Team Name: Pharmacy and Therapeutics Team Lead: Regional Director - Pharmacy Approved by: Regional Lead – Medical Services & Chief Medical Officer	Reference Number: CLI.6010.SG.011 Program Area: Pharmacy and Therapeutics Policy Section: General
Issue Date: September 5, 2023 Review Date: Revision Date:	Subject: Ectopic Pregnancy: Medical and Expectant Management Guideline

Use of pre-printed documents: Users are to refer to the electronic version of this document located on the Southern Health-Santé Sud Health Provider Site to ensure the most current document is consulted.

POLICY SUBJECT:
Ectopic Pregnancy: Medical and Expectant Management Guideline

PURPOSE:
Ectopic pregnancy is a significant cause of morbidity and mortality in the first trimester of pregnancy. Currently, a high index of suspicion, serial hormone assays, and transvaginal ultrasonography facilitate the diagnosis and treatment of ectopic pregnancy before rupture occurs. Early nonsurgical diagnosis and timely treatment have resulted in a dramatic decline in mortality due to ectopic pregnancy. Evidence indicates Methotrexate is an effective and safe pharmaceutical agent for the medical management of an ectopic pregnancy. Methotrexate is a folic acid antagonist preventing DNA replication. It inhibits the rapidly dividing trophoblast cells of an ectopic pregnancy.

BOARD POLICY REFERENCE:
Executive Limitation (EL-2) Treatment of Clients

POLICY:
To guide the effective and safe use of Methotrexate as a pharmaceutical agent for the medical management of an ectopic pregnancy and pregnancy of unknown location.

For the purpose of this document, ectopic pregnancy and pregnancy of unknown location will be referred to as ectopic pregnancy.

DEFINITIONS:
Definitive Ectopic Pregnancy: extrauterine gestational sac with yolk sac and/or embryo (with or without cardiac activity)

Probable Ectopic Pregnancy: Inhomogenous adnexal mass or extrauterine saclike structure

Pregnancy of Unknown Location: no signs of either ectopic pregnancy or intrauterine pregnancy

Persistent Pregnancy of Unknown Location: the serum hCG level fail to decline, there is no evidence of trophoblastic disease and the location of pregnancy cannot be identified using transvaginal ultrasound or laparoscopy

Probable Intrauterine Pregnancy: Intrauterine echogenic sac-like structure

Definitive Intrauterine Pregnancy: Intrauterine gestational sac with yolk sac and/or embryo (with or without cardiac activity)

GUIDELINE:

Indications:

- Hemodynamically stable without active bleeding or signs of hemoperitoneum,
- Patient able and willing to return for follow-up care,
- Unruptured mass 3.5 cm or less, No fetal cardiac activity,
- Plasma/serum B-hCG less than 5000 units/L,
- Patient is experiencing only moderate, well controlled pain,
- Patient has no contraindications to methotrexate.

Absolute Contraindications:

- Immunodeficiency,
- Known hypersensitivity to methotrexate,
- Signs of impending or ongoing ectopic mass rupture (severe or persistent abdominal pain or more than 300 mL of free peritoneal fluid outside pelvic cavity),
- Hemodynamically unstable,
- Coexistent viable intrauterine pregnancy,
- Non-compliant patient.

Relative Contraindications:

- Breast feeding,
- Abnormal creatinine clearance, elevated AST, alcoholism or liver disease,
- Pre-existing blood dyscrasias such as bone marrow hypoplasia, leucopenia, thrombocytopenia or anemia.

Necessary Lab Testing Prior to Methotrexate Therapy:

- Transvaginal ultrasound,
- CBC,
- Liver function tests (AST, ALT, GGT, LDH, Alkaline Phosphatase),
- Creatinine, Quantitative beta-hCG (day 1),

- RH status
    - Unknown: determine,
    - Negative: treat with RH Immumoglobulin (refer to Best Blood Manitoba Guidelines for Perinatal Testing and Administration of WinRho SDF (Rh Immune Globulin),
    - Positive: no treatment.

Single-Dose Regimen and Follow-up:

- The most commonly used regimen is a single dose of Methotrexate of 50 mg/m^2 IM (day 1),
- Patients should be counseled about the ongoing risk of tubal rupture,
- They should avoid NSAIDs, alcohol, and folic acid supplements during therapy,
- If the B-hCG level does not decrease at least 15% between days 4 and 7, then a repeat dose of Methotrexate 50 mg/m^2 IM would be given and repeat the B-hCG measurements on days 4 and 7,
- Once the B-hCG level decreases appropriately, the B-hCG level should be followed weekly until it reaches the nonpregnant level,
- Provide CLI.6010.SG.011.SD.01 - Discharge Information: After Methotrexate Treatment for Ectopic Pregnancy to patient,
- Provide CLI.6010.SG.011.SD.02 - Methotrexate Treatment for Ectopic Pregnancy Patient Information to patient.
- Refer to CLI.6010.SG.011.FORM.01- Ectopic Pregnancy: Methotrexate Standard Orders which is to be used in Regional Centres only, all other sites will need to transfer patient to regional centres.

Methotrexate Toxicity:

- Elevated liver enzyme,
- Gastritis, stomatitis,
- Bone marrow suppression,
- Dermatitis, pleuritis, pneumonitis,
- Toxicity occurs in 5% of cases when multi-dosing is used. Reported cases of toxicity were mild and transient. Complications can occur with a single-dose regimen but these are rare.

Bereavement Support:

- Where a woman and her partner are particularly distressed by their loss, referral to a bereavement support worker may be appropriate; or utilize the following resources:
    - Chapter 7: Loss and grief - Canada.ca
    - Support Groups/Self-Help - Portage la Prairie Resource Guide (portageresourceguide.com)
    - Always Loved, Never Forgotten – Angel Baby
    - Manitoba Angel Dresses

SUPPORTING DOCUMENTS:

CLI.6010.SG.011.FORM.01	Ectopic Pregnancy: Methotrexate Standard Orders
CLI.6010.SG.011.SD.01	Discharge Information: After Methotrexate Treatment for Ectopic Pregnancy
CLI.6010.SG.011.SD.02	Methotrexate Treatent for Ectopic Pregnancy Patient Information