Misoprostol for maternal health

Description

Misoprostol can be used for a number of obstetric indications that address maternal health concerns. Misoprostol acts as a uterotonic by stimulating strong contractions of the uterus and also softens and dilates the cervix, similar to the natural process of labor. Its uses related to maternal health are many and include the prevention and treatment of postpartum hemorrhage, labor induction, treatment of incomplete abortion and miscarriage, induced abortion, treatment of missed abortion, treatment of intrauterine fetal death, and cervical ripening.

Dosing regimens vary depending on the medical indication. For labor induction and cervical ripening, the dose can be as low as 25 mg; however, the other indications require a dose of between 400–800 mg. Recommended routes of administration are oral, sublingual, rectal, or vaginal. Dosage guidelines for all indications listed above have been issued by the International Federation of Gynecology and Obstetrics (FIGO).1 See also http://www.misoprostol.org.

Misoprostol is available in tablet form, and marketed products typically have a shelf life of 18–36 months when stored below 25–30°C (77–86°F) in a dry area.

Efficacy

For the prevention of postpartum hemorrhage (PPH): Misoprostol is an effective alternative uterotonic, where use of oxytocin or other injectable uterotonics requiring refrigeration and administration by a skilled provider is not feasible. For these reasons, misoprostol can be especially useful in home deliveries. In a multi-center study conducted in hospitals, oxytocin performed marginally better than oral misoprostol in controlling blood loss.2 In a study of women delivering at home in India, oral misoprostol was associated with a significant reduction in the rate of acute postpartum hemorrhage compared to women not using a uterotonic.3 A significant reduction in PPH was also observed with oral misoprostol when administered by traditional birth attendants during home deliveries in Pakistan.4

In 2000, the World Health Organization (WHO) recommended the prophylactic use of a uterotonic immediately after delivery for all women, as part of the active management of the third stage of labor,5 and oxytocin is recommended as the first line drug. In March 2011, the WHO included the use of 600 µg oral misoprostol for prevention of PPH in the 17th Model List of Essential Medicines.6

For the treatment of PPH: In women who were given prophylactic oxytocin as part of the active management of the third stage of labor, misoprostol and oxytocin were found to be clinically equivalent when used to stop excessive post-partum bleeding.7 In women not exposed to prophylactic oxytocin, although oxytocin was found to be more effective at controlling bleeding within 20 minutes, researchers concluded that 800 µg sublingual misoprostol might be a suitable first-line treatment in settings in which use of oxytocin is not feasible.8

For the treatment of incomplete abortion and miscarriage: The efficacy of misoprostol to treat incomplete abortion and miscarriage is between 91 to 99 percent, equivalent to the use of manual vacuum aspiration.9 Medical management of incomplete abortion and miscarriage with misoprostol provides a good opportunity to scale up post-abortion care services.1 Use of 600 µg oral misoprostol for this indication was included in the WHO 16th Model List of Essential Medicines in 2009 and in the WHO Priority Medicines for Mothers and Children issued in 2011.7,9

* For a complete list of references and discussion, please refer to the medial Post-abortion care (PAC) toolkit located at www.vsinnovations.org/resources.html or www.ipas.org/ma/mpactoolkit.
† 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 induced abortion: Effectiveness of misoprostol-alone regimens for early-term medical abortion range from 76 to 96 percent. Even though it is not as effective as the combination of mifepristone and misoprostol, misoprostol is more widely available than mifepristone and has been used safely and successfully for medical abortion around the world.10

For labor induction: Cochrane Reviews have concluded that oral misoprostol is more effective than placebo and at least as effective as vaginal dinoprostone for induction of labor with doses not exceeding 50 μg;11 similarly, while vaginal misoprostol is more effective than other conventional methods, low dose oral misoprostol is preferable.12 In 2011, the WHO recommended the use of both oral (25 μg, two-hourly) or vaginal (25 μg, six-hourly) misoprostol for the induction of labor.13

Current program/sector use

In the developed-world setting, misoprostol is used off-label for many of its clinical indications, including induction of labor and cervical ripening, and in combination with mifepristone for medical abortion, where legally permissible.14

In developing countries, programs to introduce misoprostol into the health system for a variety of obstetric indications are being implemented. For the prevention of PPH, pregnant women have been taught to self-administer 600 μg misoprostol tablets orally as soon as their baby is delivered. Studies in Afghanistan,15 Nepal,16 and Bangladesh17 show that women can use misoprostol consistently and safely (even for twin deliveries) when the drug is distributed by community health workers to women planning to deliver at home. Programs in Ethiopia, Kenya, Tanzania,18 Mozambique, Zambia, Bangladesh, Uganda, Nigeria, and Senegal have shown that distribution at antenatal-care checks and through community health workers is effective and that misoprostol is used safely and correctly at home deliveries. Some countries are now taking steps to scale up the use of misoprostol in national safe motherhood programs and are also including the use of misoprostol for treatment of incomplete abortion and miscarriage in post-abortion care programs.

Manufacturer/supplier

More than 50 branded and non-branded generic versions of 200 mg misoprostol tablets are manufactured by pharmaceutical companies in high-, middle-, and low-income countries including India, Bangladesh, Brazil, Egypt, China, Peru, South Korea, Chile, Argentina, Mexico, the United States, France, and Russia.19 Some of these manufacturers are making products for export to low- and middle-income countries, but many only make products for their local markets. Cytotec® (manufactured by Pfizer) is the most widely available misoprostol product. There are few manufacturers of the 25 mg tablet. As of May 2010, misoprostol became eligible for the WHO’s Prequalification of Medicines Programme,20 and efforts are underway to support applications from generic manufacturers of misoprostol.

Registration status

Registration, or market approval of a drug by a country’s drug regulatory agency, grants permission for a product from a specific manufacturer to be marketed in that country by a pharmaceutical distributor for the medical indications for which the application was made. The registration status of misoprostol varies. It is often only registered for some of its many obstetric indications, while in many countries it is not registered for these indications at all. For example, misoprostol is most commonly registered for prevention and treatment of gastric ulcers; Cytotec®, is registered in more than 80 countries but only for these two indications. As noted previously, in many countries misoprostol may be legally used for off-label indications.

Misoprostol is increasingly being registered for obstetric indications. A limited number of manufacturers make misoprostol for export. Exporting manufacturers that have registered products for obstetric indications include Acme Formulations, Cipla, Sigma Pharmaceuticals, Square Pharmaceuticals, and Zizhu Pharmaceutical, and there are likely to be others.

Products are registered for obstetric indications in more than 15 countries, including Bangladesh, Bolivia, India, Ethiopia, Kenya, Malawi, Mali, Mozambique, Myanmar, Nepal, Pakistan, Senegal, Sudan, Somaliland, Tanzania, Uganda, and Zambia. More registrations are expected in the coming years as interest in misoprostol grows. The approved indications vary across countries; in some countries, products are only registered for PPH prevention and treatment, while in others they are registered for multiple obstetric indications. The indications for which the drug is granted approval usually depend on the level of commitment and willingness of governments to integrate misoprostol into safe motherhood programs. More information on the global status of misoprostol registration can be found at http://www.vsinnovations.org/resources.html.

‡ For more information on misoprostol for induced medical abortion, please see the Caucus on New and Underused RH Technologies brief on Medical Abortion.
Public-sector price agreements

There are no global public-sector price agreements for misoprostol. Governments can purchase a misoprostol product that is registered in their country and can negotiate the price with the distributor that holds the market approval.

References