Medical Management of Ectopic Pregnancy Protocol (CG623)

Approval and Authorisation

<table>
<thead>
<tr>
<th>Approved by</th>
<th>Job Title</th>
<th>Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gynaecology Clinical Governance</td>
<td>Chair, Gynaecology Clinical Governance</td>
<td>15th February 2019</td>
</tr>
</tbody>
</table>

Change History

<table>
<thead>
<tr>
<th>Version</th>
<th>Date</th>
<th>Author</th>
<th>Reason</th>
</tr>
</thead>
<tbody>
<tr>
<td>Version 2</td>
<td>Jan 2019</td>
<td>B Chohan, Consultant Obs &amp; Gynae</td>
<td>Reviewed in line with current NICE guidelines</td>
</tr>
</tbody>
</table>
Contents

1.0 Purpose .............................................................................................................. 3

2.0 Definition ........................................................................................................... 3

3.0 Patient Selection Criteria .................................................................................. 3

4.0 Exclusion Criteria .............................................................................................. 4

5.0 Treatment Protocol ........................................................................................... 4

6.0 Information for Clinician ................................................................................... 5

7.0 Information for Patients .................................................................................... 6

8.0 References ......................................................................................................... 7

Appendix A Criteria for Assessment of Competence ........................................... 8

Appendix B Guidelines for Assessors ................................................................ 10

Appendix C Assessment Summary ................................................................ 11
1.0 Purpose

This protocol has been developed in line with the Joint Royal College of Obstetricians and Gynaecologists & AEPU: Green Top Guideline No. 21: Diagnosis and Management of Ectopic Pregnancy (2016)

The purpose of this protocol is to offer to carefully selected patients medical management of ectopic pregnancy by the administration of intramuscular Methotrexate.

2.0 Definition

Systemic Methotrexate (MTX) Treatment

Methotrexate is a folic acid-antagonist (anti-metabolite) which prevents the growth of rapidly dividing cells by interfering with DNA synthesis. It can be administered systematically (IV, IM or orally). However, it is most commonly given according to a single-dose protocol which involves a single intramuscular dose of 50 mg/m². A single injection of methotrexate is well tolerated and is effective. Published studies have shown a success rate varying from 52% to 94% for single dose administration.

3.0 Patient Selection Criteria

- NO significant pain
- No intrauterine pregnancy
- Unruptured ectopic pregnancy (diagnosed with serial hCG and TVS) – mass <35mm. No FH
- B-hCG values <1500 IU/litre - Offer as first line treatment (NICE 2012)
- B-hCG level 1500 - 5000 IU/litre - Offer MTX or surgery (NICE 2012) – mass <35mm. No FH increases the chance of further intervention and has higher risk of rupture.
- Haemodynamically stable
- Normal LFT’s, U&E’s and FBC
- Failed surgical treatment.
- B-hCG value <1000 IU/litre - repeat serum hCG in 48 hours if the patient remains stable
- Treatment should begin if the levels plateau
- If the levels are rising one must exclude intrauterine pregnancy before starting treatment
- Patient aware of possible lengthy follow-up process and is able to comply
4.0 Exclusion Criteria

- The presence of cardiac activity in an ectopic pregnancy (live ectopic).
- Adnexal mass =&gt;35mm diameter
- Evidence of intra-peritoneal haemorrhage (either clinically or on TVS)
- Active pulmonary disease
- Active infection or immuno-suppressed state including steroid use
- Peptic ulcer or ulcerative colitis
- Hepatic dysfunction, thrombocytopenia (platelet count &lt;100,000), blood dyscrasia (WCC &lt;2000/cm³), severe anaemia
- Difficultly or unwillingness of patient for prolonged follow-up (average follow-up 35 days).
- Patient unsure of choice of treatment

5.0 Treatment Protocol

- Registrar review and Consultant agreement
- Satisfy eligibility and exclusion criteria
- Discuss options for management surgical/medical
- Satisfy eligibility and exclusion criteria
- Counsel the patient and explain treatment protocol.
- Give information leaflet.
- Informed written consent should be obtained and documented, including unlicensed (‘off label’) use of methotrexate
- Record height and weight.
- Organise baseline blood tests: FBC, G&S, LFT’s, U&E’s and hCG.
- Prescribe methotrexate
- Methotrexate should be given as prescribed by appropriately trained staff in line with Trust Policy for administration of cytotoxic drugs.
- An appropriate area should be available for the patient to rest for up to one hour post administration of methotrexate. Before discharge home check patient has no local reaction to the drug.
- Before discharge ensure patient is fully aware of follow-up arrangements within the 602 Clinic.
- Do not prescribe anti-D for medical management of ectopic pregnancy (NiCE2012)
- Patient should attend on Day 4 and Day 7 for serum hCG; FBC;LFT
- If serum hCG has fallen less than 15% of original value, between Day 4 and Day 7, a second dose of methotrexate should be considered after discussion with on-call consultant.
**Single Dose Regime:**

<table>
<thead>
<tr>
<th>Day</th>
<th>Management</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>Serum hCG, FBC, U&amp;E, LFT, G&amp;S</td>
</tr>
<tr>
<td>0</td>
<td>Intramuscular methotrexate 50 mg/m²</td>
</tr>
<tr>
<td>4</td>
<td>Serum hCG</td>
</tr>
</tbody>
</table>
| 7   | Serum hCG, FBC, LFT  
   - If hCG has decreased > 15% repeat hCG weekly until < 10 u/L  
   - **2nd Dose of methotrexate may be necessary between Day 4 and Day 7 if the hCG levels have decreased < 15%** |

**Outcome:**
- 90% successful treatment with single dose regime.
- Recurrent ectopic pregnancy rate 10 – 20%.
- Tubal patency approximately 80%.
- 10% patients require surgery for either ruptured ectopic pregnancy or the hCG does not decline as expected.

Serum hCG levels are expected to rise initially up to Day 4 and then should decline by at least 15% between Day 4 and Day 7. If it does not decline as expected or plateaus, then consider second dose or surgery after discussion with consultant on-call. Trans-vaginal scan may be considered on Day 7 only if there is a suboptimal decline in hCG between Days 4-7 or if the patient is symptomatic with worsening pain.

**6.0 Information for Clinician**
- Up to 75% of patients may complain of pain on days 3 – 7 (thought to be due to tubal miscarriage).
- hCG levels may initially rise between days 1 – 4 (up to 86% of patients)
- The Mean time to resolution is 35 days
- A second dose of methotrexate may be given at Day 7 if the hCG level fails to fall by more than 15% between days 4 – 7 (3-27% (in published literature), 14% of medically treated women will require more than one dose of methotrexate).
- Risk of tubal rupture is 7% and the risk remains while there is persistent hCG.
- Avoid vaginal examination. TVS may be undertaken during first treatment week or subsequently if clinically indicated.
7.0 Information for Patients

- Medical treatment for ectopic pregnancy is now well established, and approximately 90% of patients do not require further surgery. Methotrexate is used for a variety of clinical conditions e.g. psoriasis, as well as for malignancies.

- It is important that all patients considering methotrexate understand that the companies manufacturing methotrexate have not licensed it (‘off-label’) to treat ectopic pregnancy, mainly because it was never anticipated for this use. This off-label treatment occurs fairly frequently (most medicines administered to children are off-label) in medicine. The treatment has been proven to work in selected patients and is recommended by NICE.

- Prolonged follow-up (up to 7 weeks) is required with blood tests until the serum hCG level is below 10 u/L.

- A further dose of methotrexate may be necessary.

- Three quarters of women experience (worsening) abdominal pain following treatment, which is due to the drug acting on tubal pregnancy. It usually occurs on days 3-7 and normally lasts between 4-12 hours. However the patient should be advised to come in urgently if the pain is severe or there are other symptoms such as dizziness or shoulder tip pain.

- Some women will also experience some vaginal bleeding ranging from dark brown spotting to heavier bright red loss, which may last a few days to weeks. Advice is to contact 602 clinic if it is excessive or the patient is concerned.

- Pregnancy should be avoided for 3 months after methotrexate has been given, because of a possible teratogenic effect – advice should be to use barrier contraception (RCOG)

- Side effects of the drug are minimal but may include nausea, vomiting, stomatitis and diarrhoea.

- Maintain ample fluid intake.

- Please avoid:
  - Alcohol or folic acid containing vitamins during treatment as they may interfere with the effectiveness of methotrexate treatment.
  - Sexual intercourse until resolution of the ectopic pregnancy.
  - Exposure to sunlight.
  - Heavy lifting.

- No difference in subsequent fertility rates between medical or surgical treatment
8.0 References


Appendix A Criteria for Assessment of Competence

Administration of Methotrexate Treatment for Patients undergoing Medical Management of Ectopic Pregnancy

Name:  
Date:  
Ward:  
Clinical Services Unit:  

Appointed staff will be able to demonstrate the knowledge, skills and competence necessary to safely administer Methotrexate treatment to patients undergoing Medical Management of Ectopic Pregnancy.

<table>
<thead>
<tr>
<th>COMPETENCES</th>
<th>Signature</th>
<th>OUTCOME SAFE/UNSAFE</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Understands professional accountability with regard to advice and information given to patients</td>
<td>Candidate</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Assessor</td>
<td></td>
</tr>
</tbody>
</table>

GENERAL

<table>
<thead>
<tr>
<th></th>
<th>Signature</th>
<th>OUTCOME SAFE/UNSAFE</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Able to discuss local and national policy for safe handling and administration of cytotoxic drugs</td>
<td>Candidate</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Assessor</td>
<td></td>
</tr>
<tr>
<td>2. Able to discuss the management of spillage (and skin/eye/equipment contamination) of cytotoxic chemotherapy according to local guidelines</td>
<td>Candidate</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Assessor</td>
<td></td>
</tr>
<tr>
<td>3. Demonstrates competence in providing patient/carer education regarding all aspects of methotrexate treatment (selection and exclusion criteria, side effects, general advice etc.).</td>
<td>Candidate</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Assessor</td>
<td></td>
</tr>
</tbody>
</table>

PREPARATION AND ADMINISTRATION

<table>
<thead>
<tr>
<th></th>
<th>Signature</th>
<th>OUTCOME SAFE/UNSAFE</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Able to discuss the procedures of ordering, transporting and storage of methotrexate relevant to own clinical area.</td>
<td>Candidate</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Assessor</td>
<td></td>
</tr>
<tr>
<td>2. Demonstrate awareness of the local policy for obtaining informed consent for administration of methotrexate.</td>
<td>Candidate</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Assessor</td>
<td></td>
</tr>
</tbody>
</table>

Author: Baljinder Chohan  
Job Title: Consultant Obs & Gynae  
Policy Lead: Group Director Urgent Care  
Location: Policy hub/ Clinical/ Gynaecology/ CG623  
This document is valid only on date printed
3. Demonstrates competence in pre-methotrexate treatment assessment (selection and exclusion criteria, blood tests, observations etc)  
   | Candidate | Assessor |

4. Able to discuss normal blood values and their relevance in the administration of methotrexate. Able to identify abnormal blood values relevant to administration of methotrexate and take appropriate action.  
   | Candidate | Assessor |

5. Demonstrate knowledge of calculating drug doses and rate of administration.  
   | Candidate | Assessor |

6. Interprets prescription correctly. Verifies methotrexate dosage, route and expiry date for individual patient. Checks details with competent second nurse/doctor prior to administration.  
   | Candidate | Assessor |

7. Demonstrate competence in risk assessment in relation to handling, administration and disposal of cytotoxic drugs.  
   | Candidate | Assessor |

8. Provides patient with appropriate written information regarding medical management of ectopic pregnancy and administration of methotrexate.  
   | Candidate | Assessor |

9. Is able to give a full explanation of the procedure to the patient allowing time for questions. Maintains patient privacy and dignity at all times.  
   | Candidate | Assessor |

10. Administers methotrexate according to practice guidelines and infection control policy wearing appropriate personal protection.  
    | Candidate | Assessor |

11. Monitors patient and is able to identify signs of any adverse reaction during administration of methotrexate.  
    | Candidate | Assessor |

12. Accurately records administration in all relevant documents.  
    | Candidate | Assessor |

13. Disposes of equipment safely. Demonstrate the awareness of cytotoxic waste disposal and sharps disposal policy.  
    | Candidate | Assessor |
Appendix B  

**Guidelines for Assessors**

The staff will be able to demonstrate the knowledge, skills and attitude necessary to undertake administration of methotrexate for patients undergoing medical management of ectopic pregnancy.

<table>
<thead>
<tr>
<th>Criteria</th>
<th>Guidance</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Understands professional accountability and responsibility</td>
<td>Candidate is able to clearly describe the role and practice to which this protocol relates, relevant codes of practice both professional and Trust wide, and own personal accountability related to the protocol.</td>
</tr>
<tr>
<td>2. Can discuss Consent Policy and Mental Capacity Act(2005)</td>
<td>Candidate is able to accurately identify and discuss key principles. Including demonstrating an awareness of the local policy for obtaining informed consent for the administration of methotrexate.</td>
</tr>
<tr>
<td>3. Demonstrates competence in relation to handling, administration and disposal of cytotoxic drugs.</td>
<td>Candidate is able to discuss both local and national policies regarding safe handling, administration and disposal of cytotoxic drugs. Can demonstrate understanding of calculating methotrexate dosages.</td>
</tr>
<tr>
<td>4. Is able to advise patient regarding all aspects of medical management of ectopic pregnancy.</td>
<td>Candidate can demonstrate full understanding of medical management of ectopic pregnancy, including selection and exclusion criteria, side effects of methotrexate, follow up and aftercare. In line with local protocol.</td>
</tr>
<tr>
<td>5. Provides appropriate written information to patient.</td>
<td>Candidate gives patient appropriate written information regarding treatment.</td>
</tr>
<tr>
<td>6. Is able to give full explanation of the procedure prior to administration of methotrexate, allowing time for questions.</td>
<td>Candidate is able to discuss procedure with patient and can identify issues that require further explanation.</td>
</tr>
<tr>
<td>7. Is able to interpret prescription correctly and check details in line with local and national policies.</td>
<td>Candidate can demonstrate correct interpretation of prescription and check all details in line with Trust and NMC Standards</td>
</tr>
<tr>
<td>8. Is able to complete all relevant documentation appropriately.</td>
<td>Candidate demonstrates that documentation is completed accurately and legibly and in an appropriate time frame.</td>
</tr>
</tbody>
</table>
Appendix C  
Assessment Summary

ASSESSMENT SUMMARY FOR

This is to certify that ………………………………………has successfully completed the competencies related to Administration of Methotrexate for patients undergoing Medical Management of Ectopic Pregnancy.

Signed……………………………………………………………………………………

Name (Print)………………………………………………………………………………

Position …………………………………………………………………………………

Date…………………………………………………………………………………………

Author: Baljinder Chohan  
Date: February 2019  
Job Title: Consultant Obs & Gynae  
Review Date: February 2021  
Policy Lead: Group Director Urgent Care  
Version: V2 ratified 15/2/19  
Location: Policy hub/ Clinical/ Gynaecology/ CG623  

This document is valid only on date printed