PEPFAR Guidance: PrEP Ring (monthly Dapivirine Vaginal Ring) Procurement

Consistent with the long-standing PEPFAR policy of only procuring FDA-approved and tentatively approved HIV commodities, the U.S. Department of State's Office of the Global AIDS Coordinator and Health Diplomacy (S/GAC) will not utilize PEPFAR funds to procure the PrEP Ring (monthly Dapivirine Vaginal Ring) for programmatic implementation at this time. However, PEFPAR remains committed to women having informed choices and will continue to work with countries and partners to ensure the creation and support of enabling environments for multi-product HIV prevention. Although PEPFAR will not procure the Ring commodity, PEPFAR will actively work with other donors who can procure the PrEP Ring and will support programmatic implementation when procured by these other parties (e.g. the Global Fund). As part of PEPFAR's commitment to informed choice, procurements of the PrEP Ring for PEPFAR-funded implementation science studies may proceed.

Background: The PrEP Ring is a long-acting, vaginal ring that slowly releases an antiretroviral (ARV) drug, dapivirine, locally in the vagina over one month. Two Phase III clinical trials, the Ring Study (IPM-027) and ASPIRE (MTN- 020), found the PrEP Ring reduced women's risk of HIV infection by about 30% with few adverse events and no safety concerns with long-term use. Two subsequent open-label extension (OLE) studies, DREAM and HOPE, showed increased ring use compared with the Phase III trials and suggested greater risk reduction of over 50% across both OLEs. Further exploratory analyses suggest higher protection may be possible with consistent use of the Ring over a period of several months. In addition, the REACH study (MTN-034) found that adolescents and young women aged 16–21 can achieve high adherence.
In July 2020, the PrEP-Ring received a positive scientific opinion from the EMA under Article 58 for its use among women at high risk for HIV who are unable to use daily oral PrEP. In January 2021, the WHO made a conditional recommendation to offer the Ring as a safe and effective additional prevention choice for women at substantial risk of HIV infection as part of combination prevention approaches. WHO included the PrEP Ring in the WHO list of prequalified medicines under the EMA Article 58 label using the alternative listing procedure. In December 2021, the International Partnership for Microbicides (IPM) withdrew the PrEP Ring new drug application from FDA consideration following feedback during the agency's review that current data are unlikely to support FDA approval at this time and given the current HIV epidemiology and the prevention landscape for women in the United States of America. Concurrently, WHO reaffirmed their support of their conditional recommendation of the PrEP Ring. Each African National Medicines Regulatory Authority (NMRA) will make its benefit-risk assessment considering their country's specific public health need and strategy and may reach different conclusions given the persistence of the epidemic among women in countries where IPM has submitted applications or where it is approved.

PrEP Ring (monthly Dapivirine Vaginal Ring) FAQs

What is the basis for the decision not to procure the Ring?

- Following the withdrawal of the application for FDA consideration by IPM, S/GAC paused procurements and entered into a consultation phase. Internal discussions led to PEPFAR leadership reaffirming the long-standing PEPFAR policy of only procuring FDA-approved and tentatively approved HIV commodities, a policy in place since the inception of PEPFAR.

Why is PEPFAR supporting research on the PrEP Ring, but not procurement for program implementation?

- PEPFAR remains committed to women having choices and additional implementation science studies will explore safe and ethical service delivery for informed choice. This is particularly important where products are not equally efficacious to oral PrEP. These implementation studies will provide critical answers to program delivery challenges associated with a multi-product platform and will support countries in scaling up and layering on the introduction of new products in existing oral PrEP programming. Additional research into a multi-product platform with oral PrEP and the PrEP Ring will answer key technical and programmatic questions that countries can use to inform PrEP Ring implementation and promote sustainability. Further, this platform can accelerate the introduction of future products when they become available, such as injectable CAB-PrEP.

What is the status of WHO-led Global PrEP Ring consultations?

- The PrEP Ring consultations presented an opportunity to consolidate the perspectives of the global community including Ministries of Health, civil society, community advocates, end-users, relevant USG agencies, and other global stakeholders about the PrEP Ring in the wake of IPM's decision to withdraw its PrEP Ring application from the US Food and Drug Administration (FDA) approval process for use in US populations. Consultations were led by WHO and the findings were disseminated on May 24, 2022. Additionally, global and country-specific reports outlining the findings of the consultations are expected to be available from WHO at the end of May 2022. During the consultation period S/GAC reviewed the impact of the FDA non-approval as it relates to PEPFAR procurement and determined that at this time the long-standing PEPFAR policy of only procuring FDA-approved and tentatively approved ARVs will stand. The country-specific reports will support PEPFAR to work with other donors who can procure the PrEP Ring and support programmatic implementation when procured by these other parties (e.g. the Global Fund).

The PrEP Ring has been prequalified by WHO and several countries in sub-Saharan Africa have approved the PrEP Ring for national scale up throughout 2022, indicating interest in PrEP Ring implementation. Why is PEPFAR not responding to this signaled interest?

- Although PEPFAR will not procure the PrEP Ring, PEPFAR will continue to support a multi-product platform and PEPFAR country teams may support programmatic implementation of the PrEP Ring when procured by other parties. PEPFAR remains committed to the goal of creating and supporting enabling environments for HIV prevention, including a market for choice and will continue to work hand-in-hand with host governments who have approved the Ring for scale up to access oral PrEP and PrEP innovations.

Can PEPFAR funds be used to support implementation of PrEP Rings (e.g. if purchased through another source such as Global Fund)?

- Yes. Countries and/or other donors that procure PrEP Rings for program implementation outside of PEPFAR can be integrated into PEPFAR funded programs. Therefore, PEPFAR-supported programs can implement Ring activities with Rings procured by other donors.
- Donors such as UNITAID and BMGF are similarly supporting multi-product market research platforms in their new prevention product-focused implementation studies, and

PEPFAR is coordinating with these donors to make sure that our implementation studies are complementary for evidence generation to inform programming.

What if there is inter-agency agreement (during COP or otherwise), MOH interest and national regulatory approval for PrEP Ring implementation? Will PEPFAR fund the procurement of the PrEP Ring for program implementation, even if it is not related to research?

- No. At this time, PrEP Ring procurement for program implementation alone will not be funded by PEPFAR, regardless of inter-agency agreement or national medicines regulatory approval.

Is the restriction on procurement of the PrEP Ring permanent or is it subject to change based on the results of the implementation studies, the WHO consultation, changes in PEPFAR leadership, or other factors?

- PEPFAR programs should not procure PrEP Ring for program implementation, based on this guidance. Currently planned implementation science studies will provide critical answers to program delivery challenges associated with a multi-product platform, including product preferences and effective use, and may inform future decisions around the PrEP Ring.

What is the status of the PrEP Ring regulatory approvals in African countries?

- At the end of April 2022, the PrEP Ring has received national regulatory approval in 8 countries in east and southern Africa.
- In March 2022, the PrEP Ring received publicly announced regulatory approvals from the South African Health Products Regulatory Authority (SAHPRA); and was approved by the Zimbabwean authorities in July 2021, with many additional regulatory submissions and reviews ongoing in PEPFAR countries.

What is the status of the PrEP Ring approvals by other normative and regulatory bodies?

- On December 9, 2021, after IPM withdrew the PrEP Ring application from consideration by the US FDA, the WHO reiterated continued support for its conditional recommendation for the dapivirine vaginal ring as an additional prevention option for women at substantial risk of HIV.
- The PrEP Ring received a positive scientific opinion from the European Medicines Agency (EMA) Article 58 on July 23, 2020. The EMA opinion states: “DPV-VR is intended to be used to reduce the risk of acquiring HIV during vaginal sex for women aged 18 years and over, who are at higher HIV risk, in combination with safer sex practices when oral pre-exposure prophylaxis (PrEP) is not used, cannot be used or is not available.”
- The PrEP Ring received WHO prequalification in November 2020. The PrEP Ring was first recommended for HIV prevention in March 2021, and it was included in the latest iteration of the WHO Consolidated Guidelines in July 2021, with the following recommendation: “The dapivirine vaginal ring may be offered as an additional prevention choice for women at substantial risk of HIV infection as part of combination prevention approaches (conditional recommendation; moderate-certainty of evidence).”