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CLINICAL GUIDELINES ID TAG		
Title:	**Protocol for dosing and administration of Monofer® ▼ (10% intravenous iron isomaltoside) in iron deficiency anaemia in pregnancy**	
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Protocol for dosing and administration of Monofer® ▼ (10% intravenous iron isomaltoside) in iron deficiency anaemia in pregnancy

The purpose of the guideline is to advise medical and nursing staff on the safe prescribing and administration on Monofer®. Please refer to the summary of product characteristics (SPC available at www.medicine.org.uk) for full prescribing information.

Patients requiring Monofer® infusions will attend;

- Daisy Hill Hospital - Maternity ward at pre-arranged date & time
- Craigavon Area Hospital - Day Obstetric Unit (DOU) at pre-arranged date & time

Patients should have received a Monofer® information leaflet (supplied by Pharmacosmos UK) prior to attendance. The SHO on call overnight will calculate and prescribe the dose of Monofer® required using the table below.

Step 1: Calculate iron requirement:

The dose of Monofer® is expressed in milligrams (mg) of elemental iron. The cumulative dose of iron using Monofer® is based on the patient's weight and haemoglobin (Hb) level. The following table should be used to determine the cumulative iron dose:

Hb (g/L)	Patients with booking body weight < 50kg	Patients with booking body weight 50kg to < 75kg	Patients with booking body weight > 75kg
≥ 90	500mg	1000mg	1500mg
< 90	500mg	20mg/kg	20mg/kg

Note: -

- The dose of parenteral iron is calculated using **booking weight.**[1]
    - Ideal body weight should be used for obese patients (BMI ≥ 30)
      Calculation of ideal body weight = **Female (kg)**: [(height (cm) – 154) x 0.9] + 45.5

Step 2: Administration:

- No test dose is required
- Give as IV Infusion in 250ml 0.9% Sodium Chloride over 30 minutes[2]
- All infusions should be followed up with a 50ml flush of 0.9% Sodium Chloride

If the total dose exceeds 20mg iron /kg body weight the dose must be split in two administrations with an interval of at least one week. Give the 20mg/kg dose in the first administration. The second administration will be based on clinical judgement[3].

Step 3: Monitoring:

Monofer® should only be administered when staff trained to evaluate and manage anaphylactic reactions is immediately available, in an environment where full resuscitation facilities can be assured. A set of observations (including blood pressure, pulse rate and temperature) and the NEWS score should be measured and recorded before administration. The patient should be observed prior to infusion, during infusion and for at least 30 minutes following each Monofer® infusion for signs and symptoms of hypersensitivity reactions.

Caution should be exercised to avoid paravenous leakage when administrating Monofer®. The cannula site must be observed for extravasation of the infusion. Paravenous leakage of Monofer® at the injection site may lead to inflammation, tissue necrosis, sterile abscess and potentially long lasting brown discolouration at the site of injection. In case of paravenous leakage, the administration of Monofer® must be stopped immediately cannula removed and cold compress applied. Also advise the patient to avoid vigorous rubbing of the affected area for several weeks following the extravasation, as this may only exacerbate the problem.

Contraindications

- 1st trimester of pregnancy
- History of hypersensitivity to parenteral iron preparations
- Hypersensitivity to the active substance, to Monofer® or any of its excipients
- Non-iron deficiency anaemia or iron overload or disturbances in utilisation of iron
- Decompensated liver disease

Caution

- In patients with active infection, severe asthma or eczema, rheumatoid arthritis– use in discussion with Consultant Obstetrician

Important information

- For better results, stop oral iron 5 days before infusion.
- Oral iron can be started 5 days after administration of Monofer®
- A maximum dose of up to 20mg/kg can be administered
- Check Hb, and Ferritin 3 - 4 weeks post administration of Monofer® to ensure that Hb and ferritin levels are within normal reference range

Undesirable effects

Ensure adrenaline (epinephrine) is available prior to administration. As with all IV preparations, acute severe anaphylactic reactions may occur with Monofer®, although they are not common.

Flushing in the face, acute chest and/or back pain and tightness sometimes with dyspnea in association with IV iron treatment may occur (frequency uncommon). This may mimic the early symptoms of an anaphylactoid/anaphylactic reaction. The infusion should be stopped, and the patient's vital signs should be assessed. These symptoms disappear shortly after the iron administration is stopped. They typically do not reoccur if the administration is restarted at a lower infusion rate. If restarted closely observe the patient.

Acute severe hypersensitivity reactions may occur with parenteral iron preparations. They usually occur within the first few minutes of administration and are generally characterised by the sudden onset of respiratory difficulty and/or cardiovascular collapse; fatalities have been reported.

Other less severe manifestations of immediate hypersensitivity, such as urticaria and itching may also occur. In pregnancy, associated foetal bradycardia may occur with parenteral iron preparations. See Appendix 1 for reaction management algorithm.

See the Monofer® SPC for a complete list of undesirable effects.

Information for Patients Receiving Intravenous Iron Preparations

Your medical team have recommended intravenous iron to treat your anaemia / low blood count. This will be given as an infusion/drip over 15 or 30 minutes. Please read the following information prior to your treatment and if you have any questions let the nurse caring for you know.

1. Intravenous iron is used to treat a low blood count due to a low amount of iron in your body. This may have occurred due to low amounts of iron in your diet, a problem with your body's ability to absorb and use iron or be as a result of blood loss.
2. Intravenous iron is a highly effective method to replenish your body's stores of iron and hopefully allow you to increase your blood count over the coming days and weeks.
3. Intravenous iron allows a much larger dose of iron to be given than iron in tablet form.
4. All medication carries a risk of side effects and reaction. Prior to receiving your treatment it is important you are aware of the side effects / risks of intravenous iron. The nurse caring for you will ask if you understand the information below and are content to proceed prior to you treatment.

Side Effects of Intravenous Iron Therapy

1. Intravenous iron is an extremely safe and effective therapy for treatment of IV iron.
2. Staining – If your cannula was to displace from your vein during treatment the drug could be deposited in your skin rather than into your bloodstream. This could result in a brown stain to the skin. If you notice pain at the injection site during your treatment please inform the nurse caring for you immediately. This will minimise any such risk.
3. Change in total body skin colour – This is an extremely rare occurrence. It has been reported that some patients noted their skin to become darker (like a sun tan) for a period of weeks after treatment with intravenous iron. This was not permanent and resolved after a number of weeks.
4. Allergy – Historically intravenous iron preparations carried a risk of allergy (ranging from a mild reaction like itchy skin through to anaphylaxis that could be life threatening). With today's modern iron preparation this is uncommon (1 in a 100 to 1 in a 1000 risk). Please inform the nurse caring for you immediately if you experience any of the following during your treatment (swelling of lips, tongue, face or throat, shortness of breath, itching, a feeling of all over body heat, heart racing or faint like symptoms)
5. Delayed reaction – Although uncommon, some patients may experience muscle or joint pains and fever in the days after treatment. This usually lasts two to four days and can be managed with simple painkillers like paracetamol.

Intravenous iron infusions – Nursing care of the patient

- Prescriptions for intravenous iron should be prescribed using the brand name (e.g. Monofer®, Ferrinject®, Venofer®). Ensure accurate patient weight is recorded for dosing.

- Patient is placed in a recliner chair/ bed conducive to emergency care-giving if required

- Consent, to proceed, is verbally obtained after the SHSCT Patient Information Leaflet and the product Patient Information Leaflet is read by the patient/ patient's advocate. Consent is also documented in the Nursing notes

- Wide bore cannula is preferable for this infusion and inserted, using an aseptic technique, in a position less likely to dislodge

- Patient is advised to use the bathroom and hydrate, if needs be, before commencement of drug to reduce possibility of extravasation and again patient is advised to avoid unnecessary movement of arm, where cannula is sited, during administration

- Clinical observations to be obtained pre administration, at 15 mins and post administration

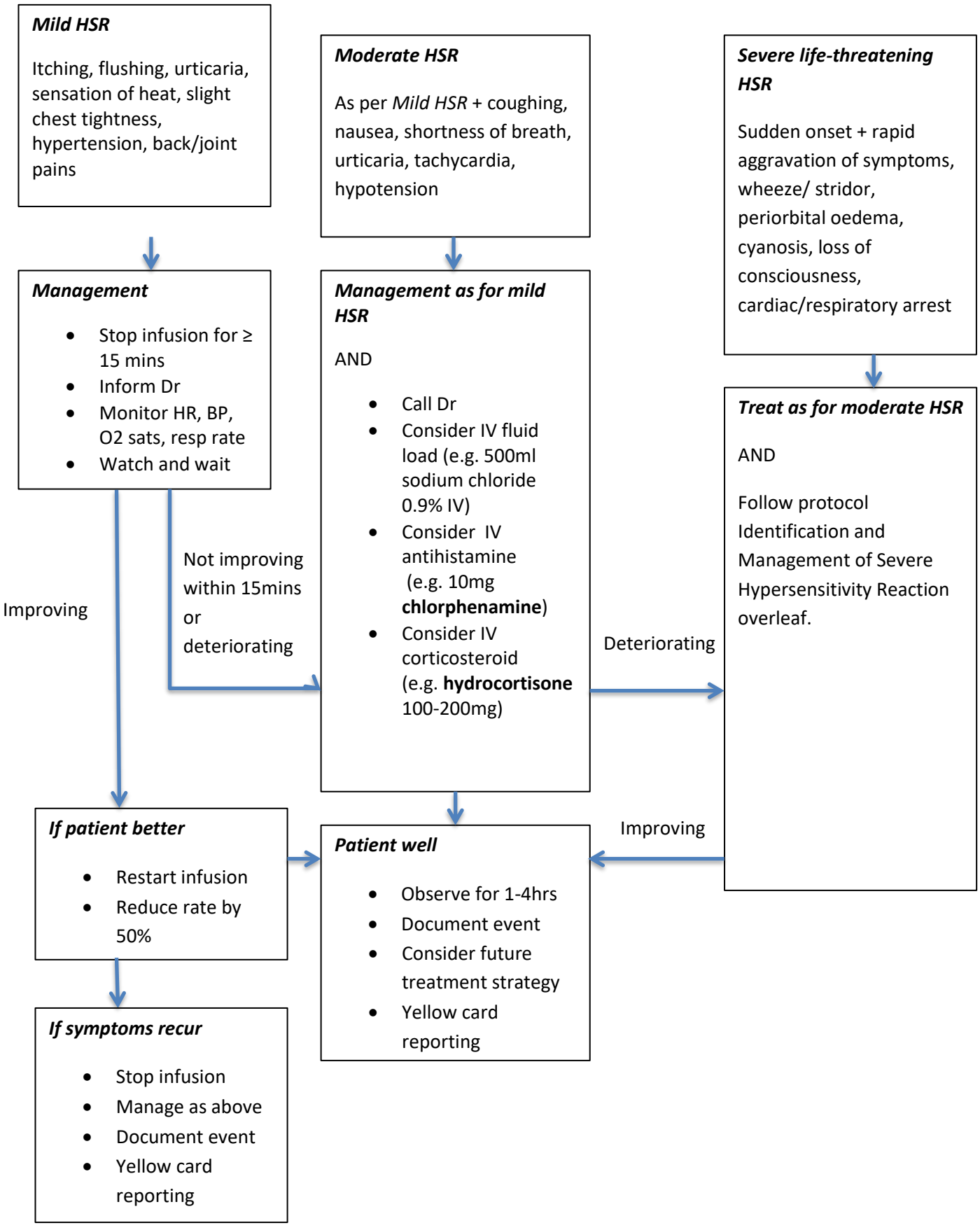
- Patients MUST be visible at all times to the nurse.
  (This avoids unforeseen staining etc occurring and side effects which can be acted upon quickly)

- Anaphylaxis kit must be readily available pre infusion

- Patient advised again on completion of the infusion that staining can occur after the infusion has stopped and they are also informed what to do should there be any issues.

Appendix 1

Algorithm grading and management of acute hypersensitivity reactions (HSR) to intravenous iron infusions[4]



IDENTIFICATION AND MANAGEMENT OF SEVERE HYPERSENSITIVITY REACTION

Sudden onset and rapid worsening of

Itching / flushing / urticaria / chest tightness / cough / shortness of breath / tachycardia / hypertension / hypotension / nausea / back pain / joint pain PLUS

Wheezing / stridor / periorbital oedema / cyanosis / loss of consciousness / cardiac arrest / respiratory arrest

↓

Stop Monofer® Infusion

↓

Alert Obstetric Emergency Response Team on 6000

↓

Initiate Local Anaphylaxis Protocol[5]

↓

Oxygen via Face Mask and Nebulised B2 Agonist

↓

Rapid Volume Load 1 – 2 l of 0.9% Sodium Chloride

↓

IV Corticosteroids (if not already administered)

↓

Advanced Cardiovascular Life Support (if necessary)

↓

Symptoms Improved/Resolved?

YES ← **Symptoms Improved/Resolved?** → **NO**

YES ↓

Do Not Restart Monofer® Infusion

↓

NO ↓

Transfer to HDU / ICU

↓

Observe for > 1 – 4 Hours (Consider Admission & Observation for up to 24 hrs)

↓

Discuss with Doctors, Discuss Future Treatment Strategy

Appendix 2

Monofer® proforma to be used for administration of Monofer®

IRON INFUSION – IRON ISOMALTOSIDE – MONOFER® PROFORMA

Before a woman is referred for a Monofer® infusion the following measures should be taken:-

- If MCV is high (macrocytosis) please check B12 and folate levels.
- If known haemoglobinopathy check serum ferritin and offer oral supplements if less than 30ug/l.
- If response to oral iron replacement is poor, exclude concomitant causes, such as folate deficiency or anaemia of chronic disease.
- Anaemic women with unknown haemoglobinopathy status should be offered a trial of iron and haemoglobinopathy screening should be undertaken in accordance with the NHS sickle cell and thalassaemia screening programme guidelines.
- The serum ferritin level is the most useful and easily available parameter for assessing iron deficiency. Levels below 15µg/l are diagnostic of established iron deficiency. A level below 30µg/l in pregnancy should prompt treatment.

TREATMENT OF IRON DEFICIENCY ANAEMIA

- Treatment must begin promptly in the community. Referral to secondary care should be considered if there are significant symptoms and/or severe anaemia (Hb less than 70) or if there is no rise in Hb following 2 weeks of oral iron therapy.
- Give 100 - 200mg elemental iron daily and repeat FBC with the GP after 2 weeks. Ferrous iron salts are the treatment of choice. See template letter Appendix 3 (three copies – patient, GP, notes)
- For nausea and epigastric discomfort, try preparations with lower iron such as ferrous sulphate.
- Once Hb levels are normal, continue supplementation for 3 months and at least until 6 weeks postpartum to replenish iron stores.

- Counsel as to how to take oral iron supplements correctly. This should be on an empty stomach, 1 hour before meals, with a source of vitamin C (ascorbic acid) such as orange juice to maximise absorption. Other medications or antacids should not be taken at the same time.

- Once all of these measures have been completed the woman should be referred for I.V Monofer®. This is done by either contacting the Day Obstetric Unit (DOU) Craigavon Area Hospital or the Maternity ward Daisy Hill Hospital and arranging an appointment. At this stage the Monofer® should be prescribed on a Kardex for the date the appointment has been made and the dose calculated using the table below.

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Note: -

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Appendix 3

PATIENT ADDRESSOGRAPH

DATE OF INFUSION: ……..

TIME ARRIVED ON WARD: ……

DOSE OF MONOFER: ……

ANY PREVIOUS IRON INFUSIONS **YES / NO**

WAS PATIENT INFORMATION LEAFLET GIVEN TO PATIENT **YES / NO**

WAS PATIENT GIVEN VERBAL INFORMATION RE THE POSSIBILITY OF SKIN DISCOLOURATION WHICH MAY TAKE SOME TIME TO RESOLVE/RISK OF ANAPHYLAXIS

YES / NO

INFORMED VERBAL CONSENT GIVEN BY PATIENT **YES / NO**

Signature of Midwife…… ……..

Signature of Patient ……

TIME CANNULA INSERTED: ……

PERIPHERAL CANNULA OBSERVATION CHART COMPLETED **YES / NO**

WAS IRON ISOMALTOSIDE (MONOFER®) PRESCRIBED ON MEDICINE PRESCRIPTION AND ADMINISTRATION RECORD/ PRIOR TO APPT

YES / NO

TIME INFUSION CONNECTED / COMMENCED: ……

BASELINE OBS PRE – INFUSION

OEWS SCORE……..

OBSERVATIONS (START OF INFUSION):

OEWS SCORE……

ARM CHECKED FOR SKIN DISCOLOURATION DURING THE INFUSION: **YES / NO**

TIME CHECKED: …… (IF YES STOP IMMEDIATELY AND RE-SITE CANNULA)

OBSERVATIONS (5 MINUTES POST COMMENCING INFUSION):

OEWS SCORE……

ANY HYPERSENSITIVITY REACTION DURING INFUSION **YES / NO** TIME CHECKED:

OBSERVATIONS (END OF INFUSION):

OEWS SCORE……

ARM CHECKED FOR SKIN DISCOLOURATION AFTER THE INFUSION: **YES / NO** TIME CHECKED:

ADVICE GIVEN TO HAVE A REPEAT FBP IN 2 WEEKS **YES / NO**

ADVICE GIVEN TO DISCONTINUE ORAL IRON POST IRON INFUSION **YES / NO**

……
……
……
……

PLEASE PHOTOCOPY AFTER COMPLETION AND FILE 1 COPY IN MHHR AND 1 COPY IN IRON INFUSION AUDIT FOLDER

TIME PATIENT LEFT WARD: ……..

DURATION OF PROCEDURE: ……..

References

1. UK Guidelines on the management of iron deficiency in pregnancy. British Journal of Haematology , 2020, 188,819-830 https://onlinelibrary.wiley.com/doi/pdf/10.1111/bjh.16221
2. Protocol for Monofer® (Iron Isomaltoside) Prescription and Administration SH&SCT Dr Aidan Cullen 19th November 2020 http://www.southernguidelines.hscni.net/?wpfb_dl=657
3. Monofer® 100mg/ml solution for injection/infusion SPC https://www.medicines.org.uk/emc/
4. Rampton et al. Hypersensitivity reactions to intravenous iron: guidance for risk minimization and management. Haematologica 2014;99(11):1671-1676.
5. SHSCT Anaphylaxis guidelines http://www.southernguidelines.hscni.net/?wpfb_dl=197