

FOR IMMEDIATE RELEASE

Monthly vaginal ring advances toward potential approval as new HIV prevention method for women

Positive opinion by European Medicines Agency paves way for IPM to pursue approvals of dapivirine ring in African countries

MTN studies of ring's safety in girls and pregnant and breastfeeding women taking place in parallel

PITTSBURGH, July 24, 2020 –A vaginal ring intended to be used for a month at a time has moved one step closer to potentially becoming a new HIV prevention method for cisgender women in sub-Saharan Africa, who despite being the face of the epidemic, have few options for protecting themselves against getting infected.

The ring, which women can insert and replace themselves, slowly releases an antiretroviral (ARV) drug called dapivirine into the vagina – the potential site of HIV infection – during the month it is worn. The nonprofit [International Partnership for Microbicides](#) (IPM) developed the monthly dapivirine ring and is seeking its approval.

Today's announcement by the European Medicines Agency (EMA) that it has adopted a positive scientific opinion on the ring's use in low- and middle-income countries is a significant step forward on the path toward potential approval of the dapivirine ring in African countries. IPM now plans to submit applications to national medical regulatory authorities in east and southern Africa, in collaboration with the World Health Organization (WHO), and to the U.S. Food and Drug Administration (FDA) later this year.

In parallel, the WHO is expected to revise its HIV/AIDS treatment and prevention guidelines with evidence-based recommendations for policymakers and healthcare providers on the ring's use, and make a determination for "prequalification," a global quality assurance designation.

Other than condoms, the only other HIV prevention product approved so far involves daily use of an ARV pill, an approach called oral pre-exposure prophylaxis, or PrEP.

If approved, the dapivirine ring would be the first biomedical prevention method specifically for cisgender women and be the first long-acting method. Importantly, it would mean women could choose the method that works best for them.

"This has been a long road, and by no means, have we reached our ultimate goal of having multiple options for women at risk of HIV. But this positive opinion by the EMA gets us closer than we have ever been. It is a monumental achievement for women's HIV prevention, and to that we owe IPM for its scientific leadership and vision, and steadfast advocacy," commented Sharon L. Hillier, Ph.D., professor and vice chair of the department of obstetrics, gynecology and reproductive sciences at the University of Pittsburgh School of Medicine and principal investigator of the National Institutes of Health (NIH)-funded [Microbicide Trials Network](#) (MTN). "The MTN has been privileged to play a role in this effort, and we are indebted to the study teams from both organizations and our study participants for getting us to where we are today."

As IPM's clinical partner, MTN conducted several of the studies that were included in IPM's application to the EMA and will be included in other regulatory submissions as well.

-more-

The EMA's review of the ring was through a procedure called Article 58, which is conducted in cooperation with the WHO and intended for products that would be used primarily in low- and middle-income countries. Reviews are conducted with the same rigor as those for products that would be marketed in the European Union.

IPM's application to the EMA included data from 183 non-clinical studies, 11 Phase I and Phase II safety and pharmacokinetics trials, and two Phase III trials: [The Ring Study](#) (IPM 027), led by IPM, and [ASPIRE](#) (MTN-020), which was conducted by the MTN, and two Phase IIIb open-label extension (OLE) studies, HOPE (MTN-025) and DREAM (IPM 032). Together, the two Phase III trials involved more than 4,500 cisgender women ages 18-45 in Malawi, South Africa, Uganda and Zimbabwe. Their results, reported in 2016, found the dapivirine ring was well-tolerated and helped reduce the risk of HIV by approximately 30 percent. Higher levels of protection were seen in women who used the ring most regularly. Results of the OLE studies suggest greater risk reduction (about 50 percent), though with no placebo group, there is less confidence in these findings. Additional data provided during the EMA's review showed the dapivirine ring reduced women's HIV risk by 35 percent with no safety concerns with long-term use.

Of the 11 supporting studies reviewed by the EMA, three were conducted by the MTN, all at U.S. clinical research sites. These included Phase IIa safety studies in adolescent girls ([MTN-023/IPM 030](#)) and post-menopausal women ([MTN-024/IPM 031](#)) and a safety and pharmacokinetic study in lactating women ([MTN-029/IPM 039](#)). Three additional MTN studies contributed supplemental information: [MTN-012/IPM 010](#), a Phase I penile safety study; [MTN-013/IPM 026](#), which augments data on the safety and pharmacokinetics of the dapivirine ring; and [MTN-015](#), an observational study of women who acquired HIV while participating in ASPIRE and HOPE.

Because initial approvals of the ring by African regulators would not apply to girls under the age of 18 or to pregnant and breastfeeding women, the MTN is also currently conducting safety studies of the ring in these populations to potentially enable the ring to be approved for use by these groups in the future.

Rates of HIV infection are especially high among adolescent girls and young women in much of Africa, as well as for women during pregnancy and breastfeeding, when they may be two- to four-times more likely to acquire HIV.

[REACH](#) (Reversing the Epidemic in Africa with Choices in HIV prevention), or MTN-034, has enrolled 247 participants ages 16 to 21, including 85 under the age of 18, at four trial sites in South Africa, Uganda and Zimbabwe. Results from REACH, expected in 2022, along with those from the MTN-023/IPM 030 study conducted in the United States among adolescent girls ages 15 to 17, are expected to provide the safety data needed to guide IPM's decision-making on seeking regulatory approvals for this group in the coming years. REACH will also help understand how to best support young women and girls to use the ring and/or PrEP as best they can, which may be important for broader implementation of these methods.

The [DELIVER](#) (MTN-042) study for pregnant women and [B-PROTECTED](#) (MTN-043) for breastfeeding women are being conducted at four sites in Malawi, South Africa, Uganda and Zimbabwe. DELIVER, which began in February 2020, is open at one site so far. Pending in-country and ethics approvals, the B-PROTECTED study is anticipated to begin in the coming weeks.

"These are populations who are among those in greatest need of HIV prevention tools, yet they are often overlooked in clinical trials of investigational products. We can't afford to wait to know whether or not the ring will be approved, which is why these studies are being conducted now, in parallel with the regulatory review process," said Jared Baeten, MD, PhD, professor of global health, medicine and epidemiology, and vice dean of the School of Public Health at the University of Washington in Seattle, who is co-principal investigator of the MTN.

-more-

“Ultimately, we are hoping the ring could be made available to all women, no matter their age or child-bearing status,” he added.

No single HIV prevention method will work for everyone – women’s needs and preferences are different and can change over time. As with contraception, the more HIV prevention options available to women, the more likely one will and can be used.

Oral PrEP is very effective, but only if taken daily as directed, and this can be challenging for some people, or may not be desired. If approved, the monthly dapivirine ring would give women who are unable to use daily oral PrEP consistently or who choose not to use a product that delivers drug systemically with another option.

“I am excited about the positive opinion from the EMA on the dapivirine ring – as are many of the women and study teams who took part in our studies. However, if we are truly committed to seeing a tangible reduction in HIV incidence in women, we need to provide them with multiple options that include much more than just oral PrEP and the vaginal ring. This is a significant positive step forward but our work must continue in this area.” said Thesla Palanee-Phillips, MMed Sci, PhD, MSc., of the Wits Reproductive Health and HIV Institute, in Johannesburg, South Africa, who with Dr. Baeten, led the ASPIRE study.

”Expanding the number of HIV prevention options is important for women here in Africa and globally.”

#

Click on the hyperlink for a [Q&A about the EMA opinion and related MTN studies](#): See also [IPM’s press release](#) and [NIAID’s statement](#), and for detailed information about the dapivirine ring and regulatory process please go to www.ipmglobal.org.

The MTN is supported by U.S. National Institutes of Health grants UM1AI068633, UM1AI068615 and UM1AI106707.

About the Microbicide Trials Network

The Microbicide Trials Network (MTN) is an HIV/AIDS clinical trials network established in 2006 by the National Institute of Allergy and Infectious Diseases with co-funding from the Eunice Kennedy Shriver National Institute of Child Health and Human Development and the National Institute of Mental Health, all components of the U.S. National Institutes of Health. Based at Magee-Womens Research Institute and the University of Pittsburgh, the MTN brings together international investigators and community and industry partners whose work is focused on the rigorous evaluation of promising microbicides – products applied inside the vagina or rectum that are intended to prevent the sexual transmission of HIV – from the earliest phases of clinical study to large-scale trials that support potential licensure of these products for widespread use.

24 July 2020