Mifepristone/misoprostol abortion care protocol

The Food and Drug Administration (FDA) updated its labeling for mifepristone on March 29, 2016. The new label incorporates most recent evidence, allowing certified prescribers to provide medication abortion in a way that minimizes adverse effects while enhancing safety, privacy, and convenience for patients and clinicians. On January 3, 2023, the FDA updated the Risk Evaluation and Mitigation Strategy (REMS) for mifepristone, removing an in-person dispensing requirement and allowing certified pharmacies to dispense mifepristone. In states that do not restrict telehealth for medication abortion, mifepristone can be sent via mail.[1]

Protocol Summary for Medication Abortion with Mifepristone and Misoprostol

Maximum gestational age	77 days from last menstrual period (LMP)[2,3]
Mifepristone dose	200 mg. orally
Misoprostol dose/route	800 mcg. Buccally, sublingually, or vaginally (4 tablets)
Misoprostol timing	24-48 hours after mifepristone* For gestational ages over 9 weeks, repeat misoprostol 3-4 hours after initial dose.
Misoprostol location	Home
Follow-up	Optional. Ensure patients have a way to reach you for questions or concerns.
Prescriber	Any prescribing clinician, including advanced practice clinicians.**
Dispensing	In-person at clinic, via mail through clinic or certified mail-order pharmacy, or in-person at certified pharmacy.

*For gestational ages under 5 weeks and over 8 weeks, recommend 24 hour administration for any route.
**In states that require abortions to be performed by a licensed physician, advanced practice clinicians cannot provide abortion care.[4]

[1] US Food and Drug Administration. Mifeprex (mifepristone) Information. January 2023. Accessed January 2023. https://www.fda.gov/drugs/postmarket-drug-safety-information-patients-and-providers/mifeprex-mifepristone-information.
[2] Dzuba I et al. A Non-Inferiority Study of Outpatient Mifepristone-Misoprostol Medical Abortion at 64-70 Days and 71-77 Days of Gestation. Contraception. 2020. 101(5):302-308.
[3] Kapp N et al. Medical Abortion in the Late First Trimester: A Systematic Review. Contraception. 2019. 99(2):77-86.
[4] Guttmacher Institute. An Overview of Abortion Laws. June 2022. Accessed June 2022. https://www.guttmacher.org/state-policy/explore/overview-abortion-laws

Initial Assessment – Day 1

Counseling

1. Options counseling: Consider abortion, or continuing the pregnancy and parenting, or adoption. Advise that medication abortion has a failure rate (i.e. ongoing pregnancy) of about 1 in 250 and an aspiration abortion may be needed in 1 to 3 of 250 cases.[5] Compared with aspiration abortion, medication abortion causes longer bleeding duration and more abdominal cramping. Medication abortion is non-invasive, avoids surgical and anesthetic risk, and can occur very early in pregnancy. It has been perceived by many patients to be more natural, and allows more privacy and control.[6] (See consent form.)

2. Review of expected effects: Bleeding and cramping (usually heavier than with menses) are expected. Diarrhea and other gastrointestinal side effects are common. There is a very small risk of prolonged bleeding requiring uterine aspiration. The patient should be instructed in how much bleeding would be considered excessive (patient is soaking through more than 2 pads per hour for 2 hours in a row) and when to call the clinician.

3. Adherence to protocol: Explain to the patient the process and the importance of finishing the medication abortion protocol. If the abortion is unsuccessful, an aspiration abortion or a repeat dosing of medications is recommended due to the possible teratogenicity of misoprostol.[7,8]

Compliance with State Requirements

Many states have specific requirements affecting abortion. Most of these laws apply both to medication and aspiration abortion. Clinicians must comply with mandatory waiting periods, parental notification, gestational age limits, and department of health reporting as required. To find out more about these regulations, consult the Center for Reproductive Rights at www.reproductiverights.org/.

Medical History and Physical Exam

1. Confirm pregnancy with a urine pregnancy test.

2. Rule out contraindications:

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[5] Committee on Practice Bulletins-Gynecology, Society of Family Planning. Medication Abortion up to 70 Days of Gestation. American College of Obstetricians and Gynecologists Practice Bulletin. 2020(225). https://www.acog.org/clinical/clinical-guidance/practice-bulletin/articles/2020/10/medication-abortion-up-to-70-days-of-gestation

[6] Winikoff B. Acceptability of medical abortion in early pregnancy. Family Planning Perspectives. 1995;27:142-148. https://www.guttmacher.org/journals/psrh/1995/07/acceptability-medical-abortion-early-pregnancy.

[7] Yip SK, Tse AO, Haines CJ, Chung TK. Misoprostol's effect on uterine arterial blood flow and fetal heart rate in early pregnancy. Obstet Gynecol 2000;95:232–5.

[8] Marques-Dias MJ, Gonzalez CH, Rosemberg S. Mobius sequence in children exposed in utero to misoprostol: neuropathological study of three cases. Birth Defects Res A Clin Mol Teratol 2003;67:1002–7.

- IUD in place (may be removed prior to medication abortion)[9]
- Allergy to prostaglandins or mifepristone
- Chronic adrenal failure
- Long-term systemic corticosteroid therapy
- Ectopic pregnancy
- Hemorrhagic disorders
- Concurrent anticoagulant therapy (excluding aspirin)

3. Ensure the patient has access to a telephone and/or transportation in case they need to reach you.

4. Obtain a medical history. A bimanual exam can assist in gestational dating if the patient is not sure about their last menstrual period.

Dating Pregnancy

Ultrasound examination should be performed if gestational age is uncertain, if there is a size/date discrepancy, if the patient's last menstrual period occurred while they were taking hormonal contraception, if the patient has a history of irregular menses, if the clinician suspects ectopic pregnancy, or if the LMP places them over 77 days.[10,11,12] If none of these conditions warrant an ultrasound, a quantitative hCG may be done prior to the administration of the mifepristone and again at a follow-up visit to monitor the success of the abortion. The hCG level does not "date" the pregnancy; it allows for a comparison of the hCG levels before and after to assure a drop of > 80% at one week after the cramping and bleeding.

Laboratory studies

A quantitative hCG level may be needed as above. A baseline hemoglobin or hematocrit level can be obtained, especially if there is a history of anemia. Testing for Rh status can be considered if the patient's status is unknown, however the evidence supporting this practice is minimal. Based on current practice guidelines, it is reasonable to forgo this testing up to 77 days LMP, however institutional policies may vary and it is important to be familiar with the standards for your practice setting.[13]

Review the required provider/patient agreement and the consent form.

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[9] Foster, Diana Greene, et al. "Interest in and experience with IUD self-removal." Contraception 90.1 (2014): 54-59.
[10] Bracken H, Clark W, Lichtenberg ES, Schweikert SM, Tanenhaus J, Barajas A, et al. Alternatives to routine ultrasound for eligibility assessment prior to early termination of pregnancy with mifepristone-misoprostol. BJOG 2011;118:17–23.
[11] Schonberg D, Wang LF, Bennett AH, Gold M, Jackson E. The accuracy of using last menstrual period to determine gestational age for first trimester medication abortion: a systematic review. Contraception 2014;90:480–7.
[12] Raymond EG, Grossman D, Mark A, et al. Commentary: No-test medication abortion: A sample protocol for increasing access during a pandemic and beyond. Contraception. 2020;101:361-366. doi:10.1016/j.contraception.2020.04.005
[13] National Abortion Federation. "Clinical Policy Guidelines 2022." (2022) https://prochoice.org/providers/quality-standards.

Give medication (or prescription for pharmacy) and directions for misoprostol administration:

Buccal/sublingual administration: The patient will insert four 200-microgram misoprostol tablets 24-48 hours after taking mifepristone.[14] They should hold two tablets in each cheek or four tablets under the tongue for 30 minutes, and then swallow any remaining fragments.
Vaginal administration: The patient will insert four 200-microgram misoprostol tablets in the vagina 6-72 hours after taking mifepristone.[15] They should then lie down for 30 minutes. If the tablets fall out after 30 minutes, they can be discarded. If your patient is concerned about privacy, you can counsel them to put the pills inside their cheeks or under their tongue. This way, there will be no pill fragments left behind.

If expulsion (i.e., cramping and heavy bleeding) does not occur within 24 hours of the initial misoprostol dose, the patient should consult the clinician. A repeat dose of misoprostol or an ultrasound exam may be indicated.

Repeat dosing: Patients with gestational age over 9 weeks should use a second misoprostol dose (four tablets by the same mucosal route) four hours after the first dose.

Advise patients in hostile environments: Patients in hostile environments (i.e. anti-abortion states, near Catholic hospitals, etc.) should consider using misoprostol buccally or sublingually to avoid having pill fragments in the vagina in the rare instance that they need an in-person follow-up exam.

Advise patient on use of supportive medications: Prescriptions for ibuprofen 800 mg and/or acetaminophen with or without an opioid should be offered to the patient. Offering anti-emetics, such as ondansetron or meclizine, may also be considered. Patients should be encouraged to fill the prescription/s in advance and to have the pain medications on hand to be taken as needed.[16,17]

Make sure the patient knows how to reach the clinician on-call: An information sheet with instructions about how to reach the clinician should be reviewed with each patient. The patient should be instructed to call their clinician if they do not bleed within 24 hours of using the misoprostol, if bleeding exceeds two maxi-pads per hour for two consecutive hours, or if they begin to feel very ill at any time during the medication abortion process.
Give mifepristone: 200-milligram tablet by mouth to be taken in the office or at home.

[14] Chen MJ and Creinin MD. Mifepristone With Buccal Misoprostol for Medical Abortion: A Systematic Review. Obstet Gynecol. 2015 Jul;126(1):12-21. doi: 10.1097/AOG.0000000000000897.
[15] Schaff EA, Fielding SL, Westhoff C, Ellertson C, Eisinger SH, Stadalius LS, et al. Vaginal misoprostol administered 1, 2, or 3 days after mifepristone for early medical abortion: A randomized trial. JAMA 2000;284:1948-53.
[16] Committee on Practice Bulletins-Gynecology, Society of Family Planning. Medication Abortion up to 70 Days of Gestation. American College of Obstetricians and Gynecologists Practice Bulletin. 2020(225). https://www.acog.org/clinical/clinical-guidance/practice-bulletin/articles/2020/10/medication-abortion-up-to-70-days-of-gestation
[17] National Abortion Federation. "Clinical Policy Guidelines 2022." (2022) https://prochoice.org/providers/quality-standards.

Offer post-abortion contraception: Patients who choose combination hormonal contraceptives (oral, patch, ring) may begin the method as soon as the next day or on the most convenient day after taking misoprostol – even if bleeding persists. The implant may be inserted the same day that the patient takes mifepristone. The progestin injection (Depo Provera) on the same day that patient takes mifepristone may somewhat decrease the effectiveness of the medication abortion, but can safely be initiated on the day of mifepristone or at a follow-up visit, depending on patient preference. Same day progestin injection is associated with increased ongoing pregnancy rate compared to initiation at follow-up (3.6% vs 0.9%), but patient satisfaction is higher.[18] IUD insertion can take place at a follow-up visit. Patients may begin to have vaginal sex with barrier contraception when they feel comfortable. Patients who choose a permanent method should be referred as appropriate to avoid delays.

Follow-up is optional.

1. To assess the completeness of the abortion, clinicians may use any of the following criteria:
    - history (patient's description of bleeding - which should be at least as much as their menses – with cramping and passage of clots accompanied by resolution of any pregnancy symptoms); or
    - declining serum hCG levels (by more than 80% at one week after the bleeding); or
    - ultrasound; or
    - negative home pregnancy test 4 weeks after mifepristone.[19,20,21,22]

2. If an at-home pregnancy test is still positive after 4 weeks after taking mifepristone, a repeat pregnancy test should be performed in office. If pregnancy is ongoing, i.e. a rising serum hCG or an ultrasound with a growing pregnancy, an aspiration procedure can be performed. If the abortion is incomplete (i.e. an ultrasound showing no interval growth and no fetal cardiac activity, but with retained tissue and continued bleeding), the patient can choose a repeat dose of misoprostol or an aspiration procedure. If the pregnancy was being followed by quantitative hCGs and levels did not fall as expected, an urgent ultrasound should be obtained to assess for failed abortion vs ectopic pregnancy.

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[18] Raymond EG, Weaver MA, Louie KS, et al. Effects of Depot Medroxyprogesterone Acetate Injection Timing on Medical Abortion Efficacy and Repeat Pregnancy: A Randomized Controlled Trial. *Obstet Gynecol*. 2016;128(4):739-745. doi:10.1097/AOG.0000000000001627

[19] Perriera LK, Reeves MF, Chen BA, Hohmann HL, Hayes J, Creinin MD. Feasibility of telephone follow-up after medical abortion. Contraception. 2010;81(2):143-9.

[20] Chen MJ, Rounds KC, Creinin MD, Casino C, Hou MY. Comparing office and telephone follow-up after medical abortion. Contraception. 2016;94(2):122-126.

[21] World Health Organization. Medical management of abortion. Geneva: WHO; 2018. Available at: https://apps.who.int/iris/bitstream/handle/10665/278968/9789241550406-eng.pdf?ua=1.

[22] Baiju N, Acharya G, D'Antonio F, Berg RC. Effectiveness, safety and acceptability of self-assessment of the outcome of first-trimester medical abortion: a systematic review and meta-analysis. BJOG 2019;126:1536–44. (Systematic Review and Meta-Analysis)