RINging the Bell for Choice
Actions and Solutions on Dapivirine Ring Access

September 22, 2022

DJ Manju Chatani
Ringing the Bell
RING RING RING

• Botswana
• Brazil
• Cambodia
• Canada
• Comoros
• Côte d'Ivoire
• Denmark
• Egypt
• Eswatini
• France
• Gambia
• Germany
• India
• Italy
• Jordan
• Kenya
• Lesotho

33 countries

262 webinar registrants

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• Nigeria
• Philippines
• Rwanda
• South Africa
• Sweden
• Switzerland
• Tanzania
• Thailand
• Uganda
• Ukraine
• United Kingdom
• United States
• Zambia
• Zimbabwe
Doxycycline for STI Prevention Evidence and Current Research

Register here: tinyurl.com/doxypep
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  - Thank you for all the questions that came in during registration!
  - Let’s hear your voice and see your face too. Raise hand to speak on camera.
- We will share links to recording and slides in follow-up email.
- Access TCA webinar resources here:
  - [www.avac.org/choice-agenda](http://www.avac.org/choice-agenda)
Press record!
Presenters

- Leonard Solai, IPM South Africa
- Yvette Raphael, APHA

Advocacy discussion

- Shakirah Namwanje, UNASO
- Natasha Mwila, Network of Zambian People Living with HIV, AVAC ‘22 Advocacy Fellow

Remarks

- Chris Obermeyer, Global Fund
- Erica Gollub, Pace University
Dapivirine Vaginal Ring Update -

The Choice Agenda

September, 2022
Monthly Dapivirine Vaginal Ring (DVR)

- Flexible silicone vaginal ring developed by IPM
- Woman-initiated and first long-acting HIV prevention product
- Slowly releases ARV dapivirine
  - Exclusive worldwide rights through Janssen Sciences Ireland Unlimited Company
- Reduced HIV risk in Phase III trials: 35% in The Ring Study, 27% in ASPIRE
- Open-label extension studies saw increased adherence, suggested greater risk reduction
- Positive Scientific Opinion from EMA in July 2020
- WHO recommendation and guidelines 2021 and Prequalification
- To date 6 approvals in Africa through the WHO Collaborative Registration Procedure
<table>
<thead>
<tr>
<th>Country</th>
<th>IPM Submission Date</th>
<th>Status</th>
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| South Africa | First electronic submission 24-Nov-2020  
  Final Submission via USB 26-Mar-2021                                               | Product Registration 08-March-2022                                      |
| Zimbabwe    | 03-February-2021                                                                     | Product Registration 06-July-2021                                      |
| Rwanda      | 11-February-2021                                                                     | Under review                                                           |
| Uganda      | 17-February-2021                                                                     | Product Registration 05-October-2021                                   |
| Malawi      | 22-February-2021                                                                     |                                                                        |
| Tanzania    | 11-March-2021                                                                        | IPM was notified on 12-April-2022 that TMDA has rejected the registration of DapiRing. IPM submitted an appeal. |
| Zambia      | 05-March-2021                                                                        | Product Registration 10-May-2021                                      |
| Kenya       | 23-March-2021                                                                        | Product Registration 16-July-2021                                      |
| Namibia     | 01-September-2021                                                                   | Under review                                                           |
| Botswana    | 08-September-2021                                                                   | Under review                                                           |
| Mozambique  | TBD                                                                                  |                                                                        |
| Ethiopia    | TBD                                                                                  |                                                                        |
| Nigeria     | TBD                                                                                  |                                                                        |
MOSAIC Project Overview

• 5-year global project funded by PEPFAR through USAID (2021-2026)

• Focuses on introduction and access for new biomedical prevention products to prevent HIV for women in sub-Saharan Africa

• Works across multiple countries to support evidence-informed and user-centered product introduction, research, research utilization, and capacity strengthening

• Supports a multi-product market with informed choice for HIV prevention as new products enter the market

• Collaborates closely with ministries of health (MOHs), missions, implementing partners (IPs), civil society, end users, providers, other local and global stakeholders, and product developers

VALUES

Country-led

Women-focused with emphasis on AGYW

Informed choice

Equitable co-leadership

Intentionality
Most countries have taken steps toward introduction of the monthly DVR

**Zambia:**
MOH indicated that it would await further research/data from other countries implementing pilot studies to inform policy and final resolution on the ring.

**Nigeria:**
MOH interest in DVR introduction

**Namibia:**
The ring is included in Namibia’s HIV ART guidelines

**Zimbabwe:**
The ring is approved in Zimbabwe and plans are underway for an implementation study – CATALYST. PSI has commenced a pilot

**Ethiopia:**
Pilot Study under iRB will be initiated. PSI

**Uganda:**
On April 26, 2022, the national prevention committee endorsed the adoption of the ring. CATALYST

**Kenya:**
The ring is included in Kenya’s HIV guidelines. CATALYST

**Eswatini:**
As of February 28, the MOH decided to introduce the ring and put in place an import waiver for the product. Pilot and MSF

**Lesotho:**
The ring is included in Lesotho’s HIV guidelines and Essential Medicines List. CATALYST

**South Africa:**
On March 11, 2022, SAHPRA has approved the ring. The DOH, through technical working groups is planning for ring implementation.
Additional Monthly Ring Research

Additional research led by MTN in partnership with IPM:

• **REACH study: Adolescent girls and young women**
  - Safety and use of dapivirine ring and oral PrEP among 300 young women ages 16-21 in South Africa, Uganda, Zimbabwe
  - Results on next slide

• **DELIVER study: Pregnant women**
  - Safety and acceptability of ring & PrEP among 750 women in Malawi, South Africa, Uganda, Zimbabwe
  - Interim results: No safety concerns seen during late pregnancy

• **B-PROTECTED: Breastfeeding women**
  - Safety and acceptability of ring & PrEP in Africa
  - Favorable safety profile
Findings from additional research

The REACH study findings showed promising results toward consistent HIV prevention product use in AGYW:

- **Choice:** 67% of participants chose to use the ring and 31% oral PrEP
- **Safety:** No safety concerns were noted for either the ring or oral PrEP
- **Acceptability:** high for both products – the ring (88.5%) and oral PrEP (64%)
- **Adherence:** The vast majority (97%) of study participants used the ring/oral PrEP some or all of the time. Adherence was higher for both products than had been observed in previous studies

No safety concerns were found in Cohort 1 = 36+ weeks (8-9 months) pregnant

No safety concerns were noted in Cohort 2 = 30-35+ weeks (7-8 months) pregnant

Cohort 3 is underway

- Results likely to be available in mid 2024
Autonomy
Countries largely look to their own regulatory bodies and WHO rather than the US FDA to make decisions

Funding Confusion
MOHs raised that an effect of the NDA withdrawal is that they need to seek funding for procurement outside of PEPFAR

“Real-world” Studies Needed
The next step to better understand how to deliver the ring as part of HIV prevention choices for AGYW are real-world studies

Choice for Women
No one product works for all women; AGYW want choice in HIV prevention options

Choice for Impact
Choice in HIV prevention products may have a greater impact on incidence, helping us to reach global and local targets

Context
Framing the ring for African women only may be problematic

Lack of clarity about NDA withdrawal
Lack of clarity about why the NDA was withdrawn could lead to distrust of US-funded products not approved by the US FDA

Information for providers and clients
Clear messaging on the product attributes of the ring is needed for providers and clients

Clear messaging to dispel myths
Without clear messaging, myths and misinformation regarding the ring and its efficacy may circulate on social media and other channels

Trust
Lack of community support for and enrollment in future US-funded trials is a potential concern

Ethical Considerations
Ethical considerations of post-trial access need to be addressed
Supply Chain Overview
Monthly DVR Procurement and Distribution Update

- First commercial DVR shipment to Zimbabwe via Chemonics (on behalf of PEPFAR)
  - ~14,500 rings Shipped in March and April Rings will be used in a PSI-Zimbabwe implementation project

- Launch of the DVR dedicated website (prepring.org) in March 2022, supporting the first batch of rings to Zimbabwe, and future countries when they start receiving the ring

  - IPM is awaiting guidance to set up this procurement pathway

- MSF has started the process to procure rings from IPM to support implementation projects in Mexico and Eswatini.
  - There is additional interest in making rings available for projects in several other African countries in the near future
Dapivirine Product Pipeline
Three-month DVR

• Off-white flexible silicone ring containing 100mg dapivirine that is self-inserted every 3 months
• Same dimensions, formulation, and manufacturing process as DapiRing
• Sustained-release *in vivo* over three-months
• No cold chain or special storage needed
• The three-month DVR will reduce the yearly cost by 66% of the current annual cost of the monthly DVR
Bioavailability Study (IPM 054)

• Phase I crossover design to investigate bioavailability of 25 mg dapivirine ring to 100 mg dapivirine ring

• Primary Objectives
  – PK: determine the bioavailability of 100 mg dapivirine ring relative to 25 mg dapivirine ring

• Secondary Objective:
  – Safety
    • Evaluate the safety of the two dapivirine vaginal ring formulations used continuously for 90 days
    • Characterize the vaginal microenvironment over the course of 90 days of ring use
Dapivirine Contraceptive Vaginal Ring: Update

- Three-month ring containing levonorgestrel for contraception and dapivirine for HIV prevention
- Two Phase I clinical trials performed with 200 mg dapivirine and 320 mg levonorgestrel in silicone matrix
  - No major safety signals for DPV or LNG
- More rigid EVA-based formulation developed as a result of slippage and expulsions with the initial silicone rings
- GMP clinical manufacturing of EVA rings completed and shipped to one of two trial sites
- CCN019b/IPM 056 Phase I study designed to compare two ring strengths
Engaging Adolescent Girls and Young Women

- Target audience include young women age 16-28 years, and older, programme managers, advocates etc.
- Content contributed by AGYW sharing personal stories on SRH, HIV and GBV issues.
Thank You to IPM’s Recent Donors

The contents of this presentation are the responsibility of IPM and do not necessarily reflect the views of its donors.
Countries where the Global Fund invests take the lead in determining where and how to best fight the three diseases (HIV/AIDS, tuberculosis, and malaria), and present funding applications and changes to current grants for review by different Global Fund structures.

Country ownership allows countries to tailor their own response, considering their political, cultural and epidemiological context.

Funding applications and changes to current grants are developed through Country Coordinating Mechanisms (CCMs).

The Global Fund is built on meaningful, transparent, and inclusive country dialogues.

Engagement of diverse individuals, groups, and organizations in country dialogues is essential to quality and impactful programs.

CCMs are responsible for coordinating an inclusive country dialogue process and are best placed to inform stakeholders about where, when and how the country dialogue will take place.
The Global Fund Supports Implementation of the PrEP Ring

- The PrEP ring is recommended by the World Health Organization (WHO) for HIV prevention.
- As a WHO recommended product, the Global Fund stands ready to support countries which wish to introduce and provide the PrEP ring if integrated into current grants (either because it is already in the grant or through reinvestments) or in new funding applications.
- Those wishing to discuss inclusion of the PrEP ring in Global Fund grants should engage with the Country Coordinating Mechanism in their country.
Engaging the Global Fund Country Coordinating Mechanism

- Those interested in being part of country dialogues should contact the Country Coordinating Mechanisms for their country by reaching out to the Administrative Focal Points found in the Coordinating Mechanism Contacts Tool.

- Those providing feedback may also wish to review the current grant for their country in order to strengthen their advocacy efforts.
Contact Information:
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