University Hospitals Sussex
NHS Foundation Trust

Management of Confirmed Ectopic Pregnancy Guideline

Maternity Protocol: GP001 Management of Confirmed Ectopic Pregnancy

Date agreed: January 2021

Guideline Reviewer:	Tasneem Singhal
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Contents

Key Principles

These guidelines and algorithms are aimed to assist in decision making. They are not designed to be prescriptive and you are not expected to use them in exclusion of discussions with senior colleagues.

Evidence used to inform these guidelines had been drawn from National Institute for Health and Clinical Excellence (NICE) and Royal College of Obstetricians and Gynaecologists (RCOG) guidelines. Where applicable other references are quoted.

These guidelines have been reviewed by all clinicians involved in early pregnancy care, including consultants, trainees, pharmacists, and specialist and senior nursing staff.

A protocol is a set of measurable, objective standards to determine a course of action. Professional judgement may be used in the application of a protocol.

Scope

These guidelines apply to women who have a confirmed diagnosis of Ectopic pregnancy.

Responsibilities

Nurses, Midwives & Gynaecologists & Obstetricians:

- To access, read, understand and follow this guidance
- To use their professional judgement in application of this guidance

Management Team

- To ensure the protocol is reviewed as required in line with Trust and National recommendations
- To ensure the protocol is accessible to all relevant staff
- To ensure protocols are available to service users on request

1 Introduction:

Ectopic pregnancy is defined as implantation of the pregnancy outside the normal endometrial cavity.

1.1 Commonly occurring symptoms

- Abdominal/ pelvic pain (often unilateral)
- PV bleeding (with or without clots or tissue) or amenorrhoea
- Syncope, dizziness
- Shoulder-tip pain
- Urinary and bowel symptoms (tenesmus/ diarrhoea)

1.2 Risk Factors

- Previous pelvic surgery
- Pelvic infection (PID)
- Smoking
- IVF pregnancy
- Subfertility
- Contraception failure (particularly Intrauterine device (IUD) or Progesterogen-only pill (POP))
- Previous ectopic pregnancy

1.3 Clinical Signs

- Lower abdominal or pelvic tenderness
- Cervical motion tenderness and mass in adnexa

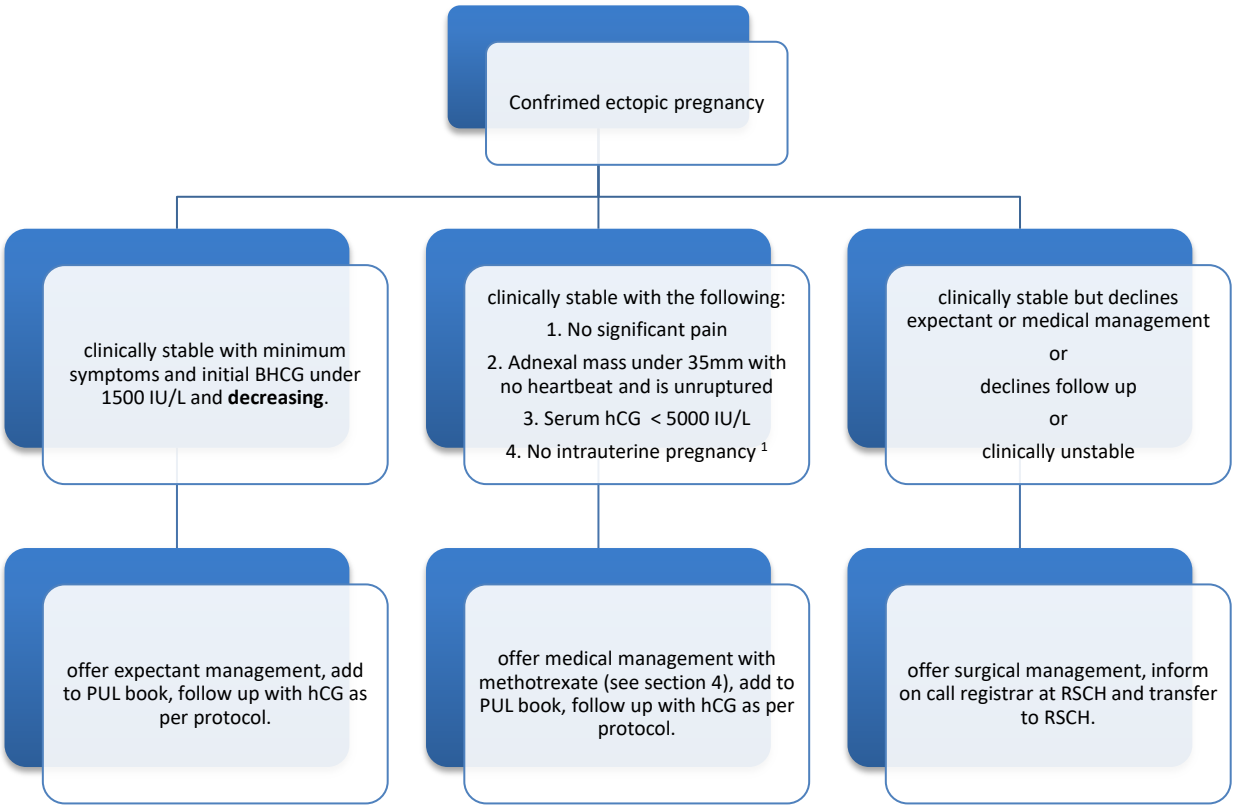
One third of women with ectopic pregnancy will have no clinical signs and 9% are asymptomatic.

For management of non-tubal ectopic pregnancies – i.e. interstitial, corneal, ovarian, abdominal, cervical and caesarean scar pregnancies please refer to: Diagnosis and Management of Ectopic Pregnancy. Green-top Guideline No. 21 RCOG/AEPU Joint Guideline | November 2016

2 Management of a confirmed tubal ectopic pregnancy

Verbal and written information needs to be given to patients with confirmed ectopic pregnancy.

Management of all women with an ectopic pregnancy must be discussed with the consultant on call.



3 Expectant Management

Can be offered to women with an initial level of ≤1500 IU/L and decreasing.

3.1 The beta -Human chorionic gonadotrophin (BHCG) levels are repeated after 48 and 96hours. Ultrasound scan (USS) is repeated in a week

3.2 The hCG levels must drop to < 50% of the initial value in 7days and there should be a reduction in the size of the adnexal mass

3.3 If the hCG level is dropping, it is repeated weekly until it drops to < 15IU/L or the patient has a negative pregnancy test. (See Section 9 for explanation)

3.4 An ultrasound scan is repeated weekly

3.5 If the hCG levels are rising or static, consider medical or surgical management as appropriate

3.6 There may be mild separation pain

3.7 If there is any pain clinically assess the woman and arrange an urgent scan

3.8 In suitable women this form of management is successful in 70% of women

3.9 25-30% may require further treatment with Methotrexate or surgery

3.10 Advise women to avoid sexual intercourse until the ectopic pregnancy is completely resolved

3.11 Advise the women to attend A&E should they experience severe pain or feel unwell.

4 Medical Management

Methotrexate can be offered to women with an unruptured ectopic pregnancy, with no foetal heartbeat and an adnexal mass of size less than 35mm in diameter and the hCG is < 5000IU/L

4.1 Contraindications

- Significant renal disease
- Hepatic dysfunction (raised transaminases (ALT, AST or GGT) >2 times upper limit of normal)

- Leukopenia (WBC <3 x 10^9/L)
- Thrombocytopenia (platelet count <150 x 10^9/L)
- Significant anaemia (Hgb <100 g/L)
- Active peptic ulcer disease
- Immunodeficiency
- Breastfeeding
- Known sensitivity to methotrexate
- Desired coexistent intrauterine pregnancy (heterotopic pregnancy)
- Active pulmonary disease
- Haemodynamic instability
- If patient unable to comply with follow-up

4.2 The woman should be given a leaflet and the treatment plan should be explained in detail

4.3 The following blood tests are to be performed on Day 1 and Day 7 FBC, LFTs and U&E.

4.4 Document on the patients' drug chart, maternal weight (kg) and height (cm)

4.5 Methotrexate dose (50mg/m^2), to be **prescribed by a consultant only** (see below for Dosage Calculations).

Please see Appendix I -Flowchart for Calculating & Obtaining IM Methotrexate for Medical Management of Confirmed Ectopic Pregnancy

Dosage Calculations:

Calculate the Body Surface Area (BSA), to 1 decimal place, using the patient's height and weight. The BSA is calculated using the formula shown below, however to reduce user error it is recommended that an online BSA calculator tool is used (please see link below).

$$BSA\ (m^2) = ([H(cm) \times W(kg)] / 3600)^{1/2}$$

Dosage of IM Methotrexate: 50 mg x BSA(m^2) = Total dose to be given (mg)

The following link for an approved online calculator can be used to calculate the dose of IM Methotrexate:

https://www.calculosaurus.com/methotrexate-dose-calculator

Obtaining IM Methotrexate:

Contact Pharmacy who will inform regarding the closest available dose (+/-5%)

in prefilled pens. The consultant should then prescribe accordingly.

For Pharmacy requests for IM methotrexate during:

- **Normal work days** (Monday–Friday 8am-4pm excluding bank holidays), the Aseptics Team should be contacted on ext. 4045.
  The Aseptics pharmacist will advise on dosage and their capacity to dispense a syringe with the exact dose of methotrexate or provide pre-filled pen(s) to the nearest available dose (within 5% of the calculated dose). If Aseptics do not have capacity to dispense a syringe with the exact dose the patients' treatment may need to be delayed**.
- **Weekends & Bank Holidays** (9.30am-1.30pm), the Dispensary in the main Pharmacy department (RSCH) should be contacted on ext. 3119.
- **Out of Hours**, contact the On-Call pharmacist (RSCH) via switchboard.

The Dispensary/On-Call pharmacist will advise on dosage and whether they can provide the closest available dose (within 5% of the calculated dose) as pre-filled pens or whether Aseptics will need to make/supply the dose during pharmacy opening hours. If Aseptics are required to make the dose, they will need to be contacted during opening hours which may require the patients dose to be delayed**.

** Please note the Aseptics Unit is not open at weekends and bank holidays therefore patients' treatment may potentially be delayed by up to 1-2 working days if the exact dose is required to be made/ supplied by Aseptics

The Pharmacy carry several different strengths of Methotrexate prefilled Pens and the patient may require more than 1 injection to make up the necessary dose.

Please see Appendix II regarding Methotrexate pre-filled pens held in pharmacy.

If the closest available dose is more than +/- 5% of the calculated dose, and Aseptics have confirmed their capacity to supply, then prescribe the exact dose but it may be necessary to inform the woman that there could be a delay of 1-2 working days until the methotrexate is available.

-Once IM methotrexate dose has been agreed with the Pharmacist, the Consultant should prescribe in the 'ONCE ONLY PRESCRIPTIONS' section on the front of the patients' drug chart. The patients' drug chart must then be sent to Aseptics/main Pharmacy on Level 3, Tower block for dispensing.

4.6 Methotrexate is to be administered intramuscularly using the Z technique via the prefilled pens which have sub-cutaneous needles (See Appendix II) or syringes prepared by Aseptics.

4.7 Methotrexate must not be administered by registrars or SHOs on their own.

4.8 Methotrexate may be administered by:

- junior doctors who have adequate training and under the direct supervision of a consultant
- nursing staff who have witnessed and been observed administrating IM Methotrexate and been signed off by their line manager (or equivalent) to perform the procedure unsupervised.

4.9 All staff administering IM Methotrexate must have completed the relevant Trust training packages including administration, disposal of a cytotoxic agent and dealing with spillages of cytotoxic agents,

See MM0007: Policy for Dealing with Cytotoxic Spillages in Wards and Departments; MM0001: Cytotoxic Chemotherapy policy; Appendix III for guidance on Z-technique.

4.10 Serum beta-hCG levels need to be measured on Day 4 and Day 7 post treatment

4.11 Then one serum beta-HCG measurement per week is required until the results are <15IU/L

4.12 Discuss further management with the consultant if hCG levels plateau or increase.

4.13 Advise the woman to avoid alcohol, sexual intercourse and use of folic acid containing vitamins until hCG <15IU/L or the patient has a negative pregnancy test. (see explanation in Section 9).

4.14 The hCG level may increase or she may have pain at Day 4- therefore a reassessment is needed

4.15 If the hCG is not <15% of initial value at Day 7 repeat a transvaginal ultrasound scan to rule out foetal cardiac activity or significant haemoperitoneum.

4.16 If above is ruled out on scan, consider second dose of methotrexate or laparoscopy. Explain to the woman that if her HCG level is more than 2000IU/L, the second dose of methotrexate is more likely to be unsuccessful.

4.17 If a second dose of methotrexate is given,(3-27% of women may need a second dose) serum beta-hCG levels need to be measured on Day 4 and Day 7 post treatment. If the hCG is not <15% of initial value (before second dose) at Day 7 discuss management with the Consultant on call, and consider surgery.

4.18 The decision for intervention at all times is based on the woman's clinical condition and her wishes and must be discussed with the Consultant on call. Treat the woman, not the numbers.

4.19 She must avoid pregnancy for 3 months after methotrexate treatment

4.20 The side effects of Methotrexate are nausea and vomiting, gastritis, diarrhoea, stomatitis, conjunctivitis and transient elevation of liver enzymes

4.21 Inform the consultant if Hb has fallen by >10g/L, ALT rise >25% or urea and creatinine rise >25%

5 Surgical Management

5.1 When surgical treatment is indicated for women with an ectopic pregnancy, it should be performed laparoscopically whenever possible, taking into account the condition of the woman and the complexity of the surgical procedure.

5.2 Surgeons providing care to women with ectopic pregnancy should be competent to perform laparoscopic surgery.

5.3 Offer a salpingectomy to women undergoing surgery for an ectopic pregnancy unless they have other risk factors for infertility.

5.4 Consider salpingotomy as an alternative to salpingectomy for women with risk factors for infertility such as contralateral tube damage.

5.5 Inform women having a salpingotomy that up to 1 in 5 women may need further treatment. This treatment may include methotrexate and/or a salpingectomy.

5.6 For women who have had a salpingotomy, take 1 serum hCG measurement 7 days after surgery, then 1 serum hCG measurement per week until hCG is <5IU/L or negative pregnancy test.

5.7 Advise women who have had a salpingectomy that they should take a urine pregnancy test (UPT) after 3 weeks. Advise women to return for further assessment if the test is positive.

6 Anti-D rhesus prophylaxis

6.1 Offer anti-D rhesus prophylaxis at a dose of 250 IU (50 micrograms) to all rhesus negative women who have a surgical procedure to manage an ectopic pregnancy or a miscarriage

6.2 Do not offer anti-D rhesus prophylaxis to women who receive solely medical management for an ectopic pregnancy

6.3 Do not use a Kleihauer test for quantifying foeto–maternal haemorrhage.

7 Post-treatment care

7.1 Debriefing and discussion with the patient and family is recommended.

7.2 Inform patients they can self-refer to the Early Pregnancy Assessment Clinic (EPAC) for early USS in future pregnancies if they are concerned.

7.3 Information on who to contact and where to go in emergencies, needs to be discussed.

7.4 Any follow-up arrangements need to be documented clearly in the discharge letter and the patient needs to be informed.

8 Management of persistent trophoblast

8.1 This is diagnosed when the fall in hCG has failed to reach less than 10% of the initial value after 14 days (without treatment, or following salpingotomy).

8.2 Out-patient medical therapy with single-dose methotrexate is the treatment of choice, in the haemodynamically stable patient as a consultant decision.

8.3 Check hCG at D4, D7 and D14

8.4 If trophoblast is still persistent then the case should be discussed with a consultant and consideration be given to a further dose of methotrexate or laparoscopy.

8.5 Patients with significant pain may require further surgical intervention

8.6 All women being managed with methotrexate should be given information leaflet on 'Management of persistent trophoblast' and Methotrexate Leaflet

8.7 Persistent Pregnancy of Unknown Location (PUL) may in some circumstances be treated with Methotrexate if decided by the consultant gynaecologist.

9 Notes for all EPAC Nurses

There are 3 conditions in which women are followed up with weekly HCGs.

1- Women with PUL
2- Women with expectant management of ectopic pregnancy
3- Women with medical management of ectopic pregnancy.

There has been some confusion with regards to their follow up mainly because of how the original guidelines were written. Some state follow up until HCG <20IU/L , while others say <15IU/L or< 5IU/L, and some say until UPT is negative.

For practical purposes ALL of the original papers on which these guidelines are based follow up women until to a Negative pregnancy test result.

For this reason and to reduce the number of unnecessary blood tests and visits to EPAC, the Trust policy is as follows:.

If in any of the above 3 conditions where a woman's HCG has been DECREASING over the weeks with an HCG result which is less than 50IU/L, but more than 15IU/L, instead of asking for a further blood test in a week, we will ask the woman to do a pregnancy test at home in a week and we will ring her for the results.

If the UPT is negative – no further follow up is required

If the UPT is positive -offer a further blood test.

So, ALL women will be followed up to an HCG less than 15IU/L or a NEGATIVE pregnancy test.

The most important aspect of the follow up is the ***safety netting***. This is because woman can need emergency surgery for a bleeding ectopic pregnancy even with a decreasing HCG or after a negative pregnancy test.

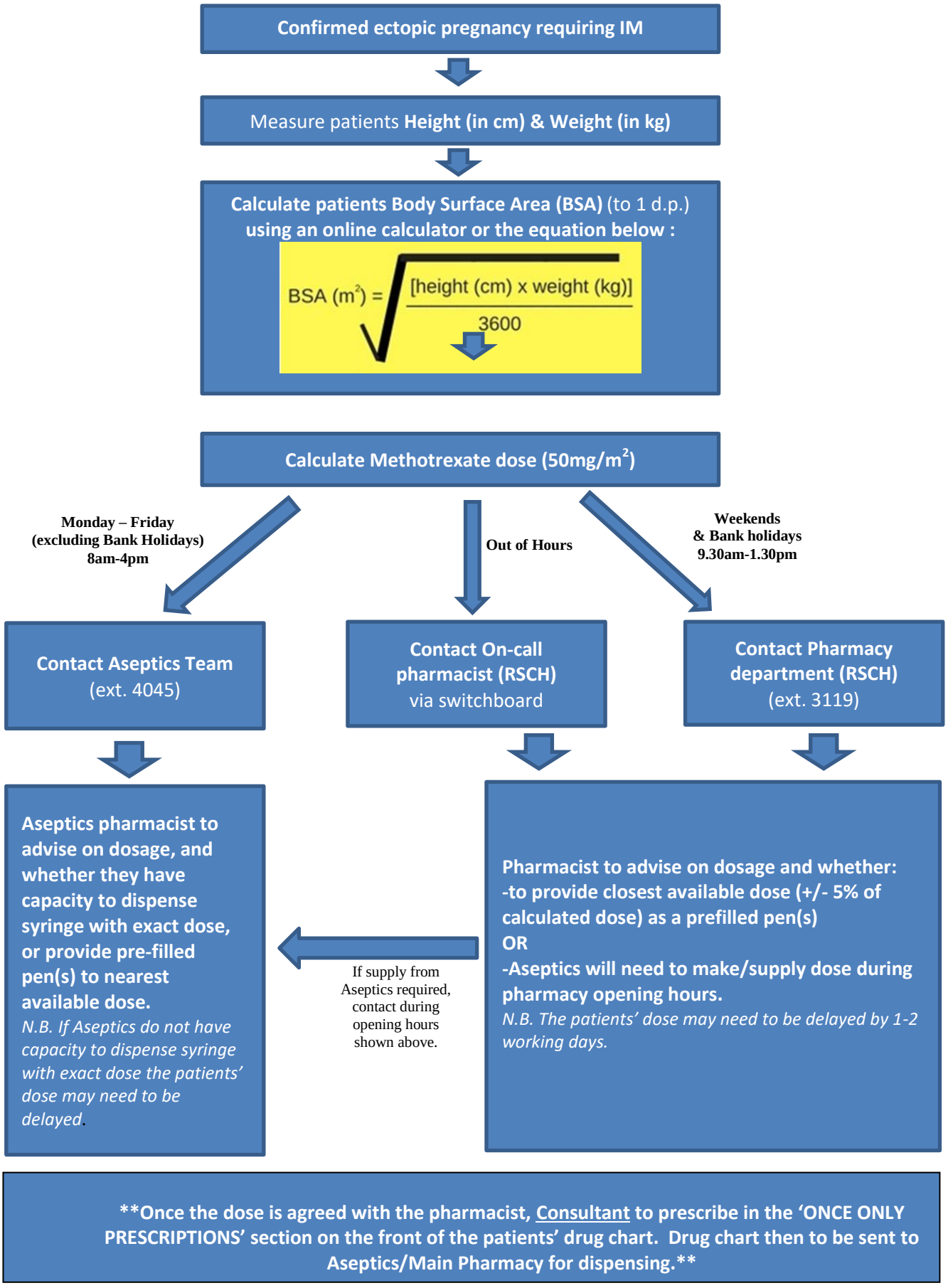
The HCG levels provide a trend view only. Treat the woman, not the numbers.

References

1. National Institute for Health and Clinical Excellence (2019) Ectopic pregnancy and miscarriage: diagnosis and initial management (NG126). London. NICE. | 17 April 2019

2. Diagnosis and Management of Ectopic Pregnancy. Green-top Guideline No. 21 RCOG/AEPU Joint Guideline | November 2016

Appendix I: Flow Chart for Calculating & Obtaining IM Methotrexate for Management of Confirmed Ectopic Pregnancy



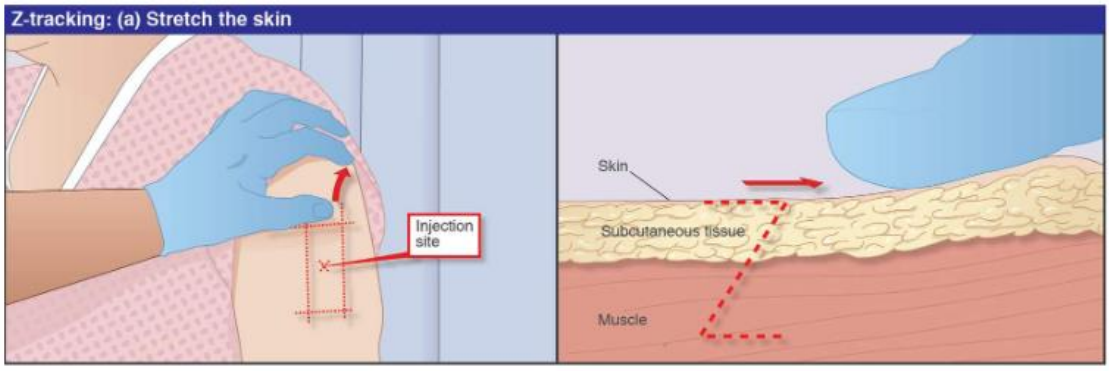
Appendix II

Pharmacy should hold sufficient stock of methotrexate pre-filled pens in 20mg and 30mg strength to cover doses of 50mg-120mg. Other strengths may be available, but direct discussions with Pharmacy will be required to confirm availability.

Pharmacy currently stocks Metoject pre-filled pens which are a licensed product within the UK but are not licensed to be used intramuscularly. Currently in the UK, there are no available pre-filled products that are licensed for use intramuscularly. When such product becomes available we will be obliged to switch to the licensed brand.

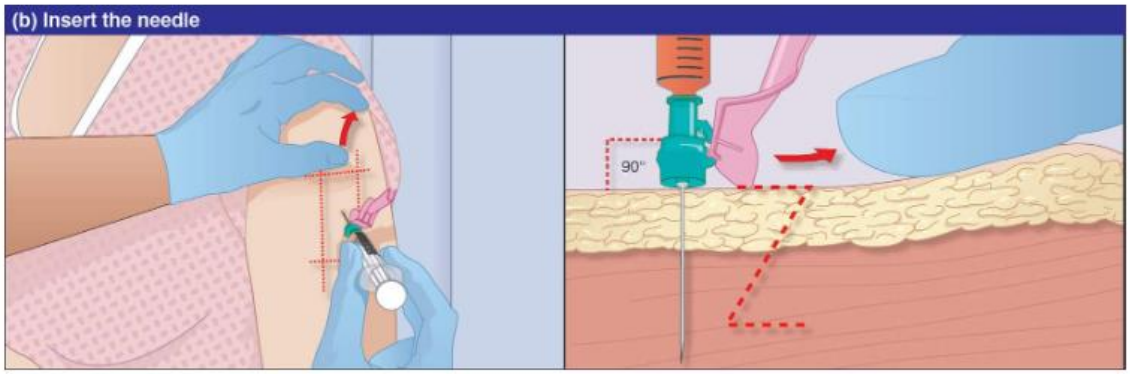
Appendix III

Z-tracking: (a) Stretch the skin



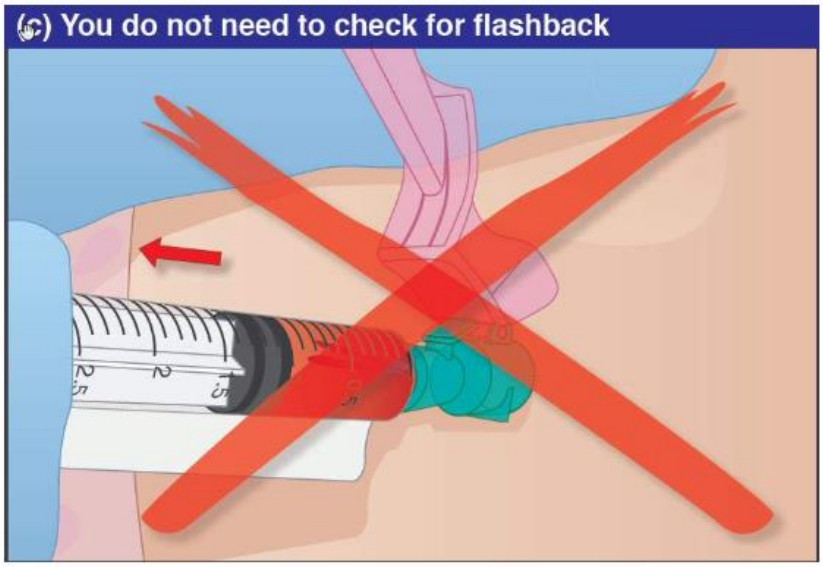
Stretch the skin 2 to 3 cm, using your thumb, as shown. This technique is known as Z-tracking; it reduces pain and leakage from the injection site (Ogston- Tuck, 2014; Nicoll and Hesby, 2002; Rodger and King, 2000).

Z-tracking: (b) Insert the needle



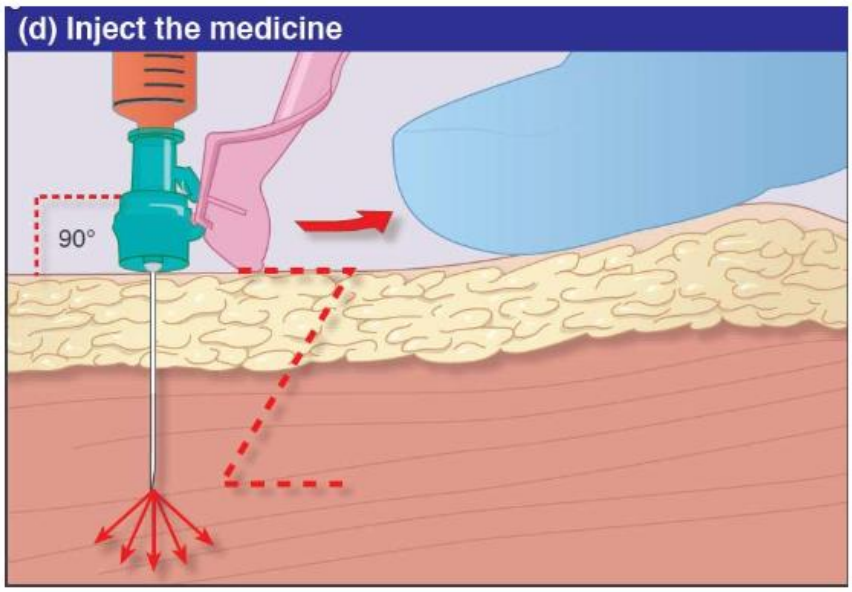
Using a darting motion, insert the needle at an angle of 90º to the skin, as this gives optimum opportunity to reach the target muscle. Insert the full length of the needle; do not leave a gap between the skin and the hub (Malkin, 2008).

Z-tracking: (c) You do not need to check for flashback



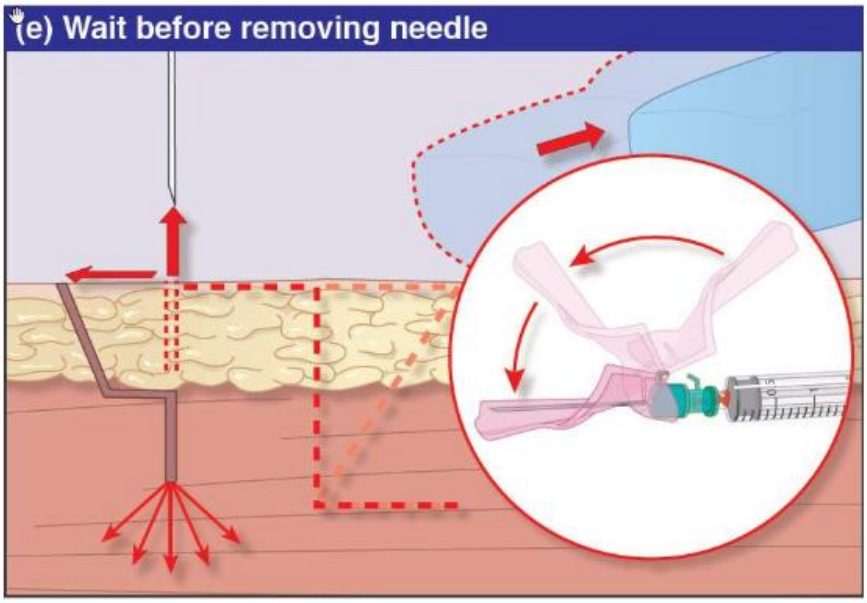
There is no need to pull back on the plunger and check for flashback of blood, as there is no risk of striking a blood vessel at this site (Sisson, 2015; Malkin, 2008).

Z-tracking: (d) Inject the medicine



While maintaining skin traction, inject slowly (approx 1 millilitre per 10 seconds) (Beckton Dickinson, 2003). It is important to inject slowly in order to reduce the pain of the injection, and to allow the muscle fibres to stretch to accommodate the fluid.

Z-tracking: (e) Wait before removing needle



Wait 10 seconds before removing the needle (Ogston-Tuck, 2014). Once the needle is out, immediately release the retracted skin, to allow the medication to disperse evenly, and activate the safety device on the needle (inset).