



Frequently Asked Questions about Mifepristone

The Food and Drug Administration's (FDA) approval of the early option pill (RU-486 or mifepristone) was a milestone for U.S. women. American women now have access to a method of very early abortion that millions of women worldwide have used safely and effectively since it was first licensed in France and China in the late 1980's. In September 2000, the FDA approved mifepristone based on extensive medical and scientific evidence. Since its approval, legislators on both the federal and state levels have introduced legislation that would attempt to restrict women's ability to access this safe and effective method for very early abortion.

What is mifepristone?

Mifepristone (RU-486) is a medication that blocks the action of the hormone progesterone. Progesterone is needed to sustain a pregnancy. In the United States, mifepristone is used in combination with another medication, a prostaglandin analogue called misoprostol. Misoprostol causes the uterus to contract and helps expel the pregnancy.

Is mifepristone safe?

Yes. Mifepristone in conjunction with misoprostol is a safe and effective regimen for early medical abortion. More than 840,000 women in the United States have used mifepristone/misoprostol to terminate their pregnancies since its approval in 2000, and millions of women around the world in 37 countries have safely used mifepristone since it was first licensed in France and China in 1988. Major complications associated with its use are rare.

Since its approval by the FDA in 2000, there have been two revisions to the labeling for mifepristone, most recently in July 2005, in order to incorporate expanded safety information including precautions and warning signs for infection, ectopic pregnancy, and excessive bleeding. Corresponding patient education materials from the manufacturer have been amended to reflect these changes, and have been incorporated into NAF's educational materials accordingly.

Seven deaths in the United States have been reported in women following the use of mifepristone/misoprostol. One death reported following the use of mifepristone and misoprostol was due to a ruptured ectopic pregnancy. Ectopic pregnancy is a pre-existing condition not caused by the use of mifepristone and misoprostol, and these medications are not an effective treatment for ectopic pregnancy. Ectopic pregnancies develop outside of the uterus, usually in the fallopian tube, occur in 2% of all pregnancies, and are the most common cause of death in the first trimester of pregnancy. As an ectopic pregnancy grows, it damages the tube causing it to rupture (burst) and bleed.

Reports of fatal infection in women using mifepristone/misoprostol are very rare. Five deaths have been attributed to sepsis following *Clostridium sordellii* infection; one death has been linked to another clostridial organism, *Clostridium perfringens*. *Clostridium sordellii* is a species of bacteria that in very rare cases causes toxic shock that is rapidly fatal. Four of the confirmed cases of *Clostridium sordellii* have occurred in California. No causal relationship has been established between mifepristone and/or misoprostol (or the route of administration of misoprostol) and these outcomes.

Clostridium sordellii has also been identified as a cause of death following childbirth, trauma, and surgery. Because it is difficult to isolate and identify clostridium species, additional cases in other settings probably exist, but have not been identified or reported. Very little is known about how or why *Clostridium sordellii* becomes lethal (see references below).

Is misoprostol safe?

Yes. The FDA approved the mifepristone/ oral misoprostol regimen as safe and effective for early abortion. These medications have a long history of safety both here and throughout the world. Misoprostol (marketed under the brand name Cytotec®) was approved years ago by the FDA as a medication to prevent gastric ulcers in individuals using a lot of aspirin, ibuprofen, or similar products to treat a medical condition. Misoprostol has also been prescribed for other purposes, including for labor induction and, since the early 1990s, as part of various regimens which induce early abortion. Misoprostol may be administered buccally (dissolving between the cheek and the gum), vaginally, or orally for medical abortion.

In August 2000, the then manufacturer of misoprostol, Searle, sent a letter to health care professionals stating that the medication should not be used by pregnant women since it "can cause abortion" (Searle letter, 8/23/00). Misoprostol had been used for years to induce labor in pregnant women, and some questions had been raised as to its safety for labor induction. Additionally, because the letter was issued shortly before the mifepristone/misoprostol regimen was approved by the FDA for early abortion, many organizations, including the American College of Obstetricians and Gynecologists (ACOG), questioned

its timing and suggested it was motivated by political, rather than medical considerations. In a letter sent to the FDA in response to the Searle statement, ACOG expressed its concern with the “content, timing, and tone of this [Searle] letter,” and reaffirmed that misoprostol is a “safe and effective agent for cervical ripening and labor induction” (ACOG release, 10/27/00).

In April 2002, the FDA made changes to the labeling of misoprostol to specify that the contraindication for its use in pregnancy refers specifically to the use of Cytotec® in patients taking it for the prevention of gastric ulcers. The FDA also created a new “Labor and Delivery” section of the label that acknowledges its use for cervical ripening, labor induction, and for treatment of serious postpartum hemorrhage in the presence of uterine atony.

What are alternative evidence-based or “off-label” regimens?

Evidence-based regimens, or “off-label” use of a medication, are part of standard medical practice. This occurs when the prescribing clinician uses a medication in a way that differs from the FDA-approved label but is based on sound scientific evidence. Many evidence-based regimens are recommended by medical textbooks, research institutes, journal articles, and professional organizations. The FDA has recognized that such use by clinicians is often appropriate and may represent the standard of practice. The American Medical Association (AMA) has estimated that 40-60% of all prescriptions are for alternative evidence-based uses.

The AMA's policy is that a physician may use an FDA-approved product “off-label” when such use is based on sound scientific evidence and sound medical opinion. Historically, the FDA has not attempted to regulate off-label drug administration and has disclaimed any interest in regulating physicians' prescribing practices.

Evidence gathered in clinical trials since the FDA trials and published in peer-reviewed medical journals has shown that a number of alternative mifepristone/misoprostol regimens are safe and effective. These alternative regimens can include a lower dose of mifepristone, different administration of misoprostol, home use of misoprostol, and flexibility in the timing of the regimen, and are as safe and effective as, and in some cases more effective than, the FDA-approved regimen (see references below). Health care providers have the option of following either the FDA-approved regimen or alternative evidence-based regimens when using mifepristone.

What has been the experience of women in the U.S. with mifepristone?

More than 840,000 women in the U.S. have used mifepristone/misoprostol since its approval by the FDA in September 2000. Medical abortion is generally well accepted by patients and providers. 96% of women in U.S. clinical studies stated they would recommend mifepristone to a friend or family member.

Was mifepristone fast tracked through the approval process?

No. The FDA approved mifepristone in September 2000, following a 54-month review period, contrasting with a median 15.6 month approval time for all other new molecular entities approved in that year. The approval of mifepristone was not accelerated, nor did mifepristone bypass the standard review process for new medications. The safety and efficacy of the drug were thoroughly reviewed during regular clinical trials, which were not abbreviated. Mifepristone was approved under Subpart H of the FDA regulations, which allows the FDA to establish a distribution system to assure safe use of certain drugs the agency has found to be effective. Subpart H was only invoked after the clinical trials had been concluded and an approvable letter had been issued.

Where is mifepristone manufactured?

Danco Laboratories, LLC is a women's health pharmaceutical company that has been granted an exclusive license from the Population Council to manufacture, market and distribute mifepristone in the United States. Danco secured a manufacturer for the production of mifepristone in accordance with FDA manufacturing standards. Mifepristone, like many other FDA-approved drugs, is produced in China. As part of the approval process, the FDA thoroughly inspected and reviewed the manufacturing process and plant. The manufacturer met the specifications of the FDA. Mifepristone's safety, efficacy, and manufacturing were thoroughly reviewed and approved by the FDA.

How is mifepristone distributed?

Mifepristone is available only through a qualified physician. Women who are seeking information about this option or referrals to providers who offer mifepristone can call NAF's toll-free hotline at 800-772-9100.

Should additional restrictions be placed upon the use of mifepristone?

No. Additional restrictions are not medically necessary and would only serve to impede women's access to mifepristone, a safe and effective medication. Restrictions similar to the ones being proposed in Congress have been considered and rejected by the FDA as not medically necessary and not in keeping with the way medicine is practiced in the United States.

Are there additional benefits of mifepristone?

Yes. There is evidence that mifepristone could be effective for a variety of other medical uses, including treatment of meningioma, breast cancer, ovarian cancer, psychotic depression, uterine fibroids, and endometriosis. With the approval of mifepristone in the United States, additional trials and studies have been able to proceed.

Where can I receive more information on mifepristone?

The National Abortion Federation (NAF) is playing a key role in educating health care providers and the public about this early abortion option and providing women with referrals to health care providers who offer quality medical abortion care.

For more information, please contact our offices at 202-667-5881 or visit our website at www.prochoice.org.

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