Pharmacists' Roles in Medication Abortion

Continuing Pharmacy Education Program

Goal

To review evidence-based provision of medication abortion, as well as current and future roles for pharmacists.

Faculty and disclosures

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- **No conflicts of interest to disclose**

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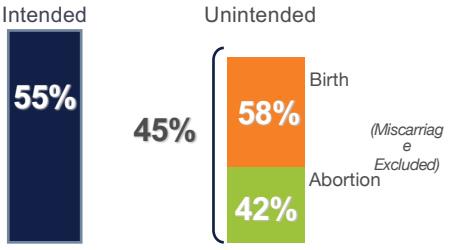
Learning objectives

- → Describe the current climate of access to abortion services in the United States.
- → Review the mechanisms, indications, safety, and effectiveness of mifepristone-based regimens for medication abortion.
- → List patient counseling points on medication use for medication abortion.
- → Explain the effects of the US FDA REMS requirement that prohibits pharmacy dispensing of mifepristone on access to medication abortion.
- → Discuss current and future pharmacist roles in the delivery of medication abortion services.

Current climate

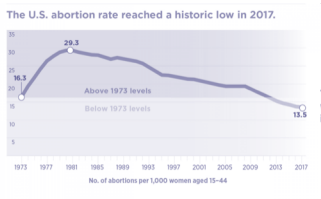
Unintended pregnancy in the US

→ 6.1 million pregnancies in the US each year

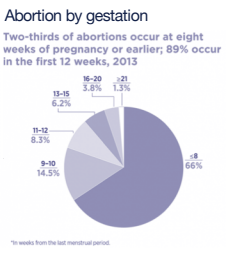


Abortion trends

Abortion rate in the US since 1973



Abortion by gestation



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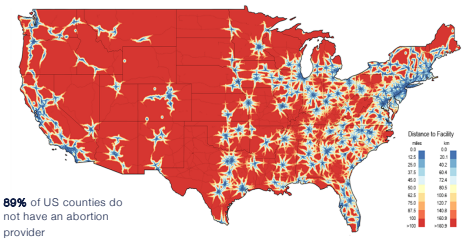
Limited clinic access to abortion

Estimated distance to nearest abortion facility



89% of US counties do not have an abortion provider

38% of reproductive age women live in one of those counties

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Who has abortions?

1 in 4 U.S. women will have an abortion by age 45

INCOME
75% poor or low income

RELIGION
62% religiously affiliated

FAMILY SIZE
59% already have a child

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Methods of abortion

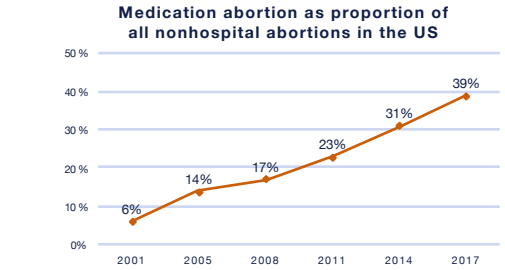
Methods of abortion

	1st trimester (4-14 weeks)	2nd trimester (14-24 weeks)
Medication	Medication (MAB) (≤10 weeks) • Mifepristone + Misoprostol • Misoprostol only	Labor induction • Mifepristone +/- Misoprostol
Procedural	Uterine aspiration (previously dilation & curettage or D&C) • Manual vacuum aspiration • Electrical vacuum aspiration	Dilation and evacuation (D&E) • Standard D&E • Intact D&E

Medication vs. procedures

Medication Abortion	"Surgical" Abortion
Usually avoids procedure	Involves procedure
Usually avoids sedation	Allows use of sedation if desired
Days to weeks to complete	Single day to complete
1st trimester (2nd trimester off-label)	1st and 2nd trimester
High success rate (~97%)	High success rate (99%)
Bleeding commonly not perceived as light	Bleeding commonly perceived as light
Patient participation throughout a multiple-step process	Patient participation in a single-step process
Requires follow-up to ensure completion of abortion	Does not require follow-up in most cases

Increasing proportion of medication abortions



Mifepristone approved in 2000

Guttmacher Institute. October 2019.

Check your learning

What portion of women in the United States will have an abortion in their lifetime?

- 1 in 3
- 1 in 4
- 1 in 10
- 1 in 12

Medication abortion (MAB)

Clinical Visit

Pregnancy confirmation

Pregnancy options counseling

MAB counseling and consents

Contraception counseling

Determining eligibility

- Determine gestational age
  - Up to 70 days (10 weeks from LMP)
  - Determined from menstrual history and clinical examination
  - Ultrasound used if the duration of pregnancy is uncertain or ectopic pregnancy is suspected

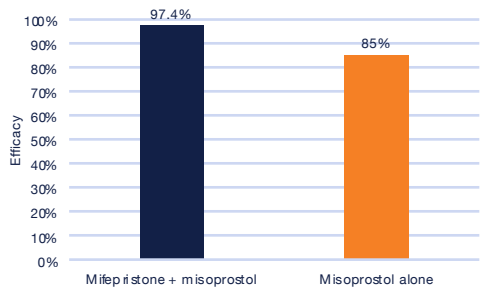
Determining eligibility (cont.)

- Evaluate for other contraindications
  - Confirmed/suspected ectopic pregnancy
  - Current IUD (must be removed before MAB)
  - Hemorrhagic disorders or concurrent anticoagulant therapy
  - Current long-term systemic corticosteroid therapy
  - Inherited porphyria
  - Chronic adrenal failure: antiglucocorticoid effect may impair action of cortisol replacement
  - Allergy to mifepristone or misoprostol: rash, urticaria and facial edema have been rarely reported
- Review RH status. If none; consider testing if >8 weeks gestation and patient is interested in RhD immunoglobulin, if needed

Ectopic pregnancy

- Ectopic pregnancy is **rare** (<1%) among medication abortion patients
- Mifepristone and misoprostol are contraindicated in case of ectopic pregnancy because treatment believed to be **ineffective**
- Medication abortion may be used with pregnancy of unknown location, but must **follow closely** to confirm completion
  - Ectopic may be diagnosed if hCG does not fall appropriately, and then patient may be treated for ectopic
- Patients at high risk of ectopic should have **ultrasound** to confirm IUP:
  - Prior ectopic, permanent contraception or tubal surgery, IUD in place, lateralizing pain, unusual bleeding

Efficacy before 10 weeks gestation



FDA-approved regimen

FDA-approved regimen as of 2016 is evidence-based	
Timeframe	10 weeks (70 days)
Pregnancy dating	LMP or Ultrasound
Progesterone receptor antagonist	Mifepristone 200 mg orally
Prostaglandin analogue	Misoprostol 800 mcg buccally 24-48 hours later
Follow-up evaluation	7-14 days after mifepristone to confirm abortion (by history, drop in beta HCG, or ultrasound)

Medications

Mifepristone

- Brand and generic available
- Progesterone receptor antagonist
- 200 mg PO

Misoprostol

- Brand and generic available
- Prostaglandin
- 800 mcg buccally 24-48 hours after mifepristone
  - Alternative evidence-based / off-label route: vaginal 6-72 hours after mifepristone

Administering misoprostol after mifepristone

	FDA regimen 2016 Buccal Misoprostol	Alternative: Vaginal misoprostol+
Maximum gestational age	70 days from LMP	70 days from LMP
Mifepristone dose/location	200 mg. orally Dispensed in office	200 mg. orally
Misoprostol dose/route	800 mcg. Buccally (4 tablets)	800 mcg. Vaginally (4 tablets)
Misoprostol timing	24-48 hours after mifepristone	6-72 hours after mifepristone
Misoprostol location	Home	Home
Follow-up timing & location	7-14 days after mifepristone, location not specified	7-14 days after mifepristone, location not specified

+ Indicates off-label use

Bleeding

- All patients with a successful medication abortion have some bleeding
- Mifepristone has boxed warning regarding serious and sometimes fatal bleeding
- Bleeding reported in the US registration trial
  - Median duration of bleeding or spotting: 13-15 days
  - 9% reported some bleeding after 30 days
  - 1% reported some bleeding after 60 days
  - 4 blood transfusions (0.2%); larger studies show transfusion rate of <0.1%

Pain management

- NSAIDs first line
- Ibuprofen more effective than acetaminophen
- NSAIDs block production of prostaglandins but do not block prostaglandin receptors, therefore do not interfere with misoprostol – a prostaglandin – used for medication abortion
- Oxycodone 10 mg did not reduce pain or improve satisfaction

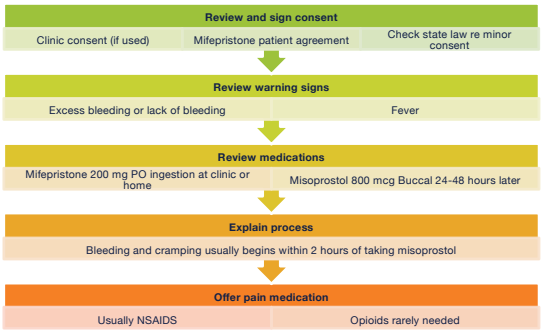
Infection and use of prophylactic antibiotics

- Uterine infection is rare, but may occur
  - Mifepristone has boxed warning regarding serious and sometimes fatal infections
  - Although Clostridial infections have been reported with medication abortion, as well as with miscarriage and delivery, neither pregnancy nor abortion causes Clostridial infections
  - Buccal administration of misoprostol may result in an even lower risk of serious infection compared to vaginal administration
  - Prophylactic antibiotics are not recommended
- Historically Doxycycline for 7 days was used
  - Data do not support its effectiveness
  - Patients likely had low adherence to this regimen

Nausea management

- Nausea reported in 50-75% of patients
- Vomiting reported in 37-48% of patients
- Treatment includes
  - Prochlorperazine
  - Ondansetron, consider ODT tablets

If patient is eligible for medication abortion…



In case patient has questions or concerns

- Patients are given a **telephone number** they can call 24 hours a day, 7 days a week to speak with a clinician if they have questions or concerns
- Clinician discusses with patient to go to **Emergency Department (ED)** in case of signs of serious complication
- Patients encouraged to bring **Medication Guide** with them to ED or if they see a different clinician

What's normal

Some women bleed after taking mifepristone, but they should still take misoprostol 24-48 hours later

- Bleeding and cramping
  - May start after taking mifepristone
  - Most women experience this after taking misoprostol
  - 23-38% report expulsion within 3 hrs after misoprostol, over 90% within 24 hrs
  - Bleeding tends to gradually increase and then decrease; pregnancy tissue is sometimes visualized
- Other common side effects
  - Nausea/vomiting/diarrhea
  - Dizziness/headache/weakness
  - Fever/chills

What's not normal

Call if…

- Bleeding that soaks 2 full-size pads per hour for 2 consecutive hours
- Signs of infection:
  - Fever > 101°F or prolonged (>4 hours) fever > 100.4 °F
  - Pain not responsive to pain meds or diffuse/severe abdominal pain
  - General malaise > 24 hours after the last misoprostol dose
- Patient has minimal bleeding, does not believe passed pregnancy, or has continued pregnancy symptoms after 7 days

Safety

- Antiglucocorticoid effect expressed at single doses >400 mg or repeated doses of 200 mg
- No clinical or laboratory signs of adrenal failure observed with chronic administration to people with normal adrenal function
- No mineralocorticoid effect
- Specific drug/food interactions have not been studied but may occur given metabolism by CYP 3A4
  - Use with caution in conjunction with CYP 3A4 inducers & inhibitors

Safety (cont.)

- Major complications (hospitalization, surgery, blood transfusion) occurs in 0.31% of patients taking medication abortion
- Death among patients using medication abortion is exceedingly rare—about 14 times less common than death associated with childbirth
  - 0.65 deaths per 100,000 medication abortions

Teratogenic potential with ongoing pregnancy

- Exposure to **mifepristone** alone is not associated with increased risk of birth defects over baseline
- **Misoprostol** may be teratogenic, associated with limb defects and Mobius syndrome
- In case of ongoing pregnancy after patient takes mifepristone and misoprostol, pregnancy options should be revisited with information about risk of birth defects resulting from use of misoprostol
- If patient elects to continue pregnancy, ultrasonographic monitoring is recommended

Follow-up

- Important to make sure there is no ongoing pregnancy (~3% ongoing pregnancy rate at 56-70 days).
- Follow-up options include:
  - Repeated measurements of serum hCG (day 1 and 8)
  - Return to clinic for ultrasound around day 8
  - Home urine pregnancy test at 4 weeks
- Contraceptive method can be started
  - Return to ovulation: 3 weeks on average but can soon as 8 days
  - For IUD, patient must return to clinic for insertion

Incomplete abortion and ongoing pregnancy

- Ongoing pregnancy occurs in 1-3% of patients, depending on gestational age
- Incomplete abortion occurs in 2-5%
  - If the patient does not have unusual symptoms, debris or thickened endometrial stripe seen on ultrasound is not an indication for treatment
- Treatment of ongoing pregnancy and incomplete abortion
  - Vacuum aspiration (surgical abortion)
  - Repeat misoprostol 800 mcg buccally
  - In case of incomplete abortion with minimal symptoms, may continue to follow the patient expectantly

Contraception

- All methods can be provided immediately after uncomplicated medication abortion – US MEC Category 1
- DMPA injection and etonogestrel implant may be provided on day of mifepristone
  - With DMPA, risk of ongoing pregnancy higher if injection given on day of mifepristone compared to giving at follow-up visit, but overall risk of needing aspiration is the same
- Pill, patch, and ring may be started on day of misoprostol administration
- IUD insertion early (5-9 days after mifepristone) vs delayed (3-6 weeks after mifepristone) had similar expulsion rates
  - Fewer women in the delayed group attended the follow-up visit for IUD insertion. Weigh expulsion rate vs risk of not returning
- Tubal ligation can be performed once abortion is confirmed

FAQ

- With multiple gestations, what regimen is used?
  - Same regimen can be administered for singleton and multiple pregnancies
- Does medication abortion affect future pregnancy outcomes?
  - Limited data, but no adverse outcomes have been reported in patients who become pregnant after a surgical or medication abortion

Other uses for these drugs

Mifepristone

- Hyperglycemia 2/2 Cushing's syndrome
- Cervical preparation/ripening for dilation and evacuation *
- Cervical preparation for induction in the second trimester *
- Early pregnancy loss *
- Emergency contraception (10 mg – not in U.S.) *
- Adjunctive treatment of uterine leiomyomata *
- Adjunctive treatment of endometriosis *
- Adjunctive treatment of unresectable/malignant meningioma *

Misoprostol

- NSAID-induced gastric ulcer prophylaxis or treatment
- Cervical preparation/ripening for dilation and evacuation *
- Cervical preparation for induction in the second trimester *
- Early pregnancy loss *
- Duodenal or gastric ulcer treatment unrelated to NSAID use *
- Postpartum bleeding, prophylaxis or treatment *

* Indicates off-label use

Early pregnancy loss (miscarriage) management

- Loss of intrauterine pregnancy in 1st trimester (aka **miscarriage**)
- Medical management can be considered in women who want to shorten the time to complete expulsion but prefer to avoid surgical evacuation and are without:
  - Infection
  - Hemorrhage
  - Severe anemia
  - Bleeding disorders
- **Medical management decreases the time to expulsion and increases the rate of complete expulsion** without the need for surgical intervention, compared with expectant management

Early pregnancy loss (miscarriage) management

- Misoprostol historically used alone
- Addition of mifepristone prior to misoprostol increases treatment efficacy (ACOG Level A recommendation)
- Treatment:
  - Mifepristone 200 mg PO 24 hours before misoprostol
  - 24 hours later, misoprostol 800 mcg PV
  - If no response, repeat misoprostol 800 mcg PV 3 hours – 7 days after first dose

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Check your learning

In the context of medication abortion, pregnancy dating, or gestational age, begins at what point?

→ First day of last menstrual period

→ Last day of last menstrual period

→ Date of ovulation

→ Date of intercourse

Check your learning

Mifepristone and misoprostol are approved by the FDA for use in medication abortion up to what gestational age?

→ 6 weeks

→ 8 weeks

→ 10 weeks

→ 12 weeks

Check your learning

When taken during the first 10 weeks of pregnancy, medication abortion with mifepristone and misoprostol is how effective?

→ 58%

→ 79%

→ 85%

→ 97%

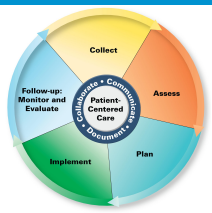
Pharmacists' roles in medication abortion

Pharmacists' roles

- Environment
- Inventory & Dispensing
- Counseling
- Privacy

Pharmacist patient care process

- Collect
  - Allergies
  - Concurrent medication list
  - Confirm no IUD in uterus
- Assess
  - Appropriate medication, dose, schedule
  - Assess potential drug interactions
- Plan
  - Call provider for verification, if needed
  - Dispense products
- Implement
  - Counsel patient on how/when to use medications, side effects, when to seek medical attention
- Follow-Up
  - Call patient in 1 week to assess therapy and wellbeing
  - Discuss contraceptive options, if patient interest



Administration considerations

Consider the timing of medication administration and the expected vaginal bleeding and abdominal pain to ensure patient comfort and minimize impact and stress.

Recommended Administration Schedule (if Mon-Fri 9-5 work schedule)

- Day 1: Thursday
  - → Take mifepristone in the morning. Minimal vaginal bleeding may occur; be prepared with panty liners.
- Day 2: Friday
  - → If possible, it is recommended to take the day off work. Take misoprostol in the morning. Expect heavy bleeding and cramping to start within 4 hours and last throughout the day. Be prepared with large sanitary pads.
- Day 3-4: Saturday & Sunday
  - → Bleeding is expected to continue through Saturday. Take the weekend to rest

Buccal administration

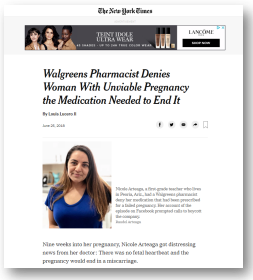
Misoprostol:
2 tablets placed in each cheek pouch for 30 minutes, then swallowed

Pharmacy counseling checklist

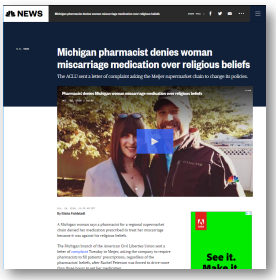
See PDF material

Media attention

Arizona June 2018



Michigan October 2018



Pharmacy workflow considerations

- If a pharmacist does not wish to participate in dispensing these medications, refer to state pharmacy regulations
- Alert pharmacy owner/manager to develop process to ensure patient care

REMS and the potential of pharmacy-dispensing of MAB

REMS

FDA Risk Evaluation and Mitigation Strategy (REMS) limits who can dispense mifepristone and where

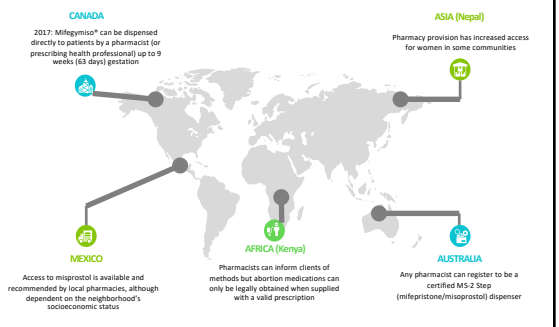
- → Prescribers complete "Prescriber Agreement Form" and give patient Medication Guide
- → Patients must sign "Patient Agreement Form"
- → Dispensed only in clinics, offices, or hospitals under supervision of certified prescriber.
  - → As of 2020…
    - → Physicians
    - → Nurse midwives
    - → Physician Assistants
    - → Nurse Practitioners

REMS During COVID-19

In place until at least 30 days after the end of the Secretary of HHS's declared "Public Health Emergency"

- → Blocks enforcement action where a health care provider arranges to have **mifepristone mailed or delivered directly to a medication abortion patient** (does not apply to other indications)
- → Patient Agreement form can be signed physically and mailed in or electronically during a telemedicine encounter
- → ***Does not authorize clinicians to dispense mifepristone through a retail or mail-order pharmacy***
- → Applies to many but not all states (check state laws)

Pharmacy dispensing abroad



Exploring expanding pharmacist roles in the US

- →UCSF Multi-Site Study: Alternative Provision of Medication Abortion via Pharmacy Dispensing
- →Designed to assess the feasibility, effectiveness, and acceptability of pharmacy dispensing of mifepristone

Check your learning

Misoprostol should be taken how long after mifepristone?

- → Right away
- → 2-4 hours
- → 24-48 hours
- → 46-72 hours

Check your learning

Patients should be counseled to call their medication abortion provider or seek immediate medical attention if they experience which of the following?

- → Heavy bleeding (soaking 2 full pads per hour for 2 hours)
- → Little or no bleeding
- → Feeling ill for 24 hours after misoprostol
- → All of the above

Check your learning

If the REMS was removed, U.S. pharmacies could:

- → Stock mifepristone to fill and dispense prescriptions
- → Prescribe mifepristone and misoprostol
- → Sell medication abortion behind the counter
- → Sell medication abortion over the counter

Thank you



For more information

Advancing New Standards in Reproductive Health

- Research
- Publications
- Resources

https://www.ansirh.org/

Birth Control Pharmacist

- Courses and Events
- Resources

https://birthcontrolpharmacist.com/