NAF Protocol for Early Abortion with Mifepristone and Misoprostol

Note: The NAF protocol describes evidence-based regimens for medical abortion. The regimens recommended within this protocol are based on the published scientific literature. Additional information on the evidence base for medical abortion with mifepristone and misoprostol is provided in NAF's Clinical Policy Guidelines (CPGs). National and local laws may restrict what can be offered. The regimens approved in the United States and Canada is included for comparison purposes.

Key Findings from Medical Abortion Research

1. Mifepristone 200 mg is as effective as mifepristone 600 mg.(1-3)
2. Home administration of misoprostol has been found to be safe and effective and is highly acceptable to patients.(4)
3. Compared to regimens using misoprostol 400 µg orally, regimens using misoprostol 800 µg vaginally are more effective.(5, 6)
4. When using 200 mg mifepristone and 800 µg misoprostol vaginally, the time interval between mifepristone and misoprostol may range from 0 to 72 hours.(7-9)
5. In regimens using 200 mg mifepristone and 800 µg misoprostol buccally, efficacy is high, similar to vaginal administration and superior to oral administration.(10, 11) To use the buccal route, women place two tablets of misoprostol 200 µg in each cheek (total of four tablets) for 30 minutes. Any remnants of tablets are to be swallowed after 30 minutes.

ELIGIBILITY:

1. Women considering medical abortion with mifepristone and misoprostol:
   a. Should not have any of the following:
      - hemorrhagic disorder or concurrent anticoagulant therapy
      - chronic adrenal failure
      - concurrent long-term system corticosteroid therapy
      - confirmed or suspected ectopic pregnancy or undiagnosed adnexal mass
      - inherited porphyrias
      - IUD in place (must remove before treatment);
      - history of allergy to mifepristone, misoprostol, or other prostaglandin; and
   b. Should have gestation no more than 70 days LMP
   c. Must be able to give informed consent and comply with treatment requirements.
   d. Should have access to a telephone and transportation to a medical facility equipped to provide emergency treatment for serious complications, including prompt evacuation of the uterus and blood transfusion for hemorrhage.
2. Special considerations:
   a. Breastfeeding. No evidence supports pumping and discarding of breast milk while undergoing medical abortion. Mifepristone levels in breast milk after a mother receives 600

mg of mifepristone are low, and are undetectable after a 200 mg dose.(12) Levels of misoprostol in breast milk are also low, and the small amounts ingested by infants should not cause any adverse effects.

b. Anemia. As in the case of surgical abortion, current severe anemia should be considered when assessing eligibility. Most early research studies of medical abortion regimens did not include women with a hemoglobin <10 gm/dl, although clinical practice varies.
c. Serious systemic illness. Any patient with serious systemic illness (e.g. severe liver disease, significant cardiac disease, renal failure, uncontrolled seizure disorder) should be evaluated individually to determine the safest method of pregnancy termination. As a general rule, the earlier a pregnancy ends, the safer it is for the woman.

COUNSELING, EDUCATION, and INFORMED CONSENT

Counseling and education should be conducted to ensure that desires of the patients are met and the purpose and the process is understood. Informed consent should be documented. It is also important to remain in compliance with applicable national, state, and local laws and regulations governing the consent process. The process of counseling, education, and informed consent should include the following items:

1. Discussion of the decision to have an abortion and assurance that the decision is the patient's own and without coercion.
2. Discussion of available abortion methods (e.g., medical abortion, uterine aspiration) and the risks and benefits of each in relation to the alternative of continuing the pregnancy, including the risk of death for all options.
3. A review of aftercare instructions, including 24-hour emergency contact information.
4. Discussion of known side effects and possible complications of abortion with mifepristone and misoprostol. This discussion should include the following information:
    a. Expected side effects and the differences between side effects and complications. The following symptoms warrant contacting the provider immediately:
        i. soaking two or more maxi-pads per hour for two consecutive hours
        ii. sustained fever >38ºC (100.4ºF) or onset of fever more than 24 hours after taking misoprostol
        iii. abdominal pain or discomfort, or "feeling sick" including weakness, nausea, vomiting, or diarrhea more than 24 hours after taking misoprostol
        iv. light bleeding or spotting, accompanied by one-sided, severe lower abdominal pain, with dizziness, shoulder pain or shortness of breath, particularly when an intrauterine pregnancy (IUP) was not confirmed by pre-treatment ultrasound (these symptoms are strongly suggestive of rupturing ectopic pregnancy and the clinician should assist with arranging the patient's immediate access to emergency services).
    b. The possibility of continued pregnancy, particularly in the absence of bleeding.
    c. Fetal malformations have been reported after first-trimester use of misoprostol.

5. Anticipatory guidance for the length of time involved in the medical abortion process and the need to confirm termination of pregnancy.
6. Instruction on the administration of misoprostol
    a. For the buccal use, the importance of retaining the tablets between check and gum for 30 minutes prior to swallowing the residual tablets should be discussed.
    b. For vaginal use, hand washing prior to placement deep in the vagina should be discussed.
    c. For the subligual use, the importance of retaining the tablets under the tongue for 30 minutes prior to swallowing the residual tablets should be discussed.
    d. For buccal and sublingual usage, gastrointestinal side effects and their management should be addressed.
7. Anticipatory guidance for the variation in pain experienced by patients and the use of pain medications. Pain is typically described by patients as cramping and is self-limiting. It is often most intense during the actual expulsion of the pregnancy, commonly for a two- to four-hour period, although possibly preceded and followed by intermittent mild cramping. Once treatment has been initiated, the patient should have ready access to a supply of pain medication and instructions for use. A non-steroidal anti-inflammatory drug (NSAID) should be provided to patients. The best studied of these is ibuprofen.(13, 14) An opioid such as codeine is also commonly given.(7, 8)
8. Anticipatory guidance for the amount and quality of bleeding and the passage of tissue associated with the abortion process, including the following key points:
    a. Bleeding is typically heavier than menses and may be greater as gestational age increases.
    b. The passage of clots is common.
    c. In the earliest pregnancies, an embryo is usually not distinguishable, but even when the gestation is close to 10 weeks and the embryo may be visible, it is very small and often passes unnoticed within a clot.
    d. Bleeding is uncommon before misoprostol is used. If bleeding occurs in the interval between using mifepristone and misoprostol, misoprostol should still be used as instructed.
    e. Patients should be instructed to call if little or no bleeding occurs within 24 hours following administration of misoprostol.
    f. Patients should be advised that they may (rarely) experience a second episode of heavy bleeding several weeks after initiating medical abortion.
9. Local and national regulations should be followed, such as special consent forms or other information that must be provided to patients. If a mandated informed consent form is used, a facility-specific informed consent form for medical abortion should also be used. If the provider is using an evidence-based regimen that differs from the nationally approved regimen, the facility's informed consent should detail the evidence-based regimen being used and should specify how the regimen differs from the nationally approved labeling.

10. Information regarding privacy and confidentiality precautions.
11. The availability of contraception and contraceptive counseling, with initiation of contraception, if desired by the patient, as soon as possible. Hormonal contraception should be initiated as soon as possible after the misoprostol, ideally within 7 days. Contraceptive implants may be provided safely on the day of *mifepristone* administration.(15) Ovulation may occur as soon as 8 days after mifepristone use.(16)

MEDICAL HISTORY and PHYSICAL EXAMINATION should include the following:

1. Pertinent medical and obstetrical history, including history of allergies and all current medications
2. Vital signs and pertinent physical examination as indicated
3. Determination of gestational age by clinical assessment, which may include history, physical exam, and/or ultrasonography.

LABORATORY EVALUATION should include**:**

1. Test to confirm pregnancy, if not confirmed by other means such as ultrasonography.
    a. If follow-up with serum hCG is planned, the initial serum hCG should be obtained at the initial lab evaluation.
    b. If follow-up with a multi-level urine pregnancy test (MLPT) is planned, the first MLPT should be used at this time to establish the initial level.
2. Rh testing, if not known
3. Hemoglobin or hematocrit, if indicated
4. Other tests as medically indicated.

ULTRASONOGRAPHY**:**

Ultrasonography is often used to determine gestational age. However, its use is not required for safe provision of medical abortion with mifepristone and misoprostol. When used, the guidelines for ultrasonography in NAF's Clinical Policy Guidelines [http://prochoice.org/education-and-advocacy/cpg/] should be followed. If an ectopic pregnancy is suspected, further evaluation is warranted. Mifepristone should not be administered until a suspected ectopic pregnancy has been definitively ruled out.

MEDICATION

1. Mifepristone 200 mg is given to the patient to take orally.
2. Misoprostol 800 mcg is given to the patient to use vaginally or buccally at home.
    a. If used vaginally, the misoprostol can be used from 0 to 72 hours after the mifepristone, though it is recommended that the patient return home before using the misoprostol.
    b. If used buccally, the misoprostol can be used 24 to 48 hours after the mifepristone.

FOLLOW-UP:

Success of the medical abortion must be assessed by ultrasonography, hCG testing, or clinical means in the office, by telephone, or electronic communication.(17-19) Follow-up evaluation should be scheduled within 14 days after starting medical abortion.(20)

1. When ultrasonography is used, the goal is to confirm absence of the previously visualized pregnancy. Absence of the pregnancy confirms success. Endometrial thickness alone should not be used to guide management after medical abortion.(21, 22)
2. When serum hCG levels are used, at 6-10 days after mifepristone, blood is drawn for beta-hCG, at clinic or lab.
    a. If beta hCG drops by at least 60% in comparison to the initial hCG level, then the abortion was successful (23, 24).
    b. If beta hCG drops by less than 60%, further evaluation is warranted. A continuing pregnancy is unlikely unless the beta-hCG has increased.
3. Urine pregnancy testing is not recommended for follow-up evaluation until multi-level urine pregnancy tests become available. High-sensitivity urine hCG testing should not be checked within 3 weeks of medical abortion due to the high-risk of false positive tests.(25-27)
4. When continuing pregnancy is diagnosed at the follow-up visit, the patient has two management options: (1) additional misoprostol, usually 800 mcg vaginally (28, 29) or (2) uterine aspiration completion. Patients given additional misoprostol for continuing pregnancy should return in 2-8 days for evaluation.

Absent a persistent gestational sac or fetal pole, the diagnosis of incomplete abortion and indications for uterine aspiration should be based on a combination of history, physical exam, and ultrasound findings, rather than on ultrasound imaging alone.

CONCLUSION OF TREATMENT

Comprehensive follow-up care is important. Delivery of all abortion care requires 24-hour availability of a clinician for assessment of potential complications. This is especially critical with medical abortion as the patient is expected to participate in monitoring her own process and may need assistance in determining whether or not intervention is indicated. Uterine aspiration may be offered as an option for any patient experiencing unexpected distress with the process of medical abortion.

Once completion of the medical abortion is confirmed, information on the expected length and quantity of normal post-abortion bleeding, the signs and symptoms of complications, and any pertinent instructions should be provided to the patient. At this time, providers should also follow up with the contraceptive counseling initiated during the first visit, revising method planning and supplies as needed.

COMPARISON OF FDA-APPROVED AND OTHER EVIDENCE-BASED REGIMENS FOR MIFEPRISTONE AND MISOPROSTOL IN EARLY ABORTION

	NAF vaginal regimen	NAF buccal regimen	Original US FDA Labeling	2016 US FDA Labeling	Canadian labeling
Mifepristone	200 mg p.o.	200 mg p.o.	600 mg p.o.	200 mg p.o.	200 mg p.o.
Misoprostol	800 µg per vagina	800 µg buccal	400 µg p.o.	800 µg buccal	800 µg buccal
Interval between drugs	0-72 hours	24-48 hours	48 hours	24-48 hours	24-48 hours
Location of misoprostol use	Home	Home	In the office or clinic	"at location appropriate for the patient"	
Gestational age limit	≤70 days	≤70 days	≤49 days	≤70days	≤49days
Risk of continuing pregnancy	0.5%	0.5%			
Timing of follow-Up	Before day 14	Before day 14	Day 14	Day 7-14	Day 7-14
Method of follow-up	Multiple	Multiple	In office	medical history, clinical exam, hCG testing, or sonography	

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Appendix I. FDA-APPROVED LABEL

Clinicians should be familiar with the manufacturers' labeling and offer patients the corresponding educational materials; this information is beyond the scope of this document but is available from Danco Laboratories. Medications must be administered by or under the supervision of a healthcare provider who prescribes and has been appropriately trained to: assess the pregnancy's gestational age; diagnose ectopic pregnancies; provide uterine aspiration intervention or have plans in place to provide such care through others if needed; and assure patient access to emergency medical facilities equipped to provide blood transfusions and emergency resuscitation during the treatment procedure.

A brief outline of the regimen follows:

DAY 1:

a. Mifepristone 200 mg is given as a single oral dose.
b. Rh immune globulin is administered to Rh-negative patients.

DAY 2-3:

Misoprostol Administration (minimum 24-hour interval between MIFEPREX and misoprostol) Four 200 mcg tablets (total dose 800 mcg) of misoprostol are taken by the buccal route. Patients taking MIFEPREX must take misoprostol within 24 to 48 hours after taking MIFEPREX. The effectiveness of the regimen may be lower if misoprostol is administered less than 24 hours or more than 48 hours after mifepristone administration.

DAY 7-14:

Patients should follow-up with their healthcare provider approximately 7 to 14 days after the administration of MIFEPREX. This assessment is very important to confirm that complete termination of pregnancy has occurred and to evaluate the degree of bleeding. Termination can be confirmed by medical history, clinical examination, human Chorionic Gonadotropin (hCG) testing, or ultrasonographic scan. Lack of bleeding following treatment usually indicates failure; however, prolonged or heavy bleeding is not proof of a complete abortion.

Disclaimer

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 care in which they are not expressly and directly involved in the role of primary caregiver