



INTRODUCTION:

Both methotrexate and misoprostol have been approved by the U.S. Food and Drug Administration (FDA) for purposes unrelated to abortion. Administration of methotrexate and misoprostol for induction of abortion in very early pregnancy has been reported in the medical literature, and the scientific evidence indicates that it is safe and efficacious for this use. Clinicians can prescribe methotrexate and misoprostol at their discretion for this off-label use.

These protocol recommendations were initially developed at a meeting convened by the National Abortion Federation (NAF) and Planned Parenthood Federation of America (PPFA) on June 6, 1996. It was attended by the leading researchers who have published in this field as well as clinicians experienced with medical abortion techniques. These recommendations have been updated to reflect the use of methotrexate and misoprostol as supported by the current evidence in the medical literature.

These recommendations were developed to facilitate quality care for women seeking medical abortion, because we recognize that women are increasingly asking for access to medical abortion options, that clinicians are increasingly using it for early abortion, and that practice protocols are necessary to ensure quality care. As further research is completed and additional experience is gained, these recommendations will continue to be modified.

These protocol recommendations are not *Clinical Policy Guidelines*. Rather, they are recommendations based on a medical review of all published literature through October, 2000. All applicable NAF *Clinical Policies Guidelines* should, however, be followed when providing any abortion, either medical or surgical.

Several considerations must be stressed:

- There have been no studies to assess whether routine vs. selective ultrasound use impacts final outcomes in clinical use of medical abortion regimens. However, all published studies using methotrexate/misoprostol have relied upon routine ultrasound for determination of gestational age and confirmation of the completed medical abortion. Since the efficacy of methotrexate/misoprostol regimens decreases after 49 days' gestation, accurate determination of gestational age is critical for this method. For these reasons, transvaginal ultrasound is recommended, especially for practitioners inexperienced with clinical dating of very early pregnancies;
- we urge that great care be taken to provide appropriate and comprehensive options and medical counseling; and
- follow up care to assure complete abortion is critical.

Additionally, delivery of all abortion services requires twenty-four hour availability of a clinician for assessment of potential complications. This is especially critical with medical abortion where bleeding may be greater and delays before expulsion of the pregnancy will be common. Vacuum aspiration may be offered at the clinician's discretion at any time for a patient experiencing a delay in passage of the pregnancy and who is unwilling to wait for the medical abortion to be complete.

In addition to these protocol recommendations, clinicians are strongly encouraged to read the published literature on the subject of medical abortion and attend accredited training programs in medical abortion and early ultrasound diagnosis. We have included a bibliography of important articles. Additionally, NAF's publication "Early Medical Abortion with Mifepristone and Other Agents: Overview and Protocol Recommendations" includes a comprehensive outline and review of the published literature. These resources will provide information that may be useful to you, your clinic staff, and/or your patients.

ELIGIBLE PATIENTS:

1. must be in overall good health and have none of the following:
 - a. acute or chronic renal or hepatic disease;
 - b. coagulopathy or current severe anemia (hematocrit less than 30%; hemoglobin less than 10gm/dl);
 - c. acute inflammatory bowel disease;
 - d. uncontrolled seizure disorders;
 - e. unwillingness to undergo a surgical abortion if indicated;
2. must have gestation no more than 56 days from the first day of the last menstrual period (LMP). Confirmation with ultrasound is strongly recommended. The failure rate for methotrexate/misoprostol increases steadily with gestational age. The failure rate (curettage for bleeding or for viable pregnancy two weeks after methotrexate) at 50-56 days is approximately twice that at 43-49 days. Many providers will choose to limit provision of methotrexate/misoprostol abortions to pregnancies under 50 days. It is recommended that providers who offer methotrexate/misoprostol at 50-56 days' gestation have a full understanding of the data and medical literature regarding appropriate care when using methotrexate/misoprostol at that gestational age range;
3. must be able to give informed consent and comply with treatment requirements;
4. must have ready access to a telephone, emergency medical care, and transportation;
5. must have no other medical contraindications or known intolerance to either methotrexate or misoprostol.

PRECAUTIONS:

1. Although there are no data available on the effect of folate supplementation on the efficacy of methotrexate/misoprostol for abortion, it may be advisable for patients to discontinue use of vitamins containing folate for one week after methotrexate administration.
2. Although there are no data available on the effects of methotrexate while breast-feeding, it is prudent to advise patients to discontinue breast-feeding for 72 hours after methotrexate injection.

COUNSELING, EDUCATION, and INFORMED CONSENT should include:

1. discussion of the decision to have an abortion and assurance that the decision is patient's own;
2. discussion of available abortion methods (e.g. medical abortion, vacuum aspiration) and the risks and benefits of each, as well as discussion about the need to consent to vacuum aspiration or other treatment if and when it is recommended by the clinician;
3. discussion of known side effects and possible complications of methotrexate and misoprostol; explanation that both methotrexate and misoprostol can cause serious fetal anomalies, so that *once methotrexate has been administered, the abortion must be completed, either medically or with vacuum aspiration;*

4. explanation that while both methotrexate and misoprostol have been approved by the FDA for other uses, neither has been approved for induction of abortion;
5. discussion of the amount of time involved, the requirement of multiple visits (with one dose of misoprostol, 67% of patients will abort within 1 week; with a second dose of misoprostol, 80-85% of patients will abort within 2 weeks; in about 1% of cases, non-viable pregnancy tissue may be retained for as long as 6 to 10 weeks), and the failure rate of methotrexate-induced abortions resulting in the need for a surgical abortion; patients should be advised that if their gestational age is greater than 49 days, the success rate for medical abortion will likely be lower; patients should also be advised that if the pregnancy is not fully expelled from the uterus it could cause infection or other complications.
6. discussion of amount of pain that might occur and the use of pain medications;
7. instruction concerning the vaginal insertion or administration of misoprostol tablets or suppositories;
8. discussion of the amount of bleeding associated with the abortion process and, in particular, the size of the clots and embryo. An embryo is approximately the size of a grain of rice at the time when medical abortion with methotrexate/misoprostol is most commonly provided, and is typically not seen;
9. availability of contraception and contraceptive counseling;
10. a review of the consent form;
11. compliance with additional applicable state and local laws, ordinances, regulations, and common law governing the consent process and standard of care for abortion procedures.

MEDICAL HISTORY and PHYSICAL EXAMINATION should include:

1. a thorough medical and obstetrical history, including history of allergies and all current patient medications;
2. pelvic examination, and pertinent physical examination, including height and weight for calculation of intramuscular methotrexate dose;
3. baseline blood pressure.

ULTRASOUND:

1. Transvaginal ultrasound is recommended to confirm gestational age. Document ultrasound examination (gestational sac; embryonic pole; presence of cardiac activity; yolk sac) in the medical record before administering methotrexate.
2. As soon as the embryonic pole is visible, use this measurement instead of gestational sac measurement.
3. If an intrauterine sac is not present, this could indicate early intrauterine pregnancy or ectopic pregnancy (or miscarriage if patient has had bleeding).
 - a. If patient is *at low risk for possible ectopic pregnancy*:
 - 1) give precautions for ectopic pregnancy signs and re-evaluate in 1 week; **OR**
 - 2) measure quantitative serum -hCG
 - a) -hCG \geq 2,000 IU/L: pregnancy is very likely ectopic and patient should be treated accordingly;
 - b) -hCG <2,000 IU/L: could be consistent with an intrauterine or ectopic pregnancy. Management based on the clinician's judgment should be to:
 - (1) give precautions for ectopic pregnancy and re-evaluate in 1 week; **OR**
 - (2) proceed with methotrexate/misoprostol abortion treatment regimen and follow the serum quantitative -hCG to zero at an interval deemed appropriate by the clinician.

- b. If patient is *at high risk of possible ectopic pregnancy*, measure quantitative -hCG:
- 1) -hCG $\geq 2,000$ IU/L: pregnancy is very likely an ectopic pregnancy and patient should be treated accordingly;
 - 2) -hCG $< 2,000$ IU/L: could be consistent with an intrauterine or ectopic pregnancy. Management based on the clinician's judgment should be to:
 - a) give precautions for ectopic pregnancy and follow the patient until intrauterine or extrauterine pregnancy is confirmed, and then give appropriate treatment; **OR**
 - b) proceed with methotrexate/misoprostol treatment regimen and follow the serum quantitative -hCG to zero at an interval deemed appropriate by the clinician.

LAB WORK:

1. Hemoglobin or hematocrit;
2. Rh factor;
3. Evaluation of renal function (serum creatinine) and/or hepatic function (aspartate transaminase) only if clinically indicated;
4. Quantitative serum -hCG:
 - a. not necessary if transvaginal ultrasound demonstrates gestational sac;
 - b. perform if clinically indicated for evaluation of possible ectopic pregnancy;
5. Other tests as medically indicated.

MEDICATION and FOLLOW-UP:

OPTION I:

DAY 1:

- a. Methotrexate 50 mg/m² IM or 50 mg po
- b. Rh immune globulin for Rh-negative patients (can be administered on Day 1 or any day prior to misoprostol administration).
- c. Provide patient with adequate analgesic information and prescription.
- d. Provide patient with misoprostol 800 µg (as 4-200 µg tablets) with instructions for self-insertion on Day 3-7.

DAY 8:

Obtain patient history and perform transvaginal ultrasound.

- a. If gestational sac is absent, treatment is complete.
- b. If gestational sac is still present, repeat misoprostol dose. This can either be administered by the clinician or given to the patient to self-administer in the office or later at home.
 1. If no cardiac activity is present in the gestational sac, follow-up in approximately 3-4 weeks.
 2. If cardiac activity is present in the gestational sac, follow-up in 1 week.

DAY 15: (if completed abortion has not been confirmed)

Obtain patient history and perform transvaginal ultrasound.

- a. If gestational sac is absent, treatment is complete.
- b. If gestational sac is still present with cardiac activity, perform vacuum aspiration.

- c. If gestational sac is still present without cardiac activity, follow-up in approximately 3 weeks. Patients should be given appropriate instructions regarding what to expect with delayed passage of the pregnancy.

DAY 29-45: (if completed abortion has not been confirmed)

Obtain patient history and perform transvaginal ultrasound.

- a. If gestational sac is absent, treatment is complete.
- b. If gestational sac is still present, perform vacuum aspiration.

OPTION II:

DAY 1:

- a. Methotrexate 50 mg/m² IM or 50 mg po.
- b. Rh immune globulin for Rh-negative patients (can be administered on Day 1 or any day prior to misoprostol administration).
- c. Provide patient with adequate analgesic information and prescription.
- d. Provide patient with two doses of misoprostol 800 µg with instructions for self-insertion of the first dose on Day 3-7. The second dose should be administered 24 hours later if little or no bleeding occurs.

DAY 8:

Optional office visit if bleeding has occurred. Perform transvaginal ultrasound to determine status of pregnancy and provide patient reassurance.

DAY 15: (if completed abortion has not been confirmed)

Obtain patient history and perform transvaginal ultrasound.

- a. If gestational sac is absent, treatment is complete.
- b. If gestational sac is still present with cardiac activity, perform vacuum aspiration.
- c. If gestational sac is still present without cardiac activity, follow-up in approximately 3 weeks. Patients should be given appropriate instructions regarding what to expect with delayed passage of the pregnancy.

DAY 29-45: (if completed abortion has not been confirmed)

Obtain patient history and perform transvaginal ultrasound.

- a. If gestational sac is absent, treatment is complete.
- b. If gestational sac is still present, perform vacuum aspiration.

CONCLUSION OF TREATMENT:

When a transvaginal ultrasound confirms expulsion of the gestational sac, the abortion has been completed. The patient should receive follow-up instructions to include information about expected length of bleeding, increased heavy vaginal bleeding (which may indicate an incomplete abortion), and any other pertinent medical information.

SELECTED STUDIES ON REGIMENS WITH METHOTREXATE/MISOPROSTOL:

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These education materials are intended as guidelines and do not dictate an exclusive course of management. These materials contain recognized methods and techniques of medical care that represent currently appropriate clinical practice. Variations in the needs of individual patients and differences in the resources available to clinical providers may justify alternative approaches to those contained in these materials. Neither the National Abortion Federation, its officers, employees, or members are responsible for adverse clinical outcomes that might occur in the course of delivery of abortion services in which they are not expressly and directly involved in the role of primary caregiver.

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