

MIFEPRISTONE: EXPANDING WOMEN'S OPTIONS FOR EARLY ABORTION IN THE UNITED STATES

Mifepristone, also known as medication abortion or “the abortion pill” (formerly known as RU-486), is an antiprogesterone drug that blocks receptors of progesterone, a key hormone in the establishment and maintenance of human pregnancy. Used in combination with a prostaglandin such as misoprostol, mifepristone induces abortion when administered in early pregnancy, providing women with an alternative to aspiration (suction) abortion.

Mifepristone was approved by the U.S. Food and Drug Administration (FDA) on September 28, 2000, for use as an abortifacient despite anti-women’s health lobbying efforts to prevent its approval. In the United States, the brand name for mifepristone is Mifeprex®, which is manufactured by Danco Laboratories, LLC (Danco, 2000).

EFFECTIVENESS AND SAFETY

Since its approval in France in 1988, mifepristone has proven to be a safe, effective, and acceptable option for women seeking abortion during the first several weeks of pregnancy.

- By the time the FDA approved mifepristone for use in the U.S., more than 600,000 women in Europe had medication abortions using mifepristone (FDA, 2000).
- Between 1994 and 1995, 2,121 women in Planned Parenthood and other U.S. health centers participated in clinical trials of mifepristone sponsored by the Population Council (Spitz et al., 1998).
- In the 14 years following FDA approval, more than 2 million U.S. women have used Mifeprex (Danco, n.d.). Planned Parenthood has provided approximately 875,000 women with this option (PPFA, 2014).
- Using the FDA-approved regimen up to 49 days’ gestation (measured from the first day of the last menstrual period), about 92-96 percent of women will complete their abortion without the need for a vacuum aspiration (ACOG, 2014; Kahn et al., 2000).
- Evidence-based alternative regimens use a lower dose of mifepristone and a higher dose of misoprostol than the FDA-approved regimen. Some of these alternative regimens have been found to be effective for longer than 49 days’ gestation. Planned Parenthood currently provides medication abortion up to 63 days’ gestation. Evidence-based alternative regimens have a success rate of up to 98 percent (ACOG, 2014; Fjerstad et al., 2009; Middleton et al., 2005; Schaff et al., 2002).
- Some women may begin bleeding after taking mifepristone, *before* taking misoprostol. For most, the bleeding and cramping begins *after* taking misoprostol. More than 50 percent of women who use mifepristone abort within four to five hours after taking the misoprostol (Newhall & Winikoff, 2000; Peyron et al., 1993).
- An overwhelming majority of women who choose mifepristone for medication abortion are satisfied with the method. One study found that 97 percent of women would recommend the method to a friend. Additionally, 91 percent of the women reported that they would choose the mifepristone regimen again if they had to have another abortion (Hollander, 2000; Jensen et al., 2000).

- Because it is a noninvasive procedure, successful abortion eliminates certain risks associated with manual vacuum aspiration and dilation and suction curettage (D&C) such as perforation or risks related to anesthesia (Aguillaume & Tyrer, 1995).
- The most common side effects reported by women using mifepristone plus misoprostol for early abortion are similar to those of a spontaneous miscarriage: abdominal pain, bleeding, dizziness, fatigue, nausea, and vomiting. Changes in body temperature are also common (ACOG, 2014; Creinin & Aubény, 1999; Stewart et al., 2005).
- In some instances, rare, but potentially serious, side effects can occur. These adverse events include allergic reaction, heavy bleeding, incomplete abortion, infection, and undetected ectopic pregnancy – a dangerous condition that mifepristone does not cause or treat. In extremely rare cases, death is possible from very serious complications (ACOG 2014; Creinin & Aubény, 1999; Hausknecht, 2003).
- On the basis of data currently available, it is believed that the risk of death from medication abortion through 63 days' gestation is about one per 100,000 procedures (Grimes, 2005). The risk of death with surgical abortion is thought to be about one per 1,000,000 through 63 days' gestation (Bartlett et al., 2004). The risk of death from miscarriage is about one per 100,000 (Saraiya et al., 1999). The risk of death associated with childbirth is about 10 times as high as that associated with all abortion (Christiansen & Collins, 2006).

WHO PROVIDES PATIENT WITH MIFEPRISTONE

Mifepristone has been found to be most effective when administered in combination with a prostaglandin such as misoprostol. Elements of the procedure, such as who may prescribe, the type of prostaglandin, the method of administration, the dosage, and the number of days of pregnancy in which mifepristone is an option, vary worldwide.

In the United States, medication abortion using mifepristone and misoprostol may be provided by a physician or other clinician under the supervision of a physician who is

- capable of providing vacuum aspiration or is capable of referring for vacuum aspiration

- able to diagnose ectopic pregnancy
- able to assess gestational age

HOW MIFEPRISTONE IS USED

In the U.S., the approved FDA regimen involves three steps: 1) a visit to a clinician to discuss the procedure and its alternatives and to receive a 600 mg dose of mifepristone, 2) a second visit two days later for an oral dose of 400 mcg of misoprostol, a prostaglandin used to treat ulcers that the FDA approved for off-label use to induce contractions for abortion, and 3) a third, follow-up visit on day 14. The FDA approved mifepristone for use up to 49 days after the first day of the last menstrual period.

It is generally common for a large majority of clinicians in the U.S. to follow evidence-based alternatives to FDA regimens when they have been shown by published scientific evidence to have notable benefits, including a higher rate of effectiveness, causing fewer side effects, and allowing patients more flexibility. Ways in which the mifepristone regimen is often adapted include

- changing the dosage of the medications – It has been found that 200 mg of mifepristone and 800 mcg of misoprostol is equally as or more effective than using 600 mg of mifepristone and 400 mcg of misoprostol.
- eliminating the second visit – At-home administration of the second drug – the prostaglandin – allows a woman to control the timing and location of the cramping and bleeding associated with the medication abortion process. Studies have shown at-home administration to be both safe and effective (Fiala et al., 2004).
- extending the time period for using mifepristone – Studies have found that mifepristone can be effective up to 63 days after the first day of the last menstrual period, dependent upon the regimen used (buccal and/or vaginal administration of the prostaglandin allows the 63-day limit) (Boonstra, 2002; Creinin et al., 2006; Dzuba, et al., 2007; Middleton et al., 2005; Schaff et al., 2001).
- eliminating the follow-up ultrasound visit – Some health centers allow women to take a blood test in place of the repeat ultrasound to determine if the medication abortion process was complete (Fiala et al., 2003).

IMPLICATIONS FOR THE FUTURE

As mifepristone has become widely available, more women have elected to choose this option. These are some of the effects that are expected to continue:

- In France, Great Britain, and Sweden, where mifepristone has been available for at least 20 years, the proportion of abortions that are performed early in pregnancy has increased significantly in the years following its approval for medication abortion (Boonstra, 2002).
- More providers have been willing to offer the medication regimen than vacuum aspiration services.
- Mifepristone has offered women more privacy in the abortion decision, along with greater personal control over the process of pregnancy termination.

There is no evidence that the availability of mifepristone for medication abortions increases a nation's rate of abortion. In France, England, and Wales, the abortion rate remained stable from the year prior to mifepristone's approval to 2000. The abortion rate in Sweden fell following mifepristone approval (Jones & Henshaw, 2002). And the rate of abortion fell nine percent in the first five years of its use in the U.S. (Jones et al, 2008).

OTHER USES

Medical uses for mifepristone are likely to expand in the future.

Researchers have identified a number of potential uses for mifepristone beyond pregnancy termination, including the treatment of breast cancer, Cushing's syndrome, endometriosis, glaucoma, meningioma, ovarian cancer, prostate cancer, severe depression, and uterine fibroids (DeBattista & Belanoff, 2006; Institute of Medicine, 1993).

Although not currently available in the United States for this use, mifepristone may be used in very low doses to prevent pregnancy as a method of emergency contraception within five days of unprotected intercourse (WHO, 1999). In higher doses, of course, it can be used to terminate pregnancy. Other medications currently used for emergency contraception in the U.S. cannot be used to terminate pregnancy because they are not abortifacients.

HISTORY

In spite of its demonstrated effectiveness, safety, and acceptability, mifepristone was continuously targeted by opponents of safe and legal abortion, causing numerous and lengthy delays in the efforts to make the drug legal and available to the many Americans it might benefit.

Mifepristone/RU-486 was first approved for use in September 1988 in France, where it was developed by the pharmaceutical firm Roussel-Uclaf. In October 1988, Roussel Uclaf, the sole manufacturer of the drug and holder of the patents, took the unprecedented action of suspending its distribution, citing protests by anti-abortion groups in the U.S., France, and West Germany. Two days later, the French Minister of Health ordered the company to resume distribution in the interests of public health (Aguillaume & Tyrer, 1995).

In 1991, mifepristone was approved by the United Kingdom Licensing Authority for use in Great Britain, and in 1992, it was approved for use in Sweden (Aguillaume & Tyrer, 1995).

Even while the use of mifepristone was expanded to the U.K. and Sweden, however, Roussel-Uclaf announced that it had no intention of marketing the drug in the U.S. or any other country where the company perceived that political and social conditions were unreceptive to the drug. The George H. W. Bush administration, with its overall hostility to abortion, took the additional step of placing mifepristone on a list of drugs banned by the FDA from importation into the U.S. for personal use (Aguillaume & Tyrer, 1995).

In July 1992, Leona Benten attempted to bring mifepristone into the U.S. for personal use – the drug was seized and, in spite of a lower court ruling in Benten's favor, the confiscation was upheld by the U.S. Supreme Court (Talbot, 1999).

The Clinton administration, in one of its first administrative actions in January 1993, asked the FDA to reexamine the import ban. Subsequently, an FDA deputy commissioner indicated that the agency might consider clinical trials in Europe as evidence in determining the drug's safety, an important step for expediting the process of approval.

In May 1994, Department of Health and Human Services Secretary Donna Shalala announced that as a result of encouragement by the Clinton administration, Roussel-Uclaf had donated the U.S. rights for mifepristone to the Population Council, a New York-based nonprofit research institution. The Population Council conducted U.S. clinical trials from 1994–1995. Results of the Population Council clinical trials, showing mifepristone to be highly effective, safe, and acceptable for early abortion, were published in the *New England Journal of Medicine* and the *Archives of Family Medicine* in 1998.

Following public hearings on the subject, the FDA Advisory Committee for Reproductive Health Drugs recommended approval of mifepristone in the summer of 1996. The FDA issued an approvable letter for mifepristone in September 1996, indicating that the drug was safe and effective, but that the Population Council and the manufacturer needed to provide additional manufacturing, labeling, and other information in order to obtain final approval (Talbot, 1999).

The Population Council granted the Danco Group, a new women's health pharmaceutical company, an exclusive license to manufacture, market, and distribute mifepristone in the United States. Danco entered into a series of agreements with a manufacturer to produce mifepristone. However, the manufacturer backed out of the project in early 1997. This further delayed the availability of mifepristone in the U.S. Danco then identified manufacturers willing to produce mifepristone, worked with them toward production, and provided the FDA with the information it needed to make a final review of the application (Talbot, 1999).

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Politicians opposed to safe and legal abortion continued their efforts to deny women access to this safe, convenient method of abortion. In June 1998, Representative Tom Coburn (R-OK) attempted to prevent the possibility of FDA approval by offering an amendment to a spending bill that would have prohibited the FDA from spending any money to test, develop, or approve any drug for the chemical inducement of abortion. This measure was approved by the House, but it did not make it into the final version of the spending bill. In June 1999, Coburn again introduced – and the House passed – the amendment (Talbot, 1999). In July 2000, a similar amendment was again introduced, but this time rejected by the House (Zimmerman & Lueck, 2000).

Despite anti-women's health lobbying efforts that began in 1988 to prevent its approval, mifepristone was finally approved for use as an abortifacient by the FDA on September 28, 2000. In the U.S., the brand name for mifepristone is Mifeprex®, which is manufactured by Danco Laboratories, LLC (Danco, 2000).

Additional Resources

Mifeprex® The Early Option – <http://www.earlyoptionpill.com/>

U.S. Food and Drug Administration Mifepristone Information – <http://www.fda.gov/drugs/drugsafety/postmarketdrugsafetyinformationforpatientsandproviders/ucm111323.htm>

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