

EDITORIAL

Improving access to medicines for early medical abortion: learning from experiences of medicines licensing and service delivery

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INTRODUCTION

Governments worldwide have an obligation to ensure that reproductive health information, supplies and services are available, accessible, acceptable and of good quality.¹ The World Health Organisation (WHO) advises that everyone has the right to access safe and effective abortion care². However, in 2023, there remain many factors working against people's access to such care.^{3,4} This editorial discusses two key areas which continue to restrict women's rights to obtain safe and effective medical abortion.

MEDICINES LICENSING

Misoprostol was initially licensed in the 1980s solely for the treatment of peptic ulceration and its use in reproductive health since then has been widely off-label. It has become the prostaglandin of choice for early medical abortion (abortion at less than 10 weeks' gestation) even though the product licence still does not include this indication.⁵

In contrast, mifepristone's sole indication is for termination of pregnancy. Since mifepristone was registered in France in 1988, it has become clear that adding mifepristone to misoprostol significantly improves efficacy.² Used alone, misoprostol will abort about 80% of early pregnancies, although this may take some time and may involve multiple doses.⁶ A combined mifepristone/misoprostol regimen results in complete abortion in 95-98% of cases.⁶ Despite this evidence, and the fact that mifepristone is on the World Health Organization (WHO) Essential Medicines List,² around half (98/193) of countries have not licensed it for early medical abortion, including Brazil, Egypt, Indonesia, Pakistan and the Philippines⁵. Therefore, nearly 200 million women of childbearing age in these five countries cannot access mifepristone through health services. Regulators who hesitate or decline marketing authorisation of mifepristone are not making their decisions based on scientific evidence.

The safety of mifepristone is now well established after more than three decades of use, approval in 94 countries and more than 100 studies demonstrating its safety.⁷⁻¹⁰ In the USA, among 4.9 million people who had a medical abortion using mifepristone over a period of 20 years, the mortality rate associated with early medical abortion using mifepristone is 0.63 per 100,000, 14 times less than that of childbirth.¹¹

Restrictive regulations attached to authorisation of mifepristone are unnecessary and impair access.^{11, 12} A list of such regulations in three countries is shown in Table 1. In the USA, a range of conditions were imposed by the Food and Drug Administration (FDA) when mifepristone was first licensed in 2000 and a Risk Evaluation and Mitigation Strategy (REMS) was applied in 2011. REMS programmes are intended for drugs that are known or suspected to cause serious adverse effects that cannot be mitigated simply by the label instructions.¹¹ This REMS requirement has had the effect of limiting the number of clinicians able to prescribe medical abortions, has necessitated an in-person visit to a health care setting and has meant patients could not obtain the medication from a retail pharmacy or by mail. In January 2023, the FDA modified the REMS, removing the in-person dispensing requirement, maintaining the prescriber certification and patient consent requirement and *adding* a requirement that pharmacies that dispense mifepristone must be certified.¹³ These continuing restrictions are sufficiently onerous to limit access to abortion care in the US states where abortion is permitted.

The example of Canada shows the negative effect of launching mifepristone with multiple restrictions applied.¹² Eight conditions initially applied to the licence in 2015 were removed in a piecemeal fashion between 2016 and 2019 (Table 1). All these imposed conditions impeded access to medical abortion; access improved once they had been removed. Admittedly, this sequence from licensing with restrictions to deregulation in Canada was much faster than in the USA, where certain restrictions and outdated advice imposed on initial licensing in 2000 were not lifted until 2016 or 2023 (Table 1).¹¹ A data-linkage study from Ontario showed that, comparing before and after deregulation, abortion complications and ectopic pregnancy remained rare.⁹ The in-person dispensing by doctors requirement insisted on in both the USA and Canada was unnecessary for doctor and patient, bypassed the safety check of a pharmacist and reduced access to medical abortion.^{14, 15}

In New Zealand, from November 2022, pharmacists have been able to dispense medicines for medical abortion.¹⁶ In Australia, from August 2023, general practitioners no longer have to undertake mandatory training and registration, pharmacists no longer have to register to

dispense mifepristone/misoprostol¹⁷ and mid-level providers (physician associates, nurses or midwives)¹ will be able to prescribe these medicines.

So far in 2023, two countries have given marketing approval for mifepristone for the first time. The National Administration of Medicines, Food and Medical Technology in Argentina approved mifepristone in March 2023 for distribution via public and private health services (in both primary and secondary care) and pharmacies, without the imposition of conditions.¹⁸ Japan's Ministry of Health and Welfare approved mifepristone in April 2023.¹⁹ ²⁰ Unfortunately, the approval is subject to various restrictive conditions, including the drug being classified as 'deleterious' (based upon the potential to harm the fetus, not the pregnant woman), mandatory training of prescribing doctors, its prescription being limited to designated gynaecologists, approved premises being hospitals only and the patient being required to stay in the hospital until the pregnancy has passed (Table 1). All these conditions are extreme and unique to Japan. The terms of this approval are not evidence-based and do not serve the 25 million Japanese women of child-bearing age in their ability to control their fertility. Until this restrictive licensing is revisited, access to medical abortion will be severely limited and most women will be denied choice, continuing to have surgical abortions.

SERVICE DELIVERY

The licensing of a medicine by a regulatory body is only one step in ensuring populations have ready access to safe and effective treatments. There is a far wider range of barriers and facilitators that determine access to abortion.^{3, 21} Many countries need reform in areas such as: abortion being criminalised, spousal or parental consent requirements, conscientious objection by medical practitioners, a lack of funding or reimbursement and harassment by protestors. Most of these aspects of access are governed by statute law, government policy or religious doctrines and we do not have space here to discuss them.

We have seen recently how minority pressure groups and political manoeuvring can interfere with reproductive rights. A ruling by a district judge in Texas in April 2023 undermined the validity of the licensing of mifepristone by the FDA (although the FDA is well known for its rigorous processes) and the status of mifepristone in the USA is now

vulnerable to unpredictable legal processes.^{10, 22} The judge relied upon papers written by members of the Lozier Institute, an overtly antiabortion organisation. One of these papers is now being investigated by the publisher over concerns about its representation of data and author conflicts of interest.²³

Other barriers to requests for medical abortion include practical issues concerning the delivery of healthcare services. Factors which facilitate access, especially in rural or remote areas, include dissemination of information about services, central booking services and delivery by general practitioners, midwives and nurses. There are examples of good primary care service delivery in Australia, Canada, France, Ireland and the USA.²⁴⁻²⁶ Medical abortion delivered in general practice (including a nurse-led service) is safe and effective.^{26, 27}

Progressive legislation permits mid-level providers to perform early medical abortions: in South Africa, Sweden, France and the Isle of Man midwives are specifically named in abortion laws. A study from Sweden showed that there was no difference in effectiveness or complications rates between early medical abortion provided by midwives compared with gynaecologists.²⁸

A key advantage of mifepristone/misoprostol for early medical abortion over a surgical procedure, especially with ongoing threats such as pandemics and gender-based violence, is the privacy that it allows. This is enhanced when treatment is facilitated by remote consultations and this option is recommended by the WHO.² Some countries have given permanent approval for telemedicine programmes to deliver early medical abortion: these include England and Wales, Scotland, the Republic of Ireland, New Zealand, France, the USA and Colombia. Experience in the UK has shown abortion by telemedicine to be effective, safe and acceptable.²⁹

Data from both Australia and Canada show that community pharmacy dispensing of mifepristone/misoprostol is safe, effective and acceptable to patients.^{9, 14, 15, 30} Pharmacists in Canada are willing and able to dispense mifepristone/misoprostol for medical abortion.^{31, 32} In Australia, pharmacist dispensing increased the number of providers and availability of medical abortion, particularly in rural areas.¹⁵ US primary care practitioners are of the view that pharmacy dispensing will increase access and contribute to the normalisation of

medical abortion.³³ This evidence supports adoption of mifepristone/misoprostol dispensing by pharmacists in countries where such approval has not yet been granted.

CONCLUSIONS

Some governments, health ministries and medicines regulators over the last decade have adopted a stance of extreme caution with regard to licensing mifepristone for early medical abortion, as if it were a new medicine. Such authorities are failing to learn from more than three decades of experience around the world. Mifepristone/misoprostol is safe and effective for medical abortion including in primary care and telemedicine services. Pharmacy dispensing of medicines for abortion has been shown to be effective and acceptable to patients. Restrictions on use of this combination serve only to deprive women of safe and effective pharmaceutical products and create unnecessary barriers to accessing them. Instead, authorities should be thinking how medicines for early medical abortion can be made more freely available and accessible so that women are empowered to control their fertility according to their personal wishes. An ultimate aim for the future would be self-management by women of their abortion, with over-the-counter status for the relevant medicines and appropriate support if needed.^{1, 34}

Table 1 Examples of conditions imposed by medicines regulators in three countries on providers for delivery of mifepristone to patients (years indicate duration condition was in place)†

Category of condition	Condition imposed	United States of America	Canada	Japan
Registration or certification of staff	Registration of prescribers with manufacturer	2000 – present*	2015 - 2017	-
	Registration of pharmacists with manufacturer	2023 -	2015 - 2017	-
Training	Training for prescribers (exemption through specified qualifications in some countries)	-	2015 - 2017	2023
	Training for pharmacists	-	2015 - 2017	-
Staff	Gynaecologists only can prescribe	-	-	2023
Premises	Hospital premises only	-	-	2023
	Treatment on approved premises only	2000 - 2023	-	-
Gestation	Gestational limit of 49 days	2000 - 2016	2015 - 2017	-
Investigations	Routine ultrasound scan	-	2015 - 2019	-
Dispensing	Doctor to dispense directly to patient	2000 – 2023**	2015 - 2017	-
	Clinician to observe mifepristone ingestion	-	2015 - 2016	-
Clinical management	Manufacturer consent form to be signed by patient	2000 – present*	2015 - 2017	-
	Patient to remain on premises until pregnancy passed	-	-	2023
	In-person follow-up	2000 - 2016	-	-
Reporting	Non-fatal adverse events to be reported	2000 - 2016	-	-

* Risk Evaluation and Mitigation Strategy (REMS)

** This condition was temporarily relaxed during the COVID-19 pandemic

† Particular types of conditions have also been used in countries other than those specified.

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Contributors

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