

# ACOG PRACTICE BULLETIN

## Clinical Management Guidelines for Obstetrician–Gynecologists

NUMBER 225

(Replaces Practice Bulletin Number 143, March 2014)

**Committee on Practice Bulletins—Gynecology and the Society of Family Planning.** This Practice Bulletin was developed jointly by the Committee on Practice Bulletins—Gynecology and the Society of Family Planning in collaboration with Mitchell D. Creinin, MD, and Daniel A. Grossman, MD.

## Medication Abortion Up to 70 Days of Gestation

*Medication abortion, also referred to as medical abortion, is a safe and effective method of providing abortion. Medication abortion involves the use of medicines rather than uterine aspiration to induce an abortion. The U.S. Food and Drug Administration (FDA)-approved medication abortion regimen includes mifepristone and misoprostol. The purpose of this document is to provide updated evidence-based guidance on the provision of medication abortion up to 70 days (or 10 weeks) of gestation. Information about medication abortion after 70 days of gestation is provided in other ACOG publications (1).*

### Background

#### **Epidemiology**

An estimated one in four women in the United States will have an abortion in her lifetime. In 2017, an estimated 60% of abortions in the United States occurred at or before 10 weeks of gestation and medication abortion comprised 39% of all abortions (2). Between 2006 and 2015, there was a shift in the timing of abortion, with abortions taking place at earlier gestational ages; this is likely due, in part, to availability of medication abortion (3). From 2014 to 2017, the number of nonhospital facilities that provided medication abortion increased by 25% (2). A recent survey of American College of Obstetricians and Gynecologists (ACOG) Fellows and Junior Fellows found that 14% had provided medication abortion in the prior year (4).

#### **Medication Abortion**

The medication abortion regimen supported by major medical organizations nationally and internationally includes two medications, mifepristone and misoprostol (5, 6). If

mifepristone is unavailable, then a misoprostol-only regimen is an acceptable alternative (5). Mifepristone is a selective progesterone receptor modulator that binds to the progesterone receptor with an affinity greater than progesterone itself but does not activate the receptor, thereby acting as an antiprogesterin (7). Mifepristone's known actions on a uterus during pregnancy include decidual necrosis, cervical softening, and increased uterine contractility and prostaglandin sensitivity (8, 9). Misoprostol is a prostaglandin E1 analogue that causes cervical softening and uterine contractions. It is approved by the FDA for oral administration to prevent gastric ulcers in individuals who take anti-inflammatory drugs on a long-term basis, and it is included in the FDA-approved labeling of mifepristone for use in abortion (10).

The FDA currently restricts mifepristone access under the risk evaluation and mitigation strategy (REMS) program, which includes a requirement that the drug be “dispensed to patients only in certain health-care settings, specifically clinics, medical offices, and hospitals, by or under the supervision of a certified prescriber” (10). However, the REMS

restrictions for mifepristone do not make the care safer, are not based on medical evidence or need, and create barriers to clinician and patient access to medication abortion (4, 11, 12). The American College of Obstetricians and Gynecologists advocates the removal of REMS restrictions for mifepristone (12).

## Clinical Considerations and Recommendations

### ► *How should patients be counseled about abortion methods?*

Only when patients have considered their options and decided to have an abortion does the discussion about the different methods become clinically relevant. Patients who choose abortion should be counseled about all methods available as well as the risks, advantages, disadvantages, and the different features of these options (5, 6). Most patients who initially are unsure about the method will have some preference after counseling (13). Generally, patients are satisfied with the method they choose (12, 14, 15). Patients who choose medication abortion tend to do so because of a desire to avoid a procedural intervention; a perception that medication abortion is safer, more natural, and private compared with uterine aspiration; or a combination of these reasons (16). Compared with uterine aspiration, medication abortion takes longer to complete and requires more active patient participation as the pregnancy expels outside of a clinical setting. The uterine aspiration procedure for a first-trimester abortion takes place most commonly in one visit, is slightly more effective, and allows for direct assessment of pregnancy tissue by the clinician.

### ► *What information and counseling should be provided to patients who are considering medication abortion?*

#### **Eligibility and Contraindications**

Most patients at 70 days of gestation or less who desire abortion are eligible for a medication abortion. There are medical conditions for which a medication abortion may be preferable to uterine aspiration. Such examples include uterine fibroids that significantly distort the cervical canal or uterine cavity (17, 18), congenital uterine anomalies (19), or introital scarring related to infibulation (20). Patients with asthma are candidates for medication abortion because misoprostol does not cause bronchoconstriction and actually acts as a weak bronchodilator (21). Multiple gestation

pregnancy is not a contraindication; patients with twin gestations can be treated with the same regimens as those with singleton gestations (22).

Medication abortion is not recommended for patients with any of the following: confirmed or suspected ectopic pregnancy, intrauterine device (IUD) in place (the IUD can be removed before medication abortion), current long-term systemic corticosteroid therapy, chronic adrenal failure, known coagulopathy or anticoagulant therapy, inherited porphyria, or intolerance or allergy to mifepristone or misoprostol (23). Patients with significant comorbidities may still have a medication abortion but may need more monitoring during the process depending on the stability of the conditions. The safety of medication abortion in patients with anemia is unknown because studies have excluded patients with anemia who have hemoglobin levels of less than 9.5 or 10 g/dL. Although the transfusion rates associated with medication abortion are low (less than 0.1%), they exceed those reported for uterine evacuation procedures in early pregnancy (0.01%) (24, 25). Patients may also not be good candidates for medication abortion if they are unable or unwilling to adhere to care instructions, desire quick completion of the abortion process, are not available for follow-up contact or evaluation, or cannot understand the instructions because of comprehension barriers.

#### **What to Expect**

Most patients who have a medication abortion will experience bleeding and cramping, which are necessary for the process to occur. Patient counseling should emphasize that bleeding likely will be much heavier than menses (and potentially with severe cramping).

Adverse effects can occur after mifepristone administration but are more typically experienced after misoprostol administration. Adverse effects commonly associated with misoprostol use include nausea (43–66%), vomiting (23–40%), diarrhea (23–35%), headache (13–40%), dizziness (28–39%), and thermoregulatory effects such as fever, warmth, hot flushes, or chills (32–69%) (26–29). The incidence of each adverse effect varies by regimen used, the dose and route of administration of the prostaglandin analogue, and the gestational age.

Patient counseling before medication abortion should include discussion of when patients should contact their clinician in the case of heavy bleeding (soaking more than two maxi pads per hour for 2 consecutive hours) and when to access urgent intervention (5, 6, 30). In rare cases, patients who undergo medication abortion may need to obtain an additional intervention, such as uterine aspiration. If the prescribing

clinician does not perform the intervention, it is medically appropriate to provide a referral. In patients who receive mifepristone and vaginal misoprostol, the need for intervention within the first 24 hours of treatment is rare, occurring in 0.2% of patients (31). The need for intervention is based on how the patient is feeling and whether the bleeding seems to be slowing. For patients with heavy bleeding, a baseline hemoglobin or hematocrit, if known, may also influence when to seek urgent care. Overall, less than 1% of patients will obtain an emergency intervention for excessive bleeding (13–15, 32), and the need for blood transfusion is rare (0.1% of patients or less) (24, 33). Should a rare medical emergency arise, patients should be advised to seek care at the closest emergency facility.

### ***Teratogenicity and Ongoing Pregnancy***

Before undergoing medication abortion, patients should be counseled regarding the teratogenicity of misoprostol in the event of an unsuccessful medication abortion. All patients with a continuing pregnancy after using mifepristone and misoprostol should be provided with all pregnancy options and a thorough discussion of the risks and benefits of each. Most individuals with a continuing pregnancy opt to complete the abortion, but patients should be supported in their choice of how to proceed. No evidence exists to date of a teratogenic effect of mifepristone (34). However, misoprostol can result in congenital anomalies, such as limb defects with or without Möbius' syndrome (ie, facial paralysis), when used during the first trimester (35–39). Because misoprostol is the common agent used with every medication abortion regimen, clinicians should counsel all patients regarding potential teratogenic effects.

In the very rare case that patients change their mind about having an abortion after taking mifepristone and want to continue the pregnancy, they should be monitored expectantly (40). There is no evidence that treatment with progesterone after taking mifepristone increases the likelihood of the pregnancy continuing (41, 42). However, limited available evidence suggests that use of mifepristone alone without subsequent administration of misoprostol may be associated with an increased risk of hemorrhage (43).

### **► *What evaluation and ancillary testing is needed before a medication abortion?***

Before medication abortion is performed, the clinician should confirm pregnancy and estimate gestational age. For patients with regular menstrual cycles, a certain last menstrual period within the prior 56 days, and no signs, symptoms, or risk factors for ectopic pregnancy, a

clinical examination or ultrasound examination is not necessary before medication abortion. Rh testing is recommended in patients with unknown Rh status before medication abortion, and Rh D immunoglobulin should be administered if indicated (44). In situations where Rh testing and Rh D immunoglobulin administration are not available or would significantly delay medication abortion, shared decision making is recommended so that patients can make an informed choice about their care. Other laboratory evaluations are not routinely indicated but may be required by local and state laws (2). Preoperative assessment of hemoglobin or hematocrit is indicated only when anemia is suspected.

Most abortion care globally is provided without ultrasound examination. Although most U.S.-based studies have used ultrasonography to confirm gestational age and intrauterine location of the pregnancy, more recent evidence has shown that a patient's certain last menstrual period when within the prior 56 to 63 days is accurate (45–48). In one study, use of certain last menstrual period alone would have resulted in medication abortion being provided to only 26 of 3,041 (0.8%) patients with pregnancies beyond 70 days of gestation (45).

A potential concern when providing early abortion services is the possibility of an undiagnosed ectopic pregnancy. The overall ectopic pregnancy rate in the U.S. general population is low and declining and is approximately 6 per 1,000 pregnancies among insured patients and 14 per 1,000 among patients who receive Medicaid (49, 50). However, in studies of patients who seek abortion, ectopic pregnancy rates generally are lower. A U.S. study of uterine evacuation procedures performed at less than 6 weeks of gestation found the ectopic pregnancy rate to be 5.9 per 1,000 pregnancies (51) at a time when the national rate was three times higher (52). The largest published study of first-trimester medication abortion patients involved 16,369 patients with pregnancies of 49 days of gestation or less and yielded a calculated ectopic pregnancy rate of 1.3 per 1,000 pregnancies (53). Although ectopic pregnancy among individuals who seek early abortion is rare, patients with a medical history of ectopic pregnancy, medical risk factors (prior tubal surgery, pregnancy with progestin-only or IUD contraception use) or symptoms (ie, unilateral pain, vaginal bleeding) suggestive of ectopic pregnancy should have pretreatment clinical evaluation, which may include ultrasonography (5, 6).

Most patients with clinical indications for an ultrasound examination before medication abortion can be initially screened with transabdominal ultrasonography, reserving transvaginal ultrasonography for situations in which further clarification is required (54, 55).

If ultrasonography is medically indicated, transabdominal ultrasonography is sensitive for diagnosing the presence or absence of a gestational sac in patients who are not obese (54). A randomized trial that compared the use of transabdominal ultrasonography with transvaginal ultrasonography for eligibility assessment before medication abortion found that 80% of patients who received initial transabdominal ultrasonography did not require further testing to proceed with medication abortion, thus avoiding use of more invasive and resource-intensive screening with transvaginal ultrasonography (55).

Recommendations on whether Rh D immune globulin should be given to patients before medication abortion in early pregnancy are primarily based on expert opinion because available evidence is limited (6, 56). Rh D alloimmunization that is left undiagnosed and untreated can lead to significant perinatal morbidity and mortality in future pregnancies (57). And, guidelines from ACOG and various other major medical societies include recommendations for Rh D immune globulin prophylaxis for Rh D-negative patients undergoing medication abortion within the first 12 weeks of gestation (44, 58–60). For patients undergoing medication abortion before 10 weeks of gestation, some experts recommend against routine Rh testing and anti-D prophylaxis (6) or advise that forgoing Rh typing and Rh prophylaxis can be considered (61). Research regarding Rh alloimmunization during early pregnancy continues to evolve (62). However, based on currently available indirect evidence and the theoretical risk of Rh D alloimmunization in future pregnancies, ACOG recommends Rh D immune globulin prophylaxis for Rh D-negative patients undergoing medication abortion. In situations where Rh testing and anti-D prophylaxis are not available or would significantly delay medication abortion, shared decision making is recommended so that patients can weigh the benefits and risks of their options and make an informed decision about their care.

► ***What regimens are used for medication abortion, and how do they compare in effectiveness for treatment?***

Combined mifepristone–misoprostol regimens are recommended as the preferred therapy for medication abortion because they are significantly more effective than misoprostol-only regimens. If a combined mifepristone–misoprostol regimen is not available, a misoprostol-only regimen is the recommended alternative (5, 63, 64). Mifepristone is approved by the U.S. FDA to be used with misoprostol for medication abortion through 70 days of gestation (23), but evidence also exists to support use with more advanced gestations (1, 5). The recommended medi-

cation abortion regimens are listed in Table 1. With all regimens, the mifepristone dose is the same: 200 mg taken orally. The misoprostol portion of the regimen is more variable in terms of dose, route, and timing. Oral use of misoprostol is not recommended because it may result in lower overall efficacy (65). In general, patients prefer a shorter interval between the two medications (66). These regimens have been extensively studied and are similarly safe and effective (5). Offering options provides patients with flexibility in the timing of abortion and the ability to avoid possible adverse effects related to the misoprostol route. Gastrointestinal adverse effects are less common when misoprostol is administered vaginally as compared with regimens that use oral, buccal, or sublingual misoprostol (65, 67). Buccal and sublingual administration cause similar adverse effects, with the sublingual route associated with a higher rate of chills (68).

Complete abortion rates with all regimens are highest at earlier gestational ages (Table 2). *Medication abortion failure* (defined as the need for uterine aspiration because of ongoing pregnancy or retained tissue) increases with advancing gestational age through 70 days of gestation (Table 2), although failure rates remain low even at this point. Clinicians should counsel patients that medication abortion failure rates, especially continuing pregnancy rates, increase as gestational age approaches 10 weeks.

► ***Who is qualified to provide medication abortion, and in what settings can medication abortion be provided?***

Any clinician with the skills to screen patients for eligibility for medication abortion and to provide appropriate follow-up can provide medication abortion. Clinicians who wish to provide medication abortion services should be trained to perform uterine evacuation procedures or should be able to refer to a clinician who has this training (5, 69).

In addition to physicians, advanced practice clinicians, such as nurse–midwives, physician assistants, and nurse practitioners, possess the clinical and counseling skills necessary to provide first-trimester medication abortion (70). Randomized trials in Mexico, Nepal, and Sweden have consistently found that patients randomized to receive medication abortion under the care of a nurse or nurse–midwife had a statistically equivalent risk of complete abortion compared with those under the care of a physician, without increased risk of adverse events (71–73). In some U.S. states, advance practice clinicians can provide medication abortion; however, many states require that a physician perform an abortion and prohibit provision of medication abortion by nonphysician clinicians (2).

**Table 1. Medication Abortion Regimens Up to 70 Days of Gestation**

| Regimen                       | Mifepristone Dose | Misoprostol Dose                                      | Interval Between Drugs              |
|-------------------------------|-------------------|-------------------------------------------------------|-------------------------------------|
|                               |                   | <b>Preferred</b>                                      |                                     |
| Combination, FDA-approved*    | 200 mg (orally)   | 800 micrograms (buccally)                             | 24–48 h                             |
| Combination, WHO recommended† | 200 mg (orally)   | 800 micrograms (vaginally, sublingually, or buccally) | 24–48 h                             |
|                               |                   | <b>Alternative</b>                                    |                                     |
| Misoprostol only              | N/A               | 800 micrograms (vaginally, sublingually, or buccally) | Repeat every 3 h for up to 3 doses‡ |

Abbreviations: h, hours; FDA, U.S. Food and Drug Administration; N/A, not applicable; WHO, World Health Organization.

\*U.S. Food and Drug Administration. Mifeprex (mifepristone) information. Postmarket drug safety information for patients and providers. Silver Spring, MD: FDA; 2018. Available at: <https://www.fda.gov/Drugs/DrugSafety/PostmarketDrugSafetyInformationforPatientsandProviders/ucm111323.htm>. Retrieved March 3, 2020.

†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>. Retrieved March 3, 2020.

‡Although studies typically use no more than three doses for the initial treatment regimen, the World Health Organization guidelines do not specify a maximum number of misoprostol doses (Raymond EG, Harrison MS, Weaver MA. Efficacy of misoprostol alone for first-trimester medical abortion: a systematic review. *Obstet Gynecol* 2019;133:137–47 and 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>. Retrieved March 3, 2020).

According to the requirements of the FDA REMS program, clinicians who want to prescribe mifepristone must complete a “prescriber agreement form” before ordering and dispensing mifepristone, and the clinician and patient need to sign a “patient agreement form” before the drug is dispensed (10).

The actual location of where a patient takes the medication abortion drugs has evolved over time. Although the FDA REMS program for mifepristone continues to require dispensing in the clinician's office, the U.S. labeling for mifepristone no longer indicates that the medication should be used only in the clinician's office (10). Patients can safely and effectively use mifepristone at home for medication abortion (74–77). A clinician can prescribe misoprostol and pain medications or can maintain an office supply and directly dispense to the patient. Patients can safely and effectively self-administer misoprostol at home for medication abortion (5, 78–80).

Medication abortion can be provided safely and effectively by telemedicine with a high level of patient satisfaction, and telemedicine improves access to early abortion care, particularly in areas that lack a health care practitioner (81, 82). Telemedicine involves the use of video and information technology to provide a medical service at a distance. Medication abortion through telemedicine has been evaluated in observational studies and found to be equally effective as an in-person visit (33, 83–85). In an analysis of nearly 20,000 medication abortions, adverse events

were rare (0.3% overall) and did not differ between those who choose telemedicine or in-person services (33, 84). Patients who choose telemedicine medication abortion are significantly more likely to say they would recommend the service to a friend compared with those who have an in-person visit (90% versus 83%) (83). Telemedicine also may help reduce the rate of delays to care because of barriers in access to abortion care in remote areas (82). After medication abortion through telemedicine was introduced in Iowa, a significant reduction in second-trimester abortion was reported, and patients in remote parts of the state were more likely to obtain a medication abortion (82). Despite this evidence, some states have passed legislation that bans the use of telemedicine to provide medication abortion (86).

#### ► *Should prophylactic antibiotics be used in medication abortion?*

The routine use of prophylactic antibiotics is not recommended for medication abortion (6). Following concern about serious, rare, and deadly infection with clostridial bacteria in patients undergoing medication abortion, it has since become evident that no specific connection exists between clostridial organisms and medication abortion (87, 88). Uterine infection with medication abortion is uncommon, and published data do not support the routine use of prophylactic antibiotics in medication abortion. In a systematic review of 65 studies

**Table 2. Outcome by Gestational Age After Mifepristone 200 mg and Misoprostol for Outpatient Medication Abortion**

|                   | Misoprostol Dose                              | Interval Between Mifepristone and Misoprostol (h) | Gestational Age |            |            |            |
|-------------------|-----------------------------------------------|---------------------------------------------------|-----------------|------------|------------|------------|
|                   |                                               |                                                   | ≤49 days        | 50–56 days | 57–63 days | 64–70 days |
| Complete abortion | 800 micrograms buccally*                      | 24–48                                             | 98.1%           | 96.8%      | 94.7%      | 92.7%      |
|                   | 800 micrograms vaginally <sup>†‡§¶  ††</sup>  | 24–72                                             | 98.3–99.7%      | 95.3–98.6% | 95.1–98.3% | 94.9%      |
|                   | 800 micrograms vaginally <sup>§</sup>         | 6–8                                               | 97.1%           | 94.2%      | 95.2%      | N/A        |
|                   | 800 micrograms vaginally <sup>  ¶</sup>       | 0–0.25                                            | 95.5–95.7%      | 93.7–94.3% | 91.6–95.3% | N/A        |
|                   | 400 micrograms sublingually <sup>¶***††</sup> | 24–48                                             | 95.4%           | N/A        | 94.8%      | 91.9%      |
| Ongoing pregnancy | 800 micrograms buccally*                      | 24–48                                             | 0.3%            | 0.8%       | 2.0%       | 3.1%       |
|                   | 800 micrograms vaginally <sup>†‡§¶  ††</sup>  | 24–72                                             | 0–0.4%          | 0–1.2%     | 0–2.2%     | 3.4%       |
|                   | 800 micrograms vaginally <sup>§</sup>         | 6–8                                               | 0.4%            | 0          | 0.8%       | N/A        |
|                   | 800 micrograms vaginally <sup>  ¶</sup>       | 0–0.25                                            | 1.4–2.3%        | 1.9–2.8%   | 1.6–5.0%   | N/A        |
|                   | 400 micrograms sublingually <sup>¶***††</sup> | 24–48                                             | N/A             | N/A        | 1.8–3.5%   | 2.2%       |

Abbreviations: h, hours; N/A, not available.

\*U.S. Food and Drug Administration. Mifeprex (mifepristone) information. Postmarket drug safety information for patients and providers. Silver Spring, MD: FDA; 2018. Available at: <https://www.fda.gov/Drugs/DrugSafety/PostmarketDrugSafetyInformationforPatientsandProviders/ucm111323.htm>. Retrieved March 3, 2020.

<sup>†</sup>Schaff EA, Eisinger SH, Stadalius LS, Franks P, Gore BZ, Poppema S. Low-dose mifepristone 200 mg and vaginal misoprostol for abortion. *Contraception* 1999;59:1–6.

<sup>‡</sup>Schaff EA, Fielding SL, Westhoff C. Randomized trial of oral versus vaginal misoprostol at one day after mifepristone for early medical abortion. *Contraception* 2001;64:81–5.

<sup>§</sup>Creinin MD, Fox MC, Teal S, Chen A, Schaff EA, Meyn LA. A randomized comparison of misoprostol 6 to 8 hours versus 24 hours after mifepristone for abortion. MOD Study Trial Group. *Obstet Gynecol* 2004;103:851–9.

<sup>||</sup>Creinin MD, Schreiber CA, Bednarek P, Lintu H, Wagner MS, Meyn LA. Mifepristone and misoprostol administered simultaneously versus 24 hours apart for abortion: a randomized controlled trial. Medical Abortion at the Same Time (MAST) Study Trial Group. *Obstet Gynecol* 2007;109:885–94.

<sup>¶</sup>Lohr PA, Starling JE, Scott JG, Aiken AR. Simultaneous compared with interval medical abortion regimens where home use is restricted [published erratum appears in *Obstet Gynecol* 2018;132:219]. *Obstet Gynecol* 2018;131:635–41.

<sup>#</sup>Raghavan S, Tsereteli T, Kamilov A, Kurbanbekova D, Yusupov D, Kasimova F, et al. Acceptability and feasibility of the use of 400 µg of sublingual misoprostol after mifepristone for medical abortion up to 63 days since the last menstrual period: evidence from Uzbekistan. *Eur J Contracept Reprod Health Care* 2013;18:104–11.

<sup>\*\*</sup>Bracken H, Dabash R, Tsertsvadze G, Posohova S, Shah M, Hajri S, et al. A two-pill sublingual misoprostol outpatient regimen following mifepristone for medical abortion through 70 days' LMP: a prospective comparative open-label trial. *Contraception* 2014;89:181–6.

<sup>††</sup>von Hertzen H, Huong NT, Piaggio G, Bayalag M, Cabezas E, Fang AH, et al. Misoprostol dose and route after mifepristone for early medical abortion: a randomised controlled noninferiority trial. WHO Research Group on Postovulatory Methods of Fertility Regulation. *BJOG* 2010;117:1186–96.

<sup>‡‡</sup>Hsia JK, Lohr PA, Taylor J, Creinin MD. Medical abortion with mifepristone and vaginal misoprostol between 64 and 70 days' gestation. *Contraception* 2019;100:178–81.

of heterogeneous design (prospective, retrospective, and randomized), the overall proportion of diagnosed or treated infection after medication abortion was 0.9% in more than 46,000 patients (89). In these studies, as in most studies of abortion by uterine evacuation, the diagnostic criteria for infection were variable, leading to possible overestimation of infection.

Although serious infections occur rarely in patients after medication abortion, clinicians need to be aware of the signs and symptoms. Tachycardia, severe abdominal pain, or general malaise with or without fever that occur more than 24 hours after misoprostol administration should increase suspicion of a serious infection (90). Clostridial toxic shock often resembles a flu-like illness, so clinicians should have a high level of suspicion for infection when symptoms consistent with flu are present (90). Patients with such infections typically have hemoconcentration and significant leukocytosis without fever and can rapidly progress to refractory hypotension and death (91).

► ***What is the recommended pain management approach for patients undergoing medication abortion?***

Nonsteroidal anti-inflammatory drugs are recommended for pain management in patients who undergo a medication abortion. Pain management during medication abortion is an important consideration because many patients report pain that requires analgesia. Studies of pain control and medication abortion have found that the duration of pain for most patients is no longer than 24 hours after misoprostol administration (92, 93). The most severe pain occurs approximately 2.5–4 hours after misoprostol use and lasts about 1 hour (94). One randomized trial found that ibuprofen taken when needed was more effective than acetaminophen to reduce pain associated with medication abortion (95). Another randomized trial found ibuprofen given prophylactically at the time of misoprostol administration did not significantly reduce pain associated with medication abortion compared with ibuprofen taken when needed (93). Nonsteroidal anti-inflammatory drugs do not appear to counteract misoprostol or affect the success of the medication abortion (96). Opioids have not been found to decrease the amount or duration of maximum pain associated with medication abortion up to 70 days of gestation (94). Other medications, like pregabalin, have been studied for pain control but have not been effective (97).

Patients should be sent home with appropriate instructions for analgesia with over-the-counter medications. If opioids are requested or desired, the Centers for Disease Control and Prevention (CDC) advises that “clinicians should prescribe the lowest effective dose of immediate-release opioids and should prescribe no

greater quantity than needed for the expected duration of pain severe enough to require opioids” (98).

► ***What kind of assessment is recommended after medication abortion?***

Routine in-person follow-up is not necessary after uncomplicated medication abortion. Clinicians should offer patients the choice of self-assessment or clinical follow-up evaluation to assess medication abortion success. If medically indicated or preferred by the patient, follow-up evaluation can be performed by medical history, clinical examination, serum human chorionic gonadotropin (hCG) testing, or ultrasonography (5, 6, 99).

The type of follow-up visit after medication abortion has evolved over time. The mifepristone FDA label includes recommendations for follow up (23). However, some patients choose not to return for follow-up; this likely is due to the high success rates and because patients are able to self-assess abortion completion (100–102).

***Remote Assessment and Self-Assessment***

Follow-up can be performed by telephone at 1 week, with subsequent at-home urine pregnancy testing at 4 weeks after treatment, which avoids the need for the patient to go to a facility (103–106). Most studies have used a short series of questions that ask patients whether they have experienced bleeding and cramping (including how much and for how long) and whether they still feel pregnant or if they think the pregnancy has passed (104, 107). When the clinician and the patient think that expulsion has occurred based on symptomatology, they are correct 96–99% of the time (104, 108). Although urine pregnancy testing alone with standard high-sensitivity or low-sensitivity tests has not been shown to be a viable alternative to other forms of follow-up, newer semiquantitative or multilevel at-home urine hCG tests have shown promise in accurately identifying ongoing pregnancies after medication abortion (109–112).

***Clinical Follow-Up***

When a patient obtains in-person follow-up after medication abortion, transvaginal ultrasonography is commonly used, although it is not required (5). If an ultrasound examination is performed at follow-up after medication abortion, the sole purpose is to determine whether the gestational sac is present or absent. The measurement of endometrial thickness or other findings do not predict the need for subsequent uterine aspiration (113). In research trials, when a transvaginal ultrasound examination shows no evidence of a gestational sac

1 week after mifepristone use, only 1.6% of patients needed subsequent uterine evacuation (113).

Serum hCG testing before treatment and 1 week after treatment is another option for follow-up examination after medication abortion; however, data about use of this approach are lacking for gestations beyond 63 days. This strategy may be more effective than ultrasonography to confirm abortion completion in patients who were below the threshold for visualization of a gestational sac at the time of their medication abortion (114). Patients do not need to return to the same facility; they can obtain serum hCG testing at a convenient location (114, 115). The patient should then be informed of the result. A serum hCG level decrease of at least 80% over 6–7 days after initiating treatment with mifepristone and misoprostol indicates a successful abortion (114). In a randomized trial of in-clinic transvaginal ultrasound examination or serum hCG testing follow-up, 24.5% of patients were lost to follow-up, there were no significant differences reported in unplanned visits and interventions by 2 weeks (6.6% versus 8.2%, respectively) or in uterine evacuation rates by 4 weeks (4.4% and 1.4%, respectively) (116).

### ► *How is incomplete medication abortion or ongoing pregnancy managed?*

Guidelines for intervention vary for patients who have delayed expulsion, an incomplete medication abortion (ie, persistent gestational sac on ultrasonography without evidence of embryonic cardiac activity or retained tissue), or an ongoing pregnancy (ie, continuing development with embryonic cardiac activity).

### **Delayed Expulsion**

After induced or spontaneous expulsion, the uterus will normally contain sonographically hyperechoic tissue or “thick” endometrial stripe that consists of blood, blood clots, and decidua. Rarely does this ultrasound finding in patients who have undergone medication abortion indicate a need for intervention. In the absence of excessive bleeding or pain by patient report, clinicians can monitor such patients based on symptoms.

### **Incomplete Medication Abortion**

An incomplete medication abortion can be treated with a repeat dose of misoprostol, uterine aspiration, or expectant management, depending on the clinical circumstances and patient preference (23, 30, 117, 118). Studies indicate that even with a retained sac at 2 weeks after medication abortion, intervention is unnecessary, and that expulsion will typically occur in the ensuing weeks (30). However, some patients with incomplete expulsion will have bothersome symptoms, such as prolonged and irregular bleeding epi-

sodes. Patients with incomplete medication abortion 1 week after treatment can safely receive another dose of misoprostol (28, 118) or repeat misoprostol doses can be used for a persistent gestational sac (117). Patients who prefer not to wait or do not desire medical management can choose to have a uterine evacuation at any time.

### **Ongoing Pregnancy**

Ongoing pregnancy after medication abortion can be treated with a repeat dose of misoprostol or uterine aspiration, depending on the clinical circumstances and patient preference. In an analysis of data from two randomized trials with 14 cases of ongoing pregnancy, treatment with a repeat dose of misoprostol, 800 micrograms administered vaginally, resulted in expulsion of the products of pregnancy in five cases (36%); in an additional four cases (29%), gestational cardiac activity was no longer present at the next follow-up visit (118). If gestational cardiac activity persists at follow-up after a second dose of misoprostol, uterine aspiration should be performed.

### ► *What is the recommended timing of contraception initiation after medication abortion?*

Patients undergoing medication abortion who desire contraception should be counseled that

- almost all contraceptive methods, except IUDs and permanent contraception, can be safely initiated immediately on day 1 (mifepristone intake) of medication abortion.
- all contraceptive methods can be safely initiated after successful medication abortion.

Patients who select depot medroxyprogesterone acetate (DMPA) for contraception should be counseled that administration of DMPA on day 1 of the medication abortion regimen may increase the risk of ongoing pregnancy (119).

Providing desired contraception as soon as possible to patients undergoing medication abortion enables the greatest flexibility in care and decreases barriers to initiating contraception. The CDC and World Health Organization (WHO) support the initiation of almost all methods of contraception on day 1 of the medication abortion or on the same day as mifepristone administration (5, 6, 120). Permanent contraception procedures may be performed once abortion is confirmed complete.

Concern has been raised that the immediate use of hormonal contraception that contains progestins could theoretically interfere with medication abortion efficacy. Etonogestrel implant use does not affect medication abortion outcomes (121, 122). However, DMPA injection at the time of mifepristone administration may slightly increase the risk of an ongoing pregnancy

(119). In a randomized trial that evaluated the effects of DMPA injection timing on medication abortion outcomes, ongoing pregnancy was more common among those randomized to receive DMPA injection on the day of mifepristone administration compared with those who received DMPA at a follow-up visit (3.6% versus 0.9%; 90% CI, 2.7 [0.4–5.6]), although the proportion undergoing aspiration for any reason did not significantly vary (6.4% versus 5.3%; 90% CI, 1.1 [–2.8 to 4.9]) (119). Patients should be counseled about this small risk of ongoing pregnancy, which needs to be weighed against the risk of potentially not receiving their desired method of contraception.

Patients do not experience a higher rate of IUD expulsion with placement in the first week after medication abortion as compared with 3 to 6 weeks later (123, 124). However, IUD placement within 6 weeks after medication abortion is associated with a higher expulsion rate compared with IUD placement remote from pregnancy; the time frame after 6 weeks at which this rate decreases is unknown. Placement of a copper or levonorgestrel IUD close to the time of abortion results in improved uptake of a desired IUD compared with placement at an additional follow-up visit several weeks after the abortion (123–125), although overall use rates at 6 months may not differ (126). The IUD expulsion risk should be weighed against the potential for more patients to receive their desired IUD if it is placed sooner rather than later.

► ***How should patients be counseled about the effect of medication abortion on future fertility and pregnancy outcomes?***

Patients can be counseled that medication abortion does not have an adverse effect on future fertility or future pregnancy outcomes (5, 6). Studies consistently demonstrate that medication abortion has no negative effect on future fertility or pregnancy outcomes. A study from China found that patients who had a prior mifepristone abortion had lower odds of preterm birth compared with those who had never been pregnant (adjusted OR, 0.77; 95% CI, 0.61–0.98), and the frequencies of low-birth-weight infants and mean lengths of pregnancy were similar in both groups (127). No significant differences were reported in risk of preterm delivery, frequency of low-birth-weight infants, or mean infant birth weight in the comparisons of patients who had previous mifepristone abortion and patients who had uterine evacuation. In a registry-based study from Scotland, no association was found between prior abortion and subsequent preterm birth during the period 2000–2008, when 68% of abortions were medication-induced (128).

## Summary of Recommendations

***The following recommendations are based on good and consistent scientific evidence (Level A):***

- Combined mifepristone–misoprostol regimens are recommended as the preferred therapy for medication abortion because they are significantly more effective than misoprostol-only regimens. If a combined mifepristone–misoprostol regimen is not available, a misoprostol-only regimen is the recommended alternative.
- Clinicians should counsel patients that medication abortion failure rates, especially continuing pregnancy rates, increase as gestational age approaches 10 weeks.
- Any clinician with the skills to screen patients for eligibility for medication abortion and to provide appropriate follow-up can provide medication abortion.
- Patients can safely and effectively use mifepristone at home for medication abortion.
- Patients can safely and effectively self-administer misoprostol at home for medication abortion.
- Nonsteroidal anti-inflammatory drugs are recommended for pain management in patients who undergo a medication abortion.
- Routine in-person follow-up is not necessary after uncomplicated medication abortion. Clinicians should offer patients the choice of self-assessment or clinical follow-up evaluation to assess medication abortion success. If medically indicated or preferred by the patient, follow-up evaluation can be performed by medical history, clinical examination, serum human chorionic gonadotropin (hCG) testing, or ultrasonography.
- If an ultrasound examination is performed at follow-up after medication abortion, the sole purpose is to determine whether the gestational sac is present or absent. The measurement of endometrial thickness or other findings do not predict the need for subsequent uterine aspiration.

***The following recommendations are based on limited or inconsistent scientific evidence (Level B):***

- Medication abortion is not recommended for patients with any of the following: confirmed or suspected ectopic pregnancy, intrauterine device (IUD) in place (the IUD can be removed before medication abortion), current long-term systemic corticosteroid therapy, chronic adrenal failure,

known coagulopathy or anticoagulant therapy, inherited porphyria, or intolerance or allergy to mifepristone or misoprostol.

- ▶ Before undergoing medication abortion, patients should be counseled regarding the teratogenicity of misoprostol in the event of an unsuccessful medication abortion.
- ▶ Before medication abortion is performed, the clinician should confirm pregnancy and estimate gestational age. For patients with regular menstrual cycles, a certain last menstrual period within the prior 56 days, and no signs, symptoms, or risk factors for ectopic pregnancy, a clinical examination or ultrasound examination is not necessary before medication abortion.
- ▶ Most patients with clinical indications for an ultrasound examination before medication abortion can be initially screened with transabdominal ultrasonography, reserving transvaginal ultrasonography for situations in which further clarification is required.
- ▶ Medication abortion can be provided safely and effectively by telemedicine with a high level of patient satisfaction.
- ▶ The routine use of prophylactic antibiotics is not recommended for medication abortion.
- ▶ An incomplete medication abortion can be treated with a repeat dose of misoprostol, uterine aspiration, or expectant management, depending on the clinical circumstances and patient preference.
- ▶ Ongoing pregnancy after medication abortion can be treated with a repeat dose of misoprostol or uterine aspiration, depending on the clinical circumstances and patient preference.
- ▶ Patients undergoing medication abortion who desire contraception should be counseled that
  - almost all contraceptive methods, except IUDs and permanent contraception, can be safely initiated immediately on day 1 (mifepristone intake) of medication abortion.
  - all contraceptive methods can be safely initiated after successful medication abortion.
- ▶ Patients who select depot medroxyprogesterone acetate (DMPA) for contraception should be counseled that administration of DMPA on day 1 of the medication abortion regimen may increase the risk of ongoing pregnancy.
- ▶ Patients can be counseled that medication abortion does not have an adverse effect on future fertility or future pregnancy outcomes.

***The following recommendations are based primarily on consensus and expert opinion (Level C):***

- ▶ Patients who choose abortion should be counseled about all methods available as well as the risks, advantages, disadvantages, and the different features of these options.
- ▶ Most patients at 70 days of gestation or less who desire abortion are eligible for a medication abortion.
- ▶ Patient counseling before medication abortion should include discussion of when patients should contact their clinician in the case of heavy bleeding (soaking more than two maxi pads per hour for 2 consecutive hours) and when to access urgent intervention.
- ▶ All patients with a continuing pregnancy after using mifepristone and misoprostol should be provided with all pregnancy options and a thorough discussion of the risks and benefits of each.
- ▶ In the very rare case that patients change their mind about having an abortion after taking mifepristone and want to continue the pregnancy, they should be monitored expectantly.
- ▶ Rh testing is recommended in patients with unknown Rh status before medication abortion, and Rh D immunoglobulin should be administered if indicated. In situations where Rh testing and Rh D immunoglobulin administration are not available or would significantly delay medication abortion, shared decision making is recommended so that patients can make an informed choice about their care.
- ▶ Clinicians who wish to provide medication abortion services should be trained to perform uterine evacuation procedures or should be able to refer to a clinician who has this training.

## References

1. Second-trimester abortion. Practice Bulletin No. 135. American College of Obstetricians and Gynecologists. *Obstet Gynecol* 2013;121:1394–406. (Level III)
2. Jones RK, Witwer E, Jerman J. Abortion incidence and service availability in the United States, 2017. New York, NY: Guttmacher Institute; 2019. Available at: <https://www.guttmacher.org/report/abortion-incidence-service-availability-us-2017>. Retrieved March 4, 2020. (Level II-3)
3. Jatlaoui TC, Boutot ME, Mandel MG, Whiteman MK, Ti A, Petersen E, et al. Abortion surveillance—United States, 2015. *MMWR Surveill Summ* 2018;67:1–45. (Level II-3)
4. Grossman D, Grindlay K, Altshuler AL, Schulkin J. Induced abortion provision among a national sample of

- obstetrician-gynecologists. *Obstet Gynecol* 2019;133:477–83. (Level II-3)
5. 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>. Retrieved March 3, 2020. (Level III)
6. National Institute for Health and Care Excellence. Abortion care. London, UK: NICE; 2019. (Level III)
7. Gravanis A, Schaison G, George M, de Brux J, Satyaswaroop PG, Baulieu EE, et al. Endometrial and pituitary responses to the steroidal antiprogesterin RU 486 in postmenopausal women. *J Clin Endocrinol Metab* 1985;60:156–63. (Level III)
8. Swahn ML, Bygdeman M. The effect of the antiprogesterin RU 486 on uterine contractility and sensitivity to prostaglandin and oxytocin. *Br J Obstet Gynaecol* 1988;95:126–34. (Level II-3)
9. Johannisson E, Oberholzer M, Swahn ML, Bygdeman M. Vascular changes in the human endometrium following the administration of the progesterone antagonist RU 486. *Contraception* 1989;39:103–17. (Level III)
10. U.S. Food and Drug Administration. Mifeprex (mifepristone) information. Postmarket drug safety information for patients and providers. Silver Spring, MD: FDA; 2018. Available at: <https://www.fda.gov/Drugs/DrugSafety/PostmarketDrugSafetyInformationforPatientsandProviders/ucm111323.htm>. Retrieved March 3, 2020. (Level III)
11. Raymond EG, Blanchard K, Blumenthal PD, Cleland K, Foster AM, Gold M, et al. Sixteen years of overregulation: time to unburden mifeprex. Mifeprex REMS Study Group. *N Engl J Med* 2017;376:790–4. (Level III)
12. American College of Obstetricians and Gynecologists. Improving access to mifepristone for reproductive health indications. Position Statement. Washington, DC: American College of Obstetricians and Gynecologists; 2018. Available at: <https://www.acog.org/Clinical-Guidance-and-Publications/Position-Statements/Improving-Access-to-Mifepristone>. Retrieved March 4, 2020. (Level III)
13. Creinin MD. Randomized comparison of efficacy, acceptability and cost of medical versus surgical abortion. *Contraception* 2000;62:117–24. (Level I)
14. Henshaw RC, Naji SA, Russell IT, Templeton AA. Comparison of medical abortion with surgical vacuum aspiration: women's preferences and acceptability of treatment. *BMJ* 1993;307:714–7. (Level II-3)
15. Rorbye C, Norgaard M, Nilas L. Medical versus surgical abortion: comparing satisfaction and potential confounders in a partly randomized study. *Hum Reprod* 2005;20:834–8. (Level II-3)
16. Ho PC. Women's perceptions on medical abortion. *Contraception* 2006;74:11–5. (Level III)
17. Creinin MD. Medically induced abortion in a woman with a large myomatous uterus. *Am J Obstet Gynecol* 1996;175:1379–80. (Level III)
18. Mark K, Bragg B, Chawla K, Hladky K. Medical abortion in women with large uterine fibroids: a case series. *Contraception* 2016;94:572–4. (Level III)
19. Goldthwaite LM, Teal SB. Controversies in family planning: pregnancy termination in women with uterine anatomic abnormalities. *Contraception* 2014;90:460–3. (Level III)
20. Mistry H, Jha S. Pregnancy with a pinhole introitus: a report of two cases and a review of the literature. *Eur J Contracept Reprod Health Care* 2015;20:490–4. (Level III)
21. Rooney Thompson M, Towers CV, Howard BC, Hennessy MD, Wolfe L, Heitzman C. The use of prostaglandin E<sub>1</sub> in peripartum patients with asthma. *Am J Obstet Gynecol* 2015;212:392.e1–3. (Level II-2)
22. Hayes JL, Achilles SL, Creinin MD, Reeves MF. Outcomes of medical abortion through 63 days in women with twin gestations. *Contraception* 2011;84:505–7. (Level III)
23. GenBioPro, Inc. Mifepristone tablets, 200mg for oral use. Highlights of prescribing information. Las Vegas, NV: GenBioPro, Inc.; 2019. Available at: <https://genbiopro.com/wp-content/uploads/2019/05/genbiopro-prescribing-information.pdf>. Retrieved June 2, 2020. (Level III)
24. Cleland K, Creinin MD, Nucatola D, Nshom M, Trussell J. Significant adverse events and outcomes after medical abortion. *Obstet Gynecol* 2013;121:166–71. (Level III)
25. Hakim-Elahi E, Tovell HM, Burnhill MS. Complications of first-trimester abortion: a report of 170,000 cases. *Obstet Gynecol* 1990;76:129–35. (Level II-3)
26. Creinin MD, Schreiber CA, Bednarek P, Lintu H, Wagner MS, Meyn LA. Mifepristone and misoprostol administered simultaneously versus 24 hours apart for abortion: a randomized controlled trial. Medical Abortion at the Same Time (MAST) Study Trial Group. *Obstet Gynecol* 2007;109:885–94. (Level I)
27. Creinin MD, Fox MC, Teal S, Chen A, Schaff EA, Meyn LA. A randomized comparison of misoprostol 6 to 8 hours versus 24 hours after mifepristone for abortion. MOD Study Trial Group. *Obstet Gynecol* 2004;103:851–9. (Level I)
28. Winikoff B, Dzuba IG, Creinin MD, Crowden WA, Goldberg AB, Gonzales J, et al. Two distinct oral routes of misoprostol in mifepristone medical abortion: a randomized controlled trial. *Obstet Gynecol* 2008;112:1303–10. (Level I)
29. Schaff EA, Eisinger SH, Stadalius LS, Franks P, Gore BZ, Poppema S. Low-dose mifepristone 200 mg and vaginal misoprostol for abortion. *Contraception* 1999;59:1–6. (Level II-3)
30. Creinin MD, Danielsson KG. Medical abortion in early pregnancy. In: Paul M, Lichtenberg ES, Borgatta L, Grimes DA, Stubblefield PG and Creinin MD, editors. Management of unintended and abnormal pregnancy: comprehensive abortion care. Hoboken, NJ: Blackwell Publishing Ltd; 2009. p. 111. (Level III)
31. Allen RH, Westhoff C, De Nonno L, Fielding SL, Schaff EA. Curettage after mifepristone-induced abortion: frequency, timing, and indications. *Obstet Gynecol* 2001;98:101–6. (Level III)

32. Aubeny E, Peyron R, Turpin CL, Renault M, Targosz V, Silvestre L, et al. Termination of early pregnancy (up to 63 days of amenorrhea) with mifepristone and increasing doses of misoprostol [published erratum appears in *Int J Fertil Menopausal Stud* 1996;41:56]. *Int J Fertil Menopausal Stud* 1995;40(suppl 2):85–91. (Level II-3)
33. Grossman D, Grindlay K. Safety of medical abortion provided through telemedicine compared with in person. *Obstet Gynecol* 2017;130:778–82. (Level II-2)
34. Bernard N, Elefant E, Carlier P, Tebacher M, Barjhoux CE, Bos-Thompson MA, et al. Continuation of pregnancy after first-trimester exposure to mifepristone: an observational prospective study. *BJOG* 2013;120:568–74. (Level II-2)
35. 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. (Level III)
36. Gonzalez CH, Vargas FR, Perez AB, Kim CA, Brunoni D, Marques-Dias MJ, et al. Limb deficiency with or without Mobius sequence in seven Brazilian children associated with misoprostol use in the first trimester of pregnancy. *Am J Med Genet* 1993;47:59–64. (Level III)
37. Marques-Dias MJ, Gonzalez CH, Rosenberg 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. (Level III)
38. Pastuszak AL, Schuler L, Speck-Martins CE, Coelho KE, Cordello SM, Vargas F, et al. Use of misoprostol during pregnancy and Mobius' syndrome in infants. *N Engl J Med* 1998;338:1881–5. (Level II-3)
39. Wiebe ER. Abortion induced with methotrexate and misoprostol: a comparison of various protocols. *Contraception* 1997;55:159–63. (Level II-3)
40. National Abortion Federation. 2020 clinical policy guidelines for abortion care. Washington, DC: NAF; 2020. Available at: <https://prochoice.org/resources/clinical-policy-guidelines/>. Retrieved June 1, 2020. (Level III)
41. Grossman D, White K. Abortion “reversal”—legislating without evidence. *N Engl J Med* 2018;379:1491–3. (Level III)
42. Grossman D, White K, Harris L, Reeves M, Blumenthal PD, Winikoff B, et al. Continuing pregnancy after mifepristone and “reversal” of first-trimester medical abortion: a systematic review. *Contraception* 2015;92:206–11. (Systematic Review)
43. Creinin MD, Hou MY, Dalton L, Steward R, Chen MJ. Mifepristone antagonization with progesterone to prevent medical abortion: a randomized controlled trial. *Obstet Gynecol* 2020;135:158–65. (Level I)
44. Prevention of Rh D Alloimmunization. Practice Bulletin No. 181. American College of Obstetricians and Gynecologists. *Obstet Gynecol* 2017;130:e57–70. (Level III)
45. 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. (Level II-3)
46. 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. (Systematic Review)
47. Raymond EG, Bracken H. Early medical abortion without prior ultrasound. *Contraception* 2015;92:212–4. (Meta-Analysis)
48. Raymond EG, Tan YL, Comendant R, Sagaidac I, Hodorogea S, Grant M, et al. Simplified medical abortion screening: a demonstration project. *Contraception* 2018B;97:292–6. (Level III)
49. Hoover KW, Tao G, Kent CK. Trends in the diagnosis and treatment of ectopic pregnancy in the United States. *Obstet Gynecol* 2010;115:495–502. (Level II-2)
50. Stulberg DB, Cain LR, Dahlquist I, Lauderdale DS. Ectopic pregnancy rates and racial disparities in the Medicaid population, 2004–2008. *Fertil Steril* 2014;102:1671–6. (Level II-2)
51. Edwards J, Creinin MD. Surgical abortion for gestations of less than 6 weeks. *Curr Probl Obstet Gynecol Fertil* 1997;20:11–9. (Level II-2)
52. Centers for Disease Control. Ectopic pregnancy—United States, 1988–1989. *MMWR Morb Mortal Wkly Rep* 1992;41:591–4. (Level II-3)
53. Ulmann A, Silvestre L, Chemama L, Rezvani Y, Renault M, Aguilhaume CJ, et al. Medical termination of early pregnancy with mifepristone (RU 486) followed by a prostaglandin analogue. Study in 16,369 women. *Acta Obstet Gynecol Scand* 1992;71:278–83. (Level II-3)
54. Lohr PA, Reeves MF, Creinin MD. A comparison of transabdominal and transvaginal ultrasonography for determination of gestational age and clinical outcomes in women undergoing early medical abortion. *Contraception* 2010;81:240–4. (Level II-3)
55. Fu A, Weber CE, Gilmore E, Davis AR, Hirsch G, Westhoff CL. A noninferiority randomized controlled trial to compare transabdominal and transvaginal sonography for eligibility assessment prior to medical abortion. *Contraception* 2018;98:199–204. (Level I)
56. Karanth L, Jaafar SH, Kanagasabai S, Nair NS, Barua A. Anti-D administration after spontaneous miscarriage for preventing Rhesus alloimmunisation. *Cochrane Database of Systematic Reviews* 2013, Issue 3. Art. No.: CD009617. DOI: 10.1002/14651858.CD009617.pub2. (Systematic Review)
57. Management of alloimmunization during pregnancy. ACOG Practice Bulletin No. 192. American College of Obstetricians and Gynecologists. *Obstet Gynecol* 2018;131:e82–90. (Level III)
58. Fung KF, Eason E. No. 133-Prevention of Rh Alloimmunization. *J Obstet Gynaecol Can* 2018;40:e1–10. (Level III)
59. Vayssi re C, Gaudineau A, Attali L, Bettahar K, Eyraud S, Faucher P, et al. Elective abortion: clinical practice guidelines from the French College of Gynecologists and Obstetricians (CNGOF). *Eur J Obstet Gynecol Reprod Biol* 2018;222:95–101. (Level III)

60. World Health Organization. Safe abortion: technical and policy guidance for health systems. 2nd ed. Geneva: WHO; 2012. Available at: [https://www.who.int/reproductivehealth/publications/unsafe\\_abortion/9789241548434/en/](https://www.who.int/reproductivehealth/publications/unsafe_abortion/9789241548434/en/). Retrieved June 1, 2020. (Level III)
61. Mark A, Grossman D, Foster AM, Prager SW, Winikoff B. When patients change their minds after starting an abortion: guidance from the National Abortion Federation's Clinical Policies Committee. *Contraception* 2020; 101:283–5. (Level III)
62. Horvath S, Tsao P, Huang ZY, Zhao L, Du Y, Sammel MD, 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 [published online March 2, 2020]. *Contraception*. DOI: S0010-7824(20)30064-0. (Level III)
63. Kapp N, Baldwin MK, Rodriguez MI. Efficacy of medical abortion prior to 6 gestational weeks: a systematic review. *Contraception* 2018;97:90–9. (Systematic Review and Meta-Analysis)
64. Raymond EG, Harrison MS, Weaver MA. Efficacy of misoprostol alone for first-trimester medical abortion: a systematic review. *Obstet Gynecol* 2019;133:137–47. (Systematic Review and Meta-Analysis)
65. Kulier R, Kapp N, Gülmezoglu AM, Hofmeyr GJ, Cheng L, Campana A. Medical methods for first trimester abortion. *Cochrane Database of Systematic Reviews* 2011, Issue 11. Art. No.: CD002855. DOI: 10.1002/14651858.CD002855.pub4. (Systematic Review and Meta-analysis)
66. 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 [published erratum appears in JAMA 2000;284:2597] *JAMA* 2000;284:1948–53. (Level I)
67. Honkanen H, Piaggio G, Herten H, Bartfai G, Erdene-tungalag R, Gemzell-Danielsson K, et al. WHO multinational study of three misoprostol regimens after mifepristone for early medical abortion. WHO Research Group on Post-Ovulatory Methods for Fertility Regulation. *BJOG* 2004;111:715–25. (Level I)
68. Chai J, Wong CY, Ho PC. A randomized clinical trial comparing the short-term side effects of sublingual and buccal routes of misoprostol administration for medical abortions up to 63 days' gestation. *Contraception* 2013; 87:480–5. (Level I)
69. Abortion training and education. Committee Opinion No. 612. American College of Obstetricians and Gynecologists. *Obstet Gynecol* 2014;124:1055–9. (Level III)
70. Yarnall J, Swica Y, Winikoff B. Non-physician clinicians can safely provide first trimester medical abortion. *Reprod Health Matters* 2009;17:61–9. (Level III)
71. Warriner IK, Wang D, Huong NT, Thapa K, Tamang A, Shah I, et al. Can midlevel health-care providers administer early medical abortion as safely and effectively as doctors? A randomised controlled equivalence trial in Nepal. *Lancet* 2011;377:1155–61. (Level I)
72. Kopp Kallner H, Gomperts R, Salomonsson E, Johansson M, Marions L, Gemzell-Danielsson K. The efficacy, safety and acceptability of medical termination of pregnancy provided by standard care by doctors or by nurse-midwives: a randomised controlled equivalence trial. *BJOG* 2015;122:510–7. (Level I)
73. Olavarrieta CD, Ganatra B, Sorhaindo A, Karver TS, Seuc A, Villalobos A, et al. Nurse versus physician-provision of early medical abortion in Mexico: a randomized controlled non-inferiority trial. *Bull World Health Organ* 2015;93:249–58. (Level I)
74. Tan YL, Singh K, Tan KH, Gosavi A, Koh D, Abbas D, et al. Acceptability and feasibility of outpatient medical abortion with mifepristone and misoprostol up to 70 days gestation in Singapore. *Eur J Obstet Gynecol Reprod Biol* 2018;229:144–7. (Level II-3)
75. Platais I, Tsereteli T, Grebennikova G, Lotarevich T, Winikoff B. Prospective study of home use of mifepristone and misoprostol for medical abortion up to 10 weeks of pregnancy in Kazakhstan. *Int J Gynaecol Obstet* 2016; 134:268–71. (Level II-2)
76. Conkling K, Karki C, Tuladhar H, Bracken H, Winikoff B. A prospective open-label study of home use of mifepristone for medical abortion in Nepal. *Int J Gynaecol Obstet* 2015;128:220–3. (Level II-1)
77. Chong E, Frye LJ, Castle J, Dean G, Kuehl L, Winikoff B. A prospective, non-randomized study of home use of mifepristone for medical abortion in the U.S. *Contraception* 2015;92:215–9. (Level II-1)
78. Winikoff B, Dzuba IG, Chong E, Goldberg AB, Lichtenberg ES, Ball C, et al. Extending outpatient medical abortion services through 70 days of gestational age. *Obstet Gynecol* 2012;120:1070–6. (Level II-3)
79. Ngo TD, Park MH, Shakur H, Free C. Comparative effectiveness, safety and acceptability of medical abortion at home and in a clinic: a systematic review. *Bull World Health Organ* 2011;89:360–70. (Systematic Review and Meta-analysis)
80. Raghavan S, Tsereteli T, Kamilov A, Kurbanbekova D, Yusupov D, Kasimova F, et al. Acceptability and feasibility of the use of 400 mug of sublingual misoprostol after mifepristone for medical abortion up to 63 days since the last menstrual period: evidence from Uzbekistan. *Eur J Contracept Reprod Health Care* 2013;18:104–11. (Level II-3)
81. Hyland P, Raymond EG, Chong E. A direct-to-patient telemedicine abortion service in Australia: retrospective analysis of the first 18 months. *Aust N Z J Obstet Gynaecol* 2018;58:335–40. (Level II-3)
82. Grossman DA, Grindlay K, Buchacker T, Potter JE, Schmertmann CP. Changes in service delivery patterns after introduction of telemedicine provision of medical abortion in Iowa. *Am J Public Health* 2013;103:73–8. (Level II-3)
83. Grossman D, Grindlay K, Buchacker T, Lane K, Blanchard K. Effectiveness and acceptability of medical abortion provided through telemedicine. *Obstet Gynecol* 2011; 118:296–303. (Level II-3)
84. Kohn JE, Snow JL, Simons HR, Seymour JW, Thompson TA, Grossman D. Medication abortion provided through

- telemedicine in four U.S. States. *Obstet Gynecol* 2019; 134:343–50. (Level II-2)
85. Endler M, Lavelanet A, Cleeve A, Ganatra B, Gomperts R, Gemzell-Danielsson K. Telemedicine for medical abortion: a systematic review. *BJOG* 2019;126:1094–102. (Systematic Review)
86. Guttmacher Institute. An overview of abortion laws. New York, NY: Guttmacher Institute; 2020. Available at: <https://www.guttmacher.org/state-policy/explore/overview-abortion-laws>. Retrieved March 3, 2020. (Level III)
87. Ho CS, Bhatnagar J, Cohen AL, Hacker JK, Zane SB, Reagan S, et al. Undiagnosed cases of fatal clostridium-associated toxic shock in Californian women of childbearing age. *Am J Obstet Gynecol* 2009;201:459.e1–7. (Level III)
88. Chong E, Winikoff B, Charles D, Agnew K, Prentice JL, Limbago BM, et al. Vaginal and rectal clostridium sordellii and clostridium perfringens presence among women in the United States. NCT01283828 Study Team. *Obstet Gynecol* 2016;127:360–8. (Level II-2)
89. Shannon C, Brothers LP, Philip NM, Winikoff B. Infection after medical abortion: a review of the literature. *Contraception* 2004;70:183–90. (Level III)
90. Cohen AL, Bhatnagar J, Reagan S, Zane SB, D'Angeli MA, Fischer M, et al. Toxic shock associated with Clostridium sordellii and Clostridium perfringens after medical and spontaneous abortion. *Obstet Gynecol* 2007;110: 1027–33. (Level III)
91. Fischer M, Bhatnagar J, Guarner J, Reagan S, Hacker JK, Van Meter SH, et al. Fatal toxic shock syndrome associated with Clostridium sordellii after medical abortion. *N Engl J Med* 2005;353:2352–60. (Level III)
92. Jackson E, Kapp N. Pain control in first-trimester and second-trimester medical termination of pregnancy: a systematic review. *Contraception* 2011;83:116–26. (Systematic Review)
93. Raymond EG, Weaver MA, Louie KS, Dean G, Porsch L, Lichtenberg ES, et al. Prophylactic compared with therapeutic ibuprofen analgesia in first-trimester medical abortion: a randomized controlled trial. *Obstet Gynecol* 2013; 122:558–64. (Level I)
94. Colwill AC, Bayer LL, Bednarek P, Garg B, Jensen JT, Edelman AB. Opioid analgesia for medical abortion: a randomized controlled trial. *Obstet Gynecol* 2019;134: 1163–70. (Level I)
95. Livshits A, Machtinger R, David LB, Spira M, Moshe-Zahav A, Seidman DS. Ibuprofen and paracetamol for pain relief during medical abortion: a double-blind randomized controlled study. *Fertil Steril* 2009;91:1877–80. (Level I)
96. Creinin MD, Shulman T. Effect of nonsteroidal anti-inflammatory drugs on the action of misoprostol in a regimen for early abortion. *Contraception* 1997;56:165–8. (Level III)
97. Friedlander EB, Soon R, Salcedo J, Davis J, Tschann M, Kaneshiro B. Prophylactic pregabalin to decrease pain during medication abortion: a randomized controlled trial. *Obstet Gynecol* 2018;132:612–8. (Level I)
98. Dowell D, Haegerich TM, Chou R. CDC guideline for prescribing opioids for chronic pain—United States, 2016 [published erratum appears in *MMWR Recomm Rep* 2016;65:295]. *MMWR Recomm Rep* 2016;65(RR-1):1–49. (Level III)
99. National Academies of Sciences, Engineering, and Medicine. The safety and quality of abortion care in the United States. Washington, DC: National Academy of Sciences; 2018. (Level III)
100. Creinin MD, Potter C, Holovanisin M, Janczukiewicz L, Pymar HC, Schwartz JL, et al. Mifepristone and misoprostol and methotrexate/misoprostol in clinical practice for abortion. *Am J Obstet Gynecol* 2003;188:664–9. (Level II-3)
101. Prine L, Lesnewski R, Berley N, Gold M. Medical abortion in family practice: a case series. *J Am Board Fam Pract* 2003;16:290–5. (Level III)
102. Haimov-Kochman R, Arbel R, Sciaky-Tamir Y, Brzezinski A, Laufer N, Yagel S. Risk factors for unsuccessful medical abortion with mifepristone and misoprostol. *Acta Obstet Gynecol Scand* 2007;86:462–6. (Level II-3)
103. 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)
104. Perriera LK, Reeves MF, Chen BA, Hohmann HL, Hayes J, Creinin MD. Feasibility of telephone follow-up after medical abortion. *Contraception* 2010;81:143–9. (Level II-3)
105. Cameron ST, Glasier A, Dewart H, Johnstone A, Burnside A. Telephone follow-up and self-performed urine pregnancy testing after early medical abortion: a service evaluation. *Contraception* 2012;86:67–73. (Level II-3)
106. Chen MJ, Rounds KM, Creinin MD, Cansino C, Hou MY. Comparing office and telephone follow-up after medical abortion. *Contraception* 2016;94:122–6. (Level II-2)
107. Michie L, Cameron ST. Simplified follow-up after early medical abortion: 12-month experience of a telephone call and self-performed low-sensitivity urine pregnancy test. *Contraception* 2014;89:440–5. (Level II-3)
108. Rossi B, Creinin MD, Meyn LA. Ability of the clinician and patient to predict the outcome of mifepristone and misoprostol medical abortion. *Contraception* 2004;70: 313–7. (Level II-3)
109. Godfrey EM, Anderson A, Fielding SL, Meyn L, Creinin MD. Clinical utility of urine pregnancy assays to determine medical abortion outcome is limited. *Contraception* 2007;75:378–82. (Level II-3)
110. Grossman D, Berdichevsky K, Larrea F, Beltran J. Accuracy of a semi-quantitative urine pregnancy test compared to serum beta-hCG measurement: a possible screening tool for ongoing pregnancy after medication abortion. *Contraception* 2007;76:101–4. (Level II-3)
111. Raymond EG, Shochet T, Bracken H. Low-sensitivity urine pregnancy testing to assess medical abortion out-

- come: a systematic review. *Contraception* 2018A;98:30–5. (Systematic Review and Meta-Analysis)
112. Raymond EG, Shochet T, Blum J, Sheldon WR, Platais I, Bracken H, et al. Serial multilevel urine pregnancy testing to assess medical abortion outcome: a meta-analysis. *Contraception* 2017;95:442–8. (Meta-Analysis)
113. Reeves MF, Fox MC, Lohr PA, Creinin MD. Endometrial thickness following medical abortion is not predictive of subsequent surgical intervention. *Ultrasound Obstet Gynecol* 2009;34:104–9. (Level III)
114. Fiala C, Safar P, Bygdeman M, Gemzell-Danielsson K. Verifying the effectiveness of medical abortion; ultrasound versus hCG testing. *Eur J Obstet Gynecol Reprod Biol* 2003;109:190–5. (Level III)
115. Pocius KD, Bartz D, Maurer R, Stenquist A, Fortin J, Goldberg AB. Serum human chorionic gonadotropin (hCG) trend within the first few days after medical abortion: a prospective study. *Contraception* 2017;95:263–8. (Level II-2)
116. Dayananda I, Maurer R, Fortin J, Goldberg AB. Medical abortion follow-up with serum human chorionic gonadotropin compared with ultrasonography: a randomized controlled trial. *Obstet Gynecol* 2013;121:607–13. (Level I)
117. Chen MJ, Creinin MD. Mifepristone with buccal misoprostol for medical abortion: a systematic review. *Obstet Gynecol* 2015;126:12–21. (Systematic Review)
118. Reeves MF, Kudva A, Creinin MD. Medical abortion outcomes after a second dose of misoprostol for persistent gestational sac. *Contraception* 2008;78:332–5. (Level III)
119. Raymond EG, Weaver MA, Louie KS, Tan YL, Bousie-guez M, Arangure-Peraza AG, et al. Effects of depot medroxyprogesterone acetate injection timing on medical abortion efficacy and repeat pregnancy: a randomized controlled trial. *Obstet Gynecol* 2016a;128:739–45. (Level I)
120. Curtis KM, Tepper NK, Jatlaoui TC, Berry-Bibee E, Horton LG, Zapata LB, et al. U.S. medical eligibility criteria for contraceptive use, 2016. *MMWR Recomm Rep* 2016; 65(RR-3):1–103. (Level III)
121. Hognert H, Kopp Kallner H, Cameron S, Nyrelli C, Jawad I, Heller R, et al. Immediate versus delayed insertion of an etonogestrel releasing implant at medical abortion—a randomized controlled equivalence trial. *Hum Reprod* 2016; 31:2484–90. (Level I)
122. Raymond EG, Weaver MA, Tan YL, Louie KS, Bousie-guez M, Lugo-Hernandez EM, et al. Effect of immediate compared with delayed insertion of etonogestrel implants on medical abortion efficacy and repeat pregnancy: a randomized controlled trial. *Obstet Gynecol* 2016;127:306–12. (Level I)
123. Shimoni N, Davis A, Ramos ME, Rosario L, Westhoff C. Timing of copper intrauterine device insertion after medical abortion: a randomized controlled trial. *Obstet Gynecol* 2011;118:623–8. (Level I)
124. Saav I, Stephansson O, Gemzell-Danielsson K. Early versus delayed insertion of intrauterine contraception after medical abortion - a randomized controlled trial. *PLoS One* 2012;7:e48948. (Level I)
125. Pohjoranta E, Suhonen S, Mentula M, Heikinheimo O. Intrauterine contraception after medical abortion: factors affecting success of early insertion. *Contraception* 2017; 95:257–62. (Level I)
126. Dewan R, Bharti N, Mittal A, Dewan A. Early IUD insertion after medically induced abortion. *Eur J Contracept Reprod Health Care* 2018;23:231–6. (Level II-2)
127. Chen A, Yuan W, Meirik O, Wang X, Wu SZ, Zhou L, et al. Mifepristone-induced early abortion and outcome of subsequent wanted pregnancy. *Am J Epidemiol* 2004; 160:110–7. (Level II-2)
128. Oliver-Williams C, Fleming M, Monteath K, Wood AM, Smith GC. Changes in association between previous therapeutic abortion and preterm birth in Scotland, 1980 to 2008: a historical cohort study. *PLoS Med* 2013;10: e1001481. (Level II-3)

The MEDLINE database, the Cochrane Library, and the American College of Obstetricians and Gynecologists' own internal resources and documents were used to conduct a literature search to locate relevant articles published between January 2000 and February 2020. The search was restricted to articles published in the English language. Priority was given to articles reporting results of original research, although review articles and commentaries also were consulted. Abstracts of research presented at symposia and scientific conferences were not considered adequate for inclusion in this document. Guidelines published by organizations or institutions such as the National Institutes of Health and the American College of Obstetricians and Gynecologists were reviewed, and additional studies were located by reviewing bibliographies of identified articles. When reliable research was not available, expert opinions from obstetrician–gynecologists were used.

Studies were reviewed and evaluated for quality according to the method outlined by the U.S. Preventive Services Task Force:

- I Evidence obtained from at least one properly designed randomized controlled trial.
- II-1 Evidence obtained from well-designed controlled trials without randomization.
- II-2 Evidence obtained from well-designed cohort or case–control analytic studies, preferably from more than one center or research group.
- II-3 Evidence obtained from multiple time series with or without the intervention. Dramatic results in uncontrolled experiments also could be regarded as this type of evidence.
- III Opinions of respected authorities, based on clinical experience, descriptive studies, or reports of expert committees.

Based on the highest level of evidence found in the data, recommendations are provided and graded according to the following categories:

Level A—Recommendations are based on good and consistent scientific evidence.

Level B—Recommendations are based on limited or inconsistent scientific evidence.

Level C—Recommendations are based primarily on consensus and expert opinion.

Published online on August 14, 2020.

Published concurrently online on August 14, 2020, in *Contraception*.

Copyright 2020 by the American College of Obstetricians and Gynecologists. All rights reserved. No part of this publication may be reproduced, stored in a retrieval system, posted on the internet, or transmitted, in any form or by any means, electronic, mechanical, photocopying, recording, or otherwise, without prior written permission from the publisher.

**American College of Obstetricians and Gynecologists**  
**409 12th Street SW, Washington, DC 20024-2188**

Medication abortion up to 70 days of gestation. ACOG Practice Bulletin No. 225. American College of Obstetricians and Gynecologists. *Obstet Gynecol* 2020;136. DOI: 10.1097/AOG.0000000000004082. Epub 2020 Aug 14.

---

*This information is designed as an educational resource to aid clinicians in providing obstetric and gynecologic care, and use of this information is voluntary. This information should not be considered as inclusive of all proper treatments or methods of care or as a statement of the standard of care. It is not intended to substitute for the independent professional judgment of the treating clinician. Variations in practice may be warranted when, in the reasonable judgment of the treating clinician, such course of action is indicated by the condition of the patient, limitations of available resources, or advances in knowledge or technology. The American College of Obstetricians and Gynecologists reviews its publications regularly; however, its publications may not reflect the most recent evidence. Any updates to this document can be found on [acog.org](http://acog.org) or by calling the ACOG Resource Center.*

*While ACOG makes every effort to present accurate and reliable information, this publication is provided “as is” without any warranty of accuracy, reliability, or otherwise, either express or implied. ACOG does not guarantee, warrant, or endorse the products or services of any firm, organization, or person. Neither ACOG nor its officers, directors, members, employees, or agents will be liable for any loss, damage, or claim with respect to any liabilities, including direct, special, indirect, or consequential damages, incurred in connection with this publication or reliance on the information presented.*

*All ACOG committee members and authors have submitted a conflict of interest disclosure statement related to this published product. Any potential conflicts have been considered and managed in accordance with ACOG’s Conflict of Interest Disclosure Policy. The ACOG policies can be found on [acog.org](http://acog.org). For products jointly developed with other organizations, conflict of interest disclosures by representatives of the other organizations are addressed by those organizations. The American College of Obstetricians and Gynecologists has neither solicited nor accepted any commercial involvement in the development of the content of this published product.*