PROJECT REPORT

REGISTERING MIFEPRISTONE FOR INDICATIONS OTHER THAN FIRST TRIMESTER ABORTION: A LANDSCAPE ANALYSIS REPORT

Background and Justification

Mifepristone is an antiprogestin that blocks the activity of progesterone, the hormone which is needed to maintain a pregnancy. Mifepristone also plays a role in softening and dilating the cervix and thus has been used for cervical ripening prior to medical procedures. It is most commonly known for its use in combination with the drug misoprostol to induce abortion. The safety and efficacy of mifepristone for first trimester abortion has been well-documented and its use for this purpose has expanded greatly over the past two decades.

Global availability of the commodity "mifepristone" has also expanded; there are now WHO pre-qualified products, three SRA approved products, and two SRA approved combi-packs. Nonetheless, while mifepristone is registered more than 68 countries for first trimester abortion, it is not always available or used. Additionally, given its antiprogestin and cervical ripening properties, mifepristone can be used for alternative indications both in reproductive health and other therapeutic areas. However, there have been limited efforts to pursue labeling for non-abortion indications (although, the innovator product, Mifegyne®, is registered for four indications). For these reasons, mifepristone is a highly underutilized medication, specifically for improving women's health, and this underutilization threatens market sustainability.

Mifepristone registration for indications other than first trimester abortion has the potential to be a major game changer by creating the framework to facilitate greater commodity access in restricted settings. Furthermore, expanding registration has the potential to move mifepristone from its status as an "abortion drug" used only by abortion providers to being known as a medication for improving women's health used by a broad range of health care providers. More indications could also increase demand, and thus improve market sustainability, which may in turn generate interest by pharmaceutical companies to pursue its marketing and distribution, including private sector distributors and social marketing organizations (SMOs).

Gynuity Health Projects has worked for almost two decades to develop clinical evidence on the safety and efficacy of mifepristone for indications outside of first trimester abortion. This work serves as a strategy for expanding mifepristone access in countries with restrictive abortion laws or increasing the market in countries where mifepristone is registered for first trimester abortion but remains underutilized. Indications include early pregnancy loss, intra-uterine fetal death (IUFD), cervical ripening, second trimester abortion for maternal health or fetal indication, and menstrual regulation. These indications are legal and less politically and culturally sensitive in most relevant jurisdictions, and, in turn, registration may not pose the same problems as have been encountered for registration for first trimester elective abortion. Further, registration provides an entry point for mifepristone to be added to national drug registries, stocked in hospitals and other health care facilities, and integrated into health care systems.

We conducted a landscape analysis of the registration and marketing feasibility for alternative mifepristone indications in six countries with limited abortion availability (legal and otherwise), global representation, and some of which had a sizeable potential market share. The goal was to identify the indication(s) with the greatest promise for registration and recommendations for what steps would help to move registration forward successfully as well as ensure availability and use post-approval.

Selection of organizations and key informants for global stakeholder interviews

We conducted interviews with eight organizations (pharmaceutical companies, international NGOs, and social marketing organizations) to assess their interest in the alternative indications, geographic and market priorities, and perceived barriers to pursuing registration for additional mifepristone indications. Stakeholder organizations play various roles related to mifepristone availability and use—from registration to distribution to marketing.

Country selection for national-level assessment

Country-level assessments were conducted in six countries (see text box). Countries were selected to ensure regional representation – with at least one country from West Africa, one from Latin America, one from East Africa, one from South Asia and one from Eastern Europe/Caucuses. Countries selected fell into at least one of the following categories: 1) no mifepristone product currently registered for any indication, 2) limited legal abortion status, 3) known interest in exploring mifepristone registration for indications other than first trimester abortion. There was also an interest in selecting countries where abortion is legally permitted and mifepristone is or has been registered, but where the market is not stable. Key stakeholders represented a range of groups involved in reproductive health care including staff from ministries of health or drugs and regulatory bodies, health care providers and national staff of international NGOs.

Countries Selected and Number of Interviews Per Country

Burkina Faso (2)	Colombia (4)
Kenya (2)	Latvia (3)
Pakistan (3)	Senegal (3)

Learnings from Global Stakeholder Interviews

Interest in registering mifepristone for alternative indications

Stakeholder organizations were overwhelmingly supportive of registering mifepristone for alternative indications. Most stakeholders were aware of the four indications that were the focus of this assessment (early pregnancy loss, IUFD, second trimester abortion, and cervical ripening). There was interest in registering all four indications and no consensus as to which indication would be most promising.

Interestingly, one stakeholder stated that future registration efforts should be focused on registering the combi-pack, not just mifepristone. The reason they cited was that mifepristone is used in conjunction with misoprostol for most indications other than first trimester abortion, including second trimester abortion, IUFD, and missed abortion.

Stakeholders were also widely aware of mifepristone's other reproductive health indications, such as for emergency contraception, menstrual regulation, and treatment of endometriosis and fibroids. They expressed interest in knowing more about the evidence available on these indications and exploring opportunities for registration. Finally, stakeholders were aware that mifepristone can be used for indications beyond reproductive health, like Cushing's syndrome. However, for those indications, the pill size may be different. For this reason, such indications were not the focus of this assessment. Yet, given potential interest in these indications, relevant stakeholders may consider convening an expert meeting to explore a path forward for registration.

GEOGRAPHIC PRIORITIES FOR REGISTRATION

Sub-Saharan Africa, West Africa specifically, was most frequently mentioned as a priority by nearly all organizations. This regional priority likely reflects both the legal context for abortion (which limits opportunities for mifepristone registration for first trimester abortion) and donor priorities and funding. Several stakeholders specifically indicated that geographic priority is largely based on available funds and funder priorities. Further, most stakeholders indicated that their geographical priorities would align with regions of the world where abortion is most restricted. Two organizations expressed interest in the Latin America and Caribbean (LAC) market, Mexico, Colombia and Argentina specifically. LAC could be a promising market, especially for commercial entities.

Barriers to registration

Barriers to registration fall into three categories: 1) political/legal, 2) financial, and 3) knowledge.

Political barriers relate primarily to legal restrictions on abortion and the widespread understanding that mifepristone is an abortion drug. Several key informants mentioned both a lack of political will and significant regulation burdens. One key informant did emphasize that the fact that mifepristone can be used for abortion should not determine the success of registration for non-abortion indications. Whether or not mifepristone is used for but not approved for abortion is related to regulations regarding distribution. Additionally, even if mifepristone is approved for abortion under limited circumstances, this does not mean that it will be made available for unapproved uses, since it is possible to restrict distribution channels to approved indications. This critical distinction, between approval and availability, needs to be reflected in registration strategies and approaches.

Financial barriers are also relevant to the cost of registration and the sustainability of the market post-registration. There can be significant cost to supporting activities needed for registration. One issue raised by stakeholders was the preparation of the regulatory dossier, even when clinical and other data exist. In addition, issues related to market sustainability were high on the list of perceived barriers: it is not commercially viable to register a product if there is not a sustainable market, and/or one that is highly profitable. Stakeholders raised several important factors related to market sustainability: perceived supply problems and lack of competition; market monopoly and failure to collaborate; and, inability to pool orders for multiple countries as is done by UNFPA and others with condoms and oral contraceptive pills.

Finally, **knowledge** gaps pose a critical barrier. For example, stakeholders demonstrated inconsistent understanding of the meaning of the terms: "registration" and "distribution." Understanding of these terms and their functional differences is critical when designing and implementing strategies for expanding mifepristone access, especially for selecting indications, countries, and distributors. Second, not all stakeholders were aware of the possible indications or the evidence base that supports registration. Third, not all stakeholders demonstrated understanding of what it would take to register mifepristone for non-abortion indications, including the evidence needed, the product that could or should be registered, the need or potential for collaboration, the processes for registration, and strategies for distribution post-registration. The latter is a critical element of any successful registration effort. If the sector were to invest in registering mifepristone for non-abortion indications it should have a parallel strategy that will ensure availability (distribution) and use (trained, invested providers and appropriate clinical guidelines).

BURKINA FASO

The context of abortion in Burkina Faso is like that in other Francophone countries in West Africa: it is legally restricted and highly socially stigmatized. Abortion is legal in cases where it is necessary to save the mother's life, in cases of rape or incest, and in cases of severe fetal malformation. It is widely understood that abortion is provided, but it is not discussed. Services are largely clandestine and most frequently provided by non-governmental organizations.

The combi-pack is registered in Burkina. However, the social and political environment has posed a challenge for widespread marketing and distribution of mifepristone for first trimester abortion. Mifepristone is not registered for other indications. It is not clear the extent to which the combi-pack is available or used or whether off-label use for other indications is common or happens at all. Assumedly, because it is registered for abortion, and because abortion is highly restricted and stigmatized, mifepristone is not currently being used off-label for the alternative indications. However, data are lacking. Key informants were not aware that any organizations were seeking to register mifepristone for other indications now or in the future. For these reasons, stakeholders consider mifepristone to be under-utilized for first trimester abortion as well as for other indications.

Both key informants expressed interest in registration of mifepristone for indications other than first trimester abortion, in part because, in the context of Burkina Faso, those indications are more likely to be perceived as needed for treating medical conditions; whereas first trimester abortion is not perceived as a medically necessary procedure. They agree that due to the highly political and stigmatized nature of mifepristone (because it is seen as an abortion medication), registering mifepristone for one or more of the indications outside first trimester abortion could expand use in reproductive health care. They also believe that in order to increase the use of mifepristone, more work with providers is necessary, as one of the greatest challenges to use was said to be lack of correct and appropriate information among doctors.

For promising indications, both key informants felt that registration for second trimester abortion would be beneficial to women and seen as medically necessary despite the restrictive context of abortion. In the rare case that an abortion is permitted in the second trimester, procedures with medications are perceived as safer and less complex than surgical procedures. One key informant believed that the most promising indication was cervical ripening.

There was disagreement, however, around whether it would be possible or desirable to register mifepristone for menstrual regulation. One informant believed this indication to be one of the most promising indications because he deemed the indication non-political and the need potentially high. The other informant felt that it would be undesirable to register mifepristone for menstrual regulation because it is not seen as a medical problem and would only foment mistrust, because it would be perceived as a disguise for abortion.

COLOMBIA

The legal environment in Colombia is favorable to mifepristone use for first, and more recently, second trimester abortion. In 2006, the constitutional court ruled that abortion be available in cases of rape or incest, to save or preserve a woman's health, or where the fetus has a malformation incompatible with life. Since then, National Guidelines include mifepristone as an option for abortion through 10 weeks' pregnancy, and a 2018 resolution mandates that all facilities provide abortion, at least by referral. In practice, however, medical abortion is still almost exclusively available at private clinics. Orientame and Profamilia (IPPF affiliate) are the two main providers. A recently published national guideline for maternal and perinatal health (June 2018) allows for outpatient use of mifepristone in the second trimester, as long as referral systems are in place for emergency and higher-level care.

Although mifepristone was registered in Colombia in 2017 and national guidelines support use in the first and second trimesters, there remain several barriers to widespread availability and use. For one, the guidelines are more up to date than the product label (which only goes to 63 days) which has the potential to create confusion among providers as to when mifepristone can and should be used. Also, there are two registered products however the most recently registered one is not yet available and at present only Profamilia distributes mifepristone. Finally, most hospitals do not stock mifepristone (as it is not currently included in the "*plan de beneficios*"), and there is a lack of political will on the part of hospitals to request mifepristone be stocked. Unlike misoprostol, mifepristone is not available at pharmacies.

According to key informants, providers lack information about mifepristone, which has resulted in misunderstandings about how the product can be safely used. Since provision of first trimester abortion with mifepristone is not a required service, many providers simply do not know about mifepristone and/or do not know how to manage first trimester abortion using mifepristone. There is also confusion about the law regarding abortion since while decriminalized in the law, it is still in the penal code, and therefore many women also do not know that they can obtain a legal abortion in certain circumstances.

There was no consensus among stakeholders as to whether registration of alternative indications should be a stand-alone priority at this time, although many believed it should be. Key informants felt that improving provider and client awareness of the legal status of abortion and the option of medical abortion was a priority, as well as improving and increasing distribution of mifepristone. One key informant believed that updating the National Guidelines would be beneficial to improving availability and use. In terms of an actual indication to pursue for additional uses, key informants generally felt that second trimester abortion was a priority, although there was also some interest in cervical priming and missed abortion.

KENYA

Abortion has been available in Kenya since 2010, when the constitution was changed, and is legal in cases where a mother's life is at risk by consent of one trained healthcare provider. According to one key informant, the law is interpreted and applied more liberally: in the private sector at least, women essentially can request abortion on demand. However, abortion is politically sensitive, according to a second key informant, and that is one reason why it is provided almost exclusively in the private sector.

The first registration of mifepristone was approved in 2013. Three combi-pack products are registered in Kenya (Medabon, Sun Pharma/Concept Foundation, Ma Kare, DKT; Marie Prist, MSI). Mifepristone with misoprostol is also included in the Kenyan National Essential Medicines List (2016)(EML), on the specialist list[1] under oxytocics not abortion. For a medication to be available in the public sector it must be on the EML; registration alone is not enough. Key informants both confirmed that mifepristone is only available in the private sector, where it is used for first trimester abortion. There was lack of agreement as to whether mifepristone was available in pharmacies—with one key informant claiming it was not and the other that it was.

There was lack of agreement as to whether labelling mifepristone for alternate indications was desirable and would expand mifepristone availability and use. One respondent did not see the need to change the label in order to expand mifepristone availability for first trimester, because it is widely available in the private sector. Both key informants, however, saw utility to adding indications to the label to expand mifepristone use for all indications and potentially expand availability to the public sector. Interestingly, one key informant believed that a new label could also serve as a reason for the Ministry of Health to support public sector training of providers and consequently improve proper use of mifepristone for all indications including first trimester abortion. Both key informants also agreed that expanding the label might help to change the mindset about mifepristone, and therefore, increase its availability, as was the case for misoprostol, which is approved for multiple indications.

There are three main challenges expressed by key informants as regards to expanding mifepristone availability generally, and labelling new indications, specifically. First, while there is awareness by the health ministry of mifepristone provision for first trimester abortion in the private sector, they do not support expanding mifepristone use for abortion by expanding availability to the public sector. Second, the mindset of key stakeholders about mifepristone needs to change which would require investment in advocacy. Finally, there is concern among key informants that adding further indications to the mifepristone label would results in a political backlash and further limit mifepristone availability for first trimester abortion, specifically in the private sector where it is widely available currently.

In terms of indications: one key informant felt that labelling mifepristone for second trimester abortion was a priority. The second key informant strongly agreed that mifepristone should be approved for all alternate indications, except for cervical preparation. That informant further explained that mifepristone use for missed abortion and IUFD were most likely to be approved.

LATVIA

In Latvia, abortion is legally available on demand until 12 weeks of pregnancy. However, there are several barriers to medical abortion in Latvia. First, there are two different guidelines for very early medical abortion (up to 49 days) and later gestational ages in the first trimester of pregnancy (49-63 days), thus creating confusion among providers about the upper gestational limit for medical abortion. Second, accessing the procedure is burdensome to women, who must visit the clinic three times: for abortion counseling and pre-abortion tests; 72 hours later, for giving consent and administering mifepristone; and, 14 days later, for a follow-up visit. Abortion services are an out of pocket cost for women and the much higher cost of medical abortion service (approximately 400 euros) persuades women to seek surgical abortion (approximately 100 euros). Lastly, an increased presence of vocal anti-choice groups, including anti-choice policymakers, has contributed to negative media attention and stigmatization of the service. Fewer providers in the capital city provide abortion services and women travel to clinics in rural areas where abortion providers experience less scrutiny from the media and general public.

Several mifepristone products have been registered in Latvia, including Mifegyne (Exelgyne), Mifepristone (Linepharma), and Medabon (Concept Foundation). All products were registered for termination of pregnancy in the first trimester of pregnancy, up to 63 days LMP. Since medical abortion is provided almost exclusively through the private sector and the volume of service delivery is low, demand for the product is low. Both Concept Foundation and Linepharma did not renew registration of their product in 2017 and 2018, respectively.

According to key informants, the biggest barrier to expanded mifepristone use for first trimester abortion is drug availability and the fact that mifepristone is not provided in the public sector. As it is not available in the public sector, cost is an issue for many women. The price of a Mifegyne tablet was reported at more than 150 Euros, which does not include fees associated with visiting private clinics. The lack of routine abortion service delivery data is also a barrier to understanding use and to developing subsequent strategies for expanding use.

Key informants felt that given that mifepristone is available in Latvia, focused attention on reducing barriers to use for medical abortion is a primary goal. They all felt that having alternative indications would ease the burden on providers who are concerned with lawsuits. They agreed that this strategy could also expand use of mifepristone and, in turn, expand demand for the medication. Specific recommendations related to expanding use of mifepristone included: 1) increase public sector availability, 2) lower the cost, as a means of increasing demand and in turn increase the number of providers who stock mifepristone, 3) educate and train providers on existing national guidelines and protocols for medical abortion in the first trimester, 4) inform providers of all potential uses of the drug, and 5) dispel the misconception that medical abortion is only allowed up to 7 weeks of pregnancy.

[1] Items on the specialist list are "essential medicines for priority conditions for which specialized diagnostic or monitoring facilities, and/or specialist medical care, and/or specialist training are needed." See Kenyan Essential Medicines List 2016, last accessed 11 August 2019 at: https://apps.who.int/medicinedocs/documents/s23035en/s23035en.pdf.

PAKISTAN

In Pakistan, abortion is available by law in cases where is it needed to save a woman's life or as a necessary health treatment. While it is legally restricted, abortion is commonplace. Misoprostol is registered in Pakistan for both PAC and PPH, and there is a locally manufactured product that is available and of high quality (Zafa), according to a key informant. It is widely used by providers (pharmacists and ob-gyns) as an abortifacient, although it is not registered for first trimester abortion. Despite legal restriction, abortion is less culturally stigmatized as compared to countries included in the assessment in West Africa (Burkina Faso and Senegal).

All three key informants expressed interested in registering mifepristone for alternative indications, agreeing that the most promising indications are for pregnancy failure (missed abortion or IUFD). There was also interested in registration for menstrual regulation. One key informant reflected that some efforts have been made to introduce and expand menstrual regulation services, emulating Bangladesh's successful service delivery model. Those efforts, however, did not meet the same success in Pakistan as in Bangladeh, so there remained a question of whether registration of mifepristone for menstrual regulation would be possible or practical, given the potentially low demand for the service. Menstrual regulation is not well-known or understood.

In terms of barriers and suggestions for how to be successful in registering and making the product available, there was near universal agreement that a focus on provider education and guidelines would be essential. For example, one key informant recommended that a "solid strategy" using the total market approach would be critical, which indicates the need for doing more than registering the product, but also implementing parallel activities focused on use and availability. Specifically, informants recommended provider education and training as well as clear labelling in the local language (Urdu). One informant indicated that in other countries (like Nepal) the manufacturer was not willing to adopt labelling and provider materials to the local context and/or provide them in local language, as the volume was small (and therefore assumedly the cost of doing so not beneficial).

The greatest barrier in Pakistan was the fact that misoprostol use for abortion, PAC and PPH is already widespread and misoprostol is cheaper than mifepristone. Therefore, key stakeholders might question both the need and the cost. However, at least two of the three informants argued that choice as well as clinical benefit of a safer, less painful, and/or a more effective product are important benefits that could be useful points of advocacy—resonating with a strong women's rights argument for the availability of mifepristone.

SENEGAL

Abortion in Senegal is severely limited by the law. It is completely banned by the criminal code, although permitted to save a woman's life by the medical code. Further, abortion is highly stigmatized, including within the medical profession, especially first trimester abortion. According to one key informant, first trimester abortion is not seen as medically necessary, and most doctors will not conduct abortions for that reason.

In Senegal, health care providers have limited knowledge about mifepristone and its use. According to key informants, there are no real efforts to register mifepristone – for first trimester abortion or alternative indications, although DKT and MSI have explored the possibility, at least for first trimester abortion. A recent global landscape analysis completed by Mann Global Health recommended registration for PAC and not for first trimester abortion—which is consistent with the perspectives expressed by key informants. Misoprostol is registered and used widely both to prevent and treat PPH and for PAC. Further, it is popularly known that there are medications (presumably misoprostol) available in pharmacies that can be used for abortion.

Several important challenges or barriers were raised by key informants. They expressed a need for objective clinical evidence on mifepristone's utility to foster a more widespread understanding that mifepristone is clinically useful for indications beyond abortion that benefit women's reproductive health such as miscarriage. Multiple key informants mentioned that strategies to register misoprostol for PPH and PAC were successful, because those indications are not politically controversial. Therefore, the same could happen for mifepristone, especially if the knowledge of alternative indications became more widespread. Finally, one key informant expressed the importance of identifying or fostering development of champions within the government who can serve as local experts and advocates and be trusted voices within the formal organizations responsible for registration. For this informant, changing the mentality within the government was critical to successfully registering mifepristone for any indication.

All country-level stakeholders recommended a strategy of registering mifepristone for multiple alternative indications, not just one. They reflected that registration of multiple indications is more likely to result in availability and utilization of mifepristone, as compared being focused on a single indication. Informants recommended registration for menstrual regulation (2 of 3) and missed abortion (3 or 3) most commonly, but there was also interested in registration for IUFD (1 of 3). One key informant expressed concern with registering mifepristone for menstrual regulation, because the procedure is not seen as a life-saving procedure. For this reason, that informant also did not see second trimester abortion as a viable indication, as it is also not perceived as a life-saving procedure.

Conclusion

Key findings

The results of this landscape analysis reflect significant interest in mifepristone registration for indications beyond first trimester abortion—both at the global and national level. Critically, stakeholders believe that a registration strategy for expanding mifepristone use should include registration for multiple indications simultaneously (and wherever possible). Country-level stakeholders' judgments of the most promising indications for registration varied by country. At the national level, while there was strong agreement that registering mifepristone for alternative indications would be desirable and would contribute to greater utilization of mifepristone, there was not agreement on the indications. Regionally, while different strategies would be needed to reflect local contexts, it is clear there are opportunities to pursue registration in multiple jurisdictions, including in Africa, Asia and Latin America. However, much of the funding in the sector is focused on activities in Africa and South Asia. Our findings in Latvia did not justify a current focus there given other priorities.

Barriers to registration related to financial, political and knowledge aspects and all need to be considered and addressed as strategies for registration moving forward and for those strategies to be maximally successful and sustainable in increasing access to and use of mifepristone. Stakeholders appreciate that registration is only one part of a larger strategy for expanding mifepristone access and use. To this end, a winning strategy will ensure that stakeholders work strategically and collaboratively to ensure that registration results in distribution and use. As reflected in a recent landscape analysis conducted by Mann Global Health on mifepristone for first trimester abortion, where a market is small and profit margins low, distributors may not be willing to conduct marketing activities, which are needed to expand and stabilize the market and in turn ensure that women can benefit from mifepristone availability. This finding would also apply to mifepristone use for other indications and confirms the wisdom of a collaborative and holistic strategy.

This analysis was limited in size and scope. Therefore, there are likely perspectives and insights that may not have emerged. Moving forward, it will be critical to involve a larger group of stakeholders both globally and at the country-level.

Recommended Next Steps

1. *Share findings among a larger group of stakeholders, including donors and other investors* interested in supporting expanded access to mifepristone, specifically through registration. Greater knowledge sharing is critical to address financial and political barriers.
2. *Convene multiple strategy meetings, globally and locally.* Such meetings are critical to forming consensus on who, what and how to register mifepristone for alternative indications – at both the global- and country-level—and thus, defining a unified strategy. At the global level, a meeting would be helpful to define and align strategy among global stakeholders and to ensure collaboration and rational use of resources. At the country level, a meeting would define strategy and identify champions who can provide critical advocacy, especially within formal government structures whose buy-in is essential for successful registration.
3. *Develop a global strategy to expand mifepristone availability and use that includes registration for indications other than first trimester abortion.* Registration may be the first step, but it is not the only step to increasing availability and use. Investments in registration must be complemented by investments to ensure competent, knowledgeable and trained providers; a supportive health infrastructure; and, predictable drug supply. Thus, investments should also focus on developing provider capacity, revising or introducing national practice guidelines; determining where and how drug will be made available; and striving to collaborate in-country and within-country around drug procurement. There remain real concerns over market stability. Therefore, strategies for how to stabilize the market need to be built into strategies for registration. Otherwise, mifepristone could be successfully registered for alternative indications in multiple countries, yet not be available. A unified strategy would help to foster greater collaboration and ensure greatest use of available resources, both at the global- and national-levels. Many key informants reflected that this is a humanitarian endeavor, not a commercial one. Finally, the strategy would indicate where investments could be made, with tailored recommendations for specific countries based on national-level strategy meetings.
4. *Convene webinars to improve knowledge and understanding of mifepristone registration, marketing, distribution and availability.* A webinar should focus on growing understanding within the sector and among critical stakeholder as to what these concepts mean and how they are related to availability, access and use of a drug for an indication.
5. *Expand efforts to educate providers about mifepristone and its use in reproductive health beyond first trimester abortion.* Lack of knowledge about mifepristone including its alternative indications and the perception that it is "just" an abortion drug are cited by multiple stakeholders as a critical barrier to greater mifepristone availability and use. Therefore, strategies for educating providers and other key stakeholders would help to bolster the success of efforts to register mifepristone for alternative indications, and ultimately expand use and access.
6. *Bolster advocacy efforts around mifepristone use for indications other than first trimester abortion* in countries where mifepristone is not currently registered or registered but not used, with a focus on countries where abortion is highly restricted. Lack of political support was almost universally cited as a barrier to registration and consequently greater access and use. Additionally, where efforts to register and make misoprostol available for women's health indications were successful, political support was often mentioned as one of the key factors. Therefore, strategies to generate political support are needed, starting with education. Investment in local advocates and champions is essential to any registration effort. Such advocates are necessary to generate the needed political will, especially in environments where abortion is both highly restricted legally and greatly stigmatized socio-culturally.

Characteristics of countries assessed

	Legal abortion indications	Abortion rate (per 1,000 women of reproductive age)	Available medical abortion commodities*
Burkina Faso Population 20.3M	• Protect mother's life or health • Rape or incest • Severe fetal impairment	25 (2012 estimate)	Misoprostol (Cytotec, Pfizer; Misoclear, Acme) Combi-pack (Mifepack, Naari)
Colombia Population 50.3M	• Threat to mother's life or health • Rape or incest • Fetal abnormality incompatible with life	30 (2008 estimate)	Mifepristone (Linepharma)
Kenya Population 54.6M	• Life or health of mother at risk • When trained medical provider believes situation is an emergency	46 (2002 estimate)	Mifepristone (Mediprist, Acme; Linepharma) Misoprostol (Cytotec, Pfizer; Misoclear, Acme; Miso-kare, Naari) Combi-pack (Ma-kare, Naair; Medabon, Sun)
Latvia Population 1.9M	• On request up to 12 weeks' gestation • Medical reasons up to 22 weeks' gestation	16 (2012 estimate)	Misoprostol (MisoOne, Nordic Pharma)
Pakistan Population 216.6M	• Preserve mother's life or health	29 (2002 estimate)	Mifepristone and misoprostol (Naari, Zafar)**
Senegal Population 16.3M	• Completely banned by criminal code • Medical code permits abortion to save a women's life, with three doctors' agreement	17 (2012 estimate)	Misoprostol (Misoclear, Acme)

* According to IPPF's medical abortion commodity database, accessed July 19, 2019.
** According to key informants, IPPF has not yet surveyed Pakistan and thus the database has no information about drug availability in Pakistan.
Population estimates from United Nations Population Division database, accessed July 19, 2019.
WRA = women of reproductive age.

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