SEMA
REPRODUCTIVE HEALTH

SEMA Medical Abortion Market Assessment and Recommendations Summary

Preventing unsafe abortions for enhanced sexual and reproductive health and rights

JULY 2023

Increasing equitable access to sexual and reproductive health (SRH) products is critical to saving lives, promoting gender equality, and advancing communities

About SEMA

Global efforts in the last decade have enabled 60 million additional women and girls to access SRH products. However, these efforts still fall short at meeting consumer needs, particularly the needs of communities in LMICs.

To address the challenges, a multi-stakeholder Steering Committee undertook a consultative process from 2020 to 2021. The committee engaged with over 100 stakeholders globally to envision how to support healthier, more equitable, and more resilient markets for sexual and reproductive health. The group consisted of country leaders, public and private implementers, civil society members, donors, and market representatives who came together to create Shaping Equitable Market Access for Reproductive Health, or SEMA Reproductive Health.

SEMA was announced in July 2021, during the Generation Equality Forum in France, and is currently being incubated within Amref Health Africa. The initiative received support from country governments in Burkina Faso, Nigeria, and Uganda, as well as strategic partnerships from the United States Agency for International Development (USAID), the Foreign, Commonwealth and Development Office of the United Kingdom (FCDO), the United Nations Population Fund (UNFPA), and the Reproductive Health Supplies Coalition (RHSC). Additionally, the Children's Investment Fund Foundation (CIFF), Gates Foundation and the French Ministry for Europe and Foreign Affairs (MEAE) provided initial funding for SEMA.

SEMA currently acts as a collaborative platform and financing vehicle that works with partners across the entire ecosystem of sexual and reproductive health. The initiative aims to better coordinate donor investments, leverage existing expertise, build additional capacity, and optimize limited resources to support healthier markets. By fostering collaboration and coordination, SEMA seeks to optimize resources and achieve greater impact in pursuit of our shared goals.

TABLE OF CONTENTS

01
Introduction

Access to sexual and reproductive health (SRH) services and products can transform the lives of women and girls. Access is currently undermined by a range of factors, including restrictive policies, weak health systems, misinformation, poor counseling and social stigma. In addition to these barriers, **inadequate product availability and choice** is also a critical and growing constraint to faster progress in many countries.

Shaping Equitable Market Access for Reproductive Health (SEMA) was established to transform markets for SRH products. SEMA envisions a world where SRH markets in low- and middle-income countries (LMICs) are healthy, equitable and resilient. In the envisioned world, all people, especially women and adolescent girls, can access the reproductive health products they need.

SEMA has partnered with country and global SRH stakeholders to identify the market challenges that are hindering access to SRH products and to develop interventions to address those challenges. Through this work, SEMA aims to catalyze action to transform private and public markets to better meet SRH needs.

02
The MA Landscape

The MA Landscape

Each year, an estimated 25 million unsafe abortions occur worldwide, with 97% occurring in developing countries in Africa, Asia, and Latin America.[1] Unsafe abortion results in over 22,000 deaths every year and 7 million women experience serious complications and injuries from unsafe abortion annually.[2] Increasing access to contraception and safe abortion services saves lives by reducing unintended pregnancies and unsafe abortion procedures.

Medical abortion (MA) is an effective and safe option for termination of pregnancy. Since MA drugs can be made available at lower levels of the health system (e.g., pharmacies) and can be taken at home, MA can offer women greater discretion, autonomy, and accessibility than the surgical alternatives.

More specifically, MA Combipack (co-packaged mifepristone and misoprostol) and misoprostol alone provide women with safe, highly effective methods for pregnancy termination. This includes induced abortion, missed abortion, and intrauterine fetal demise. misoprostol is also recommended for post-abortion care uses including incomplete abortion.

In late 2022, SEMA commissioned a comprehensive MA market assessment using SEMA's Healthy Markets Framework (HMF)[3]. This document summarizes key findings from the assessment, including the following primary takeaways:

Key takeaways

- MA Combipacks are the preferred regimen for MA, but misoprostol alone continues to be more affordable and more widely available due to its multiple indications. Of the 18 million safe MAs and post-abortion care services performed in low- and middle-income countries (LMICs) each year, an estimated 8.7 million are MAs that use a combination of mifepristone and misoprostol. Meanwhile 9.3 million use misoprostol alone.[4] Therefore, both products have an important role to play in increasing the accessibility of MA overall.

- Factors such as restrictive laws and policies, as well as social and cultural barriers, have historically contributed to limited demand for MA products and continue to do so.

- Quality continues to be a major concern for both MA Combipacks and misoprostol where products are not pre-qualified (PQ) by the World Health Organization (WHO) or else approved by a Stringent Regulatory Authority (SRA). Affordability is also a concern, specifically for WHO PQ/ SRA-approved MA Combipacks. Therefore, the focus of global market shaping has been to increase the availability of affordable, WHO PQ/ SRA-approved MA Combipacks.

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[1] Worldwide, an Estimated 25 Million Unsafe Abortions Occur Each Year | Guttmacher Institute
[2] https://www.researchgate.net/publication/331633813_Uneven_Progress_and_Unequal_Access
[3] The assessment was led by the Clinton Health Access Initiative (CHAI) and drew upon extensive research and stakeholder consultations to identify key market shortcomings and propose interventions for their mitigation
[4] https://leap.rhsupplies.org/#/abortion

- There has been significant progress made to increase the availability of affordable WHO PQ/SRA-approved MA Combipacks. However, limited procurement of such products potentially threatens these gains and presents a significant barrier to achieving a healthy MA market in the near-term.

- In order to address the wide-ranging and inter-connected shortcomings in the market, a comprehensive set of interventions are recommended.

Key Recommendations

1. Demand-side interventions, such as funding of advocacy, introduction, and support for national governments to coordinate the scaling of quality comprehensive abortion care (CAC) services
2. Ongoing efforts to secure sufficient manufacturers in the market and improve affordability of MA Combipacks. This will depend in significant part on the success of demand-side efforts.
3. Improvements in data and market intelligence
4. Strengthened market coordination both globally and nationally.

- Some of these recommendations, such as data and coordination, apply to the SRH product sector as a whole and will be better delivered through a cross-cutting, multi-product approach.

03
MA Market Assessment Scope & Background

Assessing in-scope MA products

For medical management of induced abortion, the WHO recommends the use of a combination regimen of mifepristone and misoprostol, or the use of misoprostol alone. The WHO also suggests[5] a combination regimen of Letrozole plus misoprostol. For the medical management of post-abortion care, the WHO recommends the use of misoprostol.[6]

Guided by the WHO recommendations, the SEMA MA market assessment focuses on assessing the MA Combipack (i.e., the co-packaged presentation of mifepristone and misoprostol) and misoprostol products. As underscored in those recommendations and reinforced in stakeholder consultations, it is critical to consider MA Combipack and misoprostol as a basket of MA product options to meet end-user needs in all LMICs across varied legal and political environments.

A high-level summary on the Letrozole and misoprostol combination regimen is also included in the appendix for reference. However, the HMF assessment was not completed for this regimen since it is 'suggested' but not yet 'recommended' by the WHO given the current level of evidence.

Geographically, the assessment is specifically focused on LMICs.[7] However, it also considers the broader global market, reflecting the perspective and supply decisions of manufacturers.

This assessment is based on publicly available data on MA. However, it is worth noting that publicly available data sources are limited, as is the level of disaggregation they contain. There is also limited data on consumer demand and provider preferences as well as private sector purchasing. ultimately, to identify key MA market shortcomings, this analysis leverages both publicly available data sources and trends from private data collection efforts. It also draws on interviews with donors, procurers, manufacturers, government representatives, implementing partners, and other stakeholders actively engaged in the supply and delivery of MA in LMICs.

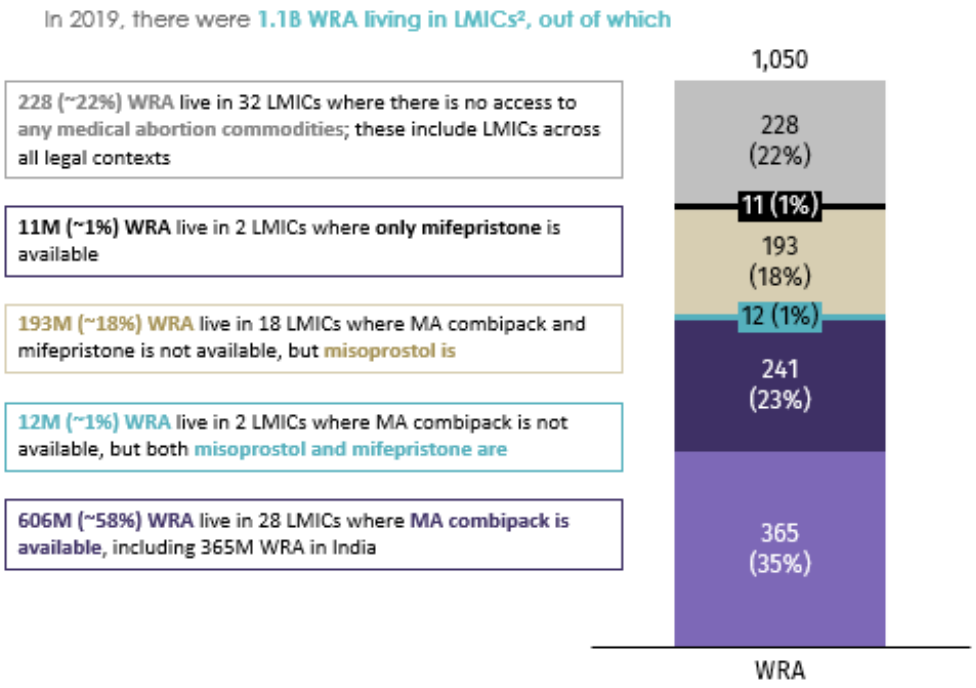
Current market overview for in-scope products

Availability and use

Figure 1 below provides an overview of product availability in LMICs. It should be noted that different legal environments for safe abortion across countries affect levels of access even where products are available.

[5] 'Suggestion' is a term used by the WHO for interventions where the strength of the recommendation is weaker or conditional. This may be because the balance of benefits and harms is less clear or where choices will depend more strongly on individual patient circumstances, values, and preferences.
[6] 2022 WHO Abortion Care Guidelines
[7] WHO Income Classifications 2022

Figure 1: Women of reproductive age (WRA) in LMICs, by MA products available (2022)[8]



In terms of use, in 2019, 18 million safe[9] MAs were estimated to have been conducted across LMICs. Of these, 8.7 million were undertaken using a combination regimen of misoprostol and mifepristone (including both MA Combipack and individual pills consumed together) and 9.3 million were undertaken using misoprostol alone.

MA Combipack market overview

The **MA Combipack** is a co-packaged combination of one 200mg tablet of mifepristone and four 200µg tablets of misoprostol (totaling 800µg misoprostol).[10] The MA Combipack is a recommended option for MA as per the WHO safe abortion guidelines, which state that "evidence from clinical studies demonstrates that the combination regimen is more effective than misoprostol alone".[11]

There are two manufacturers who currently supply WHO PQ/SRA-approved products to LMICs: Sun Pharma (whose product has SRA approval) and CR Zizhu (whose product achieved WHO PQ status).[12,13] Other manufacturers of WHO PQ/ SRA-approved products exist (Exelgyn, LinePharma) but have indicated they are not focused on LMICs.[14]

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[8] CHAI Research and Analysis | Inputs include Medab, World Bank, UN Population Data, HRP
[9] https://leap.rhsupplies.org/#/abortion; includes both safe and less safe MAs and post-abortion care but excludes all least safe abortions, defines 'safe' abortions as those abortions that are both provided by an appropriately trained person and carried out using surgical or medical method recommended by the WHO appropriate to the pregnancy gestation; 'less safe' as abortions that meet only one of these criteria (e.g., abortions provided by a trained health worker using an outdated method, or if a person self-induces an abortion using a safe method including misoprostol without adequate information or support from a trained individual; and 'least safe' abortions as those that meet neither of the two criteria and are therefore provided by untrained people using dangerous methods, such as toxic substances or the insertion of sharp objects.
[10] Safe2Choose Database
[11] WHO Abortion Care Clinical Guidelines, March 2022
[12] First co-pack of mifepristone oral tablet and misoprostol for vaginal administration prequalified | WHO - Prequalification of Medical Products (IVDs, Medicines, Vaccines and Immunization Devices, Vector Control)
[13] Leveraging_the_role_of_national_distributors_to_accelerate_access_to_medical_abortion_combi-packs_in_sub-Saharan_Africa_-_Lessons_Learned.pdf (rhsupplies.org)
[14] CHAI stakeholder engagement on behalf of the MA Market Shaping Group

Two additional suppliers that serve LMIC markets do not currently have WHO PQ or SRA-approval but have indicated their intentions to seek one of those certifications.[15] Further, at least 14 non-WHO PQ or SRA-approved suppliers of MA Combipack exist, including Mylan, Cipla, Stada, and a variety of Indian pharmaceutical companies.[16]

Recent research undertaken by the Concept Foundation found that overall, over half (51.6%) of all MA Combipack products sampled included a component that was non-compliant with WHO quality standards. However, the same study found that "prequalification by WHO or approval from an SRA provides reliable assurance of product quality"; 63.5% of non-WHO PQ/SRA-approved products were found to have quality concerns, whereas only 9.1% of WHO PQ/SRA-approved products were found to have quality concerns.[17]

Currently, MA Combipacks are available in 28 LMICs across a variety of different legal contexts. MA Combipacks are procured by national governments directly from suppliers or via institutional procurers such as UNFPA or Social Marketing Organizations (SMOs). SMOs also procure MA Combipacks directly from suppliers and account for the bulk of public/social sector procurement.[18] Key SMO partners (DKT, MSI, PSI) source from a mixture of WHO PQ/SRA-approved and non-WHO PQ/SRA-approved suppliers and conduct their own quality testing procedures.[19]

Government procurement of MA Combipacks has been increasing but is still limited. This is largely due to the time, resources, and political commitment required to deliver the advocacy and awareness-building activities needed to create a more conducive enabling environment.

Since 2019, a group of MA donors and procurers called the MA Combipack Market Shaping Group (MSG) has made significant progress towards achieving multiple affordable, WHO PQ or SRA-approved MA Combipack products. These efforts were initiated after the lack of affordable, WHO PQ/SRA-approved MA Combipack suppliers serving LMICs was identified as a key barrier to MA market health. However, further efforts are required to increase procurement and demand for said products to sustain the gains made so far. In addition, data gaps and limited visibility present potential barriers to developing robust total market strategies.

Misoprostol market overview

Misoprostol belongs to a class of medications called prostaglandins. It was first developed in the US to treat peptic ulcers in patients treated with non-steroidal anti-inflammatory drugs (NSAIDs) in the 1980s. Since then, misoprostol use has expanded to several additional uses in obstetrics and gynecology, including the treatment of postpartum hemorrhage (PPH), medical management of miscarriage, induction of labor, cervical ripening before surgical procedures and MA.

The WHO recommends the use of misoprostol for MA and post-abortion care and has strengthened its recommendation of misoprostol for self-managed abortion in the recently updated guidelines, in March 2022. Although misoprostol is generally considered a secondary alternative to MA Combipack, it is an important regimen in the MA discussion because it is more affordable than the alternatives (including MA Combipack). It is also

[15] CHAI stakeholder engagement on behalf of the MA Combipack Market Shaping Group
[16] Import / Export Database, data pulled in Q1 2023
[17] Concept Foundation & IPPF: Quality Testing of mifepristone & misoprostol in 11 Countries
[18] Stakeholder Feedback
[19] MA Combipack Market Shaping Group Updates, September 2022

relatively more available than products used only for abortion, particularly in countries with more restrictive legal environments.

There are eight WHO PQ/SRA-approved suppliers of misoprostol in LMICs: Acme, Apotex, Bial, Cipla, CR Zizhu, Line Pharma, Mylan and Pfizer.[20,21] Other WHO PQ/SRA-approved suppliers exist (e.g., Pharma Science, Exelgyn, Ferring Lakemedel AB) but do not appear to prioritize LMICS.[22] Finally, there are at least 66 non-WHO PQ/SRA-approved brands[23] including those manufactured in Argentina, Bangladesh, Brazil, Chile, China, Egypt, France, India, Mexico, Pakistan, Peru, South Korea, and Vietnam[24,25].

While historic concerns about the degradation of misoprostol over time have been mitigated by the use of double aluminum blister packs (especially in WHO PQ/SRA-approved brands),[26] quality issues still persist (especially in non-WHO PQ/SRA-approved brands). Recent research undertaken by the Concept Foundation found that over half (57.1%) of all misoprostol products sampled included a component that was non-compliant with WHO quality standards. It also found one falsified sample of misoprostol.[27] Moreover, there have been reports of counterfeit misoprostol in some West African countries.[28]

Globally, misoprostol is approved in 122 countries and is procured by national governments, UNFPA, and SMOs for a mix of use cases such as labor induction, postpartum hemorrhage, ulcer treatment, and miscarriage, as well as induced abortion (to a lesser degree). The misoprostol-only regimen is included in national guidelines for induced abortion in 37 countries. Further, misoprostol is a key maternal, neonatal, and child health (MNCH) commodity and is listed on Essential Medicines Lists (EMLs) in many countries. It has therefore benefited from a relatively resilient funding and procurement picture to date, compared to other MA products. Key SMO partners and governments source from a mixture of WHO PQ/SRA-approved and non-WHO PQ/SRA-approved suppliers, depending on cost and availability.

The size of the misoprostol market specifically for MA is unknown, due to misoprostol's indication for multiple uses beyond MA. The use of misoprostol as a percentage of total MAs conducted also varies significantly from country to country. In 2019, the misoprostol-only regimen was used in 87% of all MA and post-abortion care services provided in low-income countries, compared to 46% and 65% in lower middle and upper middle-income countries, respectively.[29] However, misoprostol is assumed to have been used in all 18 million safe MAs undertaken in LMICs in 2019 (either alone or in combination with mifepristone). Assuming an estimated four misoprostol pills per MA, the amount of misoprostol used in MA amounted to at least ~72 million pills in LMICs alone.

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[20] Search | MedAb

[21] Medicines/Finished Pharmaceutical Products | WHO - Prequalification of Medical Products (IVDs, Medicines, Vaccines and Immunization Devices, Vector Control)
Bial's misoprostol vaginal tablet prequalified | WHO - Prequalification of Medical Products (IVDs, Medicines, Vaccines and Immunization Devices, Vector Control)

[22] Search | MedAb

[23] Suppliers can make multiple brands of the same product based on regulatory requirements for individual markets

[24] Search | MedAb

[25] RHSC Final Report: "Business Case: Investing in Production of High-Quality misoprostol for Low-Resource Settings", December 2014

[26] Hagen et al, "Stability of misoprostol tablets collected in Malawi and Rwanda: Importance of intact primary packaging", September 2022

[27] Concept Foundation & IPPF: Quality Testing of mifepristone & misoprostol in 11 Countries

[28] WHO Medical Product Alert: Falsified CYTOTEC, August 2021

[29] LEAP | Landscape & Projection of RH Supply Needs (rhsupplies.org)

Additional market sizing on the portion of misoprostol used for MA would require reliable collection and disaggregation of data on misoprostol consumption. However, stakeholders indicate that such efforts could negatively impact misoprostol's availability in the short term. For example, in countries with more restrictive abortion policies, quantifying the portion of misoprostol used for MA could threaten the overall quantity of misoprostol procured. However, in the long term, the lack of data on misoprostol for MA may perpetuate stigma surrounding abortion in general, as it may continue to limit discourse and visibility into actual usage following purchase.

Finally, there is limited visibility into the commercial sector for misoprostol or the amount of non-WHO PQ/SRA-approved volumes in country.

04
MA market assessment findings

SEMA utilizes the Healthy Markets Framework (HMF), an assessment tool, to understand potential market barriers, risks, and opportunities. The HMF assessment involves a collaborative approach that draws the perspectives and the insights of technical partners, practitioners, and policy experts. The HMF assessment also involves individuals from the countries where SEMA and global partners aim to enhance SRH product accessibility. The HMF Assessment seeks to reflect all dimensions of market health, to clearly identify potential areas for action and investment by SEMA and other partners.

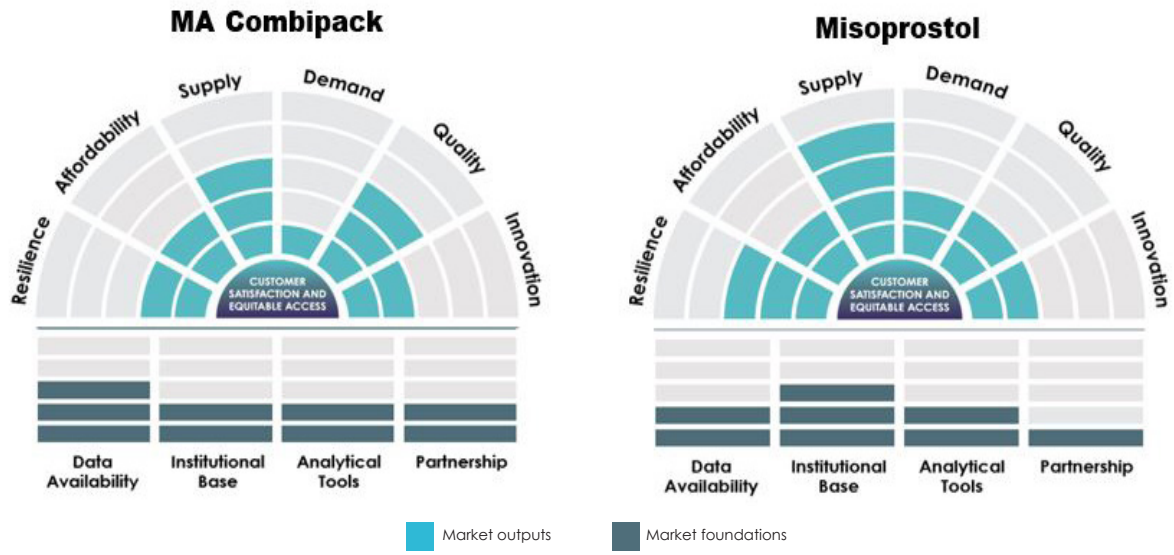
SEMA's HMF assessment is designed to help understand and build consensus around market challenges, in turn underpinning the design and discussion of potential solutions. The HMF seeks to reflect all major dimensions of market health, in order to clearly identify potential areas for action and investment by SEMA and other partners.

For SEMA, the primary dimensions of a healthy SRH market include:

- a resilient supply network capable of meeting consumer demand, even amid economic or logistical challenges;
- resilient financing to meet consumer demand;
- a pricing structure that ensures a sustainable level of affordability across varied markets;
- high levels of product quality;
- a robust innovation pipeline; and
- adequate structures for regulation, procurement, and market data collection.

SEMA has developed a list of indicators to support the assessment of these primary market dimensions. The indicators guide a data collection process for developing composite scores of 1-5 (with 1 being 'unhealthy' and 5 being 'very healthy'), which in turn are used to populate a simple visual representation of overall market health. For more detail on the HMF process, please see this background document.

The charts below summarize the market assessment findings for MA Combipack and misoprostol using SEMA's Healthy Market Framework methodology. A table with further detail for these findings is in an appendix to this document.



Based on these assessments, a wide range of **market shortcomings** emerged that were common to both MA Combipack and misoprostol. These shortcomings are interconnected. Multiple, interlinked interventions will therefore be required to mitigate these challenges and enhance overall market health.

The market shortcomings listed below represent the full breadth of the challenges that would need to be alleviated to fully improve MA market health.

1. **Restrictive laws and policy environments:** Despite various advocacy efforts, legal and policy environments remain largely restrictive in countries, while donor funding restrictions contribute to limited procurement of MA commodities (including the leveraging of available ring-fenced funding).

2. **Stigma:** Stigma can prevent key actors (e.g., regulators, policymakers, donors, procurers, distributors, service providers) from making commodities and services available. It can also prevent end-users from accessing services easily and inhibit understanding of available MA options.

3. **Lack of data and understanding of demand:** Relatively limited visibility into commercial sector volumes (including mark-ups), as well as into end-user and provider behaviors, impacts the ability of stakeholders to design informed market-shaping strategies.

4. **Limited supply and procurement:** Significant progress has been made with the MA Combipack market-shaping strategy developed by the MA Combipack MSG to increase the availability of WHO PQ/ SRA-approved products. However, procurement volumes remain relatively low, making it challenging to consistently realize affordable pricing. Continued work is required to ensure the availability of multiple affordable WHO PQ/ SRA-approved products over time.

5. **Limited coordination:** Coordination and alignment on MA vision, goals and priorities between global partnerships and groups could be further enhanced to avoid fragmented efforts. Coordination could also be improved at the country level to support more strategic resource deployment.

The following proposed interventions were recommended to address the key market shortcomings identified in the assessment. Some of these recommendations are specific to MA. However, some apply to the SRH product sector as a whole and will be better delivered through a cross-cutting, multi-product approach. This is particularly true for data and coordination shortcomings.

Priority Market Shortcomings	Proposed interventions
1. Restrictive laws and policy environments limit procurement of and access to MA **2. Stigma among key actors impacts end-user awareness and availability of MA commodities**	1. Fund advocacy activities to support more progressive abortion policies
	2. Support national governments via technical assistance (TA) to coordinate the scaling of quality CAC services (including increased procurement of WHO PQ/SRA-approved product)
	3. Fund opportunities to work within the legal framework to introduce and scale CAC services, e.g., trainings, Value Clarification and Attitude Transformation (VCAT) interventions, supply chain
3. Lack of data and corresponding limited understanding of demand	4. Enable in-depth consumer and provider research at the country level, including in the commercial sector. This could be achieved within a wider, cross-product effort to develop routine systems for collecting data on user insights.
	5. Conduct commercial sector volume tracking across products, including MA **(cross-cutting, multi-product intervention)**
4. Limited supply and procurement of affordable WHO PQ/SRA-approved MA products	6. Continue work to secure sufficient manufacturers in the market and improve affordability
	7. Build financing and demand for WHO QA Combipacks among buyers
	8. Provide TA to strengthen national regulatory capacity to approve and oversee SRH products, including MA **(cross-cutting, multi-product intervention)**
5. Limited coordination at the global and country level	9. Align the global community to a common problem and set of priorities that are both specific and actionable **(to be advanced ideally within a wider cross-cutting, multi-product approach)**
	10. Facilitate a more coordinated approach in-country across public and private channels to ensure products are available where users choose to access them

05
Next Steps

This MA market assessment aims to help SRH stakeholders to identify, prioritize and align on key interventions to increase access to safe abortion and post-abortion care services via MA over time.

In the long term, it will be important to address the full set of identified market shortcomings to realize the full potential of the MA market. However, a key barrier to MA market health in the near term is the relatively limited demand for WHO PQ/SRA-approved MA Combipack products. Therefore, SEMA stresses the importance of key supply- and demand-side interventions to address this critical market barrier.

06
Appendix

This market assessment is based on a scoring system from 1-5 for each dimension of the Healthy Market Framework. A perfectly performing market overall would score 5 on all dimensions. Scores are presented separately for the **MA Combipack** and **misoprostol.**

MA Combipack

Domain	Score	Findings
Resilience	**2**	• There are multiple WHO PQ/ SRA-approved manufacturers for the misoprostol API and the mifepristone API, sourced by WHO PQ/ SRA-approved Finished Pharmaceutical Product (FPP) MA Combipack suppliers serving LMICs. • Stigma and restrictive laws, policies, and guidelines have made it difficult to incorporate MA into national primary healthcare programs. This in turn **limits public sector funding for abortion-specific commodities like the MA Combipack**. • **The global funding picture is uncertain** in the face of shifting donor priorities. This has impacted the ability of key partners (e.g., SMOs, international NGOs) to offer abortion services, including MA. Discussion on the next phase of investments is ongoing, as donors re-evaluate strategic priorities and funding. • Some ring-fenced funding exists at the global level to support public sector introduction and scale programmatic and procurement activities related to MA Combipack. However, **such funds have historically been largely underutilized.**
Affordability	**2**	• Progress has been made in recent years to reduce the price of WHO PQ/SRA-approved MA Combipack. However, **relatively limited procurement volume for these products has led to challenges around realizing affordable prices** and achieving price parity with non-WHO PQ/SRA-approved products. • **Two suppliers have indicated their intentions to move their non-WHO PQ/SRA-approved products to WHO PQ/SRA-approved status at an affordable price point. However,** continued supplier engagement is vital to achieve supply security for affordable WHO PQ/SRA-approved products, given evolving market dynamics. • Some reports of **price gouging** in the commercial sector need to be better understood, particularly as a barrier to access.
Supply	**3**	• There is currently **sufficient WHO PQ/SRA-approved FPP supply** to meet institutional demand (i.e., from SMOs, governments, and UNFPA). However, there is **limited insight into non-WHO PQ/SRA-approved supplier capacity** and total demand. • Stigma may prevent commercial sector distributors from stocking and providing MA Combipacks.
Demand	**1**	• **User** ~8.7 million MAs take place annually in LMICs using mifepristone + misoprostol, with notable volumes occurring in the SMO sector. There are reports of limited end-user awareness of how to properly access/ use MA Combipack. Abortion rights are also limited within some countries' legal environments. There continues to be latent demand for MA, contributing to the 7.8 million abortions in LMICs that are considered 'least safe'. • **Country** Though historically public sector funding has been limited, there are positive indications of future procurement for MA Combipack, such as inclusion on EMLs, orders placed, and additions to tenders.

Quality	**3**	• **Two WHO PQ/SRA-approved products are currently available** in LMICs, with **two additional suppliers indicating their intentions to seek WHO PQ/SRA-approval for their MA Combipack products in the future**. This progress is a direct result of MA Combipack MSG efforts. WHO PQ/SRA-approved products have been found to be significantly less likely to carry quality concerns than non-WHO PQ/SRA-approved products. • There is currently limited visibility into the **quality of MA Combipack products in the commercial sector**, though some reports of counterfeit misoprostol and mifepristone have been recorded by partners.
Innovation	**2**	• There are examples across countries of technology being leveraged to increase access to safe abortions (e.g., telemedicine, applications, hotlines) and to increase consumer and provider awareness of products and services.
Data availability	**3**	• Fairly robust data collection efforts by the MA Combipack MSG have produced high volume estimates for WHO PQ/ SRA-approved products among UNFPA, SMO, and government procurement. • There is limited visibility into the commercial sector, including non-WHO PQ/SRA-approved volumes.
Institutional base	**2**	• The MA Combipack is a recommended option for MA according to the WHO. It is also considered a preferred, effective, and safe option by many providers. • There is a relatively limited number of countries that have WHO PQ/ SRA-approved products registered, though that number has been increasing over the past few years. • Governments have historically been reluctant to procure MA Combipack due to its unique indication for abortion. However, recent years have shown a shift towards higher degrees of support across LMIC public sectors.
Analytical tools	**2**	• Existing work and analysis conducted for the MA Combipack MSG has focused on tracking progress against supply- and demand-side global outcomes. Such outcomes include increased supply security for affordable, quality-assured MA Combipacks in LMICs, and increased proportion of procured MA Combipacks that are WHO PQ/ SRA-approved products in LMICs. However, this work is limited to the public and social marketing sectors and is made available only to members of the MA Combipack MSG. • Currently, no existing comprehensive market data collection or forecasting exercises take into account all MA Combipacks (i.e., WHO PQ/SRA-approved and non-approved) across all sectors.
Partnership	**2**	• In the last few years there has been notable progress in the increased availability of affordable, WHO PQ/SRA-approved MA Combipacks. However, progress is at risk due to limited procurement of WHO PQ/SRA-approved products and available financing to scale and respond to demand. • Globally, several groups have prioritized increasing access to MA products, such as the RHSC Safe Abortion Supplies (SAS), WHO Prevention of Unsafe Abortion (PUA), and the MA Combipack MSG, as well as other groups whose purviews touch on safe abortion, including PSI's Self-Care Trailblazers Group. Further, in 2022 the WHO convened a series of consultations with key actors to focus on increasing access to affordable, quality MA products and services. With the exception of the MA Combipack MSG, the focus of these groups and/or partnerships is broad, encompassing the safe abortion or MA markets and leveraging existing funded work. • Some countries (e.g., DRC, Rwanda, Zambia) are supporting coordination across public and private sectors (particularly via SMOs). These efforts are part of RH product introduction mechanisms to introduce and scale MA Combipacks. • Despite several groups and partnerships at the global and country level, coordination and alignment on MA vision, goals and priorities could be further enhanced to avoid fragmented efforts. Coordination could also be enhanced at the country level to support more strategic deployment of resources.

Misoprostol		
Domain	**Score**	**Findings**
Resilience	**3**	• There are multiple WHO PQ/SRA-approved misoprostol API manufacturers (e.g., Piramal, Everlight), with indications that Piramal has the largest market share. Looking forward, **regular engagement** with Piramal and other WHO PQ/SRA-approved manufacturers of the misoprostol API will be important to monitor key supply-side developments and mitigate any potential risks to supply security. • Misoprostol is included in country EMLs and procured by governments, UNFPA, NGOs and SMOs, often under maternal health indications instead of explicitly for MA.
Affordability	**2**	• **Misoprostol is generally more affordable than the MA Combipack** and is often covered by health insurance within maternal health. • Non-WHO PQ/SRA-approved products continue to be available at a lower price than approved options. • There is variation in price across geographical regions, including **some stakeholder reports of excessive markups**, especially in the commercial sector. Further, providers and prescribers across public and commercial sectors may levy informal surcharges.
Supply	**4**	• Misoprostol is available in more LMICs and UMICs than other MA commodities, due to its multiple indications. • There are eight WHO PQ/SRA-approved suppliers of misoprostol available in LMICs: Acme, Apotex, Bial, Cipla, CR Zizhu, Line Pharma, Mylan and Pfizer.
Demand	**2**	• In low-income countries, the relatively inexpensive misoprostol-only regimen was used in **87% of all MA** and post-abortion care services, compared to 46% and 65% in LMICs and UMICs, respectively. • Misoprostol alone was used in 9.3 million MAs in LMICs in 2019 (and as a part of the mifepristone and misoprostol combination regimen for an additional 8.7 million abortions). • There is a disconnect between policies/laws and knowledge of healthcare workers and end-users. The **end-user might not be provided with the appropriate counselling and guidance** on misoprostol use (within legal parameters), which may limit use or result in side-effects. This in turn may increase reliance on health-based facilities, despite successful completion of self-managed abortion. • Stakeholders expressed challenges with accurately **quantifying misoprostol demand due to its various indications**. This was particularly the case for MA, where misoprostol is often used as a secondary line of treatment (e.g., when the MA Combipack is not available, and for later-term abortion following MA Combipack usage to complete evacuation of the uterus). • There is limited **visibility into commercial sector procurement.**
Quality	**2**	• Some stakeholders perceive misoprostol to have a short the shelf-life. Prior **studies showed degradation over time** due to moisture. All WHO PQ/ SRA-approved suppliers have therefore upgraded to double aluminum blister packs, but some concerns remain. • WHO PQ/SRA-approved misoprostol is available in 37 of the 44 LMICs where misoprostol is available, representing 266 million women of reproductive age (WRA) with access to WHO PQ/SRA-approved misoprostol. • Further, some countries are not actively monitoring the quality of misoprostol over time, which is particularly concerning in markets with a supply proliferation. • Due to the multiple indications, instructions in packaging inserts may not give appropriate guidance on use for MA or storage, which has implications on the quality of and access to information to execute safe abortions.

Innovation	**2**	• As with MA Combipack, there are examples across countries of technology being leveraged to increase access to safe abortion, and to increase both end-user and provider awareness of products and services available within the legal framework. • In March 2023, WHO Prequalification approved Bial's Misofar vaginal tablets, which have a 36-month shelf-life. This is an improvement on the 18-24 months shelf-life of other misoprostol products on the market.
Data availability	**2**	• The size of the **misoprostol market for MA is unknown**, as misoprostol has multiple uses beyond MA (including PPH management, post-abortion care, and gastric ulcers). However, given the stigma surrounding MA, keeping information aggregated could provide certain advantages for accessibility in the short term. For example, in countries with more restrictive policies, acknowledging the portion of misoprostol used for MA could reduce the overall quantity of misoprostol procured. **In the long term, the lack of data on misoprostol for MA perpetuates the stigma**, because there is limited discourse and visibility into consumption. For example, some providers report MA as post-abortion care because they are afraid of backlash. • However, several countries have identified understanding misoprostol's usage as a key priority. Such countries conduct forecasts and quantification for misoprostol primarily for non-MA indications and post-abortion care. Other countries like Liberia have started conducting forecasts for MA regimens, including misoprostol. • Insight into the uptake of non-WHO PQ/SRA-approved products in both the public and commercial sectors is a challenge, as many LMICs have porous borders and nascent regulatory systems.
Institutional base	**3**	• The misoprostol-only regimen is recommended for MA, as per WHO guidelines. However, it is considered a secondary alternative to the MA Combipack due to its slightly lower efficacy and higher incidence of side effects. • Misoprostol has **several indications beyond MA**, which makes it widely registered and available in LMICs. It is therefore an important alternative where MA Combipack or the combination regimen of mifepristone and misoprostol is not available. A total of 37 countries have also included the misoprostol-only regimen in national guidelines for induced abortions. Overall, misoprostol is available in over 89 countries (17 LICs, 28 LMICs).
Analytical tools	**2**	• There is limited forecasting and quantification of the market for misoprostol as used for MA specifically. Further, it is unclear if key stakeholders would be interested in pursuing this kind of quantification. This is because identifying the portion of misoprostol used for MA could potentially lead to lower volumes of misoprostol being procured in countries where its presence is most valuable (i.e., those countries with restrictive abortion policies that already limit access to other abortion options). • Many countries conduct quantification for misoprostol overall. Some countries (e.g., Liberia, Uganda) have begun quantifying misoprostol underneath consumption of MA commodities.
Partnership	**1**	• Some members of the MA Combipack MSG have expressed interest in supporting interventions targeting misoprostol. However, the MA Combipack MSG's scope was determined based on an assessment of market barriers for MA products, which revealed priority concerns around MA Combipack at the global level. As a result, its market-shaping efforts have not focused on misoprostol. • As described in the MA Combipack section, several global groups prioritize access to MA products, including misoprostol. Please see above for further details.

07
‘Letrozole regimen’ market summary

Ongoing research and monitoring

In March 2022, the WHO updated its Abortion Care Guideline to include an additional MA regimen as a ‘suggestion’: a combination regimen of letrozole and misoprostol (hereafter the ‘Letrozole regimen’) that evidence suggests is a more effective alternative to misoprostol alone. The addition of Letrozole ‘significantly’ increases completion rate (i.e., successful termination of pregnancy), without increasing side effects when compared with misoprostol alone.

Clinical studies have not yet compared the Letrozole and misoprostol combination regimen to the ‘gold standard’ mifepristone and misoprostol combination or MA Combipack. In addition, the WHO currently states that the certainty of evidence from studies comparing the Letrozole combination to misoprostol alone at a gestational age of less than 12 weeks is low. Further, more evidence is needed to “determine the safety, effectiveness, and acceptability of the Letrozole plus misoprostol combination regimen at later gestational ages”. Finally, the Letrozole regimen takes at least four days to complete, whereas mifepristone in combination with misoprostol accelerates the process by two days, which is anticipated to be preferred by end-users and health workers alike.

Therefore, from a purely clinical perspective, the Letrozole regimen could be a promising option to induce MA, particularly as an alternative to misoprostol alone. However, further clinical evidence is required to understand the most suitable Letrozole regimen (i.e., correct dosage and timing) and its efficacy compared to the mifepristone and misoprostol combination and the misoprostol-only regimen.

From a market perspective, the Letrozole combination may currently offer limited upsides in terms of accessibility or affordability compared to misoprostol alone. Letrozole is currently not as accessible or affordable as taking misoprostol alone. It is included in fewer EMLs in LMICs under its primary indication (i.e., breast cancer treatment), and in some countries (e.g., Rwanda, Zambia) has only just begun to be included in the EML for MA. Moreover, while there are approximately 60 WHO PQ/SRA-approved suppliers for Letrozole, many are not actively prioritizing Letrozole for LMIC markets. And none have yet registered Letrozole with an indication of induced abortion on the label, which may be an additional barrier to increasing Letrozole use in this area. Further, the addition of any drugs to the misoprostol regimen will increase the total price of treatment. For example, based on initial landscaping, the ex-factory price of Letrozole in LMICs can range from $0.05-$0.25 per pill.

However, in countries where mifepristone is not widely available, the addition of Letrozole could be considered advantageous in terms of increasing the potential for successful pregnancy termination when compared to misoprostol alone. Due to its alternative indications (e.g., for breast cancer and fertility treatments), it may be easier to encourage public sector procurement of Letrozole over mifepristone or MA Combipack. Further, preliminary research suggests that the addition of Letrozole to a combination regimen with misoprostol may be less expensive in some regions (e.g., Latin America) than the addition of mifepristone.

Overall, more research is needed to better understand the potential clinical and market benefits that the Letrozole combination may offer compared to the MA Combipack. Therefore, we suggest continued monitoring of the Letrozole clinical evidence and market dynamics.

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