JAMA Insights | WOMEN'S HEALTH

Medication for Early Pregnancy Termination

Rebecca H. Cohen, MD, MPH; Stephanie B. Teal, MD, MPH

The US Food and Drug Administration (FDA) first approved a medication abortion regimen in 2000, which consisted of mifepristone (a progesterone antagonist that causes pregnancy tissue to detach from the endometrium) and misoprostol (a prostaglandin that induces cervical softening and uterine contractions). Current evidence-based regimens still rely on this drug combination, which is approved for abortions up to 10 weeks' gestational age. In 2017 in the US, medication abortions accounted for an estimated 60% of abortions at less than 10 weeks' gestation.[1]

Patients may opt to terminate an early pregnancy with medication rather than dilation and curettage because they perceive it as more private and less invasive.[2] Patients may prefer being in control of the timing and setting of their abortion or may have concerns about surgery and its potential complications.[2] As legislative barriers continue to reduce the ability of physicians to provide and of patients to access procedural abortions, the use of medication abortion will likely increase.[1] Medication abortion regimens are within the scope of care of clinicians who can diagnose pregnancy, estimate gestational age, discuss pregnancy options, have knowledge of medication adverse effects and safety, provide follow-up, and identify and manage (or refer for management of) complications.[3] Contraindications to medication abortion are summarized in the **Box**.

Box. Medication Abortion Contraindications and Cautions

Medication Abortion Contraindications

Pregnancy >70 days' (10 weeks') gestation[a]

Allergy to mifepristone or misoprostol

Intrauterine device in place (can proceed after removal)

Inherited porphyria

Adrenal insufficiency or chronic adrenal failure

Concurrent use of long-term corticosteroid therapy

Bleeding disorder or use of anticoagulant therapy

Current ectopic pregnancy

Use Cautiously

Patients with severe anemia

Patients at high risk of loss to follow-up (eg, lack of phone or transportation)

Obtain Ultrasonography Before Providing Medication Abortion

Irregular or uncertain last menstrual period

Vaginal bleeding

Unilateral abdominal pain

History of ectopic pregnancy

Conceived with intrauterine device in place or after tubal ligation

[a] The FDA approved medication abortion until 70 days' gestation. When clinical access is limited (eg, due to the pandemic), it can safely be offered until 77 days' gestation.

Prescribing for Medication Abortion

Gestational age is typically determined by the date of the last menstrual period. Although preprocedure ultrasonography is common, mandatory ultrasonography can pose a barrier to access.[4] In asymptomatic patients without risk factors for ectopic pregnancy (such as known tubal occlusion) or inaccurate self-estimation of gestational age (such as irregular menses or conception while using contraception), less than 1% of presumed early pregnancies are too advanced for medication abortion or are found to be ectopic pregnancies.[5,6]

The regimen for medication abortion includes mifepristone, 200 mg, given orally, followed by misoprostol, 800 µg, buccally 24 to 48 hours later or vaginally 6 to 48 hours later. Prophylactic antibiotics and routine measuring of hemoglobin levels are not recommended.[2]

The American College of Obstetricians and Gynecologists recommends offering Rh blood testing for patients with unknown Rh status and Rh immunoglobulin testing for those with Rh-negative blood types.[2] However, the risk of Rh sensitization after early abortion is negligible based on in vitro data,[7] and clinicians can consider forgoing this testing for medication abortion for patients at less than 70 days' (10 weeks') gestation.[4] As with all pregnancy-related visits, clinicians should assess partner/family support and screen for risk of violence.

Patient Experience

Patients typically have minimal or no symptoms with mifepristone and are expected to have strong cramping and heavy bleeding with use of misoprostol. Nonsteroidal anti-inflammatory drugs are more effective than acetaminophen (paracetamol) for pain management, and opioids should be used rarely, if at all.[2]

Although cramping and bleeding diminish after the pregnancy tissue passes, light cramping is normal for a few days and light bleeding is common for a few weeks. Common adverse effects of misoprostol include nausea or vomiting (up to 30% of patients), diarrhea (up to 25% of patients), and low-grade fever or chills (up to 50% of patients) within 24 hours of administration. Pregnancy symptoms, such as nausea and fatigue, typically resolve within 1 week after complete medication abortion.

Follow-up

The FDA requires that patients initiating medication abortion follow up with their clinician about 7 to 14 days after taking mifepristone to assess for completion and complications.[3] Prior to the COVID-19 pandemic, ultrasonography was typically used to document expulsion of the gestational sac. Sonographic endometrial stripe thickness varies after medication abortion and a "thickened" stripe alone does not require intervention if the patient is hemodynamically stable without heavy bleeding or signs of infection.[2] A review of 6 randomized clinical trials that involved 6886 patients reported that remote follow-up by telephone, text, or online questionnaire using symptom checklists, followed by confirmatory urine pregnancy test 4 to 5 weeks after receiving mifepristone, was preferred by patients and equally effective at detecting ongoing pregnancy compared with an in-person visit.[8]

Contraception

Fertility returns rapidly after medication abortion. Clinicians can safely provide any form of contraception, except for intrauterine devices, at mifepristone ingestion.[2] Contraceptive implants and medroxyprogesterone acetate injection can be initiated immediately, obviating the need for a second visit in many cases. Contraceptive pills, patches, or rings can be prescribed at the time of mifepristone provision and started after pregnancy expulsion.

Risks and Management of Complications

In some cases, the pregnancy is not terminated after administration of medications for inducing abortion and continues to be viable, with this risk increasing with gestational age (less than 0.5% prior to 7 weeks; up to 3.4% at 10 weeks).[2] Because misoprostol can be teratogenic, patients with ongoing pregnancy should be counseled on the risks and benefits of repeating the medication abortion regimen, having a uterine aspiration abortion, or continuing the pregnancy. Retained nonviable pregnancy tissue occurs in less than 3% of cases and can be managed expectantly with repeat misoprostol or with dilation and curettage based on patient preference.[2]

Hemorrhage and infection are rare but serious complications and require prompt evaluation. Patients should be evaluated if they have unusually heavy bleeding (soaking >2 pads/h for >2 h in a row), fever more than 24 hours after using misoprostol, recurrence of severe abdominal pain after passage of pregnancy tissue, or persistence of pregnancy symptoms more than 1 week after medication abortion. Clinicians can reassure patients and families that medication abortion has not been associated with long-term adverse mental health (anxiety, depression, or suicidality) or physical health outcomes, including future fertility.[9]

No-Test Medication Abortion

Since FDA approval, mifepristone has been subject to a Risk Evaluation and Mitigation Strategy (REMS).[3]

The REMS required that ordering clinicians register with mifepristone distributors and that the drug be dispensed directly to patients in clinics rather than sold through retail pharmacies.[3] In response to the COVID-19 pandemic, the FDA permanently removed the in-person dispensing requirement for mifepristone.[3] Protocols were developed for provision of medication abortion without ultrasonography or blood testing.[4] Pregnant individuals with a gestational age of less than 77 days who have no risk factors or symptoms of ectopic pregnancy can be offered mifepristone and misoprostol without testing, recognizing the less than 1% risk of missing an ectopic pregnancy or more advanced gestation.[5,6] Some states require that the prescribing clinician be physically present when mifepristone is administered, effectively preempting the use of telehealth abortion services.

Self-managed Medication Abortion

Some people may opt to purchase mifepristone and misoprostol outside of the formal medical system, such as from entities that provide mail-order medication and advertise these services outside of US prescribing regulations, especially in places where access to abortion care is restricted.[10] After taking the medications, these patients may present for evaluation with pain or bleeding similar to miscarriage. Evaluation should focus on confirming complete abortion via ultrasonography and managing rare complications, such as hemorrhage or infection.[10]

Although self-managed medication abortion is illegal in some states, clinicians who provide care for these patients should focus on patient safety. Clinician reporting of suspected self-managed medication abortion to authorities violates patients' right to privacy and delays effective medical care.[10]

Legal and Regulatory Issues

In 2018, the National Academies of Sciences, Engineering, and Medicine released a report that demonstrated no benefit to patient health or safety from the many regulations related to abortion provision,[9] including no benefit to assigning mifepristone a restrictive REMS. Nevertheless, clinicians must be familiar with their state laws regarding medication abortion, including gestational age limits, parental consent or notification requirements for minors, waiting periods, elements of counseling (eg, state-mandated scripts or ultrasonography viewing), and follow-up.

Summary

Medication abortion is safe, effective, and widely used in the US and it meets the needs of potential patients. Even though certain state and federal laws regarding provision of mifepristone can unnecessarily complicate care delivery, medication abortion remains an important option for patients in early pregnancy.

ARTICLE INFORMATION

Author Affiliations: Division of Complex Family Planning, Department of Obstetrics and Gynecology, University of Colorado School of Medicine, Aurora (Cohen); University Hospitals Cleveland Medical Center, Cleveland, Ohio (Teal); Departments of Obstetrics and Gynecology and Reproductive Biology, Case Western Reserve University School of Medicine, Cleveland, Ohio (Teal).

Corresponding Author: Stephanie B. Teal, MD, MPH, 11100 Euclid Ave, MAC 5034, Cleveland, OH 44106 (Stephanie.Teal@UHhospitals.org).

Published Online: June 2, 2022. doi:10.1001/jama.2022.6344

Conflict of Interest Disclosures: None reported.

REFERENCES

1. Jones RK, Witwer E, Jerman J. *Abortion Incidence and Service Availability in the United States, 2017*. Guttmacher Institute; 2019.
2. American College of Obstetricians and Gynecologists' Committee on Practice Bulletins—Gynecology, Society of Family Planning. Medication abortion up to 70 days of gestation. *Obstet Gynecol*. 2020;136(4):e31-e47.
3. Questions and answers on Mifeprex. US Food and Drug Administration. Accessed May 23, 2022. https://www.fda.gov/drugs/postmarket-drug-safety-information-patients-and-providers/questions-and-answers-mifeprex
4. Raymond EG, Grossman D, Mark A, et al. Commentary: no-test medication abortion. *Contraception*. 2020;101(6):361-366.
5. Ralph LJ, Ehrenreich K, Barar R, et al. Accuracy of self-assessment of gestational duration among people seeking abortion. *Am J Obstet Gynecol*. 2022;226(5):e1-e21. doi:10.1016/j.ajog.2021.11.1373
6. Tao G, Patel C, Hoover KW. Updated estimates of ectopic pregnancy among commercially and Medicaid-insured women in the United States, 2002-2013. *South Med J*. 2017;110(1):18-24.
7. Horvath S, Tsao P, Huang Z-Y, et al. The concentration of fetal red blood cells in first-trimester pregnant women undergoing uterine aspiration is below the calculated threshold for Rh sensitization. *Contraception*. 2020;102(1):1-6.
8. Schmidt-Hansen M, Cameron S, Lohr PA, Hasler E. Follow-up strategies to confirm the success of medical abortion of pregnancies up to 10 weeks' gestation: a systematic review with meta-analyses. *Am J Obstet Gynecol*. 2020;222(6):551-563.e13.
9. *The Safety and Quality of Abortion Care in the United States*. National Academies Press; 2018.
10. Harris LH, Grossman D. Complications of unsafe and self-managed abortion. *N Engl J Med*. 2020;382(11):1029-1040.