



# MARKET ASSESSMENT FOR MEDICAL ABORTION DRUGS IN ARGENTINA

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# ABBREVIATIONS AND ACRONYMS

|          |  |
|----------|--|
| ANLAP    | La Agencia Nacional de Laboratorios Públicos coordina y promueve la producción pública de medicamentos (National Agency of Public Laboratories)    |
| ANMAT    | Administración Nacional de Medicamentos, Alimentos y Tecnología Médica (National Administration for Medicines, Food and Medical Devices)           |
| API      | Active Pharmaceutical Ingredient   |
| CEDES    | Centro de Estudios de Estado y Sociedad (Centre for the Study of State and Society)  |
| CPR      | Contraceptive prevalence rate  |
| CTD      | Common technical document  |
| ESAR     | Fundación ESAR (Education for Reproductive Health)   |
| FEIM     | La Fundación para Estudio e Investigación de la Mujer (Foundation for the Study and Research of Women)   |
| ForoLAC  | El Foro Latinoamericano y del Caribe para el Aseguramiento de Insumos de SR (Latin American and Caribbean Forum for the Assurance of SRH Supplies) |
| GDI      | Gender development index   |
| GDP      | Gross domestic product   |
| GMP      | Good manufacturing practice  |
| ICD      | International Statistical Classification of Diseases and Related Health Problems   |
| ICH      | International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use  |
| ICD      | International Statistical Classification of Diseases and Related Health Problems   |
| ICH      | International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use  |
| INGO     | International non-governmental organisation  |
| IPPF     | International Planned Parenthood Federation  |
| IPPFWHR  | International Planned Parenthood Federation Western Hemisphere Region  |
| LIF      | Laboratorio Industrial Farmacéutico SE   |
| MA       | Medical abortion   |
| Mcg      | Micrograms   |
| MERCOSUR | Mercado Común del Sur  |
| MVA      | Manual vacuum aspiration   |
| NGO      | Non-governmental organisation  |
| PAHO     | Pan American Health Organization   |
| PGR      | Plan de Gestión de Riesgos (risk management plan)  |

|         |  |
|---------|--|
| PIC/S   | The Pharmaceutical Inspection Convention and Pharmaceutical Inspection Co-operation Scheme |
| REDAAS  | Red de Acceso al Aborto Seguro Argentina (Access to Safe Abortion Network)                 |
| RH      | Relative humidity  |
| SRA     | Stringent regulatory authority   |
| SRH     | Sexual and reproductive health   |
| UNDP    | United Nations Development Programme   |
| UNFPA   | United Nations Population Fund   |
| USD     | US Dollar  |
| WHO     | World Health Organisation  |
| WHO PQP | WHO Prequalification of Medicines Programme  |

## EXECUTIVE SUMMARY

Until recently, abortion in Argentina was carefully restricted to when the woman's life or health was in danger and in cases of rape. However, a landmark voluntary termination of pregnancy law was passed in December 2020, and it is hoped that this will pave the way to the availability of the most safe and effective medical abortion regimens containing misoprostol and mifepristone.

This market assessment for medical abortion drugs in Argentina has been undertaken to assess and understand the forward dynamics for the expansion of availability and access to medical abortion drugs following the landmark ruling. It is also intended to serve as a tool to support manufacturing companies in establishing the business proposition when considering entering the Argentinian market with a mifepristone and misoprostol combination medical abortion product (combipack).

Misoprostol in Argentina was first registered in 2010, when a 25mcg vaginal tablet received marketing authorization, indicated for induction of labour by the national drug regulatory authority, – Administración Nacional de Medicamentos, Alimentos y Tecnología Médica (ANMAT). The product was subject to a risk management plan, requiring the close monitoring of its distribution to prevent illegal use. In 2018, a 200mcg misoprostol product was registered, for both institutional use and commercial sale. Since 2018, an additional, publicly manufactured lower cost 200mcg misoprostol product has been in development and has had limited distribution in its home province whilst finalising stability studies. This culminated with national registration of the latest product in February 2021.

To date, mifepristone has not been registered or made legally available in Argentina, although small volumes of the drug have appeared sporadically through informal channels.

Clinical guidelines have historically preceded drug availability in Argentina. The first guidelines for post abortion care were published by the Ministerio de Salud (Ministry of Health) in 2005. Several guidelines have since been issued, and in 2019, mifepristone was included as part of national comprehensive abortion care guidelines in alignment with WHO recommendations.

Before 2020, medical abortion could theoretically be provided at all levels of public healthcare facilities, including hospitals and primary healthcare centres. In practice, around 700 public health institutions are estimated to currently offer abortion services, with irregular distribution throughout the country's provincial based healthcare system. The status of abortion services in the private healthcare system is largely unknown, although the single misoprostol product may be widely available in private pharmacies. Training of healthcare providers on comprehensive safe abortion care has been very limited. The new law requires that all public and private facilities in Argentina offer free and comprehensive abortion and post-abortion care, as recommended by WHO. As such, a major clinical and programmatic scale-up is anticipated.

Most abortions in the public health sector are provided by medical abortion, following misoprostol-only regimens. For surgical abortion, manual vacuum aspiration is primarily practiced and is only provided at secondary or tertiary level institutions. Medical abortion appears to be preferred over surgical options by both clients and providers. There are additionally, a number of NGO clinics and providers that offer clinical abortion services, and some who support women to self-administer.

The process of drug registration in Argentina is governed by ANMAT and is largely transparent and consistent. Several pathways exist for the registration of both externally and locally manufactured products, and for temporary waivers of quality-assured products under certain conditions. It is feasible

that mifepristone products could be made available in public supply chains within months under a waiver. However, due to the technical attributes of mifepristone and misoprostol products, uncertainties remain about the requirements and best route to register new misoprostol and mifepristone products, including combipacks.

Limited data and metrics are currently available to guide accurate forecasting for procurement of medical abortion products, which will present a challenge as demand increases and new products are introduced. Public procurement and distribution systems are clear and well established. However, the mechanisms for private sector procurement and distribution are less transparent and consequently, the market potential is difficult to predict and market trends will be challenging to track.

Whilst political, legal and administrative barriers have historically held back availability of medical abortion medicines in Argentina, these barriers have shifted greatly, and support for increasing access to medical abortion is now widespread. In this new environment, a stakeholder meeting is recommended to bring key players together to facilitate the rapid and sustainable availability of quality assured medical abortion products in Argentina in a systematic manner.

# 1. INTRODUCTION

Misoprostol and mifepristone are safe, effective, and low-cost drugs that have become the gold standard of medical abortion care globally.

*Table 1: Medical abortion regimen safety and efficacy, up to 13 weeks gestation [1]*

| <b>Regimen</b>             | <b>Efficacy</b> | <b>Continuing pregnancy</b> | <b>Complication</b>                     |
|----------------------------|-----------------|-----------------------------|---|
| Misoprostol only           | 80 – 85%        | 3-10%                       | 1-4%                                    |
| Mifepristone & Misoprostol | >95%            | <2%                         | <1% up to 10 weeks<br>3% 10 to 13 weeks |

Whilst misoprostol was initially registered for gastrointestinal indications only, it has since been registered for obstetric indications in more than 90 countries. Mifepristone has been approved in 62 countries [2]. The co-packaged presentation of mifepristone and misoprostol tablets (commonly known as a combipack) is now included in the WHO Model Essential Medicines List and its distribution is rapidly increasing in both public and private supply chains worldwide.

Historically, the situation in Latin America has been different, where most governments have been inactive or have unreasonably delayed or obstructed the registration of misoprostol and mifepristone products. Abortion has been legal in Argentina since 1921 however, until recently was restricted to when the woman's life or health was in danger and in cases of rape, with severe punishments to those violating the law.

There have been several attempts over the years to reform the Argentinian legal position in line with international norms, most notably in 2018, when the Senate narrowly voted against a bill that would have effectively legalised abortion. However, activists and NGOs were mobilised, and worked collectively with politicians to prepare a new bill and build momentum around it. Finally in December 2020, both chambers of the National Congress voted to approve a law legalising voluntary abortion up to the 14th week of pregnancy.

Several essential activities have since begun to ensure the introduction and availability of medical abortion drugs in Argentina. Among these, the Centro de Estudios de Estado y Sociedad (CEDES), a local NGO whose focus includes technical and advocacy activities around sexual and reproductive health, hopes to convene a stakeholder meeting during 2021, bringing together key government and other stakeholders to facilitate the registration of new medical abortion products in Argentina, their distribution and safe clinical use throughout public and private sectors of the Argentinian health system.

This paper is written to provide a landscape of the status of medicines for medical abortion and medicines regulation, which can serve to inform the stakeholder meeting and other interested parties.

## 2. BACKGROUND – ARGENTINA & REPRODUCTIVE HEALTH

### 2.1. DEMOGRAPHIC AND DEVELOPMENT CONTEXT

Just over half of the Argentinian population of approximately 45 million are female, with the population highly concentrated in urban areas. Nearly 65% of the population is concentrated in the central Pampas region, particularly in the province of Buenos Aires where 38.9% of the country's population lives including in and around Buenos Aires. There are 24 sub-divisions (provinces), including the capital city (Ciudad de Buenos Aires) [3].

### 2.2. HEALTH SYSTEM

Argentina's extensive health system includes the public, private, and social security sectors. It is a fragmented system, whereby each of the province's function independently and have constitutional responsibility for the leadership, financing, and delivery of health services [4].

The public sector comprises a network of hospitals and public health centres that provide universal free healthcare to all, but particularly serves those in lower income brackets who lack social security coverage or cannot pay for services. The National Ministry of Health has normative and regulatory functions and provides some essential supplies. The provincial governments and some municipal bodies are responsible for healthcare provision through hospitals and healthcare centres. Hospitals can be either provincial or municipal, but most are provincial. By contrast, more primary healthcare centres are municipal than provincial.

The compulsory social security sector applies to all formal workers, active and retired, and to their families, covering an estimated 60% of the population. It is a very fragmented subsystem with 292 national and 24 provincial workers organisations. The social security sector has to comply with an essential package of care defined in agreement with the national government.

The private sector consists of health professionals and facilities that offer services to prepaying private clients and to beneficiaries of the workers organisation and private insurers. It is voluntary and is utilised by approximately 5% of the population. Private sector entities are likewise regulated to provide an essential package of care.

### 2.3. COUNTRY INDICATORS – REPRODUCTIVE HEALTH

Argentina has an innovative and comprehensive sexual and reproductive health (SRH) regulatory framework, with initiatives aimed at improving adolescent SRH and reducing teen pregnancy, engaging both governmental agencies and NGOs. Despite this, and the socioeconomic growth registered in recent years, reproductive health indicators are still poor when compared to other countries in the region [5].

Table 2: Key reproductive, maternal and abortion indicators [6]

|  |                  |
|--|------------------|
| Number (and %) of women of reproductive age                        | 10,243,150 (50%) |
| Number of births per year (2018)                                   | 685,394          |
| Birth rate per 1,000   | 15.4             |
| Fertility rate per women   | 2.3              |
| Total number of pregnancies  | UNKNOWN          |
| % of deliveries attended by skilled healthcare worker              | 93.9%            |
| Maternal Mortality Rate (per 100,000 live births, 2018)            | 39               |
| Adolescent Fertility Rate (births per 1000 women aged 15-19, 2018) | 63               |

Death from pregnancy ending in abortion is among the leading causes of maternal death in Argentina, accounting for 14.8% of all maternal deaths in 2017. Adolescent fertility rate ranks as one of the highest in the region. 7/10 adolescents reported their pregnancy as unintended, and of them 8/10 were not using contraception [5].

Contraceptive prevalence rates remain relatively high, including uptake of modern contraceptive methods. Despite the availability of contraceptives for free in public facilities, they are mainly accessed through commercial/private pharmacies [7].

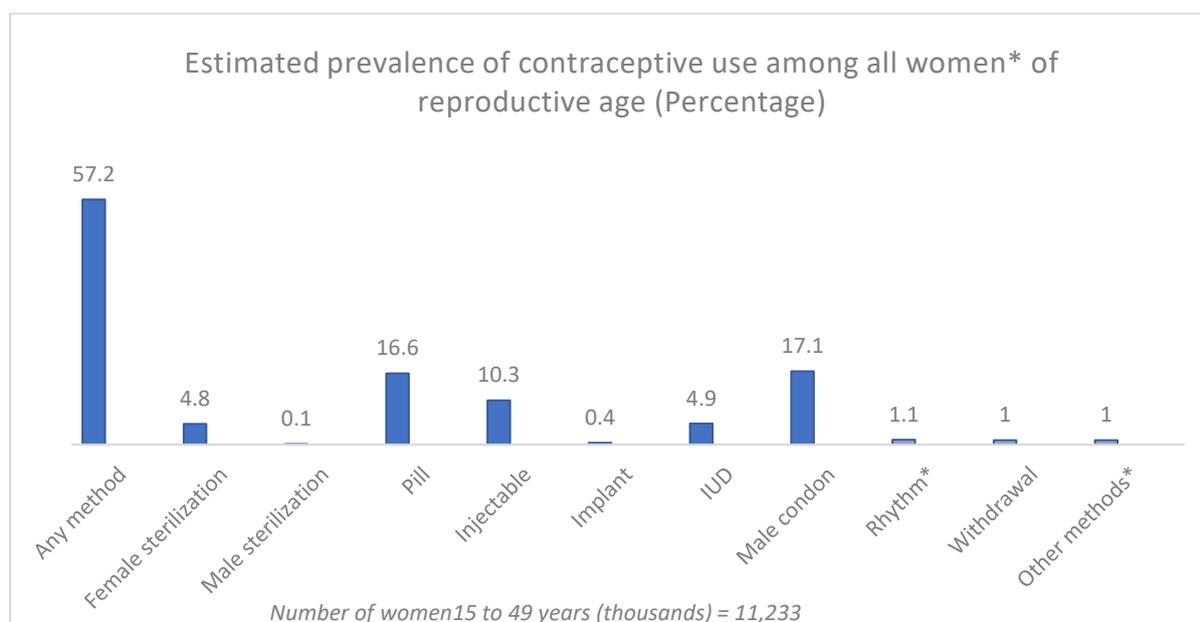


Figure 1. Estimated prevalence of contraceptive use among all women\* of reproductive age (2019 data) [8]

\* Note that most other published figures on CPR refer to married women or women in union. The above figures seek to estimate CPR in all women of reproductive age.

Whilst rates and total numbers of actual abortions per year is unknown, estimations from 2004 data using Guttmacher methodology estimated that between 352,000 and 525,000 induced abortions were carried out per year [9]. These figures are approximate since, as it has been a largely clandestine practice, accurate data is not available.

*Table 3: Key abortion statistics*

|  |                   |
|--|-------------------|
| % of unplanned pregnancies (2014)                        | 58.1% [10]        |
| % of unplanned adolescent pregnancies (aged 10-19; 2014) | 70%               |
| Rate of abortion/total number of abortions               | UNKNOWN           |
| Estimated induced abortions per year (2004)              | 352,000 – 525,000 |

Until recently, the only official information available on abortions performed in Argentina is the number of hospitalizations in public facilities for abortion-related complications. According to data available on the website of the Dirección de Estadísticas e Información de Salud (Directorate of Health Statistics and Information), 45,968 related hospital admissions were recorded in 2015 [11]. Recently, further data has been published which reveals legal abortions being carried out in public services in some provinces.

*Table 4: Select data on legal abortions*

| Area                                     | Period              | Number of legal abortions |
|--|---------------------|---------------------------|
| City of Rosario (public sector)          | 2018                | 1312 [12]                 |
| City of Buenos Aires (public sector)     | 2019                | 8388 [13]                 |
| Province of Buenos Aires (public sector) | 2020 (Jan-Jun only) | 5028 [14]                 |

Methods for unsafe abortion are not well documented but anecdotally include the use of incorrect doses of misoprostol and use of sharp objects. Statistics from public hospitals in 2016 suggested the number of discharges due to complications from unsafe abortions was 39,000 discharges (codes O00-O08 of ICD).

## 3. ABORTION POLICY ENVIRONMENT

### 3.1. ABORTION LEGAL STATUS

Up until 2020, the 1921 Penal Code 11,179 prescribed severe prison sentences for any woman obtaining an abortion, and any person participating in providing the abortion. Abortion could however

legally be performed by a certified doctor in cases of danger to the woman’s life or health, or rape [15].

Since the mid 2000’s, momentum has slowly shifted towards decriminalisation of abortion. In 2005, Resolution 989 of the Ministry of Health was enacted, protecting the right of all persons to prompt, quality, humane and confidential health care in post-abortion situations, regardless of whether the abortion is spontaneous or induced [16]. In 2018, a bill was narrowly defeated in Congress that would legalise abortion on request and make it available in all hospitals and clinics.

In December 2020, the National Congress passed the “Access to the Voluntary Termination of Pregnancy Law No. 27610” [17]. The law legalised voluntary abortion up to the 14<sup>th</sup> week of pregnancy, after which it would be legal only in cases of rape or danger to the woman’s life. The law stipulated that any woman can request the procedure at any public or private health facility, and that doctors would be legally bound to either perform it or to refer the patient to another physician or health facility. Moreover, public providers, social security and private insurance companies must provide free and comprehensive abortion and post-abortion care, in “all the forms recommended by WHO” [18]

## 3.2. POLICY ENVIRONMENT ON ABORTION

National Law 25673 (2002) and its Regulatory Decree 1282/2003 is the key overarching SRH legislation in Argentina, creating the Sexual Health and Responsible Procreation National Program within the National Ministry of Health, and among other programs, guarantees free access to any contraceptive method of the client’s choice in hospitals, health centres, social security and prepaid services. In 2020, the *Dirección de Salud Sexual y Reproductiva* (National Directorate of Sexual and Reproductive Health) was established to oversee both this program and the National Plan for the Prevention of Unintentional Pregnancy in Adolescence, which aims to address the country’s high rates of adolescent pregnancy.

The current clinical guidelines for the management of abortion and post-abortion care in Argentina are:

- 2015 *Guía para la atención integral de mujeres que cursan un aborto* (Guide for the comprehensive care of women who undergo an abortion) [19]
- 2019 *Protocolo para la atención integral de las personas con derecho a la interrupción legal del embarazo* (Protocol for the comprehensive care of persons with the right to legal termination of pregnancy) [20]

The 2015 guideline focuses on the provision of post-abortion care and includes protocols for both surgical (by manual vacuum aspiration) and medical (misoprostol-only) methods, as well as post-abortion family planning.





The 2019 guideline provides comprehensive procedural and clinical guidance for the termination of pregnancy in line with the Argentine legal framework prior to Law 27610. It includes medical and surgical methods in line with most recent WHO best practice recommendations, as well as the provision of post-abortion family planning. Notably the guideline includes the option of mifepristone where available, noting that whilst not currently available in Argentina, it nonetheless is included in the gold standard regimen for medical abortion in international guidelines.

Both guidelines are now in the process of being updated by the National Directorate of Sexual and Reproductive Health, in line with the provisions of Law 27610. It is anticipated that they will align with WHO guidelines and will be adopted by all provinces.

Two key lists determine the essential medicines distributed to the different healthcare sectors in Argentina. *Formulario Terapéutico* (Therapeutic Formulary) [21] was published in 2002 as Annex III of the Resolution 201/2002, *Programa Médico Obligatorio* (Mandatory Emergency Medical Programme) [22]. It is intended to list the essential medicines required to treat 95% of the health problems that occur in the outpatient consultation. It is updated on an ongoing basis. *Guía de Medicamentos Esenciales en el Primer Nivel de Atención* (Guide to Essential Medicines in the First Level of Care) [23] is a clinical formulary of the essential medicines distributed through Programa Remediar to all primary health care centres. It was most recently updated in 2019.

Neither list currently includes any misoprostol or mifepristone products. Despite this, misoprostol is approved by ANMAT for use in all health facility levels, and the National Reproductive Health Program procures misoprostol and supplies it to the various provinces.

### 3.3. FUNDING OF ABORTION

In 2020, the national budget expenditure on health was equivalent to USD 3.6 billion. Current health expenditure is estimated at 9.1% of GDP [6]. The 2021 budget for national sexual and reproductive health program is forecasted to be equivalent to USD 28.5 million). There are no available figures indicating the allocation of the SRH program budget to abortion services. Internationally sourced funding exists for abortion services but are likewise not available.

## 4. PROVISION OF ABORTION CARE

### 4.1. DISTRIBUTION OF SERVICES

Abortion and post abortion care can be provided at all levels of public healthcare facilities including hospitals and primary healthcare centres. Unofficial information indicates that abortion is provided at approximately 700 public health institutions throughout the country with heterogenous distribution.

With the passage of Law 27610, the number of healthcare facilities offering safe abortion services should significantly expand nationwide across all health system sectors.

Only medical doctors are authorised to provide abortions in Argentina. Primary healthcare centres all have a doctor on staff and can provide medical abortion (MA) below 13 weeks of pregnancy only. Manual vacuum aspiration (MVA) and other surgical procedures are only provided at hospital level.

Statistics from the City of Buenos Aires recorded that, of 8,388 legal abortions performed in 2019, 84% were provided at primary healthcare centres, and 16% in hospitals [24].

There is one IPPF affiliated clinic providing abortion services, and there are several Fundación ESAR (Education for Reproductive Health) members, trained by Orientame in Colombia, in different provinces. These NGO-affiliated providers are believed to provide clinical care or supportive care in the large majority of abortion services carried out in the private sector. The status of provision of abortion care in other private healthcare facilities is not clearly known, although facilities who do provide services are believed to most commonly give their clients misoprostol prescriptions to be obtained from pharmacies.

However, the operating models for how private providers will competitively offer abortion services is currently reshaping considerably in response to the new law. For example, already established abortion providers such as the NGO-affiliated providers are now offering their services to various social security and prepaid schemes, who may prefer this option to ensure compliance with the law, avoid dealing with the issue of conscientious objection from their staff, and ensure a convenient fee structure.

Currently, there are no not-for-profit social marketing organisations that distribute reproductive health medicines operating in Argentina.

## 4.2. CHOICE OF METHOD

Most abortions at the public health sector are provided by medical abortion. Medical abortion is carried out following misoprostol-only regimens, as mifepristone is not available. For surgical abortion, the Ministry of Health provides training to replace curettage with MVA, although curettage is still used in many institutions for incomplete abortions. MVA is only provided at secondary or tertiary level institutions.

Data categorising methods provided are not available for all facilities, however the City of Buenos Aires reported 92% of abortions recorded in 2019 were performed with medical abortion [24].

The IPPF and ESAR providers perform MVA and medical abortion. Information on the practice of other private providers is anecdotal only, however most are believed to have previously provided curettage but have since shifted to medical abortion and MVA.

Medical abortion is considered the most popular abortion method due to:

- the widespread dissemination of the Uruguayan experience, which follows a risk reduction model.
- it can be provided as a more ambulatory service, as indicated in national guidelines.
- the availability of the drug, when provided by the National Ministry of Health or provincial ministry of health.

Misoprostol 200 mcg tablet products are available in pharmacies, except in San Juan province where it is only allowed for institutional use. A prescription by a medical doctor is required. If the woman has medical insurance or social security and has a prescription, she can buy misoprostol at a subsidised price. Some “friendly” pharmacies sell misoprostol products without a prescription.

Misoprostol and mifepristone can be bought informally through the internet; however, this informal market sector has not been studied, and the origin and quality of the products available is unknown.

### 4.3. OBTAINING AN ABORTION

For women under 13 years old, it is required that one parent signs the consent form.

For women 13-16 years old, progressive autonomy is considered. The woman can give consent if the procedure is not a risk to her life. However, it is desirable that an adult is involved in the process and providing support.

For women 16 years old and older, they can sign their own informed consent. No further authorisation is required.

Information on abortion is made available to women by the Ministry of Health through a 0800 number that provides information and referrals. The Ministry also distributes communication materials such as a medical abortion brochure for misoprostol-only use.

Women commonly resort to public health institutions or Socorristas, a network of groups providing counselling and medicines to women, who supported 12,575 women in 2019.

Factors influencing the decision to go to private providers include a perception of higher quality of care and confidentiality, as well as shorter waiting time. Prior to the new abortion law, some private sector providers anecdotally provided abortion on request, but hidden under another medical condition (such as embryonic pregnancies) and would charge the social security insurance company according to the relevant code or charge full price to those who could afford to pay. However, such providers were difficult to find. Conversely, some liberal districts more freely offered access to abortion in the public sector in accordance with the conditions allowed by the previous law, but with a broader interpretation of “danger to the woman’s health”, in line with the WHO definition. It is hoped the implementation of the new law will equalise access across all health sectors and provinces, for people of all income levels.

#### *Locally specific information sources for abortion*

- *Public health facilities*
- *Socorristas <https://socorristasenred.org/>*
- *Professional networks, e.g. Red de profesionales de la salud por el derecho a decidir <http://redsaluddecidir.org/>; Red de acceso al aborto seguro (REDAAS) <http://www.redaas.org.ar/>*
- *NGOs, e.g. Fundación Huésped [www.huesped.org.ar](http://www.huesped.org.ar)*
- *Online books, e.g. <http://www.redaas.org.ar/archivos-recursos/Manual-abortoconpastillas.pdf>*
- *Information provided on social networks*
- *INGOs campaigning for legal abortion in Argentina, e.g. Amnesty International*
- *Word of mouth*

Telemedicine for provision of medical abortion is not yet established in Argentina. Follow-up phone calls are however often used following face-to-face consultation. Outside of the formal health system, some women self-administer medical abortion following information provided by women’s groups, web pages, and word of mouth.

Issues faced by women that undermine access to safe abortion to date include:

- Lack of access to internet: information is available to those with internet connection such as resources to get and understand legal indications and/or contact women's groups.
- Anti-choice groups' actions: harassment of physicians, harassment of women at clinics, dissemination of fake information.
- Fear of stigma and social sanctions.
- Administrative requirements, delays in accessing care.
- Unlawful use of conscientious objection by providers, mistreatment, refusal to provide abortion care.
- Subjective judgement of rape.
- Absence of comprehensive counselling for pregnant girls and adolescents including legal abortion.

The impact of the new law on access to abortion services has not yet been assessed. However, the government has established a website for the public to report issues faced in accessing abortion services in either social security or prepaid schemes [18]. Complaints can also be received at the government's free-call hotline for sexual and reproductive health and rights information.

## 5. COST OF ABORTION CARE

### 5.1. COST OF SAFE ABORTION SERVICES

Abortion and post abortion care, like other medical services, is provided free of charge if the person seeks care at a public health institution. Before the new law, patients that resorted to private abortion providers paid most, or part of the abortion services out-of-pocket.

Under the new law, social security and medical insurance companies are obliged to provide abortions. It is expected that no user costs will be charged, but it remains subject to negotiations between the government and the social security institutions. Some provincial social security organisations are already including comprehensive abortion services. In this sector, it is referred to as "uterine evacuation".

ESAR providers charge USD 150-180 for 1st trimester abortions, considering the socioeconomic status of the woman. A similar price is charged at the IPPF affiliate. Other private providers are believed to charge around USD 320 for medical abortion or MVA. Prior to the new law, many private clinics offered curettage and therefore charged a higher price, however this has recently shifted to medical abortion and MVA.

There are many anecdotes of informal providers or medical doctors who provide abortions but there is no systematic data available.

At pharmacies, the retail price of Misop 200® – misoprostol 200 mcg x 12 tablets, commercial product manufactured by Laboratorio Dominguez – is approximately USD 70, indicating a very large markup on the cost of production. If the woman has a prescription and medical insurance, she can buy misoprostol at a subsidised price of 60% of the cost, i.e., USD 42. Note that the minimum wage in Argentina is USD 232 per month.

## 5.2. COSTS OF UNSAFE ABORTION

In 2018, *Monteverde et al* quantitatively modelled the total monetary costs – including private or out-of-pocket expenditure, as well as costs for the health care system – of the status quo of illegality and unsafe practice of abortion, against potential scenarios of safe practices. They found that even the out-of-pocket cost paid by women or their families to access the practice illegally and unsafely exceeds any safe alternative according to WHO protocols, by between 30% and 80%. In turn, the resources that would be spent by the health system on treatment for complications (excluding out-of-pocket costs) would exceed the cost to the system of any safe abortion scenario by 4-5 times [25].

## 6. ARGENTINIAN MANUFACTURING SECTOR

Argentina has a strong pharmaceuticals industry. Turnover from the sector in 2017 was USD 5,902 million, or 4.9% of the country's industrial GDP. More than 71% of the total turnover is attributed to local manufacturing. There are 210 pharmaceutical companies registered in Argentina, and of the 190 manufacturing plants, 160 are Argentinian owned and 30 have multinational ownership. The local manufacturing sector produces medicines primarily for the Argentinian population, but also exports significant quantities of pharmaceuticals to neighboring MERCOSUR countries, as well as some more highly regulated markets such as in Germany, France and the US [26].

There is a national network of 40 public companies that manufacture products primarily for the public sector, overseen by the National Agency of Public Laboratories, ANLAP. These public laboratories manufacture many essential medicines and orphan drugs that typically offer lower profitability and are not produced by private companies, such as antibiotics and analgesics.

The larger private manufacturers compete with each other differentiating by proprietary brand names, whereas the smaller private manufacturers and the public laboratories focus on generic medicines.

## 7. ABORTION PRODUCTS

The list of misoprostol-containing products registered by Argentina's national regulatory agency ANMAT, as published on their website *Vademécum Nacional de Medicamentos* [27], is shown in Table 5 below. It reveals two misoprostol/diclofenac combination products; two Misop 25<sup>®</sup> misoprostol 25mcg vaginal tablet products for hospital-use only manufactured by Laboratorio Dominguez SA; and four Misop 200<sup>®</sup> misoprostol 200mcg vaginal tablet products, also manufactured by Laboratorio Dominguez. The Misop 200<sup>®</sup> products include three different pack presentations for institutional-use only, and a 12-tablet pack for private sale at the retail price of \$6,265 pesos, equivalent to approx. USD 70. Distribution of the 12-pack product is carried out by many "droguerías", and the product is widely available in private pharmacies.

Table 5: List of Misoprostol products registered by ANMAT, March 2021

| Nº Certificado | Laboratorio                        | Nombre Comercial | Forma Farmacéutica          | Presentación   | Precio Venta al Público                                 | Genérico  |
|----------------|------------------------------------|------------------|-----------------------------|--|---|---|
| 55117          | Laboratorio Domingues SA           | MISOP 25         | Comprimido vaginal          | Blister por 100 unidades   | \$0.00<br>(uso exclusivamente hospitalario)             | Misoprostol 25 mcg                              |
| 55117          | Laboratorio Domingues SA           | MISOP 25         | Comprimido vaginal          | Blister por 20 unidades  | \$0.00<br>(uso exclusivamente hospitalario)             | Misoprostol 25 mcg                              |
| 18349          | Laboratorios Beta Sociedad Anonima | OXAPROST 50      | Comprimido                  | Blister por 16 unidades  | \$2,803.41  | Diclofenaco sodico 50 mcg + Misoprostol 200 mcg |
| 18349          | Laboratorios Beta Sociedad Anonima | OXAPROST 75      | Comprimido                  | Blister por 16 unidades  | \$2,827.18  | Diclofenaco sodico 75 mcg + Misoprostol 200 mcg |
| 55117          | Laboratorio Domingues SA           | MISOP 200        | Comprimido ranurado vaginal | Blister por 12 unidades  | \$6,265.42  | Misoprostol 200 mcg                             |
| 55117          | Laboratorio Domingues SA           | MISOP 200        | Comprimido ranurado vaginal | Blister por 20 unidades<br>(uso institucional y hospitalario exclusivo)  | (uso exclusivamente hospitalario – no venta al público) | Misoprostol 200 mcg                             |
| 55117          | Laboratorio Domingues SA           | MISOP 200        | Comprimido ranurado vaginal | Blister por 48 unidades<br>(uso institucional y hospitalario exclusivo)  | (uso exclusivamente hospitalario – no venta al público) | Misoprostol 200 mcg                             |
| 55117          | Laboratorio Domingues SA           | MISOP 200        | Comprimido ranurado vaginal | Blister por 100 unidades<br>(uso institucional y hospitalario exclusivo) | (uso exclusivamente hospitalario – no venta al público) | Misoprostol 200 mcg                             |

In 2018, the public manufacturer Laboratorio Industrial Farmacéutico SE (LIF) [28] initiated development of a more affordable misoprostol 200mcg product. In line with provincial regulations, provision of initial stability data and first commercial batch analysis allowed the limited distribution within the Province of Santa Fe, prior to completing national registration. Ongoing registration efforts were assisted by ForoLAC [29] and the local NGO FEIM [30], led by Dr Mabel Bianco, and on Feb 5, 2021, ANMAT approved the product. It is unbranded, not for commercial purposes and can only be sold to Ministries of Health. The product is marketed as vaginal tablets and comes in a blister of 12.



Both the LIF and Laboratorio Dominguez products are packaged in double-aluminium blister packs. Beyond the registration and post-marketing activities of ANMAT, the quality of these products is not known to have been otherwise assessed. Both products are distributed to the Argentinian market only, and have not sought WHO prequalification, nor approval from other drug regulatory authorities.

The clinical indications for the two 200mcg products, as stated on the product information leaflets are shown as follows:

| <i>MISOP 200® BY LABORATORIO DOMINGUEZ [31]</i>   | <i>MISOPROSTOL 200MCG® BY LIF</i>   |
|---|---|
| <ol style="list-style-type: none"> <li>1. Dilatation and preparation of the cervix of a non-pregnant uterus prior to hysteroscopy</li> <li>2. Other gynaecological procedures requiring access to the uterine cavity</li> </ol> | <ol style="list-style-type: none"> <li>1. Cervix preparation before procedures that require access to the uterine cavity</li> <li>2. Uterine evacuation in cases of incomplete abortion, anembryonic pregnancy or legally permitted interruption of pregnancy</li> <li>3. Treatment of postpartum haemorrhage</li> </ol> <p>Note: For pregnancy interruption, misoprostol needs to be prescribed and indicated according to the law and regulations of the country.</p> |

Both products are vaginal tablets, however the national guidelines and WHO guidelines recommend the use of misoprostol either buccally, sublingually, or vaginally for medical abortion. In practice locally, buccal administration is preferred and is considered acceptable off-label use, while vaginal administration is more frequently used if the woman is being managed in hospital.

For MVA aspirators, cannulae and accessories, there is only one distributor registered in Argentina representing the Ipas MVA Plus® product range, Medicatec. Supplies are procured via DKT Brazil.

## 8. MEDICINE REGULATION

### 8.1. NATIONAL DRUG REGULATORY AGENCY

Law No. 16463 prescribes the regulation of human medical products in Argentina.

The drug regulatory agency in Argentina is the ANMAT, *Administración Nacional de Medicamentos, Alimentos y Tecnología Médica* (National Administration for Medicines, Food and Medical Devices) [32]. ANMAT is a decentralized agency of the Public National Administration, created by Decree 1490 in 1992. It is a branch of the Ministry of Health, but it is an autonomous body. ANMAT regulates the supply, manufacture, fractioning, import, and/or export, marketing and storage of pharmaceutical products.

ANLAP (*La Agencia Nacional de Laboratorios Públicos*) is the national agency for public laboratories and coordinates and promotes the public production of medicines [33].

Argentina is a member-state of MERCOSUR (Mercado Común del Sur) [34], together with Brazil, Uruguay, Paraguay, and Bolivia (Venezuela was suspended in 2016). Whilst there is significant regulatory collaboration with other MERCOSUR countries, there is no formal harmonised process for review, approval, or mutual recognition of marketing authorisations, nor any streamlined approval process. However, GMP inspections carried out by other MERCOSUR countries may be recognised by ANMAT.

ANMAT is a member of the international GMP harmonisation initiative PIC/S Scheme [35], and as such may recognise GMP certifications issued by other PIC/S members. However, as few signed bilateral agreements are in place, this is seldom used in practice. GMP certificates issued by the regulatory agencies of countries listed in Annex I of Decree 150/92 may be accepted.

### 8.2. REGISTRATION PROCEDURES FOR MEDICAL ABORTION MEDICINES

#### 8.2.1. Local representation

To submit and register a new medicinal product, a local representative is required who will perform the submission before ANMAT, either as the market authorization holder or as a representative of a foreign company. The local representative must hold appropriate licences to perform the required activities, such as importation, storage, distribution. It must also own the quality control laboratories where the local quality control activities will be performed and must have a Qualified Person registered with ANMAT.

#### 8.2.2. Dossier submission

ANMAT has implemented the CTD format for medicinal products. All information is exchanged through ANMAT's electronic system and e-signatures are used. Dossiers must be submitted in Spanish language.

ANMAT officials are generally reluctant to hold official meetings with applicants during the drug review process, although it is permitted. Therefore, all communication between applicants and authorities must be done in writing, in the application file, whenever requested by the agency.

### 8.2.3. Regulatory submission routes

Decree 150/92 outlines the routes for registering medicines in Argentina. The three routes relevant to medical abortion medicines are as follows:

Table 6: Key regulatory routes.

| Regulatory Route               | Eligible Products  |
|--------------------------------|--|
| Article 3 (Standard procedure) | <ul style="list-style-type: none"> <li>• products manufactured in Argentina or those authorised in any country stated in Annex II** of Decree 150/92, whereby a similar product is already registered in Argentina.</li> <li>• products manufactured in Argentina, whereby equivalent products are authorised in any country from Annex I* of Decree 150/92, even when similar products are not yet registered in Argentina.</li> <li>• products demonstrated to be similar or bioequivalent to a product registered through Article 4 route.</li> </ul> |
| Article 4 (SRA procedure)      | <ul style="list-style-type: none"> <li>• products that have a marketing authorization in any of the countries listed in Annex I.</li> <li>• this route allows a single import application by submitting the granted marketing authorization certificate among other documentation.</li> </ul>  |
| Article 5 (Standard procedure) | <ul style="list-style-type: none"> <li>• products to be manufactured in Argentina and that are chemical entities registered for the first time in Argentina even though they come from an Annex II country.</li> <li>• products manufactured in countries others than the ones listed in Annex I or II, and that they do not have authorization to be marketed in any country from Annex I.</li> </ul>   |

\* Annex I countries include: USA, Japan, Sweden, Helvetic Republic, Israel, Canada, Austria, Germany, France, UK, The Netherlands, Belgium, Denmark, Spain, Italy

\*\* Annex II countries include: Australia, Mexico, Brazil, Cuba, Chile, Finland, Hungary, Ireland, China, Luxembourg, Norway, New Zealand, India

Any foreign manufactured medical abortion products that are registered in any Annex I country would be eligible for the Article 4 (SRA) route, which is an abbreviated route.

Similarly, given the presence of misoprostol vaginal tablet products now registered in Argentina, similar foreign products registered in Annex II countries may be eligible to follow the Article 3 route.

Due to the existence of suitable reference products registered in Annex I countries, it is anticipated that locally manufactured medical abortion products – including mifepristone-only, and mifepristone and misoprostol “combipack” products – could follow the shorter Article 3 route.

Note that there is no specific pathway for the approval of products with WHO prequalification. Further, Argentina is not a participating country for WHO’s Collaborative Procedure for Accelerated Registration.

According to ANMAT Disposition 4622/12, an accelerated pathway may be applied for products indicated for rare diseases and serious diseases with risk of death and/or severe disability. This is not expected to apply for medical abortion medicines.

### 8.2.4. Marketing authorization procedure

Whilst the pathway differs according to the registration route, the general steps in the process from application to final marketing authorization may be summarised as below.



Figure 2. Marketing authorization process

### 8.2.5. Regulatory timelines

Each step of the process has legislated processing times. For example, as per Disposition 5755/96, the standard validation and review of a drug application is 8 + 72 working days, broken down as follows:

- 8 days = Filing of application
- 72 days = Review of the dossier (20 days) + Filing Department (3 days) + Evaluation / Approval (49 days)

After the technical review of a dossier, the steps until first batch release verification may take a further 115 working days.

In practice, for the standard procedure route, the processing time for a new product registration typically ranges between up to 12 months for Article 3 applications and to up to 24 months for Article 5 applications, with a further 1-2 months to first batch release.

Article 4 SRA route is a shorter process and in practice may take up to 6 months.

### 8.2.6. Marketing authorization fees

Fees for marketing authorization applications for medicinal products are outlined in Disposition 774/2021, Decree 150/92, Disposition 4622/2012, Disposition 7075/11 and Disposition 3821/20.

Table 7: Fees for Marketing Authorisation Application (updated Feb 2021) [36]

| Marketing Authorization Application Fees         |                                   |
|--|-----------------------------------|
| Regulatory Pathway                               | Fee in Argentinian Pesos \$ (USD) |
| Article 3 and 4 products                         | 22,320 - 28,920 (USD 243 - 315)   |
| Article 5 products                               | 65,140 (USD 709)                  |
| Annual Maintenance Fees for MAA Apply            |                                   |
| Products marketed to the public                  | 23,700 (USD 258)                  |
| Products authorized exclusively for hospital use | 5,100 (USD 56)                    |

Note that supplementary fees apply for situations including “New pharmaceutical form”; “New strength”.

### *8.2.7. Registration validity period*

In general, a product license is valid for 5 years. The renewal is an administrative process that must be submitted within the last month before expiration.

### *8.2.8. Registration waiver possibilities*

Waivers are sometimes possible for non-commercial purposes in circumstances determined by ANMAT, pending formal submission and registration. This route may be most feasible for products registered in Annex I countries. A reduced level of documentation is required in these circumstances, and provision of samples and reference standards may be required.

Such an approach is currently being explored by the National Directorate of Reproductive Health to accelerate the initial availability of medical abortion products.

ANMAT may also waive registration for products purchased through tender for use in the public system.

## 8.3. TECHNICAL REQUIREMENTS FOR MEDICAL ABORTION MEDICINES

### *8.3.1. Pharmacopoeias*

Argentinian Pharmacopoeia, United States Pharmacopoeia, European Pharmacopoeia, British Pharmacopoeia, and the International Pharmacopoeia are accepted. The national pharmacopoeia is the preferred option to be followed, however if a recognised compendial monograph exists it may be followed if it can be demonstrated that the specification is superior or equivalent.

Note that a misoprostol substance monograph exists in the Argentinian pharmacopoeia.

For misoprostol tablets, the only current accepted compendial monograph is the International Pharmacopoeia.

As there is no accepted compendial monograph for mifepristone tablets, complete analytical method validation would need to be submitted.

### *8.3.2. Equivalence to a reference product*

ANMAT Disposition 5040/06 details guidelines for the conduct of bioequivalence studies and establishes the requirements and documentation to be submitted for the approval of these studies. Study protocols are submitted to ANMAT along with batch records of 3 batches, for analysis and approval, prior to bioequivalence studies being initiated. ANMAT inspects clinical centres and those where bioanalytical assays are conducted [37].

However, per Disposition 3185/99, demonstrating equivalence to a designated reference product through in vivo bioequivalence studies is only mandated in Argentina for certain APIs: products categorised as high risk; or those otherwise individually advised by specific ANMAT dispositions. Bioequivalence is not currently obligatory for misoprostol and mifepristone products.

For most oral medicines, the minimum requirement is that a product demonstrates “pharmaceutical equivalence” to a suitable reference product. Pharmaceutical equivalence is defined in Disposition 3185/99 as follows (translated):

*Two medicinal products are pharmaceutically equivalent if they contain the same amount of active substance, in the same dosage form, are intended to be administered by the same route and meet identical or comparable quality standards. However, pharmaceutical equivalence does not necessarily imply therapeutic equivalence as differences in excipients, manufacturing process, or other differences may lead to disparities in the performance of the products. (WHO).*

Pharmaceutically equivalent products must be shown to meet the same compendial or other applicable standards such as identity, strength, quality, purity. When applicable, they must meet the same content uniformity, disintegration times, and/or dissolution rate and profile. Labels and leaflets must be consistent, including storage conditions and, importantly, clinical information such as indications, posology, precautions, contraindications, and adverse reactions. However, products may differ in characteristics such as shape, scoring configuration, packaging, and excipients. Guidelines from WHO, international reference pharmacopoeias, and ANMAT should be considered when designing the study protocol.

Products demonstrating pharmaceutical equivalence are termed “Similar Products”, defined in Disposition 3185s/99 as follows (translated):

*Product to be registered which is equivalent to other products approved and marketed either in Argentina or in any Annex I country (Decree 150/92), with regards to active therapeutic component, formulation, pharmaceutical presentation, dosage, indications, warnings, precautions, adverse reactions, dissolution tests and other correlative data, being able to differ in size and shape, inactive ingredients, shelf-life and primary packaging.*

In Argentina, “similar” products are widely marketed, and whilst health authorities claim the obligation to prescribe by generic name, they are unable to guarantee that drugs are truly “generic” because the bioequivalence of most approved products will not have been tested. This is believed to apply to the misoprostol products currently marketed in Argentina by Laboratorio Dominguez and LIF.

However, this approach may pose the fastest and lowest-cost route to market for new locally manufactured mifepristone and misoprostol products, whilst acknowledging that products would not be deemed “generic” medicines and may be registered with clinical particulars different to WHO recommendations for medical abortion.

Similarly, products may be more quickly registered through Article 4, but if so, they must be identical to the product registered in the designated Annex I country, in terms of strength, indications, posology, and other particulars. Such products cannot be changed later through variations.

ANMAT Disposition 1918/2013 establishes the criteria for reference medicinal products selection to conduct bioequivalence and in-vitro equivalence studies, as follows:

- Innovator product consumed and marketed in Argentina.
- Product not consumed or marketed in Argentina, if:
  - It is included as a comparator product for bioequivalence studies in the Technical Report 992/2015 of the WHO and subsequent; or
  - Innovator product consumed and coming from an ICH country, or ICH associated country.
- Product selected by ANMAT according to its safety and efficacy profile and/or pharmacokinetic profile studies, or any other information ANMAT deemed relevant.

For medical abortion products, suitable reference products meeting these criteria include those shown in Table 8 below.

*Table 8: Possible reference products for medical abortion medicines*

|  |   |
|--|---|
| Misoprostol tablets                    | Cytotec® (PFIZER, GLOBAL)<br>Gymiso (AMRING/LEON FARMA, EU)<br>Topogyne® (EXELGYN, EU)<br>Misoprostol® (NOVEL LABS, US)<br>Misoprostol® (AA PHARMA, CA)<br>PMS-Misoprostol® (PHARMASCIENCE, CA) |
| Mifepristone tablets                   | Mifegyne® (EXELGYN, EU)<br>Mifepristone® (LINEPHARMA/LEON FARMA, EU)<br>Mifeprex® (DANCO, US)<br>Korlym® (CORCEPT, US)<br>Mifepristone® (GENBIOPRO, US)<br>Mifepristone® (TEVA PHARMS, US)      |
| Mifepristone and misoprostol combipack | Medabon® (SUN/RANBAXY)<br>Mifegymiso® (LINEPHARMA, CA)  |

However, if products are registered as “similar” without bioequivalence studies, the product must be registered with identical indications, dosage, route of administration, and other clinical particulars as the reference product. This approach might render unsuitable reference products such as Cytotec® (PFIZER), which is indicated for gastrointestinal ulcer use and oral only administration, and Mifegyne® (EXELGYN), whose indications and dosage recommendation differs from WHO guidelines. This is particularly pertinent to medical abortion medicines whereby indications are determined by the abortion practice of the authorising country. Given the inconsistency of such clinical particulars across products authorised in Annex I countries, selection of the most suitable reference product that best aligns with WHO guidelines is recommended.

Anecdotally, whilst the Laboratorio Dominguez Misop 200® product is registered as vaginal tablets, off-label use by less invasive administration routes is common in clinical practice.

### 8.3.3. Stability and shelf-life

Annex III of Disposition 3555/96 describes in detail the procedures and conditions to comply with stability testing requirements in Argentina.

Argentina is considered as Climatic Zone II per ICH classification:

- Accelerated studies: 40 ± 2 °C / 60 ± 5% RH for 6 months.
- Long-term studies: 25 ± 2 °C / 60 ± 5% RH for at least 12 months

Real time studies are preferred to accelerated stability tests. Stability test results must support the shelf life, and it is preferred if the shelf life is already approved in any Annex I country.

## 8.4. PRODUCT IMPORT

The import of medicinal products into Argentina requires the intervention of ANMAT in order to release the imported product from Customs.

Local quality control of imported batches is mandatory. After the quality control tests have been performed and results are in compliance with the specifications, the batch can be released.

Costs for authorization certificate for import of medicinal products is described in Disposition 774/2021. The fee varies according to value of imported goods.

Table 9: Import certificate costs

| Value in Argentinian Pesos \$ (USD)             | Fee in Argentinian Pesos \$ (USD) |
|---|-----------------------------------|
| Up to 50,000 (USD 544)                          | 9,450 (USD 103)                   |
| From 50,000 to 500,000 (USD 544 to 5,442)       | 13,400 (USD 146)                  |
| From 500,000 to 1,000,000 (USD 5,442 to 10,884) | 26,200 (USD 285)                  |
| More than 1,000,000 (USD 10,884)                | 39,100 (USD 425)                  |

## 8.5. DISTRIBUTION CONTROLS

Medicinal products may be authorized for either:

- public use (commercial sale and non-commercial use)
- non-commercial use only
- exclusively for hospital use

Medical abortion products are available on the prescription of a medical doctor only.

The use of the generic name is mandatory in all primary and secondary labelling texts and in all technical documents/advertising for physicians.

## 8.6. PRICE CONTROL

Until recently, there has been no price control policy in Argentina. Despite strong competition from within the pharmaceutical industry, prices are typically high for the Argentine consumer compared to international standards and neighbouring countries. Prices have increased significantly on an annual basis, roughly proportionate to annual inflation in Argentina.

The final sale price of the drugs is set by the manufacturer, also taking into consideration any discounts that apply to the other intermediaries in the supply chain. At pharmacies, the consumer usually pays a portion of the full price, with the remainder paid by the pharmacy and the consumer's relevant social security organisation or private insurance scheme.

To address the high prices, the current government has established a new public bidding system for medicines. This purchasing pool has achieved a reduction in the price of some drugs, although the manufacturing companies are critical of the system as it compromises their profitability [26].

The implementation of the prescription by generic-name policy has also brought a considerable reduction in the prices of pharmaceuticals of between 50% and 75%, according to an official survey made by the Ministry of Health. This study also showed that 57% of the current prescriptions are now written using the generic name only.

## 8.7. POST-MARKETING SURVEILLANCE

Within ANMAT, the *Departamento de Farmacovigilancia* (Department of Pharmacovigilance) implements *El Sistema Nacional de Farmacovigilancia* (the National Pharmacovigilance System) [38]. Created by Resolution 706/1993, it is designed to detect, evaluate, understand, and prevent adverse effects and other drug-related problems. It bases its work mostly on voluntary reporting by healthcare professionals, but it may undertake proactive pharmacovigilance monitoring for new products where warranted.

The Laboratorio Dominguez 25mcg vaginal tablet products with specific indications for induction of labour was noted as being subject to a *Plan de Gestión de Riesgos* (PGR, risk management plan) by the *Sistema Nacional de Farmacovigilancia* (National Pharmacovigilance System) [39]. The directive is translated as follows:

*“In order to prevent the illegal use of the drug, ANMAT asked the sponsoring laboratory to present a PGR as a condition for the approval of the product. The PGR establishes certain restrictions to control access to the product:*

- The sale is made exclusively to hospital institutions that have an obstetric service.
- Hospitals complete special forms for the purchase of the medicine, reporting on the use of the medicinal product and the average number of deliveries in the institution.
- The sponsoring laboratory informs ANMAT of the movements of the product and the data collected in the drug purchase forms.”

It is not known whether the Misop 200® has been subject to similar controls, or whether this would apply to other medical abortion drugs products in the future.

## 9. PROCUREMENT AND DISTRIBUTION MECHANISMS

### 9.1. FORECASTING REQUIREMENTS

In Argentina, estimates for the number of abortions performed annually reflect a wide range according to the different methodologies implemented, compounded by underreporting in official statistics.

The estimation for acquisition of misoprostol, as well as all other abortion related supplies, is performed by the working group of pregnancy interruption access of the National Directorate of Sexual and Reproductive Health, with technical assistance from UNFPA. Forecasts are primarily based on hospital discharge data, where the recorded diagnosis at discharge was abortion. Whilst mifepristone is already included in Ministry of Health guidelines for some indications, it has not been included in previous calculations because it has not been registered or authorised for sale in the country. To date, no known forecasts have been undertaken for mifepristone, however it may be easier to estimate these volumes more accurately as a single tablet is required per total estimated medical abortions number.

In 2020, this working group forecasted the number of abortions in public sector facilities during 2020 to be 97,562, and the number across facilities in all sectors to be 168,835. Accordingly, they forecasted the number of misoprostol tablets required to meet these needs in public health facilities to be 1,170,750. For the needs of public, private and social security sectors, they forecasted 2,026,025

would be required, or nearly double. Assumptions included that medical abortion would be provided by misoprostol-only regimen, on average using 12 misoprostol 200mcg tablets per treatment [40].

Despite this, it was recorded that the national government acquired 35,000 treatments, or 420,000 misoprostol tablets, in 2020.

There is no publicly available sales information regarding the private or social security sectors, nor whether there is a market trend for misoprostol. Sales volume data of commercial products may however be purchased at some expense. Understanding the market potential for new medical abortion medicines is made more difficult by the fact that abortion care is to be provided free of charge across all sectors, and how this will be arranged is still under discussion.

The complexity of forecasting medical abortion supplies is likely to further increase with the expected rise in demand across all sectors following implementation of the new abortion law, as well as new products entering the supply chain. Prudent forecasting and regular review will be necessary to ensure commodity security during the coming years. Modifications to health statistic reporting codes may be required to accurately record different categories of abortion care in all provinces, and to improve the reliability of medical abortion product forecasting.

## 9.2. PROCUREMENT MECHANISMS

The national government procures medical abortion products for the public sector to be distributed among the different provinces. There are a few provinces that procure misoprostol independently in small quantities.

For a medicine to be included in public procurement and distributed routinely to health facilities, it must be included in the essential medicines list of the Ministry of Health's national program, *Programa Remediar*. Whilst misoprostol 200mcg tablets are not yet included in this list, an exception has been made in recent years to procure and distribute to the provincial Ministries of Health, and it is included in public sector tender listings for abortion. Considering the new abortion law, misoprostol and mifepristone are both expected to be added to the *Programa Remediar* essential list.

Similarly, there is an essential care package (*Paquete Médico Obligatorio*) of medical procedures and medicines that social security and private insurance companies are obliged to provide. Per the new abortion law, this will now include medical abortion and therefore the relevant medicines are expected to be added to the *Formulario Terapéutico*.

For a drug product to be procured for any health sector, the product has to be registered and approved by ANMAT.

Laboratorio Domínguez is the only manufacturer producing misoprostol and currently complying with all ANMAT requirements. Public laboratories primarily supply to the public health sector, however, may be able to sell certain products commercially in pharmacies if they obtain appropriate authorisations from ANMAT and relevant provincial authorities. LIF, Santa Fe's public laboratory, has a misoprostol product now approved by ANMAT, however is still completing stability requirements. Once this requirement is completed LIF can participate in public sector procurement processes and public tenders. Up to March 2021, no mifepristone or combipack products have been registered by ANMAT and are available for public procurement.

The national government is currently engaged in talks with UNFPA about the possibility of acquiring medical abortion medicines as well as contraceptives through their procurement branch. Meanwhile, IPPFWHR [41] has announced the donation of 35,000 packs of Medabon® from Sun Pharma/Ranbaxy. In these cases, a waiver from ANMAT is required for each medicine batch that enters the country. The waiver process is regulated by National Decree 150/92, and includes evaluation of each batch before being distributed, although noting that waiver requirements differ depending on which countries the product is registered in.

To participate in public tenders, the supplier, which can either be a manufacturer or distributor, needs to be registered as a provincial provider, the requirements of which differ among the provinces.

The national government establishes a fixed price for medicines included in the public tender.

The *Área de Aseguramiento de Insumos* (Commodity Security Area) of the National Directorate of Sexual and Reproductive Health published a procurement procedures guideline in 2020, which applies to procurement in the public sector [42]. The guideline outlines the criteria and basic procedures for competitive procurement through public tender, private tender, and emergency procurement, and non-competitive procurement in case of single source supply. The guideline is in line with relevant national procurement regulations, referenced as follows:

- Res SIGEN 36/2016 y modif. (Res SIGEN 228/216)
- Dto 820/2020, modificadorio del Dto. Reglamentario 1030/2016
- Disp. ONC 62/2016 “Manual de Procedimiento para Contrataciones públicas”
- Manual de Procedimiento Compr.ar; Anexo de la Disposición ONC N° 65/2016
- Decreto N° 1023/2001 y su similar reglamentario N° 1030/2016, y modificatorios
- Ley 27.437
- Decreto Reglamentario 800/2018
- Resolución 91/2018
- Decreto 963/2018

Procurement processes followed in the private and social security sectors are heterogenous and not clearly known, although may involve many negotiating actors in the supply chain, as shown in the following section.

### 9.3. DISTRIBUTION AND COMMERCIALISATION

Figure 3 illustrates the flow of products in the Argentinian market from manufacturer through to the consumer [26]. The main actors involved are laboratorios (manufacturers), distribuidoras (distributors), droguerías (drugstores), mandatarias (agents) and farmacias (pharmacies).

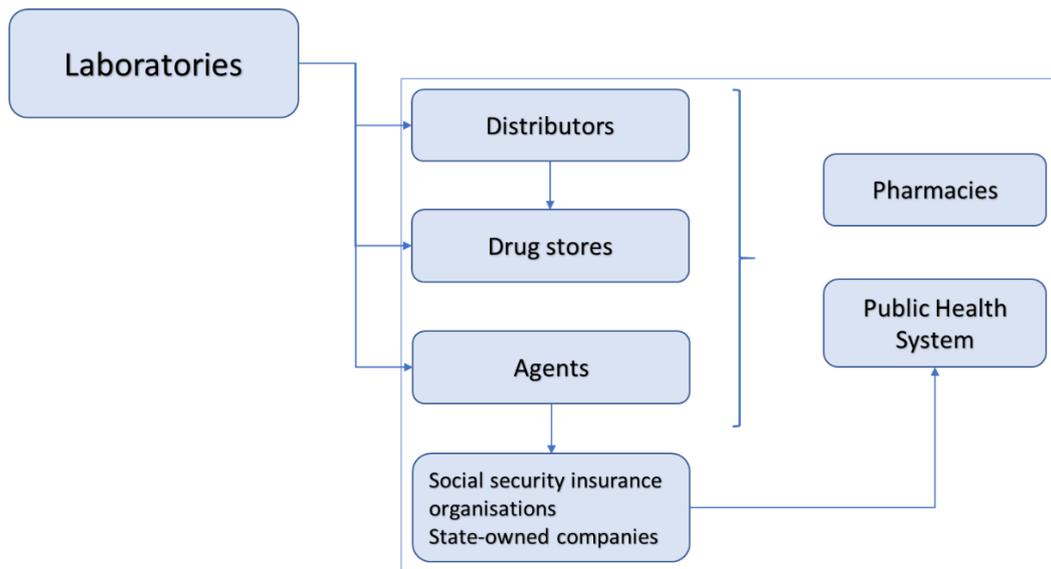


Figure 3 Pharmaceutical distribution and commercialisation supply chain (reproduced from ICEX España Exportación e Inversiones. *El mercado farmacéutico en Argentina. Oficina Económica y Comercial de la Embajada de España en Buenos Aires. 2019*) [26]

*Distribuidoras* (distributors) belong to one or more manufacturing companies and their main function is the distribution of medicines from laboratories to drugstores (or wholesalers), although some laboratories sell directly with pharmacies. There are 107 distributors currently licenced to operate in Argentina, however four main distributors cover 99% of the market: Rofina; Disprofarma; Farmanet, and; Globalfarm [43].

The main task of *droguerías* (drugstores) is the intermediation of pharmaceutical products between distributors or laboratories and pharmacies. In Argentina, according to data from the Ministry of Economics, there are 445 registered drugstores, of which three cover around 60% of the market (in order of size): Droguería del Sud; Droguería Monroe Americana (MASA); Suizo Argentina[26].

*Mandatarias* act as agents in charge of the negotiation and reaching agreements between all the industry players, such as the social security insurance companies, the private prepaid companies, hospitals, and other related agencies.

*Farmacias* (pharmacies) have traditionally followed the model of small independent businesses, however in recent years, pharmacy chains have started to develop and increase in market share. To increase negotiating power with other entities in the supply chain, pharmacies are grouped into colleges or associations.

The commercial margins of pharmacies and drugstores are decided by the manufacturer. Drugstores buy the products to laboratories with a fixed discount of 31% on the retail price, although can obtain further discounts of up to 8%, totally up to 39%. Pharmacies get an initial discount of 20% on the retail price plus additional discounts that reach 11%, so can obtain a total discount of 31%. Finally, customers with insurance from a social security or prepaid private company pay 60% of the price, with the other 40% covered by their insurer.

In the public sector supply chain, following procurement, products go from the manufacturer +/- distributor and/or drugstore to the logistics operator of *Programa Remediar*. The logistics operator distributes the products to health centres and hospitals. Users receive those products free of charge

at public facilities. The usual process is shown in Figure 4 below. In case it is a provincial manufacturer supplying to its home province, the manufacturer would usually supply directly to the provincial logistics operator.

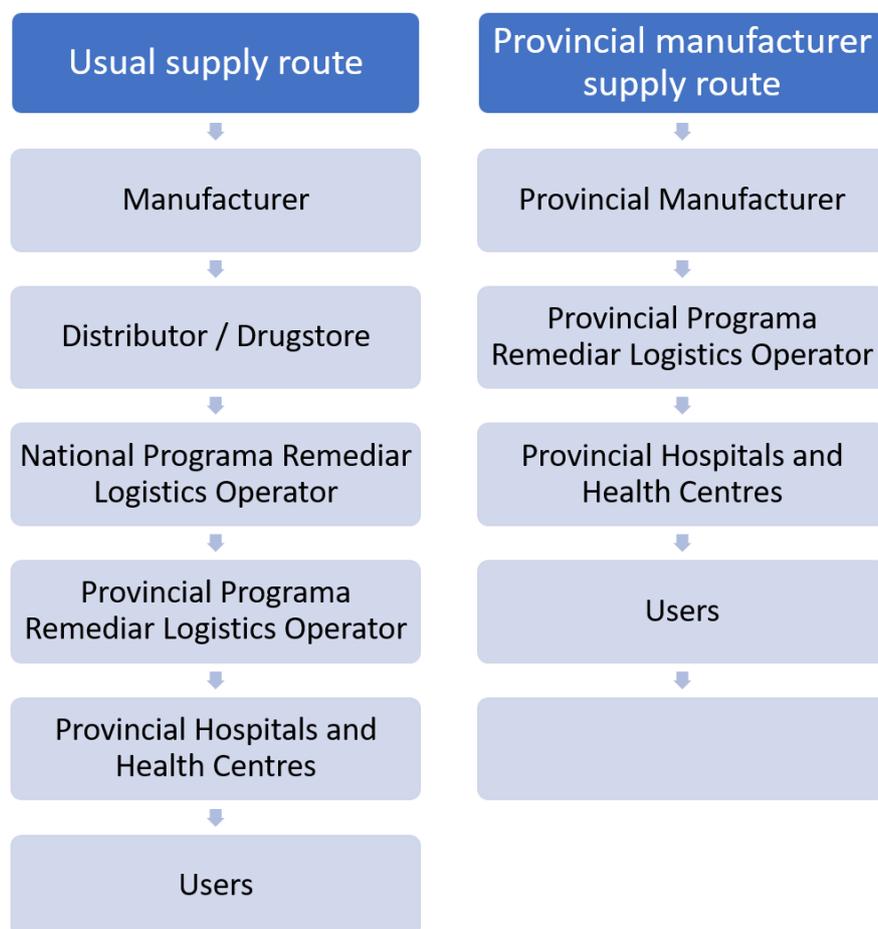


Figure 4. Journey of products in the public sector supply chain

Supply in the public sector operates by a “push mechanism”, whereby the Programa Remediar decides the quantity of products to be distributed to the facilities. Facilities can request adjustments as necessary.

Medical institutions or foundations can buy medicines from distributors or manufacturers directly, provided that the institution states in its by-laws that it provides healthcare services. If an independent clinic or provider has a licenced pharmacist on staff, they may also buy direct from distributors. However, smaller providers do not commonly meet this criterion and therefore would purchase medicines directly from pharmacies at retail prices or send their clients to pharmacies with a prescription.

Anecdotally, stockouts are known to occur from time to time for contraceptives. It is not known if this is common for misoprostol products. Informal interviews with several pharmacies in Buenos Aires indicated that Misop 200® is readily available, or if they stock out can usually be resupplied rapidly by their distributors. In other regions, availability of misoprostol in pharmacies has not been studied.

Argentina is largely a subtropical or temperate climate, and there are not known to be challenges adhering to recommended storage conditions along the supply chain that might affect the quality of medical abortion medicines.

## 10. TRAINING IN MEDICAL ABORTION

The process of training for safe abortion care is very heterogenous in Argentina and requires significant and urgent attention.

There is no formal requirement to be trained in abortion care as part of gynaecological or obstetric training. Depending on the institution, residents receive training in medical and/or surgical abortion including MVA. There have been trainings at national conferences for such specialists.

For family or general specialists, the national association is very committed to sexual and reproductive health and rights. They have offered training mostly in medical abortion. Some practitioners have been trained to perform MVA.

For midwives, nurses, pharmacists, none of these groups are currently allowed to prescribe medical abortion or carry out procedures, so training has been very limited.

Training is the most common request of health services and managers in relation to provision of medical abortion. Training needs to be provided to physicians as a matter of priority. Whilst other healthcare professionals are not permitted to perform abortions, training needs according to their respective roles in abortion care should similarly be assessed. In general, trainees are selected by local authorities and chief of services. Identified priority areas for training include abortion guidelines, counselling, pain management, MVA procedure, and second trimester abortion.

REDAAS (Safe Abortion Access Network) [44] has been providing training on safe abortion services for many years in Argentina. They have partnered with provincial and national government to develop materials and provide training on clinical procedures, counselling, and other guideline areas. Ipas has provided support and have trained many REDAAS members.

It is anticipated that some updates to training materials will be required in light of the new regulations, and in the future with the anticipated introduction of mifepristone.

## 11. KEY STAKEHOLDERS TO FACILITATE INTRODUCTION OF MA PRODUCTS

Key stakeholders that should be consulted in relation to the introduction of medical abortion medicines in Argentina are expected to include those below.

Table 10: Key stakeholders for the introduction of medical abortion medicines in Argentina

| Government agencies   | Professional associations  | UN agencies and NGOs   |
|---|--|--|
| <ul style="list-style-type: none"> <li>• National Director of Sexual and Reproductive Health</li> <li>• ANMAT (National Medicines Regulatory Agency)</li> <li>• President of ANLAP (National Agency of Public Laboratories)</li> <li>• Chief of Staff of the Minister of Health, former Secretary of Medicines</li> <li>• Programa SUMAR</li> <li>• Programa REDES</li> <li>• Superintendencia de Servicios de Salud</li> </ul> | <ul style="list-style-type: none"> <li>• Federación Argentina de Sociedades de Ginecología y Obstetricia (FASGO)</li> <li>• Sociedad de Obstetricia y Ginecología de Buenos Aires (SOGIBA)</li> <li>• Federación Argentina Medicina General (FAMG)</li> <li>• Asociación de Mujeres en Energías Sustentables (AMES)</li> <li>• Asociación Médica Argentina de Anticoncepción (AMADA)</li> <li>• Sociedad Argentina de Ginecología Infanto Juvenil (SAGIJ)</li> <li>• Federation of Midwives of Argentina (FORA)</li> <li>• Red de Profesionales por el Derecho a Decidir</li> <li>• Red de Acceso al Aborto Seguro (REDAAS)</li> <li>• La Fundación para Estudio e Investigación de la Mujer (FEIM)</li> </ul> | <ul style="list-style-type: none"> <li>• UNFPA</li> <li>• UNICEF</li> <li>• PAHO</li> <li>• Latin America Consortium Against Unsafe Abortion (ForoLAC)</li> <li>• ESAR</li> <li>• IPPFWHR</li> </ul> |

## 12. ENABLERS / BARRIERS TO INTRODUCTION

The introduction in Argentina of quality-assured mifepristone and misoprostol products for medical abortion will require careful negotiation of historical and more recent barriers to ensure access to these politically contentious products.

However, with the enactment of the landmark law legalising voluntary abortion, arguably the biggest historical barrier to introduction of these medicines has now been transformed into one of the biggest enablers. Not only has the right to access to safe abortion services been ratified, but the law mandates that comprehensive abortion care is provided in line with protocols recommended by WHO. This should provide further incentives to support and prioritise the approval and introduction of the most safe and effective medical abortion product for women in the first trimester, the misoprostol and mifepristone combipack.

A 2019 investigation report titled *Uso y acceso a Misoprostol y Mifepristona en tres países de América Latina: Argentina, Ecuador y Perú* (Mapping the use and access to Misoprostol and Mifepristone in three Latin American countries: Argentina, Ecuador and Peru), noted the below barriers and enablers to use and access.

Table 11: Barriers and enablers to use and access of misoprostol and mifepristone in Argentina, Ecuador and Peru (2019) [45]

|   |   |
|---|---|
| <p><b>Barriers to access – Misoprostol</b></p> <ul style="list-style-type: none"> <li>• Production constraints – e.g. monopoly, requirements imposed by pharmaceutical companies.</li> <li>• Conditionality for supply – e.g. need for prescriptions, refusal by providers and pharmacists.</li> <li>• Clandestine nature – e.g. potential for diversion, impact of black market</li> <li>• High cost of purchase.</li> </ul> | <p><b>Enablers to access – Misoprostol</b></p> <ul style="list-style-type: none"> <li>• Registration of misoprostol product (without diclofenac).</li> <li>• Law debate has increased availability of information about products, and demand.</li> <li>• Allied networks facilitating procurement (financing).</li> <li>• Suppliers (manufacturers) facilitating access.</li> <li>• Increased information available to public.</li> <li>• Alliances between collectives.</li> </ul> |
| <p><b>Barriers to access – Mifepristone</b></p> <ul style="list-style-type: none"> <li>• Absence of registration.</li> <li>• Cost when available.</li> </ul>  | <p><b>Enablers to access – Mifepristone</b></p> <ul style="list-style-type: none"> <li>• To be determined.</li> </ul>   |

The past 5 years has seen both unsuccessful and then successful misoprostol product registration applications with the national medicines regulator, ANMAT. As was concluded in the 2017 study, *Mifepristone y misoprostol en seis países de América Latina: procesos de registro y disponibilidad* (Mifepristone and misoprostol in six Latin American countries: registration processes and availability), the analysis of the processes that allowed or did not allow for the authorisation of the corresponding registrations can become valuable knowledge for facilitating future strategies of new MA product registrations [46]. For example, the study indicated that an in vivo bioequivalence study for misoprostol was not required and highlighted the value of additionally including less contentious indications such as prevention of post-partum haemorrhage.

Further barriers concerning the registration of quality-assured misoprostol and mifepristone products may include:

- Misoprostol and mifepristone not yet listed on national essential medicines lists or formularies.
- No formal recognition of WHO prequalified products, nor access to WHO Collaborative Registration Procedure.
- Limited participation to date in international medical abortion medicine quality initiatives.
- Lack of clarity about regulatory requirements for registration of medicines which are yet to be introduced to the country such as mifepristone and the combipack.
- Lack of consistent bioequivalence and clinical data requirements of stringent regulatory agencies and WHO PQP for misoprostol and combipack product approvals.
- Difficulty identifying suitable reference products which are marketed in highly regulated countries with indications and dosages in line with WHO recommendations.
- Lack of requirement to demonstrate bioequivalence means that lower quality products could potentially be registered.
- The high cost of quality-assured mifepristone API, and the unwillingness of API manufacturers to supply their API due to competition concerns.

Beyond registration, the prior introduction of misoprostol products for gynaecological indications in Argentina should provide a roadmap of how to successfully introduce highly effective medical abortion products additionally containing mifepristone throughout the country's health system.

Key enablers for access to quality medical abortion medicines include:

- Destigmatization of accessing abortion by the general population.
- Comprehensive and evidence-based clinical care guidelines which are already in place and regularly updated.
- Potential improvement of prescriber information leaflets specific to medical abortion indications.
- Increase of information in the public domain on safe abortion care and specifically medical abortion regimens.
- Competitive price of quality assured products.
- Prior adoption of misoprostol into the national and provincial supply chains.
- Motivated and supportive national health authorities and civil society.

Notable barriers include:

- Persistence of contrary political motivations, religious or conservative factors.
- Decentralized health system slowing implementation of new products and new clinical practices.
- Lack of professional training on the combined medical abortion regimen and the management of any complications or failures.
- Health public budget constrains if price is considered high.

## 13. CONCLUSIONS AND RECOMMENDATIONS

Whilst misoprostol tablets have been available in Argentina now for several years, the legal status of abortion has prevented widespread availability of safe medical abortion care. With the enactment of Law 27610, there is now clear political and social support for the introduction of products to Argentina that will offer Argentinian women the safest and most effective products available.

The following points have been noted in the paper:

- Law 27610 now mandates the provision of free comprehensive abortion care across Argentina, in line with WHO best practice clinical recommendations.
- Whilst two manufacturers are now making misoprostol products available, the addition of mifepristone will significantly increase the efficacy and safety of the medical abortion regimen.
- Whilst the regulatory requirements of medicines in Argentina are publicly available, specific guidance for misoprostol and mifepristone products would assist in accelerating the product development and registration time.
- Accurate forecasting of medical abortion product requirements is complicated by clinical data limitations and underreporting, and needs will change significantly with the new law and the introduction of mifepristone products.
- Good clinical guidelines are already in place which include mifepristone and are now being updated to reflect the new legal status.
- Familiarity of clinical guidelines amongst healthcare providers appears low.

To enable the rapid and sustainable introduction of quality assured medical abortion products, the following may be considered:

- Request to ANMAT for import waiver for immediate supply of mifepristone-only or combipack products registered in Annex I countries.
- Collaboration between ANMAT and manufacturers to clarify specific regulatory requirements for medical abortion products.
- Encouragement to mifepristone and combipack manufacturers holding marketing authorizations in Annex I countries to immediately initiate marketing authorization applications in Argentina via the Article 4 route.
- Technical support to local manufacturers in the development of quality-assured medical abortion products.

- Identification of most appropriate reference products for product development and to carry out equivalence studies that will allow prescribing in line with WHO recommendations.
- Careful forecasting of needs of medical abortion products across all sectors, with regular review to ensure commodity security as demand increases and new products are introduced.
- Rapid scale up of training of healthcare professionals to meet the requirements of the new law and increase the support of healthcare professionals.

A key stakeholder meeting would be invaluable in further identifying issues and proposing strategies to facilitate the rapid and sustainable availability of medical abortion products in Argentina.

## REFERENCES

- [1] IPAS, “Clinical Updates in Reproductive Health,” Chapel Hill, NC, 2020. [Online]. Available: [www.ipas.org/clinicalupdates](http://www.ipas.org/clinicalupdates).
- [2] World Health Organization Reproductive Health and Research, “GAPD - The Global Abortion Policies Database,” *GAPD - The Global Abortion Policies Database*. <https://abortion-policies.srhr.org/>.
- [3] P. A. R. Calvert, R. C. Eidt, and T. H. Donghi, “Argentina | History, Facts, Map, & Culture | Britannica.” <https://www.britannica.com/place/Argentina> (accessed Apr. 12, 2021).
- [4] “Health in the Americas 2017: Argentina,” 2017. <https://www.paho.org/salud-en-las-americas-2017/?p=2706>.
- [5] CEDES, “E-health to foster adolescents’ agency and access to sexual and reproductive services and supplies.”. [Online]. Available: [https://www.rhsupplies.org/fileadmin/uploads/rhsc/Uploads/Other/Webinar\\_Background.pdf](https://www.rhsupplies.org/fileadmin/uploads/rhsc/Uploads/Other/Webinar_Background.pdf).
- [6] United Nations Development Programme, “Human Development Reports,” 2019. <http://hdr.undp.org/en/countries/profiles/ARG>.
- [7] E. Martich, “Access to contraceptives in Argentina and Brazil,” Kathmandu, 2019. [Online]. Available: [https://www.rhsupplies.org/fileadmin/uploads/rhsc/General\\_Membership\\_Meetings/Kathmandu\\_2019/Presentations/Day\\_3/Parallel\\_Sessions/Access\\_to\\_contraceptives\\_in\\_Argentina\\_and\\_Brazil\\_-\\_Evangelina\\_Martich.pdf](https://www.rhsupplies.org/fileadmin/uploads/rhsc/General_Membership_Meetings/Kathmandu_2019/Presentations/Day_3/Parallel_Sessions/Access_to_contraceptives_in_Argentina_and_Brazil_-_Evangelina_Martich.pdf).
- [8] United Nations - Department of Economic and Social Affairs, “Contraceptive Use by Method 2019 - Data Booklet,” *Contracept. Use by Method 2019*, p. 25, 2019, [Online]. Available: [https://www.un.org/development/desa/pd/sites/www.un.org.development.desa.pd/files/files/documents/2020/Jan/un\\_2019\\_contraceptiveusebymethod\\_databooklet.pdf](https://www.un.org/development/desa/pd/sites/www.un.org.development.desa.pd/files/files/documents/2020/Jan/un_2019_contraceptiveusebymethod_databooklet.pdf).
- [9] L. López *et al.*, “Estimación de la magnitud del aborto inducido en la Argentina,” 2009. [Online]. Available: <https://repositorio.cepal.org/handle/11362/12842>.
- [10] O. Panamericana de la Salud and A. Ministerio de Salud de la Nación, “Segundo informe nacional de relevamiento epidemiológico SIP-Gestión,” 2018. [Online]. Available: <https://iris.paho.org/bitstream/handle/10665.2/49147/9789275320129-spa.pdf?sequence=3&isAllowed=y>.
- [11] “Dirección de Estadísticas e Información de la Salud | Argentina.gob.ar.” <https://www.argentina.gob.ar/salud/deis>.
- [12] Secretaría de Salud. Municipalidad de Rosario s/f., “Análisis de la problemática del aborto en la Red de Salud Pública Municipal.”
- [13] A. Aguerrido *et al.*, “Salud sexual y reproductiva en la Ciudad de Buenos Aires,” 2019. [Online]. Available: [https://www.buenosaires.gob.ar/sites/gcaba/files/situacion\\_y\\_respuesta\\_en\\_ssyrr.\\_caba\\_2019\\_para\\_publicar.pdf](https://www.buenosaires.gob.ar/sites/gcaba/files/situacion_y_respuesta_en_ssyrr._caba_2019_para_publicar.pdf).

- [14] Ministerio de la Salud de la Provincia de Buenos Aires, “Estrategia de implementación de la interrupción legal del embarazo en la Provincia de Buenos Aires,” 2020. [Online]. Available: <http://www.ms.gba.gov.ar/sitios/media/files/2020/09/Informe-de-gestión-Estrategia-de-implementación-de-la-interrupción-legal-del-embarazo-en-PBA.-Enero-junio-2020.pdf>.
- [15] Argentina InfoLEG - Ministerio de Economía y Finanzas Públicas, “Ley N° 11.179 Código Penal de la Nación.” <http://servicios.infoleg.gob.ar/infolegInternet/anexos/15000-19999/16546/norma.htm>.
- [16] Ministerio de Salud y Ambiente, “Resolución 989/2005 | Argentina.gob.ar,” 2005. <https://www.argentina.gob.ar/normativa/nacional/resolución-989-2005-108813>.
- [17] REDAAS, *Access to the Voluntary Termination of Pregnancy Law No. 27,610 1 Dispositions*. 2021.
- [18] “Ley N° 27.610 - Acceso a la Interrupción Voluntaria del Embarazo (IVE), obligatoriedad de brindar cobertura integral y gratuita | Argentina.gob.ar.” <https://www.argentina.gob.ar/noticias/ley-no-27610-acceso-la-interrupcion-voluntaria-del-embarazo-ive-obligatoriedad-de-brindar>.
- [19] Ministerio de Salud de la Nación Argentina, “Guía para la atención integral de mujeres que cursan un aborto,” 2014. [Online]. Available: <http://www.ms.gba.gov.ar/sitios/tocoginecologia/files/2014/09/Guía-para-la-atención-integral-de-mujeres-que-cursan-un-aborto.pdf>.
- [20] Ministerio de Salud y Ambiente, “Protocolo para la atención integral de las personas con derecho a la interrupción legal del embarazo,” 2019. [Online]. Available: <http://iah.salud.gob.ar/doc/433.pdf>.
- [21] Ministerio de Salud y Ambiente, “Anexo III: Formulario Terapéutico.” <https://www.argentina.gob.ar/normativa/recurso/73649/res201-2002MS-anexoIII/htm>.
- [22] Ministerio de Salud y Ambiente, “Resolución 201/2002,” 2002. <https://www.argentina.gob.ar/normativa/nacional/resolución-201-2002-73649>.
- [23] Ministerio de Salud ANMAT, “Guía de Medicamentos Esenciales en el Primer Nivel de Atención.” <https://www.argentina.gob.ar/salud/remediar/guia-medicamentos-esenciales-pna>.
- [24] M. Romero and Y. Silvina Moisés, “El Aborto en Cifras,” Buenos Aires, 2020. [Online]. Available: [http://www.redaas.org.ar/archivos-actividades/187-El aborto en cifras, 2020 - MR y SM - REDAAS.pdf](http://www.redaas.org.ar/archivos-actividades/187-El%20aborto%20en%20cifras,%202020%20-%20MR%20y%20SM%20-%20REDAAS.pdf).
- [25] M. Monteverde and S. Tarragona, “Abortos seguros e inseguros: Costos monetarios totales y costos para el sistema de salud de la Argentina en 2018,” *Salud Colect.*, vol. 15, p. e2275, Jan. 2020, doi: 10.18294/sc.2019.2275.
- [26] ICEX, “El mercado de la Siderurgia en Argentina,” no. El mercado de la Siderurgia en Argelia, pp. 1–6, 2019, [Online]. Available: <https://www.icex.es/.../GetDocumento?...%0AT>.
- [27] ANMAT, “Vademécum Nacional de Medicamentos.” <https://servicios.pami.org.ar/vademecum/views/consultaPublica/listado.zul>.

- [28] Laboratorio Industrial Farmaceutico (LIF), "ANMAT aprobó el Misoprostol fabricado por el LIF," 2021. <http://www.lif-santafe.com.ar/noticias/584/anmat-aprobo-el-misoprostol-fabricado-por-el-lif.html>.
- [29] Reproductive Health Supplies Coalition, "ForoLAC (Latin American and Caribbean Forum for the Assurance of SRH Supplies)." <https://www.rhsupplies.org/activities-resources/groups/forolac/>.
- [30] "FEIM – Fundación para Estudio e Investigación de la Mujer." <http://feim.org.ar/>.
- [31] Laboratorio Dominguez S.A., "MISOP 200 MISOPROSTOL 200 µg Comprimidos ranurados vaginales INDUSTRIA ARGENTINA VENTA BAJO RECETA ARCHIVADA," 2018. [Online]. Available: [http://www.labdominguez.com.ar/prospectos/55\\_2289\\_MIsop\\_200.pdf](http://www.labdominguez.com.ar/prospectos/55_2289_MIsop_200.pdf).
- [32] "ANMAT | Argentina.gob.ar." <https://www.argentina.gob.ar/anmat>.
- [33] Ministerio de Salud ANLAP, "Lista actualizada de laboratorios." <https://www.argentina.gob.ar/anlap/laboratorios>.
- [34] "MERCOSUR - Official website." <https://www.mercosur.int/en/>.
- [35] "Pharmaceutical Inspection Co-operation Scheme PIC/S." <https://picscheme.org/en/picscheme>.
- [36] Ministerio de Salud ANMAT, "Aranceles vigentes de los trámites ante ANMAT," 2021. <https://www.argentina.gob.ar/anmat/regulados/aranceles>.
- [37] P. A. H. Organization, "Framework for Implementation of Equivalence Requirements for Pharmaceutical Products," *PANDRH Tech. Rep. Ser. N°8*, 2011. [Online]. Available: <https://www.paho.org/hq/dmdocuments/2011/Series-Red-PARF-8--Eng.pdf>.
- [38] Ministerio de Salud ANMAT, "Acerca del Sistema Nacional de Farmacovigilancia." <https://www.argentina.gob.ar/anmat/farmacovigilancia/quees>.
- [39] "Sistema Nacional de Farmacovigilancia: Misoprostol." <http://www.anmat.gov.ar/farmacovigilancia/Misoprostol.asp>.
- [40] G. Hamilton and M. Malena, "Misoprostol: Estimación de la cantidad a adquirir por la DSSR durante el año 2020," *UNFPA*, no. 2009, pp. 2018–2020, 2020.
- [41] "International Planned Parenthood Federation Western Hemisphere." <https://www.ippfwhr.org/>.
- [42] Area Aseguramiento de Insumos, "Guía de procedimiento de Compras," 2020.
- [43] Ministerio de Salud ANMAT, "Listado de empresas habilitadas como distribuidoras y/u operadores logísticos de medicamentos," p. 6, 2021.
- [44] "REDAAS - Access to Safe Abortion Network." <http://www.redaas.org.ar/english>.
- [45] E. Juárez Chávez and M. Gonzalez, "Barreras y Facilitadores para el uso y acceso a Misoprostol y Mifepristona en tres países de América Latina," 2019.. [Online]. Available: <https://clacaidigital.info/handle/123456789/1240>.
- [46] CLACAI, "Mifepristona y misoprostol en seis países de América Latina: procesos de registro y disponibilidad Informe proyecto de indagación," 2017. [Online]. Available: [www.clacai.org](http://www.clacai.org).