Misoprostol for Treatment of Incomplete Abortion:

AN INTRODUCTORY GUIDEBOOK

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I. INTRODUCTION

The launch of this guidebook follows closely the inclusion of misoprostol for the management of incomplete abortion and miscarriage in the World Health Organization's Model List of Essential Medicines in April, 2009.¹ The Expert Committee on the Selection and Use of Essential Medicines decided that misoprostol is as effective as surgery and perhaps safer and cheaper in some settings. This new status marks a turning point in the role of misoprostol from a promising technology to an established, internationally recognized essential medicine for the treatment of incomplete abortion.

Approximately one in five recognized pregnancies are spontaneously miscarried in the first trimester² and an additional 22% end in induced abortion.³ An incomplete abortion can result from either spontaneous or induced pregnancy loss and occurs when products of conception are not completely expelled from the uterus.

Incomplete abortion is closely related to unsafe abortion in many parts of the world. Where abortion services are restricted, women may seek pregnancy terminations from unskilled providers, have procedures performed in environments lacking minimal medical standards, or both.⁴ Some women may resort to self-induction. These conditions increase the likelihood that women will experience abortion complications and will seek treatment for incomplete terminations.⁵ Safe and effective treatment for incomplete abortion is an important way to reduce abortion-related morbidity and mortality, particularly in settings where legal abortion is restricted.

Incomplete abortion can be treated with expectant management, which allows for spontaneous evacuation of the uterus, or active management, using surgical or medical methods. Expectant management is not preferred by many providers due to its relatively low efficacy and the fact that the time interval to spontaneous expulsion is unpredictable.⁶ The standard of care for active management varies by setting but has traditionally been surgery with general or local anesthesia. Surgical methods are highly effective for treatment of incomplete abortion. However, these treatments require trained providers, special equipment, sterile conditions and often anesthesia, all of which are limited in many settings.⁶ Medical methods for treatment of incomplete abortion require few resources and can be administered by low- and mid-level providers.⁷ Such technologies could increase access to services for women far from surgical care facilities. Misoprostol is the most common and thoroughly studied form of medical management and offers a highly effective alternative treatment for women wishing to avoid invasive surgery and anesthesia.⁸ In environments with few resources and limited access to surgical methods, such as primary and secondary care centers, misoprostol allows for the vast majority of cases to be treated without needing referral to higher level facilities.⁸ Additionally, misoprostol is widely available, easy to administer, stable at room temperature, accessible, and inexpensive in most countries. Misoprostol offers women and providers a safe, effective, and non-invasive treatment option for incomplete abortion that is particularly useful where supplies are limited and skilled providers are few. In settings where special postabortion care (PAC) services have been introduced to address morbidity and mortality associated with unsafe abortion, misoprostol can be integrated easily within existing services.

Information about this Guidebook

This guidebook was created for providers and policymakers who are interested in learning about misoprostol to treat incomplete abortion, whether arising from spontaneous or induced pregnancy loss. The goal of this guidebook is to synthesize the available literature to provide appropriate, effective and safe clinical guidelines for use of misoprostol in treatment of incomplete abortion. Chapter II focuses on the efficacy, safety, and acceptability of misoprostol for treatment of incomplete abortion, while Chapters III through V outline who can be offered the method, recommended regimens, schedule of clinic visits, management of side effects, counseling, and service delivery. Chapter VI addresses how misoprostol can be integrated into existing PAC services and Chapter VII provides brief information on missed abortion.

II. OVERVIEW OF MISOPROSTOL FOR INCOMPLETE ABORTION

A. What misoprostol is and how it works

Misoprostol (with a variety of trade names, the most common being Cytotec[®]) is registered in over 80 countries, mostly for prevention of gastric ulcers secondary to long-term use of non-steroidal anti-inflammatory drugs (NSAIDs). Misoprostol is a prostaglandin E1 analog which, like natural prostaglandins, affects more than one type of tissue, including the stomach lining and the smooth muscle of the uterus and cervix.^{6, 9, 10} Over the last two decades, research on use of misoprostol in reproductive health has burgeoned due to its very effective uterotonic and cervical ripening properties.^{6, 10} At present, misoprostol is an accepted and widely used treatment for cervical ripening, induction of abortion in the first and second trimester, prevention and treatment of postpartum hemorrhage, and incomplete abortion. At the same time, few misoprostol products have been registered for reproductive health uses.

B. FORMULATION

Misoprostol is most commonly manufactured as a 200 mcg tablet intended for oral administration, although 100 mcg pills also exist in some countries.¹⁰ Vaginal formulations are also available in some places, mostly as a 25 mcg suppository, but also in larger doses. Misoprostol has several important advantages over other agents with uterotonic properties. For example, it is stable at ambient temperature¹¹ while other products require refrigeration or freezing. Some other products are only administered by injection.⁹ Misoprostol is less expensive and more widely available than other treatments.¹¹ With new misoprostol products and generics appearing each year, its price can be expected to decrease as availability increases.

C. Efficacy in treating incomplete abortion

Misoprostol is effective in emptying the uterus because of its ability to induce uterine contractions and to soften the cervix. Misoprostol for treatment of incomplete abortion has been well documented in women presenting with uterine size less than or equal to a pregnancy at 12 weeks since last menstrual period (LMP).¹² Successful use of misoprostol implies complete evacuation of the uterus without recourse to surgical intervention. Infrequently, surgical completion may be needed for retained products of conception, heavy bleeding, or at the request of the woman. The efficacy rates found in the literature are inconsistent due to differences in regimens, time to determination of success, and inclusion and exclusion criteria. However, recent studies have attempted to standardize these variables and have achieved high efficacy. Overall, in studies that each enrolled more than 100 women and used misoprostol in at least one treatment arm (600 mcg oral or 400 mcg sublingual misoprostol) with at least 7 days before follow-up, efficacy averaged 95% (see Table 1), with success rates as high as 99%.¹³

Year	Author	Ν	Treatment	Time to	Success
				Success	
2009	Diop A, et al. ¹⁴	150; 150	600 mcg oral misoprostol; 400 mcg sublingual misoprostol	Days 7 & 14	94.6%; 94.5%
2007	Bique C, et al. ¹⁵	123	600 mcg oral misoprostol; MVA	Days 7 & 14	91%; 100%
2007	Dao B, et al. ¹⁶	227	600 mcg oral misoprostol; MVA	Days 7 & 14	94.5%; 99.1%
2007	Shwekerela B, et al. ¹³	150	600 oral misoprostol; MVA	Days 7 & 14	99%; 100%
2005	Ngoc NTN, et al. ¹⁷	150; 150	600 oral single or double dose*	Day 7	95.3%; 93.8%
2005	Weeks A, et al. ¹⁸	160	600 mcg oral misoprostol; MVA	Days 7 to 14	96.3%; 91.5%

Table 1: Misoprostol and Manual Vacuum Aspiration (MVA) for treatment of incomplete abortion

* 150 women received an additional 600 mcg oral misoprostol dose at 4 hrs (Ngoc NTN, et al.)

D. SAFETY

Misoprostol has been used by millions of men and women worldwide since its approval in 1988 for prevention of gastric ulcers associated with chronic NSAID use. Importantly, misoprostol has been used safely for incomplete abortion in many countries. Misoprostol has not been associated with long-term effects on women's health, and prolonged or serious side effects are virtually nonexistent.

E. ACCEPTABILITY

Women and providers find misoprostol for treatment of incomplete abortion to be highly acceptable. Many women report that they would choose misoprostol again if they were to need treatment for incomplete abortion in the future. Research in lowresource settings in several countries has indicated that over 90% of women were "very satisfied" or "satisfied" with misoprostol treatment.^{13, 16, 17, 18}

F. Comparison to other treatment methods

Incomplete abortion can be treated with expectant, surgical, or medical management. Expectant management involves allowing the uterus to evacuate the products of conception spontaneously without provider intervention. Generally, expectant management results in lower success rates compared to active (surgical or medical) management.¹⁹ Surgical evacuation procedures include dilatation and curettage (D&C), electric vacuum aspiration (EVA), and manual vacuum aspiration (MVA). These methods achieve a high success rate (91.5-100%) but carry a small risk of serious complications including infection, cervical laceration and uterine perforation. Most important, in many settings, surgical management may not be feasible. Misoprostol provides an effective, safe, and acceptable treatment option for women who do not have access to surgical treatment or who wish to avoid invasive procedures. Rates of gynecological infection after expectant, surgical, and medical management of incomplete abortion are low (2-3%) and do not differ by method of treatment.²⁰ Additionally, experience has shown that women find misoprostol to be as acceptable as MVA; in fact, in some studies, more women have reported being "very satisfied" with misoprostol treatment than MVA treatment.^{13, 16, 18} Refer to Table 2 for a comparison of methods of management of incomplete abortion.

Table 2: Comparing expectant, medical and surgical management of incomplete abortion								
Who can offer the What is needed to What are the risks?								
Expectant	Mid-level and skilled providers	Ability to diagnose the problem	Failure; need for medical or surgical					
Medical	Mid-level and skilled providers	Above plus drug supplies	Failure; need for surgical completion;					
Surgical	Skilled providers	All of the above plus sterilized equipment, surgical supplies, and a special room	Cervical laceration; uterine perforation; infrequent failure					

G. MISOPROSTOL IS AN IMPORTANT NEW TREATMENT FOR INCOMPLETE ABORTION

In countries where legal abortion is restricted, the PAC model provides a framework for care of women experiencing complications from unsafe abortion (see page 7). Treatment of incomplete abortion is an essential component of PAC services, and misoprostol can serve as an effective treatment option. Misoprostol treatment can be readily integrated into existing PAC services with basic provider training. Importantly, misoprostol is a safe and effective treatment option for PAC where there are no other treatment options or where there are few skilled providers. Essential elements of postabortion care where abortion services are restricted $^{\scriptscriptstyle 21}$

- 1. Community and service provider partnerships
 - Prevent unwanted pregnancies and unsafe abortion
 - Mobilize resources to help women receive appropriate and timely care for complications from abortion
 - Ensure that health services reflect and meet community expectations and needs
- 2. Counseling
 - Identify and respond to women's emotional and physical health needs and other concerns
- 3. Treatment
 - Treat incomplete and unsafe abortion and potentially lifethreatening complications
- 4. Contraceptive and family planning services
 - Help women prevent an unwanted pregnancy or practice birth spacing
- 5. Reproductive and other health services
 - Preferably provided on-site, or via referrals to other accessible facilities in providers' networks

III. TREATMENT OF INCOMPLETE ABORTION USING MISOPROSTOL

A. Who can receive misoprostol for treatment of incomplete abortion?

Eligibility criteria

Misoprostol can be used for early, uncomplicated incomplete abortion.

Eligible women have the following:

- > Open cervical os
- Vaginal bleeding or history of vaginal bleeding during this pregnancy
- Uterine size of less than or equal to 12 weeks' LMP

Assessment of uterine size

Providers should assess a woman's uterine size prior to misoprostol administration. A woman with a uterus 12 weeks' LMP or smaller is eligible for treatment with misoprostol. Uterine size can be estimated by conducting a physical exam. Precise dating of the initial gestational age is unnecessary as long as the uterine size at presentation for treatment is equivalent to a pregnancy of 12 weeks' LMP or less.

Women who are NOT eligible have the following:

- Known allergy to misoprostol or other prostaglandin
- Suspected ectopic pregnancy
- Signs of pelvic infection and/or sepsis
- Hemodynamic instability or shock

Precautions to use of misoprostol for treatment of incomplete abortion:

- Intrauterine device (IUD) in place: Women who have an IUD in place should have the IUD removed before misoprostol administration.
- Information to women who are breastfeeding: Misoprostol is quickly metabolized in the body,^{22,23} however, small amounts of misoprostol or its metabolite may appear in breast milk. No adverse effects in nursing infants have been reported, and there are no known consequences of such exposure.²⁴ If there is any concern, women can be advised to discard the breast milk produced for the first few hours after misoprostol administration.
- Uterine size larger than 12 weeks' LMP: Misoprostol may be used with caution in women with a uterine size larger than 12 weeks' LMP (e.g. uterine enlargement due to fibroids).

Myth: Misoprostol is not an appropriate treatment for women in rural areas

Misoprostol may be the most appropriate treatment choice for rural women because care can be provided by mid-level providers in the absence of surgical equipment and ultrasound. If a treatment facility is unable to provide surgical completion in the event of method failure, a referral clinic can provide this care.

B. Who can provide misoprostol for treatment of incomplete abortion?

Misoprostol can be provided by mid-level and skilled providers practicing in primary, secondary and tertiary care facilities. The most important skill is to know who could benefit from the treatment. Providers who are offering other reproductive health services may already have the skills needed to offer misoprostol as a treatment option for incomplete abortion. Myth: Only physicians can administer misoprostol for treatment of incomplete abortion

Given the nature of misoprostol treatment (oral medication), trained non-physician health workers can be effective treatment providers, increasing the number of providers. In some areas, nurses, midwives and other non-physician trained providers are already using misoprostol for treatment of incomplete abortion.

C. Dose and timing

High efficacy rates with acceptable side effect profiles have been obtained with both a single 600 mcg oral dose^{13, 14, 15, 16, 18} and with a single 400 mcg sublingual dose of misoprostol.¹⁴ Recent research has shown that these two regimens work equally well.¹⁴ Repeated dosing within a short interval does not seem to improve efficacy.²⁵ The recommended dosing regimen is a single administration of either 600 mcg oral or 400 mcg sublingual misoprostol (see Table 3). The lower dose may be advantageous in settings where cost of misoprostol is a concern. Success of misoprostol for treatment of incomplete abortion in the first trimester is independent of gestational age at the time of miscarriage/abortion.²⁶

Table 3: Recommended regimens of misoprostol for treatment of incomplete abortion ^{12, 27}						
Dose Misoprostol	Route of Administration					
600 mcg	oral					
400 mcg	sublingual					

Madagascar: Adapting the 400 mcg sublingual misoprostol regimen for PAC into national reproductive health norms and protocols

A large maternity hospital in Madagascar recently completed a study comparing a 400 mcg sublingual dose to a 600 mcg oral dose of misoprostol for treatment of incomplete abortion.¹⁴ Shortly after the launch of the study, it became clear to providers that treatment with the misoprostol regimen yielded high efficacy rates in addition to increased access and improved services. Over-burdened doctors saw their workload decrease as in-patient PAC patients were screened and treated by nurse midwives. Patient follow-up was also managed by these mid-level service providers. Given the lower cost of a 400 mcg versus 600 mcg dose and the similarity in efficacy, the Ministry of Health added a 400 mcg sublingual misoprostol regimen for the treatment of incomplete abortion to the Reproductive Health Norms and Protocols.

Future plans in Madagascar include expanding the use of misoprostol for incomplete abortion to lower levels of the healthcare system. The focus will be on providing training and developing curricula for lower level providers. Misoprostol's potential may best be realized as a firstline treatment in community-level health facilities when used by lower level health providers such as nurses and midwives.

D. ROUTE OF ADMINISTRATION

Misoprostol for incomplete abortion has been administered vaginally, orally, and sublingually.^{14, 28, 29, 30} A number of studies have demonstrated very high efficacy (greater than 90%) and acceptability using the oral route.^{13, 14, 15, 16, 18} The oral route is effective, simple, and acceptable to both women and providers. Recent experience has shown that lower dose sublingual administration is as effective as oral administration.¹⁴ If misoprostol is taken sublingually, the woman holds the pills under her tongue for about 30 minutes. Any remaining pill fragments can be swallowed with water.

E. SAFETY OF MISOPROSTOL FOR TREATMENT OF INCOMPLETE ABORTION

Misoprostol has been studied for treatment of incomplete abortion in many settings. It has been used safely by thousands of women seeking postabortion care with almost no side effects. Misoprostol has not been associated with long-term effects on women's health.

Frequently cited safety concerns include:

- Excessive bleeding: Excessive bleeding warranting transfusion is rare;³¹ misoprostol for treatment of incomplete abortion is no more likely to result in transfusion than other treatments.¹⁹
- Anemia: Misoprostol treatment is not associated with increased risk of anemia. A recently completed study shows no clinically significant difference in change in hemoglobin between women treated with misoprostol or MVA for incomplete abortion. Very few women had clinically significant drops in hemoglobin (0.3% misoprostol, 0.9% MVA).³²
- Infection: Risk of infection is low. The rate of infection in women who receive misoprostol for treatment of incomplete abortion is similar to the rate in women who receive other treatments.^{19, 20} There is no evidence that misoprostol increases the risk of infection.

- Ectopic pregnancy: Misoprostol will not cause, complicate, or treat an ectopic pregnancy. Suspected ectopic pregnancy is a contraindication to use of the method.¹² However, it is possible to confuse symptoms of ectopic pregnancy (e.g. pelvic pain and bleeding) with those of spontaneous pregnancy loss. Careful evaluation before treatment and good clinical judgment are essential to identify women with suspected ectopic pregnancies so that they may be referred for appropriate diagnosis and treatment.
- Use in women with history of cesarean section: There is no clinical reason to withhold misoprostol from women with previous cesarean sections. Such women have not been excluded in studies of misoprostol for treatment of incomplete abortion; misoprostol used for incomplete abortion according to the guidelines above is generally safe in this population.
- Teratogenic effects: Women seeking PAC services do not have viable pregnancies; therefore concerns about the potential teratogenic effects of misoprostol are not relevant for this indication.

IV. Service design, visit schedule and managing complications

A. Ultrasonography

Ultrasound machinery is not essential to provide misoprostol for treatment of incomplete abortion. Misoprostol can be offered in PAC facilities and at levels of care that lack ultrasound equipment or where ultrasound is too costly. An incomplete abortion can be diagnosed by clinical history and examination; complete evacuation can be assessed using the same set of clinical techniques.³³ Several recent studies in low-resource settings rarely used ultrasound to diagnose incomplete abortion (<5% of diagnoses were confirmed via ultrasound) or to confirm uterine evacuation.^{13, 14, 15, 18}

Ultrasound can be used if the provider has expertise in the technique: the biggest danger is in over-interpretation of normal amounts of debris in the uterus, leading to unnecessary surgical completion. Providers should be aware that women treated successfully with misoprostol have been found to have a wide range of endometrial thicknesses on ultrasound at follow-up; therefore it is recommended that the decision to perform surgical evacuation be based on clinical signs rather than ultrasound findings.³⁴ Unnecessary intervention to evacuate the uterus may occur when providers see debris on ultrasound but misinterpret its clinical significance.³⁵

Myth: Ultrasound is necessary prior to and after misoprostol for treatment of incomplete abortion

Many providers are concerned about offering misoprostol where ultrasound may not be available. However, ultrasound is not necessary to use misoprostol for treatment of incomplete abortion. Clinical history and examination are sufficient for diagnosis of incomplete abortion; complete evacuation can be assessed in the same way. Experience has shown the safety and efficacy of misoprostol in the absence of routine ultrasound.^{13, 14, 15, 18} Providers can refer women to facilities with ultrasound if they are uncertain of the woman's status following misoprostol treatment.

B. PROVIDER EXPERIENCE

The effectiveness of misoprostol as a treatment option for postabortion care services is in part dependent on provider familiarity with and confidence in the regimen. Clinical assessment of when and if surgical intervention is medically necessary is subjective and dependent on experience with the method. Providers who are confident and familiar with the regimen are more likely to make clinical judgments that avoid surgical intervention.³⁶ An inexperienced provider may feel uncomfortable allowing misoprostol to take its course or may misjudge the status of completion and decide to intervene surgically. Accordingly, as providers become comfortable with misoprostol for treatment of incomplete abortion, success rates will generally rise.²⁵

C. Schedule of clinic visits

A woman who chooses misoprostol for treatment of her incomplete abortion usually has one initial visit and could be encouraged to make a follow-up visit. During the initial visit the diagnosis of incomplete abortion is made, the woman is counseled, she is provided information about what to expect with treatment, and misoprostol is administered. Depending on the healthcare system and provider and patient preference, the woman can take misoprostol either at the clinic or at home. There is no medical reason to observe women in the clinic following misoprostol administration.

Myth: Women should be observed at the clinic following administration of misoprostol or until the abortion is complete

There is no medical reason to observe women in the hospital or the clinic following administration of misoprostol. Women can be sent home with the misoprostol to administer later or immediately after taking it at the clinic. They should be informed of potential side effects, how to handle them, and when to seek additional care. Several recent experiences in low resource areas have followed these guidelines and achieved high efficacy with low rates of complications.^{13, 15, 16, 18}

Providers should also be sure to allow sufficient time for misoprostol to work, as time to complete the process can vary from one day to several weeks.³⁷ To avoid unnecessary surgical intervention, the follow-up visit to assess health status should be scheduled no less than 7 days after misoprostol administration. This visit schedule is associated with consistently high success rates, but the method does fail for approximately 1 out of every 20 women. Unless medically necessary for hemostatic or infection control, surgical intervention prior to 7 days is not recommended. Women should be advised that medical help can be sought at any point during treatment if needed.

Myth: Misoprostol is not as safe as surgical methods; misoprostol has a higher rate of heavy bleeding compared to surgical methods

Women should be informed of what to expect following treatment with misoprostol, and when to seek care for heavy bleeding. Excessive bleeding requiring transfusion is no more likely to result from misoprostol for treatment of incomplete abortion than from surgical management. Some research shows that more women report heavy bleeding with medical management compared to surgical management,^{15,16,18} while other research finds similar bleeding patterns following treatment with either misoprostol or surgical methods,^{32,38}

D. MANAGING SIDE EFFECTS AND COMPLICATIONS

Side effects associated with misoprostol treatment of incomplete abortion are well-studied and generally easy to manage. Each woman should be informed about potential side effects and how to handle them. Women should also be instructed to seek additional care (either at the clinic or at an emergency facility) in the event of very heavy and/or prolonged bleeding or persistent fever. Table 4 lists common side effects and management strategies.

Table 4: Common side effects of misoprostol and their management when used for treatment of incomplete abortion

	Description	Management
Pain/ cramping	Cramping typically starts within the first few hours and can begin as early as 30 minutes following misoprostol administration. Pain may be stronger than that typically experienced during a menstrual period.	 > Sitting or lying comfortably > Hot water bottle or heating pad > Paracetamol/acetaminophen > Non-steroidal anti-inflammatory drugs (NSAIDs) such as ibuprofen
Chills/ fever	Chills are a transient but common side effect of misoprostol. Fever is less common and does not necessarily indicate infection. Temperature elevation generally does not last more than a few hours. Though infection is rare, fever or chills that persist for longer than 24 hours may indicate infection.	 Reassurance that chills and fever are common side effects of misoprostol Antipyretics if needed Women should be instructed to contact a medical provider if fever or chills persist for more than 24 hours or develop more than one day after taking misoprostol
Bleeding	Generally, vaginal bleeding will commence within an hour of misoprostol administration. Bleeding typically lasts an average of 5 to 8 days (but may continue up to 2 weeks). Spotting can persist until the next menstrual period.	 > Give women information on expected bleeding > Women should be instructed to notify a health care provider if they experience the following: Soaking more than 2 extra large sanitary pads (or local equivalent) per hour for more than 2 consecutive hours Sudden heavy bleeding after bleeding has slowed or stopped for several weeks with dizziness or light-headedness
Heavy bleeding	Heavy and/or prolonged bleeding that causes a significant change in hemoglobin is uncommon. A few women will present with heavy bleeding according to the guidelines above.	 > Surgical completion if bleeding is profuse or prolonged > Administration of intravenous fluids if there is evidence of hemodynamic compromise > Transfusion should be provided only when clearly medically indicated
Nausea/ vomiting	Nausea and vomiting may occur and typically resolve within 2 to 6 hours. ¹²	 Reassure women that nausea and vomiting are possible side effects An antiemetic may be used if necessary
Diarrhea	Diarrhea is a common, transient side effect of misoprostol that should resolve within a day.	 Reassure women that diarrhea is sometimes associated with misoprostol use and passes quickly
Infection	Documented endometrial and/or pelvic infection is rare. Infection is typically treated with oral antibiotics.	 > If infection is suspected the woman should be evaluated > If there are signs of sepsis or severe infection women should be given immediate surgical evacuation and antibiotic coverage > Severe infections could require hospitalization and parenteral antibiotics

E. Follow-up

If routine follow-up is scheduled by the providers, it should be planned for no less than 7 days after misoprostol treatment. Very few follow-up visits prove to be medically necessary for the woman. Women should be educated about the symptoms of retained tissue and infection so they will know when a follow-up visit is medically necessary.

Women who return for follow-up should be asked to report side effects and bleeding patterns. Bimanual exam will help the provider assess whether the uterus is firm, involuted, and pre-pregnancy size. Experience in low-resource settings has shown that patient history and clinical exam are sufficient to assess whether the process is complete.^{13, 14, 15, 18} If a woman is thought to have retained products of conception but is not experiencing any signs of infection or severe bleeding, she should be offered the choice between an additional follow-up visit in approximately one week and an immediate surgical evacuation (either by D&C or suction aspiration). Women may also be offered an additional dose of misoprostol at the follow-up visit, as this may offer some benefit.

V. COUNSELING, INFORMATION PROVISION AND SERVICE DELIVERY

Information provision is an important component of postabortion care. Women should be informed about medical conditions, test results, treatment and pain management options, side effect management, follow-up care, and where and when to seek help in the case of complications.²¹ Counseling and information provision are particularly important when using misoprostol for treatment of incomplete abortion. By preparing women for what to expect, providers can reduce the likelihood that women will experience anxiety and request an unnecessary surgical intervention. Women who are comfortable and confident in the method may be more likely to have a positive, satisfactory experience.

A. CHOOSING A METHOD

If the provider offers more than one treatment method, the woman should be given a brief description of each and allowed to choose the treatment that she prefers, provided there are no clinical contraindications to the use of any specific method. It is important to provide complete, accurate, and unbiased information to enable women to choose the most appropriate method for themselves. (For a comparison of expectant, surgical, and medical methods refer to Chapter II.) Providers should take the time to explain to women that if misoprostol or expectant management fails, they may need to have surgical intervention. Table 5 compares some advantages and disadvantages of surgical and medical treatment for incomplete abortion as cited by women. Table 5: Advantages and disadvantages of misoprostol treatment compared to surgical treatment of incomplete abortion as cited by women

	Misoprostol Treatment	Surgical Treatment (D&C, MVA, EVA)
Advantages	 > can avoid surgery and anesthesia > more natural, like menses > women can be more in control, involved > simple to administer > in-patient care not needed 	 > quicker > provider controlled > woman can be less involved
Disadvantages	 > bleeding, cramping and side effects (real or feared) > waiting, uncertainty 	 > invasive > small risk of uterine or cervical injury > small risk of infection > loss of privacy, autonomy

B. ESTABLISHING ELIGIBILITY

It is important that providers screen each woman to ensure that she meets criteria for eligibility (see Chapter III). Below is a brief check-list on how to determine if a woman is eligible to use misoprostol.

- Ask questions: Providers should ask questions to determine whether the woman's symptoms might indicate an ectopic pregnancy. Women with suspected ectopic pregnancies should be referred for appropriate diagnosis and treatment. Providers also need to ask the woman if she has an allergy to misoprostol or another prostaglandin.
- Clinical examination, including bimanual exam: Providers should confirm that the woman has an open cervical os and uterine size of less than 12 weeks' LMP.

- Rule out signs of severe infection: Evaluate the woman for significant uterine tenderness, fever >38°C, and foul smelling discharge. If the woman has two or more of these symptoms, she should be given an immediate surgical evacuation and not misoprostol.
- Rule out hemodynamic instability: Assess the woman's blood pressure/ pulse. Women with very low systolic blood pressure and very high pulse rates may need surgical evacuation. Reassess such women to determine if their vital signs are indicative of hemodynamic instability or fear/anxiety.
- Assess whether any additional precautions should be taken: Determine if the woman has an IUD in place and if so, remove the IUD prior to misoprostol treatment. Ask whether the woman is currently breastfeeding. While there are no known consequences of exposure to breast milk among nursing infants, if the woman is concerned, she can be advised to discard breast milk for the first few hours after misoprostol administration.

Myth: Misoprostol is not an appropriate treatment if the provider suspects that the woman may have interfered with her pregnancy

Providers are commonly concerned about treatment with misoprostol in women who they believe have interfered with their pregnancy. If a woman presents with signs of severe infection, she should be given immediate surgical treatment. Otherwise, misoprostol can be offered for treatment even if the drug was used to induce the abortion. Repeated misoprostol doses for treatment of incomplete abortion have been reported with no adverse effects.^{17, 25} Numerous studies have shown that treatment with misoprostol works well for women who may have induced their abortions with misoprostol.^{14,16}

C. PREPARING WOMEN FOR WHAT TO EXPECT

A discussion of misoprostol treatment with women seeking services for incomplete abortion should include the following:

- Answering women's questions: Women should be given the opportunity to ask questions and should receive satisfactory answers prior to selecting a treatment method.
- Misoprostol information: Explain how misoprostol is administered and how it works. Inform women that misoprostol will cause the uterus to contract and expel the remaining products of conception.
- Success rate: Explain that approximately 1 of every 20 women treated with misoprostol requires a surgical procedure to complete the process.
- Understanding the method: Explain that the contents of the uterus are likely to pass in the week after the misoprostol administration.
- Side effects: Explain that women who take misoprostol will likely experience pain, cramping, and bleeding. They may also experience chills, fever, nausea or diarrhea. Inform women that these side effects generally dissipate after a few hours although bleeding similar to a period may continue for days.
- Follow-up care: Women can be encouraged to return to the clinic in one to two weeks to assess whether the method was successful.
- Possible complications: Women should be given a complete description of possible complications. Signs and symptoms of serious complications should be carefully explained. It may be useful, where possible, to give women a telephone number to call with questions or concerns. All women should be advised to seek emergency care if they experience serious complications (see Chapter IV for complications that require medical attention).
- Cost: In treatment facilities where postabortion care is paid for by the woman, the cost of treatment options should be discussed.

D. FAMILY PLANNING AND CONTRACEPTIVE SERVICES

All women should be informed that fertility returns quickly following a first trimester pregnancy loss. By discussing family planning options with women during treatment for incomplete abortion, providers can help prevent future unwanted pregnancies. Providers should bear in mind that incomplete abortion can result from either spontaneous or induced pregnancy loss, and, while some of the women may be seeking contraception, others may want information on becoming pregnant again.

The following topics should be discussed with women:

- Reassure the woman that generally there is no reason to believe that she would have difficulty carrying another pregnancy to term in the future.
- Women who wish to become pregnant again are frequently advised to wait until they experience at least one normal menstrual period before attempting to conceive.
- Women not wishing to become pregnant in the near term should be offered contraception that they can begin immediately. These women should receive appropriate contraceptive information. An appropriate contraceptive method will depend on the needs and preferences of each woman, as well as local availability. Refer to Table 6 for contraceptive options and when they can be offered following misoprostol for treatment of incomplete abortion. Some contraceptives can be offered at the first visit while others can be integrated into a follow-up visit, if planned.

Table 6: Contraceptive methods and when they can be safely offered following misoprostol for treatment of incomplete abortion

Contraceptive method	When method can be offered
Condoms	At first visit
Oral contraceptives	At first visit
Contraceptive jellies, foams, tablets or films	At first visit
Cervical cap	Fitting should be delayed until bleeding has stopped and the uterus has returned to pre-pregnancy size (after the first menstrual period)
Diaphragm	At first visit
Injectables	At first visit
Implants	At first visit
Intrauterine devices (IUDs)	At a follow-up visit
Sterilization	Women seeking sterilization may want to opt for surgical treatment for incomplete abortion, since sterilization and completion of the abortion can be done at the same time

E. Reproductive and other health services

It is important to use the follow-up visit to determine whether the woman needs any additional reproductive or other health services. Linking such services with postabortion care allows providers to address other health issues while women are in contact with health care providers. If the facility cannot provide these additional services, appropriate referrals can be made. Other health services might include:²¹

- > Sexually Transmitted Infection (STI) education, testing and treatment
- Infertility diagnosis and treatment
- ➢ Hygiene education
- > Referral and counseling for cases of sexual and/or domestic violence
- Screening for anemia

F. PROVIDER AND STAFF TRAINING

Comprehensive training on how to use misoprostol for treatment of incomplete abortion will improve provider comfort and skill with the method. Experience with misoprostol treatment for postabortion care suggests that as provider familiarity with and confidence in the method increase, success rates and satisfaction will increase as well. A basic training course on misoprostol for treatment of incomplete abortion should include the following elements:

- Mechanism of action
- > Misoprostol availability, storage, efficacy, and acceptability
- > Eligibility, contraindications, and precautions
- Diagnosis of incomplete abortion
- Role of ultrasonography

- > Regimens for using misoprostol for treatment of incomplete abortion
- Counseling when using misoprostol as a treatment option for incomplete abortion
- > Management of side effects and potential complications
- Follow-up and assessment of health status
- > Provision of contraceptive and family planning services following abortion
- > Provision of reproductive and other health services following abortion

Case studies are generally quite helpful in training providers, particularly when discussing evaluation of health status and side effect management. Additionally, role play and group activities are often effective for training on counseling and eligibility.

G. COMMUNITY AND SERVICE PROVIDER PARTNERSHIPS

Collaboration between community members, lay health workers, service providers and traditional healers is critical in improving women's reproductive health.²¹ For example, misoprostol may be the most appropriate treatment option for rural women, because it can be provided by mid-level providers in the absence of skilled surgical providers or equipment; however, the method is not 100% effective, and providers who cannot perform surgical completion should be able to refer women to skilled providers in the event of method failure. Similarly, if the facility cannot provide emergency care, providers should be able to recognize any danger signs and refer women to appropriate facilities.

H. DESIRABLE (BUT NOT REQUIRED) FACILITIES AND SUPPLIES

- Ultrasound equipment: As discussed above, ultrasonography is not necessary for service provision. However, ultrasound may be useful for diagnosis of rare complications.
- Pain medications/antiemetics: These medications can be given to women in advance to be taken as needed to alleviate possible side effects.
- Anti-RhD immunoglobulin: Currently, there is incomplete evidence on use of anti-RhD immunoglobulin for very early first trimester abortion. If local standard of care indicates anti-RhD immunoglobulin for Rh negative women receiving treatment for incomplete abortion, then this treatment should be provided in conjunction with misoprostol.

VI. INTEGRATING MISOPROSTOL INTO EXISTING POSTABORTION CARE SERVICES

Misoprostol for incomplete abortion can be integrated easily into existing PAC services. Providers who practice surgical evacuation (D&C, MVA, EVA) for PAC can add misoprostol to their treatment choices, preferably allowing women to decide between surgical and medical methods. The basic requirements for misoprostol for treatment of PAC are trained staff and misoprostol pills. Staff should be able to diagnose incomplete abortion, determine eligibility for misoprostol treatment, confirm completed abortion, and refer to and/or provide women with emergency care if necessary. Accordingly, PAC providers already have many of the skills needed to offer misoprostol for treatment of incomplete abortion. Providers not currently offering PAC services but who are currently offering family planning services, pre-natal care, or other reproductive health services can integrate misoprostol for treatment of incomplete abortion provide they have access to a referral facility in the rare case of method failure or complication.

Integrating misoprostol into existing PAC services: Experience in two Egyptian hospitals

In 2008, a clinical study at El Galaa Teaching Hospital in Cairo and Shatby Maternity Hospital in Alexandria compared misoprostol to MVA for treatment of incomplete abortion.³² Almost 700 women were treated for incomplete abortion with high success rates (misoprostol 98.3%, MVA 99.7%). Bleeding and side effects reported by women were comparable and women were highly satisfied with their misoprostol treatment.

Integrating misoprostol into existing PAC services through the pilot study provided an important experience for providers by helping them gain confidence in the efficacy and safety of a 400 mcg sublingual regimen. Providers were initially reluctant to allow women to leave the hospital immediately after misoprostol administration, but with experience saw no reason for extending women's stay. They also became convinced of the importance of clinical history and examination in PAC treatment, and viewed ultrasonography not as a routine primary diagnostic tool but as a way to confirm clinical assessment. These changes in providers' attitudes and practices have resulted in the acceptance of misoprostol as a good treatment option for incomplete abortion and successful expansion of PAC services.

VII. MISSED ABORTION

While information presented in this guidebook pertains to use of misoprostol for treatment of incomplete abortion, misoprostol can also be used to treat missed abortion/anembryonic gestation. Missed abortion/anembryonic gestation is diagnosed by ultrasonography and is defined as a pregnancy in which there is no embryo (empty sac) or unrecognized fetal death. Women experiencing a missed abortion generally have little or no bleeding and no other overt signs or symptoms.³⁹

The recommended regimens for missed abortion/anembryonic gestation are 800 mcg of misoprostol administered vaginally or 600 mcg of misoprostol offered sublingually.³⁹ Table 7 lists several studies that have examined a range of regimens with success rates from 50-93%.

lable 7: Misoprostol for early pregnancy failure: missed abortion/anembryonic gestation							
Year	Author	N	Dose Misoprostol (mcg)	Additional Dose Misoprostol	Time to Success	Success	
2007	Shankar M, et al.4º	75	800 vaginal	400 oral 3 hrs apart up to 2 doses starting the next day	Day 7-10	77.3%	
2007	Sharma D, et al.41	50	600 sublingual	600 every 3 hrs up to 1800	72 hrs	86%	
2006	Tang OS, et al.42	180	600 sublingual	600 every 3 hrs to up to 1800; 90 pts received 400 sublingual daily for 7 additional days	Day 9	92% non-extension group; 93% extension group	
2006	Vejborg TS, et al.43	254	400 vaginal or 800 vaginal	None	Day 2-4	Missed: 43% 400 mcg; 59% 800 mcg Anembryonic: 36% 400 mcg; 47% 800 mcg	
2005	Agostini A, et al.44	276	800 vaginal	None	24 hrs	65.2%	
2005	Blohm F, et al.45	64	400 vaginal	None	Day 6-7	81%	
2005	Kovavisarach E, et al.46	114	600 or 800 vaginal	None	24 hrs	46% 600 mcg; 68% 800 mcg	
2005	Lister MS, et al.47	18	800 vaginal	800 vaginal at 24 hrs if necessary	48 hrs	83%	
2005	Sifakis S, et al.48	108	400 vaginal	400 vaginal every 4 hrs up to 1200 per day for 3 days	Day 3	91%	
2005	Zhang J, et al.49	454	800 vaginal	800 vaginal on day 3, if necessary	Day 8	88% missed abortion; 81% anembryonic gestation	

Table 7: continued								
2004	Bagratee JS, et al.50	45	600 vaginal	600 vaginal on day 2, if necessary	Day 7	87%		
2004	Davis AR, et al. ⁵¹	77	800 dry vaginal or 800 moistened vaginal	None	Day 30	85%		
2004	Gilles JM, et al. ⁵²	80	800 vaginal dry or moistened	Dose repeated at 48 hrs if necessary	Day 7	85%		
2004	Graziosi GC, et al.53	79	800 vaginal	800 vaginal at 24 hrs if necessary	48 hrs	53%		
2004	Murchison A, et al.54	44	800 vaginal	800 vaginal at 24 hours if necessary	48 hrs	78%		
2004	Ngoc NTN, et al. ³⁵	198	800 oral or 800 vaginal	None	Day 2 & Day 7	Day 2: 42% oral; 53% vaginal Day 7; 89% oral; 93% vaginal		
2004	Taner CE, et al. ⁵⁶	54	200 oral and 800 vaginal	None	24 hrs	89%		
2003	Al Inizi SA, et al. ⁵⁷	27	400 vaginal	400 vaginal every 12 hrs up to 4 doses	48 hrs	70%		
2003	Tang OS, et al.58	80	600 vaginal or 600 sublingual	Dose repeated every 3 hrs to a maximum of 1800	Day 7	87.5% (weighted avg)		
2002	Kovavisarach E, et al. ⁵⁹	27	400 vaginal	None	24 hrs	63%		
2002	Muffley PE, et al. ⁶⁰	25	800 vaginal	800 vaginal at 24 and 48 hrs if necessary	Day 3	60%		
2002	Wood SL, et al. ⁶¹	25	800 vaginal	800 vaginal at 24 hrs, if necessary	48 hrs	80%		
2001	Demetroulis C, et al. ⁶²	26	800 vaginal	None	8-10 hrs	77%		
2001	Ngai SW, et al.63	25	400 vaginal	400 vaginal day 3 and day 5	Day 15	80%		
2000	Ayres de Campos D, et al. ⁶⁴	74	600 vaginal (saline moistened)	600 vaginal at 4-5 hrs, if necessary	10-12 hrs	57%		
1999	Autry A, et al. ⁶⁵	9	800 vaginal	None	Days 10-14	89%		
1999	Chung TKH, et al. ⁶⁶	321	400 oral	400 oral every 4 hrs, up to 3 doses	24 hrs	50%		
1998	Zalanyi S, et al. ⁶⁷	25	200 vaginal	200 every 4 hrs up to 800	10 hrs	88%		
1997	Creinin M, et al. ⁶⁸	20	400 oral or 800 vaginal	Dose repeated at 24 hrs if necessary	Day 3	25% oral; 88% vaginal		
1997	Herabutya Y, et al. ⁶⁹	43	200 vaginal	None	24 hrs	83%		

VIII. LOOKING FORWARD

Given its safety, efficacy, and ease of use, misoprostol is an important option for the treatment of women with incomplete abortion. This guidebook shows how misoprostol can be provided in low-resource settings where demand for services may be high and availability of skilled providers and equipment are often scarce. Misoprostol can increase access to treatment for those who need it most—women who suffer complications from clandestine induced abortions.

Professional associations such as the American College of Obstetricians and Gynecologists recommend misoprostol for postabortion care and the World Health Organization has added misoprostol for the management of incomplete abortion and miscarriage to its Model List of Essential Medicines.^{1,7} These recommendations are based on a review of the large body of research on medical management of incomplete abortion which shows that misoprostol matches the safety and efficacy of surgical treatments. Additionally, non-surgically-trained, mid-level providers can use the method, thereby reducing the burden of care in higher level facilities that possess the equipment and skills needed for surgical treatment. Misoprostol introduction at secondary- and primary-level health facilities can increase treatment options for women while cutting costs to the healthcare system.

The stage is now set for misoprostol introduction into services. Misoprostol can be easily integrated into existing postabortion care services or established as a treatment option where other options do not exist. Suggestions provided in this guidebook can help facilitate the use of misoprostol in a simple, low-tech manner.

To optimize the use of misoprostol for treatment of incomplete abortion, adequate training for providers is needed along with a sustainable supply of drug. Next steps in programmatic research could include the development of suitable service delivery models and cost-benefit analyses that compare misoprostol to surgical methods. It will be helpful to learn more about the use of misoprostol in rural settings, among populations with high rates of untreated infection, along with documentation of any heavy bleeding and other complications. These efforts can help build momentum among policymakers to approve, promote, and scale-up the use of misoprostol systematically for treatment of incomplete abortion.

Ultimately, safe and effective induced abortion services are needed to prevent complications of abortion, not just to treat them. Services to treat incomplete abortion therefore do not obviate the need for access to family planning and safe abortion services for all women. For those who do require treatment of incomplete abortion, misoprostol should complement access to safe surgical treatment, since surgical treatment will sometimes be necessary depending upon the woman's condition, her preferences, and for back-up in case of failure of any initial treatment. Comprehensive programs to treat incomplete abortion with roles for both misoprostol and surgical services will enhance the quality of services offered to women, providing a range of treatment options and appropriate care.

Misoprostol can revolutionize how, where and by whom services can be provided to treat incomplete abortion. Misoprostol has the potential to reduce complications arising from spontaneous and induced abortion in low-resource settings where access and availability to safe and effective treatment options are still lacking. Misoprostol is an important technology for women's health, and the time to move forward is now.

IX. Appendix

FREQUENTLY ASKED QUESTIONS

Questions may arise during trainings or service delivery regarding misoprostol's use for this new indication. Below is a list of frequently asked questions and possible answers that may be helpful.

• Is misoprostol safe for treatment of incomplete abortion?

Yes, misoprostol has been used safely to treat incomplete abortion in thousands of women worldwide. There have been fewer than a dozen hospitalizations mostly for minor treatments, among over two thousand women treated in recent clinical studies.

• What are the advantages of misoprostol if a safe surgical alternative is available?

Misoprostol is a safe alternative to surgical evacuation. It may be preferable to some women who fear surgery, treatment under anesthesia, and prefer outpatient care. In addition, it may be less expensive for healthcare systems.

- Are women satisfied with misoprostol for treatment of incomplete abortion? Yes, satisfaction levels are high among women receiving treatment with misoprostol. Most women report that they would choose misoprostol if treatment were needed again in the future. Offering women a choice of treatment methods is optimal in settings where feasible.
- What skills are needed to offer misoprostol for treatment of incomplete abortion? Providers must be able to identify women in need of treatment for incomplete abortion and must be able to diagnose severe infection which requires immediate surgical care. A woman with a uterus 12 weeks' LMP or smaller is eligible for treatment. Uterine size can be estimated by providers by conducting a physical exam. Surgical skills are not needed to offer misoprostol.

• What type of referral system is needed?

Women with incomplete abortion who wish to be treated with misoprostol and who meet criteria for treatment can be treated without referral. More than nine out of ten women who were previously referred to a higher level of care will not require referral once misoprostol is available. Any referral system already in place for postabortion care can be used for women not eligible for misoprostol and for complicated cases.

• Is ultrasound necessary prior to and after the use of misoprostol for incomplete abortion?

No, ultrasound is not required when offering misoprostol for treatment of incomplete abortion. An incomplete abortion can be diagnosed by clinical history and examination; a complete evacuation following misoprostol treatment can be assessed using the same set of clinical techniques. The biggest drawback in use of ultrasound is over-interpretation of normal amounts of debris in the uterus, leading to unnecessary surgical completion.

• Is misoprostol safe for women who have never given birth and experience a miscarriage?

Yes, misoprostol is a safe method for women experiencing a miscarriage who have never given birth.

• Is misoprostol safe to use for women with a previous cesarean section? Yes, there is no clinical reason to withhold misoprostol for treatment of incomplete abortion in women with a previous cesarean section. A number of trials studying the drug's utility for treatment of incomplete abortion have not excluded these women. (Uterus of < 12 weeks' LMP size will ensure that misoprostol remains safe for women with uterine scars.)

• Can a woman with incomplete abortion be treated with misoprostol even if she may have already taken misoprostol (to induce abortion)? Yes. Some providers have expressed concerns about giving women misoprostol again if they have already taken it before presenting at the health facility. Misoprostol can be offered for treatment even if the drug was used to induce the abortion. Repeated misoprostol doses for treatment of incomplete abortion have been reported with no adverse effects. Numerous studies have shown that treatment with misoprostol works well for women who may have induced their abortions with misoprostol. • If the woman is beyond 12 weeks' LMP, can misoprostol be used?

The guidance in this booklet for misoprostol use in incomplete abortion applies when the uterine size is not larger than expected in a 12-week pregnancy. The length of amenorrhea may be longer than 12 weeks, however, since some of the contents of the uterus may have already been expelled. Typically, *lower* doses are needed for efficacy and safety when the uterus is larger.

- If a woman presents with signs of infection, should she be given misoprostol? Women presenting with two or more signs of infection (significant uterine tenderness, fever >38°C, foul smelling discharge) should be given an immediate surgical evacuation and antibiotic coverage.
- What are the side effects of misoprostol treatment? Expected side effects include pain, cramps, nausea, vomiting, fever, and chills. These side effects are easily managed, transient, and generally mild. A majority of women report the side effects to be tolerable.
- Do women who receive misoprostol for treatment of incomplete abortion become anemic?

No, this treatment is not associated with increased risk of anemia. In fact, data from a recently completed study on this point shows no clinically significant difference in change in hemoglobin between women treated with misoprostol or with MVA. Very few women had clinically significant drops in hemoglobin.

- **Does treatment with misoprostol increase the risk of infection?** No, there is no evidence that misoprostol treatment increases the risk of infection.
- Should women be given antibiotics routinely along with misoprostol? No, routine antibiotic coverage is not necessary. Local norms regarding antibiotic use should be followed. The provider may determine that the woman requires antibiotic coverage based on history or clinical exam.

• Is a follow-up visit required?

In many settings, follow-up visits are the standard of care following both surgical and medical treatment. Given the very high efficacy rates reported with both surgical and medical treatments, few follow-up visits prove medically necessary, however. It is important to educate the woman about the signs of retained tissue and infection so that she will know when a follow-up visit is needed to protect her health (see page 19).

- At the follow-up visit, if ultrasound examination reveals no debris but thickening of the endometrium, is surgical evacuation necessary? No. Studies have shown that the thickness of the endometrium is not a good predictor of the need for surgery. It is recommended that the decision to perform surgical evacuation be based on clinical signs rather than ultrasound findings.
- If the abortion is not complete at the follow-up visit is it safe to give the woman another dose of misoprostol and ask her to return one week later? Yes, if the abortion is not complete at the follow-up visit and the woman is clinically stable and willing to continue to wait for her uterus to empty, she can be offered another dose of misoprostol.

Can contraception be used after misoprostol care? Yes, contraception can be offered to women after misoprostol treatment, as with standard postabortion care services. Almost all contraceptives can be offered at the first visit while an IUD can be integrated into a follow-up visit, if planned.

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