



Special communication

Misoprostol use in obstetrics and gynecology in Brazil, Jamaica, and the United States

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Abstract

Objectives: To investigate current clinical use of misoprostol for the treatment of a range of reproductive health indications by providers in Brazil, Jamaica, and the United States. **Methods:** Using a ‘snowball’ sampling technique, we surveyed 228 gynecologists and obstetricians in Brazil ($n = 123$), Jamaica ($n = 52$), and the United States ($n = 53$). **Results:** Providers use misoprostol for labor induction (46%), postpartum hemorrhage (8%), intra-uterine fetal death (61%), cervical priming (21%), missed abortion (57%), and incomplete abortion (16%) as well as first and second trimester abortion induction (27% and 13%, respectively). **Conclusions:** There is considerable variation in the regimens used; moreover, the regimens commonly used in clinical practice often differ from those recommended in the medical literature. While misoprostol is an appealing alternative for many reproductive health indications in developing countries, the varied regimens and lack of registration raise critical medical and policy questions. © 2002 International Federation of Gynecology and Obstetrics. All rights reserved.

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1. Introduction

In most developing countries access to the latest research results and new drug therapies is

limited, especially where drugs are expensive or require sophisticated delivery systems. As a result women in many developing countries do not have access to adequate gynecological and obstetric services. Little research and even fewer funds have been devoted to finding effective and inexpensive technologies that are appropriate to developing country settings. Consequently, providers often modify standard regimens to suit their own

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needs or develop their own treatments based on available drugs. One clear example of this is the widespread off-label use of misoprostol (Cytotec®) for a host of reproductive health indications. (Cytotec, Pharmacia, NJ, USA)

Misoprostol, an E₁ prostaglandin analog, is especially well-suited for use in developing countries, as it is inexpensive, simple to administer and easy to store. Moreover, it is widely available and registered in more than 80 countries to treat and prevent gastric ulcers. Many providers throughout the world have discovered that misoprostol is also a potent and valuable drug for managing and treating a wide range of obstetric and gynecological conditions including postpartum hemorrhage, intra-uterine fetal death, labor induction, first and second trimester abortion, and incomplete and missed abortion. Two properties make misoprostol useful for these procedures. First, misoprostol causes contractions of the smooth muscles lining the uterus that are instrumental in emptying the uterus of its contents. Second, it softens the cervix, allowing greater dilation for interuterine procedures as well as facilitating expulsions from the uterus. Mounting evidence demonstrates that misoprostol is beneficial in treating an array of reproductive health conditions which fall into three main categories: (1) abortion induction; (2) uterine evacuation; and (3) labor and delivery [1,2,3].

Despite its tremendous promise for many of these gynecological and obstetric indications, there are no standard or labeled regimens for any of these conditions. Instead, providers have relied on the medical literature and colleagues in the field, as well as their own experience, for information on effective regimens. Consequently, in many cases providers have developed their own regimens. This ‘trial and error’ method of drug development, especially in the absence of large randomized clinical trials, leaves many providers guessing at the best and safest regimens.

2. Methods

From February 1999 to May 2000, we conducted a telephone survey of 228 obstetricians

and gynecologists in Brazil ($n = 123$), Jamaica ($n = 53$) and the United States ($n = 52$) to document use of misoprostol for reproductive health indications and to capture some of the variation in regimens used in clinical practice. If a provider reported using misoprostol for a particular reproductive health indication, he or she was asked to describe the regimen used, including dose, number of doses, timing of doses, and route of administration. We also asked for information on commonly observed side effects. Providers were then asked to estimate the efficacy of misoprostol and patient acceptability. We caution that these are subjective measures, as they are reports of providers’ impressions, and not based on clinical research.

In all three countries, we used the ‘snowball’ method to identify potential respondents. We started with a core of knowledgeable providers with whom we had contacts and asked them to refer us to other providers who might be willing to participate. The snowball technique has several inherent drawbacks; most notably, it does not produce a random sample from which one could generalize outcomes or estimate overall prevalence rates. We chose this method, despite this limitation, for several reasons. First, misoprostol is not registered for any reproductive health uses and its use has sparked considerable controversy. By starting with principal investigators in the field who were well-known among their colleagues and then developing a network through these colleagues, we were able to establish credibility and trust and, therefore, greater cooperation. Second, we initially speculated that use of misoprostol for a non-labeled indication may be quite rare, and therefore a random sample would have to be very large (and costly) to obtain an adequate sample of misoprostol users. Finally, the primary objective of this study is not to document the overall prevalence of the use of misoprostol among providers, but rather to investigate how providers who know about misoprostol are using it in their services.

While the snowball methodology proved successful in Brazil and Jamaica, we had difficulty expanding our pool of providers in the US. American providers repeatedly referred us to the same tightly knit circle of researchers on misoprostol.

In an effort to expand our sample size, we changed our methodology for the US and, using the Medical Directory of New York State, we called and e-mailed a random sample of obstetrician and gynecologist providers in Manhattan.

Given the wide range of responses, summarizing the data in a succinct and accurate manner poses a daunting challenge. To describe some of the differences, we often note the highest and lowest doses. We also use a standard statistical software package (SPSS 10.0) to calculate the mean maximum dosage and number of doses. We strongly caution, however, that these numbers do not represent the best, safest or most effective regimens, but rather serve as a practical measure of the diverse uses of misoprostol for various indications.

3. Results

3.1. Uses of misoprostol

Table 1 shows the characteristics of the 228 providers interviewed in Jamaica, Brazil and the US. A sizable majority of providers in both Brazil

(72%) and Jamaica (75%) were male. Providers interviewed were associated with a range of professional institutions, including both public and private hospitals and clinics, as well as university hospitals. They offered a wide range of reproductive health services, including abortion, obstetrics, gynecology, and family planning.

Table 2 provides the percentage of providers who report using misoprostol for each of the 10 reproductive health indications. These indications are sorted into three categories: (1) abortion; (2) uterine evacuation; and (3) labor and delivery. The use of misoprostol for abortion induction is well known among the providers we interviewed in all three countries. Twenty-seven percent of the providers interviewed use misoprostol alone for first trimester abortion. Slightly fewer use misoprostol for second trimester abortion in combination with D&E (23%) or as a labor induction agent (13%). Approximately one-fifth of providers (21%) use misoprostol to prime the cervix prior to surgical abortion. It is interesting to note, however, that although none of the respondents in Brazil indicate that they routinely offered abortion services, nearly 30% report that they used

Table 1
Provider characteristics (%)

	Brazil (N = 123)	Jamaica (N = 52)	US (N = 53)	All (N = 228)
<i>Sex</i>				
Male	72	75	59	70
Female	28	25	41	30
<i>Institutional affiliation</i>				
Public hospital	36	19	0	24
Private hospital	14	19	22	17
University hospital	36	23	38	33
Private practice	5	17	18	11
Clinic	9	0	22	10
Resident	0	21	0	5
<i>Services offered</i>				
First trimester abortion	0	49	69	22
Second trimester abortion	0	27	48	14
Third trimester abortion	0	0	5	1
Gynecological exams	89	76	87	86
Family planning	29	76	87	49
Obstetrics	92	97	51	84

misoprostol for first trimester abortions and a total of 37% have used it for second trimester terminations.

Misoprostol appears to be most frequently used for evacuating the uterus following a pregnancy failure. A large percentage of providers (61%) report using misoprostol for treatment of intra-uterine fetal death, while 57% use misoprostol to treat missed abortion. Reports of use for incomplete abortions were rare in all three countries ranging from 14% to 18%. Using misoprostol during labor and delivery was common (46% overall), especially in Jamaica (89%). Misoprostol is less often used in clinical practice for cervical softening or for prevention or treatment of postpartum hemorrhage (14% and 8%, respectively).

3.2. Abortion induction

Our results demonstrate that providers are exploring a wide array of regimens for each of the four abortion indications (Table 3). We found a strong preference for vaginal administration of the drug; nearly 70% of providers who report using misoprostol for these four indications used it vaginally. Several providers, particularly in Brazil, however, use a combination of oral and vaginal administration for first and second trimester abortion induction. Regimens vary tremendously both in terms of dosage amount and number of doses used for each indication. Providers report using anywhere from 50 to 900 μg and an average of three to four doses of misoprostol for first trimester abortion induction. Regimens for cervical priming prior to first trimester surgical abortion decrease the dosage to approximately half the amount, with a per dose range of 20–400 μg , and an average of two doses.

In addition to examining the range of regimens, we also report the most common regimens found in clinical practice. Although these have not been adequately tested and thus cannot be recommended by the authors, it is interesting to compare them to those recommended in the medical literature (Table 6). A recent article in the *New England Journal of Medicine* reviewed randomized controlled trials on misoprostol for various reproductive health indications and made recommen-

Table 2
Providers reporting using misoprostol for each reproductive health indication (%)

	All (N = 228)
<i>Induced abortion</i>	
First trimester induction	27
Second trimester (D&E)	23
Second trimester (labor induction)	13
Cervical priming prior to surgical abortion	21
<i>Uterine evacuation</i>	
Intra-uterine fetal death	61
Missed abortion	57
Incomplete abortion	16
<i>Labor and delivery</i>	
Cervical softening	14
Labor induction	46
Prevention of postpartum hemorrhage	8

dations for clinical practice [1]. We find that the use of misoprostol alone for first trimester medical abortion is common in clinical practice, while the authors of the review article concluded that misoprostol alone was not recommended for first trimester medical abortion when safe alternatives exist. They based this conclusion on the fact that misoprostol's efficacy is substantially improved when it is used with other drugs such as mifepristone and methotrexate. However, the article did not address whether misoprostol would be recommended in settings where these drugs were not available. The article did recommend two regimens for labor induction for second trimester abortion, which roughly concurs with the regimens we find in clinical practice. Its recommendation for cervical priming, however, contrasts sharply with the regimens often used in practice, which generally use a much lower dose further in advance of the procedure.

Our survey also asked providers to assess side effects, efficacy, and acceptability. Overall, providers do not report a large number of side effects with the use of misoprostol for abortion induction. Indeed, more than one-third of providers do not report any side effects associated

Table 3
Regimens used for induced abortion

	Route (%)	Max dose (mean)	Per dose (range)	No. of doses (mean)	Perceived efficacy (mean)	Perceived acceptability (mean)
<i>Misoprostol alone for medical abortion</i>						
Vaginal (<i>n</i> = 41)	68	720	50–800	3.6	90	89
Oral (<i>n</i> = 1)	2	200	–	3.0	–	100
Combination (<i>n</i> = 17)	30	1212	200–900	4.0	91	82
<i>Second trimester (D&E)</i>						
Vaginal (<i>n</i> = 40)	77	564	50–800	4.4	93	89
Oral (<i>n</i> = 1)	2	600	200	3.0	100	80
Combination (<i>n</i> = 11)	21	1291	200–700	4.6	89	83
<i>Second trimester (labor induction)</i>						
Vaginal (<i>n</i> = 20)	80	528	50–800	2.9	91	87
Oral (<i>n</i> = 1)	–	–	–	–	–	–
Combination (<i>n</i> = 5)	20	1440	200–400	5.0	93	82
<i>Cervical priming (prior to surgical abortion)</i>						
Vaginal (<i>n</i> = 39)	95	188	20–400	2.4	92	87
Oral (<i>n</i> = 2)	5	125	50–200	2.0	90	94
Combination (<i>n</i> = 0)	–	–	–	–	–	–

with abortion indications. By far the most common side effect reported is gastrointestinal discomfort. Some providers (usually less than 10%) also mention bleeding, vomiting, nausea, cramps, and pain. In addition, providers typically rate efficacy above 90% and gauge the acceptability to their patients to be between 80% and 90%.

3.3. Uterine evacuation

Misoprostol has also shown promise for evacuating the uterus after an early first trimester pregnancy failure or intra-uterine fetal death (Table 4). More than 60% of providers who report using misoprostol for uterine evacuation administered misoprostol vaginally, while nearly a third report using a regimen combining both vaginal and oral administration of misoprostol. In our survey, regimens using solely oral administration are uncommon (less than 5%). A wide range of regimens are described for each indication, with reported doses ranging from 25 to 800 μg and average number of doses from three to five.

With this kind of variation, it is difficult to identify the most common uterine evacuation treatment regimens. Nonetheless, Table 6 shows some of the regimens used in practice and contrasts them with those recommended in the medical literature. According to the recent review article, providers using misoprostol for intra-uterine fetal death should administer vaginal misoprostol every 12 h and decrease the dose from 200 μg in the second or early third trimester, to 100 μg in the third trimester, to only 50 μg at term. Although our study did not differentiate by trimesters, the most common regimens reported are similar. For early pregnancy failure, the review article recommends one or two doses of 800 μg administered vaginally every 24 h. In practice, we find that providers tend to use approximately half this dose. Finally, the article notes that there is too little evidence with inconsistent results to support the use of misoprostol for treatment of incomplete abortions. Yet a small percentage of providers in our study use misoprostol for incom-

Table 4
Regimens used for uterine evacuation

	Route (%)	Max dose (mean)	Per dose (mean)	Per dose (range)	No. of doses (mean)	Perceived efficacy (mean)	Perceived acceptability (mean)
<i>Intra-uterine fetal death</i>							
Vaginal (<i>n</i> = 95)	73	411	185	25–800	3.0	93	86
Oral (<i>n</i> = 2)	2	600 ^a	200	–	2.5 ^a	100	80
Combination (<i>n</i> = 33)	26	1014 ^b	209	50–400	3.4 ^b	98	83
<i>Missed abortion</i>							
Vaginal (<i>n</i> = 82)	66	591	292	25–800	3.0	93	86
Oral (<i>n</i> = 5)	4	1064	320	200–600	5.4	98	82
Combination (<i>n</i> = 38)	30	1224	248	100–600	3.8	97	82
<i>Incomplete abortion</i>							
Vaginal (<i>n</i> = 23)	64	516	273	50–800	3.1	91	84
Oral (<i>n</i> = 1)	3	200	200	–	1.0	100	80
Combination (<i>n</i> = 12)	33	842	321	100–800	2.3	96	85

^aExcludes one outlier with a maximum dose of 7200 µg and range of 16–36 doses.

^bExcludes one outlier with a maximum dose of 4000 µg and total number of doses equal to 20.

plete abortion; a sizable majority of these providers report using approximately two doses of 200 µg every 4, 6, or 12 h.

Nearly 60% of providers report that there are no side effects associated with treatment of missed abortion or intrauterine fetal death, while half of the providers do not report any side effects associated with treatment of incomplete abortion. Other side effects such as gastrointestinal discomfort, nausea, cramps, vomiting and bleeding were mentioned by less than 12% of providers. However, one provider reported two cases of uterine rupture in women with intrauterine fetal death at 6 months gestation. These women were given 1200 µg, which is far above the recommended dosage of 100–200 µg, but consistent with other providers in our survey; 18% reported giving 1000 µg or more to women presenting with intrauterine fetal death. Providers indicate that misoprostol is more than 90% effective and 80% acceptable to women when used to treat pregnancy failure.

3.4. Labor and delivery

A majority of providers reporting use of misoprostol for labor induction and cervical

softening use vaginal misoprostol (labor induction 80%, cervical softening 85%) (Table 5). While providers typically indicate that they use between 25 and 50 µg, one provider claims to use only 20 µg (which would be difficult to extract from 100 µg or 200 µg tablets) and others report using doses as high as 600 µg. These doses were administered between one and three times. In general, vaginal administration consists of lower doses, which are administered more frequently compared with oral administration. While there are only 15 providers who report use of misoprostol for prevention of postpartum hemorrhage, providers who use it for this indication are divided between those who favor vaginal (53%) and rectal (33%) administration.

Table 6 includes a comparison with the medical literature for labor induction and cervical softening. Although it is difficult to distinguish between the two, we find that in either case the amount of misoprostol typically administered is at least double the amount recommended in the review article, which is only 25 µg administered vaginally every 4–6 h. The review article also does not recommend misoprostol for prevention of postpartum hemorrhage if other drugs are available. Other studies and clinical trials, however, typi-

Table 5
Regimens used for labor and delivery

	Route (%)	Max dose (mean)	Per dose (mean)	Per dose (range)	No. of doses (mean)	Perceived efficacy (mean)	Perceived acceptability (mean)
<i>Labor induction</i>							
Vaginal (<i>n</i> = 81)	80	142	82	20–200	2.3	93	86
Oral (<i>n</i> = 2)	2	225	225	50–400	1.5	100	84
Combination (<i>n</i> = 4)	4	75 ^a	91	25–200	4.5	90	89
<i>Cervical softening</i>							
Vaginal (<i>n</i> = 23)	85	227	164	25–400	1.2	93	86
Oral (<i>n</i> = 2)	7	400	400	200–600	2.0	90	82
Combination (<i>n</i> = 0)	0	–	–	–	–	–	–
Buccal (<i>n</i> = 2)	7	400	300	200–400	1.5	93	90
<i>Prevention of postpartum hemorrhage</i>							
Vaginal (<i>n</i> = 8)	53	300 ^b	266	100–600	2.5	100	85
Oral (<i>n</i> = 1)	7	200	200	–	1.0	100	80
Combination (<i>n</i> = 1)	7	1000	300	–	3.0	100	100
Rectal (<i>n</i> = 5)	33	440	425	200–1000	1.3	80	91

^aExcludes one outlier, reporting a maximum dose of 2400 µg.

^bExcludes one outlier, reporting a maximum dose of 2400 µg.

cally administer between 400 and 600 µg orally or rectally for this indication [4–7].

Side effects mentioned by providers included cramps, gastro-intestinal discomfort, and fever or chills. For labor induction, however, providers mention a different set of side effects than reported for other indications. Although these side effects are rare, they are also potentially more serious. They include hyperstimulation of the uterus (18%), pain (6%) and precipitous labor (6%). Providers are generally pleased with this drug and plan to continue to use it for labor and delivery. They consistently judge the drug's efficacy as over 90% and perceive patient acceptability as above 80% for labor induction and cervical priming. For prevention of postpartum hemorrhage, providers report that the drug is acceptable to more than 80% of women and, somewhat surprisingly, they felt that vaginal administration is more effective (100%) than rectal (80%).

4. Discussion and conclusions

While this study demonstrated that providers in

Jamaica, Brazil, and the United States are using misoprostol to treat a range of reproductive health indications, our method of data collection prevents us from estimating the prevalence of misoprostol use among providers in these countries. Nonetheless, we were easily able to find providers in each country who report using misoprostol for each of the reproductive health indications included in this survey. Interestingly, we found providers in the US to be more reluctant to return our calls and more tepid in their support of the drug.

In sharp contrast, providers in Brazil and Jamaica eagerly participated in our study and most appeared well informed about their colleagues' use of misoprostol. In Jamaica, some respondents expressed frustration that the drug was not specifically labeled and marketed for reproductive health indications, while in Brazil providers clamored for greater access and repeatedly pressed the interviewer for information about obtaining new supplies. Respondents in all three countries mentioned the need for more research and greater information dissemination. Many providers learn of the drug's multiple uses from trusted col-

Table 6
Clinical practice and the medical literature on the use of misoprostol for induced abortion, uterine evacuation, and labor and delivery

	Clinical practice	Medical literature review
<i>Induced abortion</i>		
Misoprostol alone for medical Abortion	<ul style="list-style-type: none"> ● 400 µg vag; 2 doses; Q 6, 12 or 24 h ● 200 µg vag; 1–4 doses; Q 6 or 12 h 	● Not recommended where safe alternatives exist
Second trimester abortion (D&E)	<ul style="list-style-type: none"> ● 400 µg vag; 1 dose ● 200 µg vag; 2–4 doses; Q 4, 6, 12, or 24 h 	
Second trimester abortion (labor induction)	<ul style="list-style-type: none"> ● 200 µg vag; 2 doses; Q 6 or 12 h 	<ul style="list-style-type: none"> ● 200–600 µg vag; Q12 h ● 400 µg vag; Q 3 h
Cervical priming (prior to surgical abortion)	<ul style="list-style-type: none"> ● 50 to 100 µg vag, 1–3 doses; Q 12 h before surgery 	<ul style="list-style-type: none"> ● 400 µg vag; Q 3–4 h before surgery
<i>Uterine evacuation</i>		
Intra-uterine fetal death	<ul style="list-style-type: none"> ● 100 µg vag; 2 doses; Q 12 or 24 h ● 200 µg vag; 1–4 doses; Q 4, 6, 12 or 24 h 	<ul style="list-style-type: none"> ● 200 µg vag (2nd tri); Q12 h ● 100 µg vag (3rd tri); Q 12 h ● 50 µg vag (at term); Q12 h
Missed abortion	<ul style="list-style-type: none"> ● 400 µg vag; 1 dose ● 200 µg vag; 1–4 doses; Q 4, 6, 12, or 24 h 	<ul style="list-style-type: none"> ● 800 µg vag; 1–2 doses
Incomplete abortion	<ul style="list-style-type: none"> ● 200 µg vag; 2 doses; Q 4, 6, or 12 h 	● Not recommended
<i>Labor and delivery</i>		
Labor induction	<ul style="list-style-type: none"> ● 50–100 µg vag; 2 doses; Q 12 or 24 h 	● 25 µg vag; Q 4–6 h
Cervical softening	<ul style="list-style-type: none"> ● 50 µg vag; 1 dose ● 200 µg vag; 1 dose 	
Prevention of postpartum hemorrhage	<ul style="list-style-type: none"> ● 200 µg vag; 1 dose ● 400 µg rectal; 1 dose ● 200 µg vag; 2 doses 	● Not recommended if other drugs are available

leagues, and once they started using the drug for one indication, they quickly recognized its potential for other reproductive health indications. Our findings clearly indicate that providers, particularly in developing countries, consider misoprostol a safe and effective drug that helps to fill a critical void in their services.

Nonetheless, this ‘trial and error’ method of individual exploration entails several significant drawbacks. First, some providers may not be aware of potential adverse effects and may give their patients excessively large doses. Although we did not find much evidence of this, we did find many individual providers who consistently gave higher doses than are currently supported by the published literature or recommend by professional associations such as the *American College of Obstetrics and Gynecology* (ACOG). This is partic-

ularly problematic for labor induction. Unfortunately tablets in appropriate low doses for labor induction (approx. 25 µg) do not exist (misoprostol is sold only in 100 µg and 200 µg tablets).

Second, since misoprostol is not labeled for any reproductive health indications, it is often not available in obstetric or gynecology wards. Although some providers in each country indicated that their hospitals had specific guidelines for at least one indication, many reported that they had no such protocols and that access to misoprostol was severely limited. Even when protocols existed, many hospitals, particularly in Brazil, found it difficult ensure a reliable supply of this medication. Some providers stated that they often used less than the optimal amount of misoprostol to conserve their supplies. Third, we were surprised by the high levels of misoprostol use for labor

induction found in Jamaica. Like other labor inducing drugs, such as oxytocin, misoprostol may be used (even overused) for provider or patient convenience.

Finally, a well-specified safety profile and clear instructions on usage are particularly important in circumstances where women use misoprostol covertly. Over a decade ago, women in Brazil (where abortion is largely illegal) discovered the abortifacient properties of misoprostol and began to self-administer this drug to induce abortion [8,9]. In the absence of clear guidelines, women may either take too much of the drug (potentially causing severe side effects such as vomiting, nausea, diarrhea, chills, and fever) or too little (resulting in either incomplete abortion or an on-going pregnancy). If women with incomplete abortions are able to seek safe treatment at local clinics, misoprostol (by initiating the abortion process) may serve as a 'ticket' to safe post-abortion care services. However, if women with incomplete abortion are unable to find prompt medical attention, they are potentially at risk of serious complications such as prolonged or profuse bleeding. On-going pregnancies after exposure to misoprostol in the first trimester are also a concern since individual case reports link misoprostol to congenital abnormalities (although these studies are inconclusive about causality). On balance, though, misoprostol appears much safer than other illegal or self-initiated means of inducing abortion. Increased access to the drug and information on how to use it could significantly reduce morbidity and mortality associated with unsafe abortion, as has been documented in Brazil [10].

The combination of widespread informal use and few conclusive clinical trials leaves policy makers, drug regulators, pharmaceutical companies, providers, and women in difficult and often conflicting positions. On the one hand, a large and growing constituency of providers, particularly in developing countries, have discovered the myriad uses of misoprostol for improving reproductive health care. These providers have identified a clear need for this drug. Providers in our study appreciate its high efficacy, low cost, and

high patient satisfaction. On the other hand, the pharmaceutical company that produces and markets misoprostol, Pharmacia (formerly Searle), appears to have no interest in developing misoprostol for any of these reproductive health indications.

The conflicting attitudes of providers and the pharmaceutical company raise a series of questions for drug regulatory agencies, hospital administrators, and women. The entrance of new players may help resolve some of these dilemmas. In many countries, patents for misoprostol have expired or will expire soon. This paves the way for new drug companies, which may be interested in developing misoprostol for these indications, to produce and market a generic product. In the meantime, international organizations such as the WHO and the Population Council have initiated trials to fill several conspicuous voids in the clinical research on postpartum hemorrhage, first trimester medical abortion and incomplete abortion. Providers and research hospitals around the globe have also played a critical role in conducting often small but pertinent clinical trials on nearly every reproductive health indication. The need for affordable strategies for managing reproductive health indications, particularly in developing countries, makes continued use of misoprostol in gynecology and obstetrics almost inevitable. We need increased funding and definitive research to clarify optimal regimens and concomitant efforts to develop protocols and educational materials for providers to ensure that women receive optimal care. The question remains, however, how to find the quickest and safest way to deliver this promising drug into the hands of qualified providers and to women in need of such care.

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