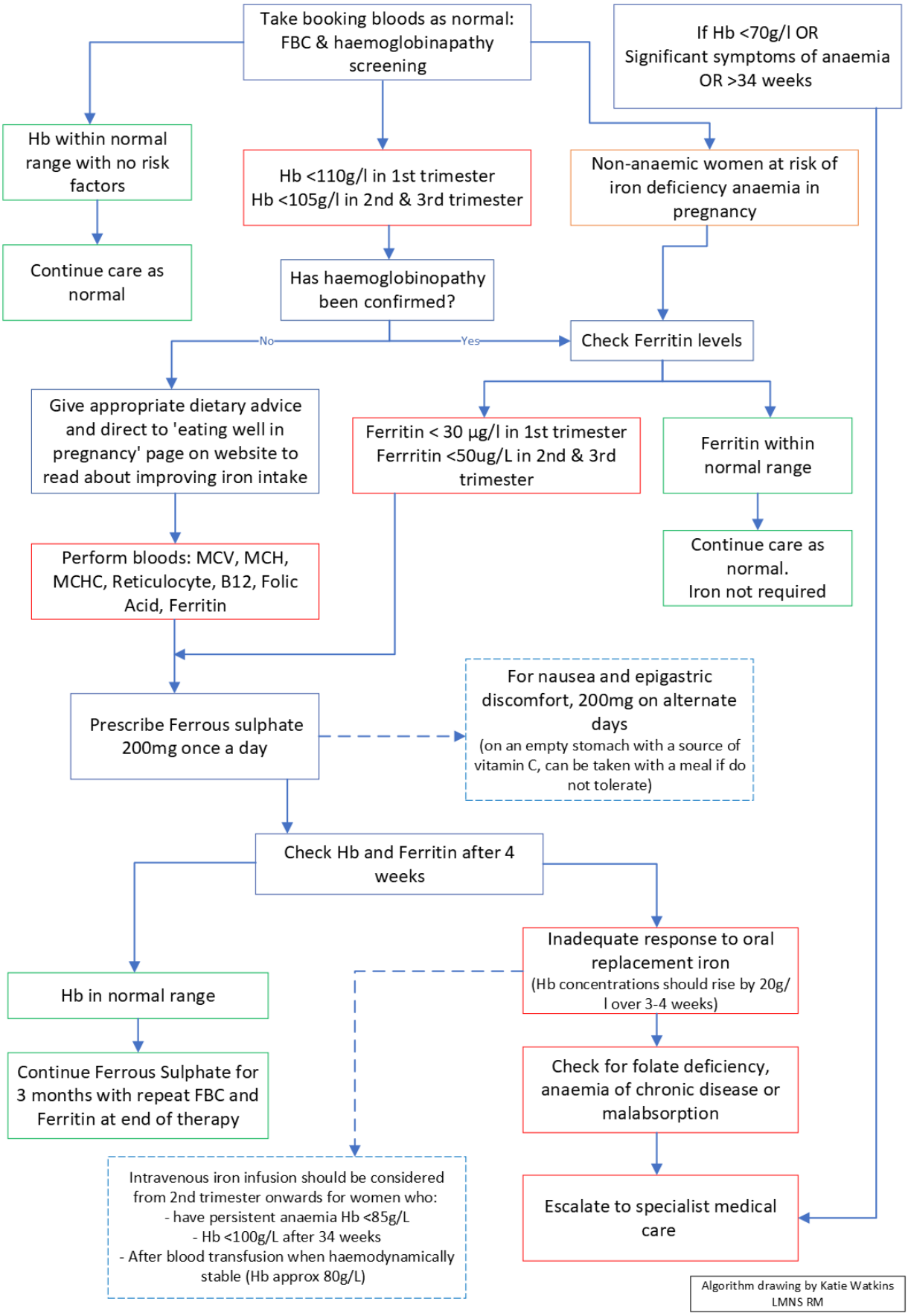
Non-anaemic women with high risk of iron depletion for empirical iron treatment with/without serum ferritin testing:

- Previous anaemia
- Multiparity ≥P3
- Twin or higher order multiple pregnancy
- Inter pregnancy interval <1 year
- Women who have poor dietary habit
- Those following a vegetarian/vegan diet
- Pregnant teenagers
- Recent history of clinically significant bleeding

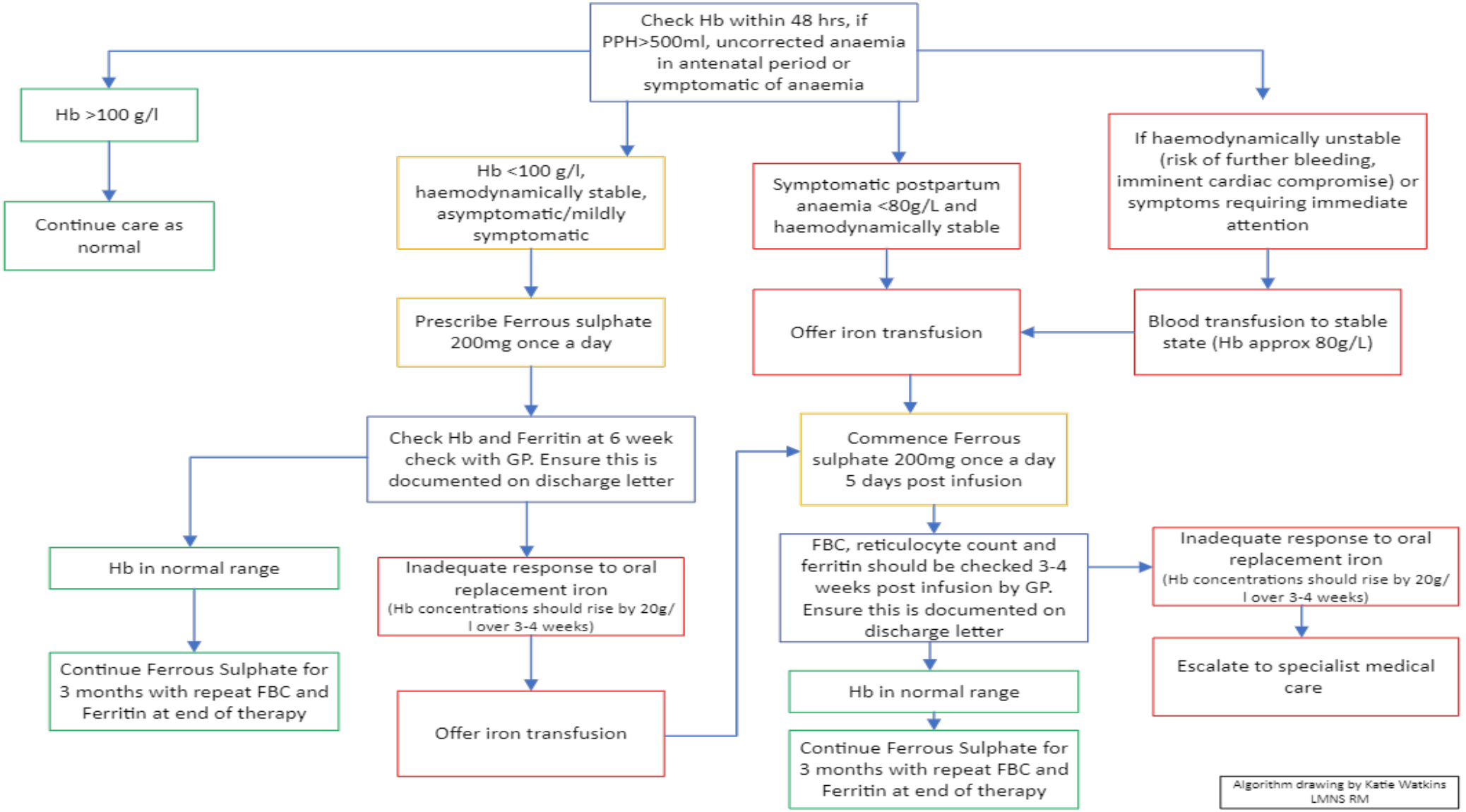
Non-anaemic women where serum ferritin may be necessary:

- High risk of bleeding during pregnancy or at birth
- Women declining blood products, such as Jehovah's Witnesses
- Women for whom providing compatible blood is challenging

Appendix 2 – Algorithm for the Antenatal Management of Anaemia



APPENDIX 3 – ALGORITHM FOR THE ANTENATAL MANAGEMENT OF ANAEMIA



APPENDIX 4 – PARENTERAL IRON INFUSION PROFORMA

Parenteral Iron infusion proforma

Ferinject

Date

Gestation

Verbal Consent ☐

Patient label

Medical History

Allergies	

Past medical history	

Contra-indications:

- Non iron deficiency anaemia (eg, low vitamin B12, low folic acid, haemolytic anaemia)
- First trimester of pregnancy
- Patients with haemoglobinopathies e.g.,. Sickle cell and thalassaemia, without proven evidence of iron deficiency
- Iron overload or disturbances in the utilisation of iron e.g., haemochromatosis
- History of hypersenstivity to parenteral iron
- History of severe asthma, eczema or anaphylatic reactions (may be possible to use cosmofer IM for these patients)
- Decompensated hepatic cirrhosis or hepatitis
- Acute or chronic bacteraemia
- Acute kidney injury
- Rheumatoid arthritis with signs or symptoms of active inflammation

Blood Results

Hb	
MCV	
Serum Ferritin	
Haemoglobinopathy screen	

Observations

Main infusion

	Before	30 mins	1 hr
P			
BP			
T			
R			

Wait one hour then may go home if feeling well.
Repeat bloods in 4 weeks
Recommence oral iron no earlier than 5 days post infusion

APPENDIX 5 – IRON RICH DIET SHEET

Improve your iron level and avoid developing anaemia in pregnancy

Iron is vital for making haemoglobin in red blood cells which carry oxygen around the your body and to your baby. During pregnancy, your body needs two to three times more iron than usual. Iron is important for your baby's growth and brain development Anaemia is when the level of haemoglobin in your blood is lower than normal.
The most common type of anaemia in pregnancy is iron-deficiency anaemia. It affects at least 4 in 10 pregnant people in the UK.

Why is maintaining good iron levels important in pregnancy and after giving birth?

It is important to optimise your iron levels during pregnancy.

Good iron levels help to:

- Maintain a healthy immune system.
- Decrease the impact of blood loss at delivery and reduce the risk of blood transfusion.
- Decrease risk of infection and depression after giving birth
- Improve postnatal recovery, especially if you need surgery or have a perineal tear.
- Avoid a decreased breast milk supply associated with severe anaemia.
- Decrease low birth weight in baby and premature birth (when delivery occurs before 37 complete weeks of pregnancy).

How will you know if you are anaemic?

The most common symptoms of anaemia are:

- Excessive tiredness.
- Weakness.
- Dizziness.
- A paler complexion than usual.
- Shortness of breath.
- Heart palpitations (awareness of a faster heart beat).

If you have any of these symptoms, talk to your midwife and we can perform a blood test. All pregnant women are routinely screened for anaemia at their first booking visit and at 28 weeks of pregnancy. If you are at increased risk of anaemia you may be screened more frequently.

What foods are rich in iron?

Unless your iron level is below expected, you should not need to take iron supplements if you eat plenty of iron rich foods as part of a healthy diet. However, a general pregnancy vitamin supplement will contain a small amount of iron and this is recommended.

The best foods to eat are:

- Red meat
- Fish
- Poultry

These contain a form of iron that is easily absorbed into the body.

Do not eat any liver products in pregnancy; even though these are high in iron they also contain high levels of vitamin A, which is dangerous for your baby.
Other vegetarian foods rich in iron include:

- Fortified cereals
- Dried fruit
- Green vegetables such as peas, broccoli, or dark leafy cabbage and spinach
- Beans and pulses such as lentils, soybeans, kidney beans or chickpeas
- Nuts and seeds
- Dark chocolate
- Tofu

The type of iron contained in these foods is more difficult for the body to absorb and it is recommended that you also have a good intake of vitamin C in your diet to improve absorption. Drinking a glass of orange juice with your breakfast can help.

Is there anything I should avoid?

There are also some foods, drinks and medicines that limit the absorption of iron, including tea and coffee and antacid medication for heartburn or indigestion

What treatment can you take if you become anaemic?

If you become anaemic, we will start you on a course of oral iron supplementation. Very occasionally, patients who do not respond to treatment will need iron infusion through a drip or blood transfusion.

Very high doses of iron can be fatal, particularly if taken by children, so always keep iron supplements out of the reach of children and only take the recommended/prescribed dose.

Reference:
1. https://www.nice.org.uk/guidance/ng201

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FULL VERSION CONTROL RECORD

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This guideline has been registered with the trust. However, clinical guidelines are guidelines only. The interpretation and application of clinical guidelines will remain the responsibility of the individual clinician. If in doubt, contact a senior colleague or expert. Caution is advised when using guidelines after the review date.

This guideline is for use in Frimley Health Trust hospitals only. Any use outside this location will not be supported by the Trust and will be at the risk of the individual using it.

Version History

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1.0		Vidya Shirol, Consultant	Final	First cross site version
2.0	Sept 2020	Shaila Banu, Post CCT Speciality Doctor, Obs and Gynae, WPH	Final	Updated and approved at OGCGC
2.1	March 2024	Shaila Banu, Post CCT Speciality Doctor, Obs and Gynae, WPH	Draft	Scheduled review.
3.0	May 2024	Shaila Banu, Post CCT Speciality Doctor, Obs and Gynae, WPH	Final	Ratified at Cross site obstetrics clinical governance meeting, 21.05.2024

Related Documents

Document Type	Document Name
Guideline	Blood Transfusion Policy for Adult Patients
Guideline	Postpartum Haemorrhage