



Mifepristone and misoprostol for medical abortion

Description

Medical abortion (MA) is a nonsurgical procedure in which drugs are used to induce abortion. The most effective and safest medical abortion regimen requires the use of two medications: mifepristone and misoprostol. Mifepristone blocks the action of progesterone to enhance the contractility of the uterus and prompt the detachment of the implanted embryo. Misoprostol stimulates strong contractions of the uterus, expelling the products of conception. This process is very similar to that of a spontaneous abortion or miscarriage.¹ Repeated administration of misoprostol alone can also be used to induce abortion. Both drugs also soften and dilate the cervix.

Quality abortion care should include counseling, confirmation of intra-uterine pregnancy, and estimation of gestational age by the patient's history, bimanual exam, or with ultrasound—although the latter is not required. Family planning and contraception counseling should be provided at the time of the abortion or afterwards. Medical abortion options have made abortion more available to women in a variety of health care settings, and home administration of medical abortion is also highly acceptable.²

Efficacy

The 2012 World Health Organization (WHO) publication “Safe Abortion: Technical and Policy Guidance for Health Systems” contains guidelines for the use of mifepristone and misoprostol for MA up to nine weeks, 9 to 12 weeks, and after 12 weeks of gestation.³ All the regimens use 200 mg of mifepristone followed by 800 µg of misoprostol administered vaginally, buccally, or sublingually. The misoprostol dose is taken 24 to 48 hours after mifepristone for pregnancies up to gestational age of 9 weeks, and 36 to 48 hours later for pregnancies of 9 to 12 weeks in gestational age and beyond 12 weeks. Additional 400-µg doses of misoprostol may be required depending on gestational age. These regimens result in complete abortion in more than 95 percent of cases; the rate of continuing pregnancy is less than 1 percent in gestations up to 63 days' amenorrhea.

Complete abortion rates in early pregnancy with misoprostol-only regimens range from 76 to 96 percent, according to existing research.^{4,5,6} Even though the combined regimen of mifepristone followed by misoprostol is significantly more effective than use of misoprostol alone for early MA, misoprostol is generally more widely available than mifepristone and has been used alone safely and successfully for MA around the world.⁷ When mifepristone is unavailable, the International Federation of Gynecology and Obstetrics (FIGO) and WHO recommend vaginal or sublingual administration of 800-µg misoprostol in pregnancies up to 12 weeks of gestation, repeated three times every 3 to 12 hours. For pregnancies of 12 to 24 weeks of gestation, the dose is halved and can be repeated up to five times every three hours.⁸

The use of mifepristone and misoprostol is very safe; MA has not been associated with long-term health impacts and is statistically less risky than continuation of pregnancy.⁹ MA may be preferable to surgical abortion for some women and their providers, as it is less invasive and can be perceived to be a more private procedure by some women.

Current program/sector use

There are a number of political, logistical, cultural, religious, financial, and other barriers that limit universal access to MA. Elective abortion is legally restricted in many countries, but almost all countries have provisions under which abortion is legal, including to save the woman's life, to preserve physical or mental health, when the pregnancy is a result of rape or incest, or on socioeconomic grounds. Where abortion is legal, challenges may arise in terms of health-system restrictions on where the services can be provided, procurement of the drugs, and provider training to properly inform and counsel patients about their options. However, MA is being made available to women in numerous countries, including some sub-Saharan African countries. The level of use in developed countries such as the United States and those in Europe suggests that women appreciate having an alternative to surgical abortion; women in Europe have been using mifepristone and misoprostol for more than 20 years.

Manufacturer/supplier

Mifepristone and misoprostol are available from generic manufacturers, as individually packaged medicines, and in combination packs made specifically for MA. There are numerous manufacturers of all three products (mifepristone, misoprostol, and combination packs).

Mifepristone

Two branded generics of mifepristone, Mifeprex® (Danco Laboratories, USA) and Mifegyne® (Laboratoire Exelgyne, France), and a non-branded generic (Linepharma, France), are available in mostly high-income countries. Linepharma's product was registered in Kenya in 2012. Many more branded and non-branded generic versions of mifepristone are made by numerous pharmaceutical companies in low- and middle-income countries such as India and China, but their export capacity is limited.

Misoprostol

More than 50 branded and non-branded generic versions of misoprostol are manufactured by pharmaceutical companies in high-, middle-, and low-income countries, including Argentina, Bangladesh, Brazil, Chile, China, Egypt, France, India, Mexico, Peru, South Korea, Russia, and the United States.¹⁰ Some of these manufacturers are making products for export to low- and middle-income countries; however, as with mifepristone, many only make products for their local markets. Cytotec® (Pfizer), registered in more than 80 countries, was the first misoprostol product on the market and is the most widely available. Misoprostol is eligible for the WHO Prequalification of Medicines Programme,¹¹ and for the United Nations Population Fund (UNFPA) Expert Review Panel process, which will assess whether misoprostol products from manufacturers that are applying for WHO prequalification could be recommended for use before achieving prequalification.¹² Efforts are underway to provide technical assistance to manufacturers applying to these programs.¹³

Mifepristone-misoprostol combination packs

Combination packs containing one tablet of mifepristone (200 mg) and four tablets of misoprostol (200 µg each) are currently only made by manufacturers in low- and middle-income countries. Most of these products are made in China and India and are for use in the local market only. Medabon®, a combination pack manufactured by Sun

Pharmaceuticals (India) is available for export, and Acme Formulations (India) also makes a product available for export.* Other manufacturers may export combination packs as interest grows globally.

The mifepristone and misoprostol combination is eligible for the WHO's Prequalification of Medicines Programme, and efforts are underway to support applications from generic manufacturers of the product.

Registration status

Misoprostol products are registered in most countries around the world, but in a large number of those countries products are only registered for the treatment and prevention of gastric ulcers. This is despite a breadth of existing evidence supporting misoprostol's effectiveness for a number of obstetric indications, including MA.** In 2005, the combination of mifepristone and misoprostol for MA was included on the WHO Model List of Essential Medicines for termination of pregnancy where legal and acceptable, up to nine weeks of gestation.¹⁴ A number of international organizations are working with policymakers and health care officials to ensure both drugs are registered for the breadth of uses for which they are effective, including MA. The information below highlights the global registration status for each drug and the combination pack.

Mifepristone

Mifepristone has been registered and approved for use in medical abortion in 50 countries worldwide; the low-income countries where mifepristone is currently registered are Cambodia, Ghana, India, Kenya, Mozambique, Nepal, Vietnam, and Zambia.¹⁵ In some of these countries, mifepristone is registered alone and in others it is registered as part of a combination pack with misoprostol.

*Misoprostol****

Registration of misoprostol for MA is far from universal. Misoprostol products have been approved for MA in only a few countries, including Ethiopia, Ghana, and Mozambique.¹⁶ Misoprostol has been registered specifically for use with mifepristone for pregnancy termination in France (registered by HRA Pharma as Gymiso®) and Russia (registered by Pentcroft Pharma as Misoprostol). In many other countries, misoprostol is prescribed off label for use with mifepristone for medical abortion.

* For a complete list of references and discussion, please refer to the Post-abortion care (PAC) Service Delivery Toolkit located at www.vsinovations.org/resources.html or <http://www.ipas.org/en/What-We-Do/Comprehensive-Abortion-Care/Elements-of-Comprehensive-Abortion-Care/Medical-Abortion--MA-/Medical-Abortion--MA--Supply-Guidance/Postabortion-Care-Educational-Resources.aspx>

** Further information on the treatment of incomplete abortion with misoprostol and service delivery guidelines for integrating misoprostol into PAC services can be found at <http://vsinnovations.org/resources.html> or <http://www.ipas.org/ma/mpactoolkit> and <http://gynuity.org/resources/info/guidebook-on-misoprostol-for-treatment-of-incomplete-abortion/>.

*** For more information on misoprostol, please see the Caucus brief on Misoprostol for Maternal Health.

Mifepristone-misoprostol combination packs

Medabon® is currently registered for medical abortion in Cambodia, Ghana, India, Mozambique, Nepal, Zambia, and 14 countries in Europe. A combination product from Acme Formulations is also registered in Mozambique, and efforts are underway to register combination packs from other manufacturers in several other countries in sub-Saharan Africa. In India, many brands of Indian-made combination packs are registered for MA, but they are not available for export.

Public-sector price agreements

The Concept Foundation has negotiated a preferential price for public-sector procurement of Medabon® in developing countries. Overall, the number of manufacturers for these drugs is large, and the market is continuing to evolve. Pricing varies by manufacturer, is country-specific, and is often dependent upon product demand.

References

1. World Health Organization (WHO). *Frequently Asked Clinical Questions About Medical Abortion: Conclusions of an International Consensus Conference on Medical Abortion in Early First Trimester, Bellagio, Italy*. Geneva: WHO; 2006.
2. Kopp Kallner H, Fiala C, Gemzell-Danielsson K. Assessment of significant factors affecting acceptability of home administration of misoprostol for medical abortion. *Contraception*. 2011;85(4):394–397.
3. World Health Organization. *Safe Abortion: Technical and Policy Guidance for Health Systems*. Geneva: WHO; 2012. Available at: http://www.who.int/reproductivehealth/publications/unsafe_abortion/9789241548434/en/.
4. Zikopoulos KA, et al. Early pregnancy termination with vaginal misoprostol before and after 42 days gestation. *Human Reproduction*. 2002;17(12):3079–3083.
5. Prasad S, A Kumar, A Divya. Early termination of pregnancy by single-dose 800 [mu]g misoprostol compared with surgical evacuation. *Fertility and Sterility*. 2009;91(1):28–31.
6. Ngoc NT, Shochet T, Raghavan S, et al. Mifepristone and misoprostol compared with misoprostol alone for second-trimester abortion: a randomized controlled trial. *Obstetrics & Gynecology*. 2011;118(3):601–608.
7. Faundes A, et al. Misoprostol for the termination of pregnancy up to 12 completed weeks of pregnancy. *International Journal of Gynecology & Obstetrics*. 2007;99(2):S172–177.
8. International Federation of Gynecology and Obstetrics. *Misoprostol Recommendations*. 2012. Available at: http://www.igo.org/publications/miscellaneous_publications/Misoprostol_Recommendation_2012.
9. Grimes DA. Estimation of pregnancy-related mortality risk by pregnancy outcome, United States, 1991 to 1999. *American Journal of Obstetrics and Gynecology*. 2006;194(1):92–94.
10. Fernandez MM, et al. Assessing the global availability of misoprostol. *International Journal of Gynecology and Obstetrics*. 2009;105:180–186.
11. World Health Organization. 5th Invitation to manufacturers of reproductive health products to submit an Expression of Interest (EOI) for product evaluation to the WHO Prequalification Programme, Geneva: WHO; 2010. Available at: http://apps.who.int/prequal/info_applicants/eoi/EOI_ReproductiveHealth-V5.pdf.
12. United Nations Population Fund (UNFPA). *Quality Assurance Policy for Reproductive Health Medicines*. New York: UNFPA; 2012. Available at: <http://www.unfpa.org/public/home/procurement/pid/10865>.
13. Concept Foundation. *Quality of Reproductive Health Medicines Program*. Available at: <http://www.conceptfoundation.org/business.php>.
14. World Health Organization. *Model Lists of Essential Medicines*. Available at: <http://www.who.int/medicines/publications/essentialmedicines/en/>.
15. Gynuity website. List of mifepristone approvals. Last updated September 2012. Available at: <http://gynuity.org/resources/info/list-of-mifepristone-approval/>.
16. Venture Strategies Innovations website. Map of misoprostol approval page. Last updated January 2013. Available at: <http://www.vsinnovations.org/resources.html>.

For more information on the Caucus on New and Underused RH Technologies, please visit our web page at <http://www.rhsupplies.org/working-groups/caucus-on-newunderused-rh-technologies.html>.

This publication forms part of a series of technical briefs, written by members of the Caucus on New and Underused Reproductive Health Technologies, a thematic group established under the auspices of the Reproductive Health Supplies Coalition. The Caucus' aim is to broaden the discussion within the Coalition of reproductive health technologies that are not well integrated into the public or commercial health sectors. Responsibility for the selection and contents of the product briefs rests solely with the Caucus and does not imply endorsement by the Coalition or its wider membership. For additional information, please contact secretariat@rhsupplies.org.