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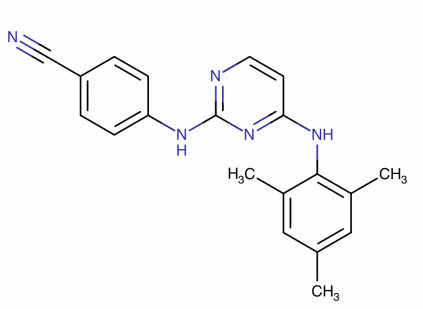


Dapivirine (DPV)

Developer(s)

Janssen Pharmaceuticals

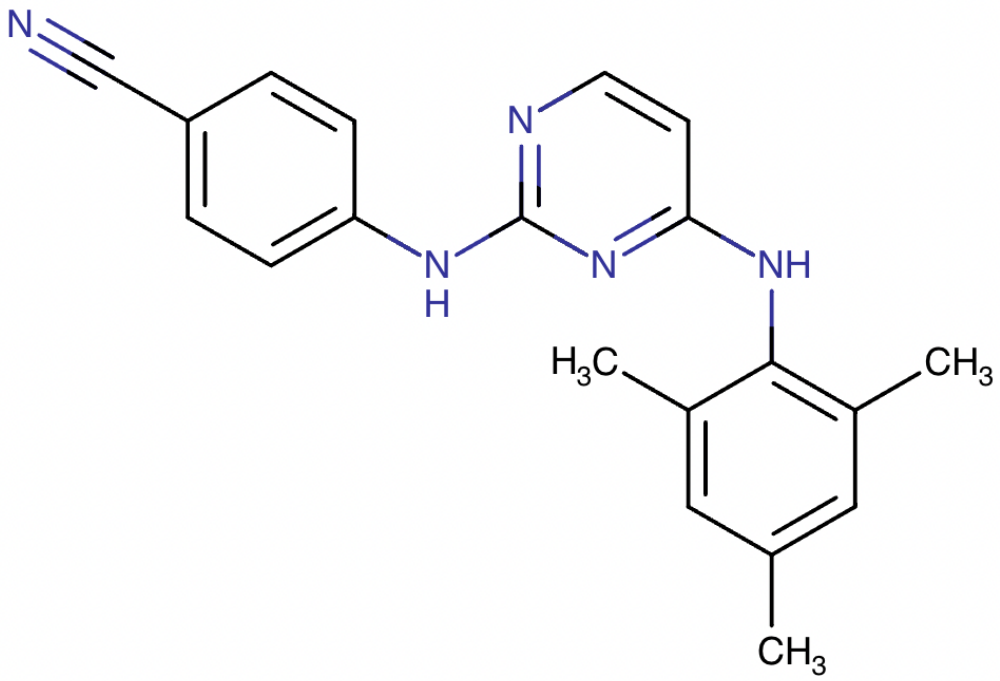
Originator

https://www.janssen.com

Belgium

Janssen Pharmaceuticals is a subsidiary company of Johnson & Johnson headquartered in Beerse, Belgium. They focus on manufacturing and developing pharmaceutical products for use in areas such as, Immunology, Infectious Diseases & Vaccines, Pulmonary Hypertension, Cardiovascular & Metabolism, Oncology, and Neuroscience.

Drug structure



Dapivirine Chemical Structure

Sourced from Drugbank

Drug information

Associated long-acting platforms

Intra-vaginal ring

Administration route

Topical (Vaginal)

Therapeutic area(s)

HIV

Use case(s)

Pre-Exposure Prophylaxis (PrEP)

Use of drug

Ease of administration

Administered by a community health worker
Administered by a nurse
Self-administered

User acceptance

Not provided

Dosage

Available dose and strength

25 mg of dapivirine in the monthly ring

Frequency of administration

once a month

Maximum dose

25 mg

Recommended dosing regimen

Not provided

Additional comments

Not provided

Dosage link(s)

Not provided

Drug information

Drug's link(s)

Not provided

Generic name

Dapivirine

Brand name

Not provided

Compound type

Not provided

Summary

Dapivirine (DPV) is a diarylpyrimidine non-nucleoside reverse transcriptase inhibitor (NNRTI) marketed as a monthly intravaginal silicone ring for the prevention of HIV-1 infection. NNRTIs function by mechanistically binding to the HIV reverse transcriptase enzyme, thereby inhibiting viral replication. Other topical microbicide formulations of dapivirine include film and gel products that are applied directly to the rectum and/or vagina to prevent the sexual transmission of HIV. Long-acting DPV intravaginal rings are constructed from a malleable silicone elastomer matrix that releases DPV over a 28-day period. DPV intravaginal rings are self-inserted and provide women with a discreet HIV PrEP option that reduces the risk of HIV infection by 31-37% (IPM 027 & ASPIRE).

Approval status

Dapivirine Vaginal Monthly Ring 25mg has received a positive opinion from European Union and it has received recommendation for its use outside EU. DVR has been approved as a HIV PrEP to reduce the risk of a woman getting infected with HIV-1

through vaginal intercourse in African countries such as South Africa, Zimbabwe, Malawi, Botswana, Zambia, Kenya, Uganda, Namibia, Rwanda, Eswatini and Lesotho. However, DVR has been rejected by United States and it is under clinical hold in United Republic of Tanzania.

Regulatory authorities

Dapivirine Vaginal Ring 25mg monthly is a non-nucleoside reverse transcriptase inhibitor that was first approved by South African Health Products Regulatory Authority (SAHPRA) followed by other African regulatory bodies. DVR is indicated for use by cisgender women as a PrEP to reduce the risk of a woman getting infected by HIV-1 during vaginal intercourse.

Delivery device(s)

No delivery device

Scale-up and manufacturing prospects

Scale-up prospects

DPV is manufactured commercially through a well-defined synthetic chemical process and undergoes a micronisation procedure to improve drug dispersion within the silicon intravaginal ring. The current DPV ring formulation (Ring-004) contains 25mg of micronised drug product and is produced with NuSil™ DDU-4870 silicone elastomer using addition-curing to prevent the formation of undesirable volatile alcohol by-products. This formulation provides high pharmacokinetic exposure with low overall manufacturing costs. Novel additive manufacturing techniques (e.g. APF) could provide new formulations.

Tentative equipment list for manufacturing

For ring manufacture: Injection molding machine, mixer, automated inspection and packaging machines.

Manufacturing

Manufacturing is a non-standard four stage workflow process: (1) preparation of the master batch, (2) pre-mix formation, (3) ring construction using injection addition-curing, and (4) packaging/inspection. For DPV Compound: stability testing indicates that the chemical compound can be stored for up to 6 months at 40ºC and 96 months at 25ºC in the pre-specified commercial packaging. DPV is photo-stable. For Finished Ring Product: stability testing shows that the product can be stored for 48 months at 30ºC. The DPV ring product is photosensitive and should be stored away from light sources.

Specific analytical instrument required for characterization of formulation

For DPV Compound: HPLC (determine chemical purity), GC (residual solvents), laser diffraction (determine particle size), Karl Fischer titration (determine water content) and FT-IR & DSC (chemical identification). For Finished Ring Product: HPLC (determine dissolution, content uniformity and degradation products), compression testing machine (determine tensile and compression properties).

Clinical trials

MTN-029/IPM 039

Identifier

NCT02808949

Link

https://clinicaltrials.gov/ct2/show/NCT02808949

Phase

Phase I

Status

Completed

Sponsor

International Partnership for Microbicides, Inc.

More details

Not provided

Purpose

Evaluate the pharmacokinetic profile of the Dapivirine vaginal ring in lactating women.

Interventions

Intervention 1

Drug: Dapivirine

Countries

United States of America

Sites / Institutions

Not provided

Trials dates

Anticipated Start Date

Not provided

Actual Start Date

2015-02-01

Anticipated Date of Last Follow-up

Not provided

Estimated Primary Completion Date

Not provided

Estimated Completion Date

Not provided

Actual Primary Completion Date

2018-03-03

Actual Completion Date

2018-03-03

Studied populations

Age Cohort

- Adults

Genders

- Cisgender female

Accepts pregnant individuals

No

Accepts lactating individuals

Yes

Accepts healthy individuals

Yes

Comments about the studied populations

Women aged 18 and over who are able and willing to express breast milk twice a day or more over the duration of the drug exposure study. After initiation of the drug product, participants must not provide any subsequently expressed breast milk to their children or to others for consumption during the study.

Health status

Negative to : HIV

Study type

Interventional (clinical trial)

Enrollment

16

Allocation

Not provided

Intervention model

Single group assignment

Intervention model description

Not provided

Masking

Open label

Masking description

None (Open Label)

Frequency of administration

Other(s) : "Intravaginal ring inserted for two weeks "

Studied LA-formulation(s)

Non-Implantable Device

Studied route(s) of administration

Topical (Vaginal)

Use case

PrEP

Key results

Type of key results	Title	Website link
Article	Pharmacokinetics of Dapivirine Transfer into Blood Plasma, Breast Milk, and Cervicovaginal Fluid of Lactating Women Using the Dapivirine Vaginal Ring	https://doi.org/10.1128/aac.01930-18

IPM 035

Identifier

NCT02858024

Link

https://clinicaltrials.gov/ct2/show/NCT02858024

Phase

Phase I

Status

Completed

Sponsor

International Partnership for Microbicides, Inc.

More details

Not provided

Purpose

Evaluate the effects of tampon use and menses on the pharmacokinetics of Dapivirine vaginal ring-004 in HIV-uninfected women.

Interventions

Intervention 1

Drug: Dapivirine Vaginal Ring-004 and no tampons

Intervention 2

Drug: Dapivirine Vaginal Ring-004 with tampons

Intervention 3

Drug: Dapivirine Vaginal Ring-004 with no menses

Intervention 4

Drug: Dapivirine Vaginal Ring-004 and same ring inserted after menses

Intervention 5

Drug: Dapivirine Vaginal Ring-004 and new ring inserted after menses

Countries

Not provided

Sites / Institutions

Not provided

Trials dates

Anticipated Start Date

Not provided

Actual Start Date

2015-01-12

Anticipated Date of Last Follow-up

Not provided

Estimated Primary Completion Date

Not provided

Estimated Completion Date

Not provided

Actual Primary Completion Date

2016-04-16

Actual Completion Date

2016-04-16

Studied populations

Age Cohort

- Adults

Genders

- Cisgender female

Accepts pregnant individuals

No

Accepts lactating individuals

No

Accepts healthy individuals

Yes

Comments about the studied populations

Women aged between 18 and ≤ 40 years.

Health status

Negative to : HIV, HBV, HCV

Study type

Interventional (clinical trial)

Enrollment

16

Allocation

Randomized

Intervention model

Cross-over assignment

Intervention model description

Not provided

Masking

Open label

Masking description

None (Open Label)

Frequency of administration

Other(s) : "Two consecutive 28-day intra-vaginal ring treatment periods separated by a washout period of 28 days. "

Studied LA-formulation(s)

Non-Implantable Device

Studied route(s) of administration

Topical (Vaginal)

Use case

PrEP

Key results

Not provided

IPM 054

Identifier

NCT05416021

Link

https://clinicaltrials.gov/ct2/show/NCT05416021

Phase

Phase I

Status

Active, not recruiting

Sponsor

International Partnership for Microbicides, Inc.

More details

Not provided

Purpose

Compare the relative bioavailability in plasma and vaginal fluid of the 25mg Dapivirine vaginal ring-004 and 100 mg Dapivirine vaginal ring-008 in HIV-uninfected women.

Interventions

Intervention 1

Drug: Dapivirine

Countries

South Africa

Sites / Institutions

Not provided

Trials dates

Anticipated Start Date

Not provided

Actual Start Date

2022-08-01

Anticipated Date of Last Follow-up

Not provided

Estimated Primary Completion Date

2024-04-01

Estimated Completion Date

2024-04-01

Actual Primary Completion Date

Not provided

Actual Completion Date

Not provided

Studied populations

Age Cohort

- Adults

Genders

- Cisgender female

Accepts pregnant individuals

No

Accepts lactating individuals

No

Accepts healthy individuals

Yes

Comments about the studied populations

Women aged 18-45 inclusive.

Health status

Negative to : HIV, HBV, HCV

Study type

Interventional (clinical trial)

Enrollment

110

Allocation

Randomized

Intervention model

Cross-over assignment

Intervention model description

Not provided

Masking

Open label

Masking description

None (Open Label)

Frequency of administration

Other(s) : "25 mg dapivirine ring (Ring-004) for 90 days (changed every 30 days) and the 100 mg dapivirine ring (Ring-008) used continuously for 90 days. "

Studied LA-formulation(s)

Non-Implantable Device

Studied route(s) of administration

Topical (Vaginal)

Use case

PrEP

Key results

Not provided

MTN-036/IPM-047

Identifier

NCT03234400

Link

https://clinicaltrials.gov/ct2/show/NCT03234400

Phase

Phase I

Status

Completed

Sponsor

International Partnership for Microbicides, Inc.

More details

Not provided

Purpose

Evaluate the safety and pharmacokinetics of extended duration Dapivirine vaginal rings.

Interventions

Intervention 1

Combination Product: Dapivirine Vaginal Ring, 25 mg

Intervention 2

Combination Product: Dapivirine Vaginal Ring, 100 mg

Intervention 3

Combination Product: Dapivirine Vaginal Ring, 200 mg

Countries

United States of America

Sites / Institutions

Not provided

Trials dates

Anticipated Start Date

Not provided

Actual Start Date

2017-12-04

Anticipated Date of Last Follow-up

Not provided

Estimated Primary Completion Date

Not provided

Estimated Completion Date

Not provided

Actual Primary Completion Date

2018-10-23

Actual Completion Date

2019-01-23

Studied populations

Age Cohort

- Adults

Genders

- Cisgender female

Accepts pregnant individuals

No

Accepts lactating individuals

No

Accepts healthy individuals

Yes

Comments about the studied populations

Women aged 18-45 inclusive.

Health status

Negative to : HIV

Study type

Interventional (clinical trial)

Enrollment

49

Allocation

Randomized

Intervention model

Parallel Assignment

Intervention model description

Not provided

Masking

Single blind masking

Masking description

Single (Participant)

Frequency of administration

Other(s) : "Participants will insert one IVR for 13 weeks (100 mg IVR or 200 mg IVR) or one IVR (25 mg VR) to be replaced every 4 weeks for 8 weeks then worn for an additional 5 weeks for a total of 13 weeks. "

Studied LA-formulation(s)

Non-Implantable Device

Studied route(s) of administration

Topical (Vaginal)

Use case

PrEP

Key results

Type of key results	Title	Website link
Article	Phase 1 pharmacokinetics and safety study of extended duration dapivirine vaginal rings in the United States	https://doi.org/10.1002/jia2.25747
Article	Users' Preferred Characteristics of Vaginal Rings for HIV Prevention: A Qualitative Analysis of Two Phase I Trials	https://doi.org/10.1089/aid.2021.0077

DREAM

Identifier

NCT02862171

Link

https://clinicaltrials.gov/ct2/show/NCT02862171

Phase

Phase III

Status

Completed

Sponsor

International Partnership for Microbicides, Inc.

More details

Not provided

Purpose

A follow-on, open label trial to assess patient adherence and continued safety of the 25mg Dapivirine vaginal ring-004 in HIV-negative women.

Interventions

Intervention 1

Drug: Dapivirine Vaginal Ring-004

Countries

South Africa

Uganda

Sites / Institutions

Not provided

Trials dates

Anticipated Start Date

Not provided

Actual Start Date

2016-07-12

Anticipated Date of Last Follow-up

Not provided

Estimated Primary Completion Date

Not provided

Estimated Completion Date

Not provided

Actual Primary Completion Date

2019-01-11

Actual Completion Date

2019-01-11

Studied populations

Age Cohort

- Adults

Genders

- Cisgender female

Accepts pregnant individuals

No

Accepts lactating individuals

No

Accepts healthy individuals

Yes

Comments about the studied populations

Participants are required to be previously enrolled in the IPM 027 trial.

Health status

Negative to : HIV

Study type

Interventional (clinical trial)

Enrollment

941

Allocation

Not provided

Intervention model

Single group assignment

Intervention model description

Not provided

Masking

Open label

Masking description

None (Open Label)

Frequency of administration

Monthly

Studied LA-formulation(s)

Non-Implantable Device

Studied route(s) of administration

Topical (Vaginal)

Use case

PrEP

Key results

Type of key results	Title	Website link
Article	Safety, adherence, and HIV-1 seroconversion among women using the dapivirine vaginal ring (DREAM): an open-label, extension study	https://doi.org/10.1016/S2352-3018(20)30300-3

MTN-024/IPM031

Identifier

NCT02010593

Link

https://clinicaltrials.gov/ct2/show/NCT02010593

Phase

Phase II

Status

Completed

Sponsor

International Partnership for Microbicides, Inc.

More details

Not provided

Purpose

Evaluate the safety of the Dapivirine vaginal ring when administered once every 28 days for twelve weeks in postmenopausal women.

Interventions

Intervention 1

Drug: Dapivirine Vaginal Ring

Intervention 2

Drug: Placebo Vaginal Ring

Countries

United States of America

Sites / Institutions

Not provided

Trials dates

Anticipated Start Date

Not provided

Actual Start Date

2013-12-01

Anticipated Date of Last Follow-up

Not provided

Estimated Primary Completion Date

Not provided

Estimated Completion Date

Not provided

Actual Primary Completion Date

2015-04-01

Actual Completion Date

2015-04-01

Studied populations

Age Cohort

- Adults
- Older Adults

Genders

Cisgender female

Accepts pregnant individuals

No

Accepts lactating individuals

No

Accepts healthy individuals

Yes

Comments about the studied populations

Women aged 45-65 inclusive.

Health status

Negative to : HIV

Study type

Interventional (clinical trial)

Enrollment

96

Allocation

Randomized

Intervention model

Parallel Assignment

Intervention model description

Not provided

Masking

Double-blind masking

Masking description

Double (Participant, Investigator)

Frequency of administration

Other(s) : "Rings inserted once every 28 days for twelve weeks "

Studied LA-formulation(s)

Non-Implantable Device

Studied route(s) of administration

Topical (Vaginal)

Use case

PrEP

Key results

Type of key results	Title	Website link
Article	Acceptability of the Dapivirine Vaginal Ring in Postmenopausal US Women	https://doi.org/10.1089/apc.2022.0002
Article	Phase 2a Safety, Pharmacokinetics, and Acceptability of Dapivirine Vaginal Rings in US Postmenopausal Women	https://doi.org/10.1093/cid/ciy654

ASPIRE

Identifier

NCT01617096

Link

https://clinicaltrials.gov/ct2/show/NCT01617096

Phase

Phase III

Status

Completed

Sponsor

International Partnership for Microbicides, Inc.

More details

Not provided

Purpose

Evaluate the effectiveness and safety of the Dapivirine vaginal ring in preventing HIV-1 infection in women at high risk of acquiring HIV-1.

Interventions

Intervention 1

Combination Product: Dapivirine Vaginal Ring

Intervention 2

Combination Product: Placebo Ring

Countries

Malawi
South Africa
Uganda
Zimbabwe

Sites / Institutions

Not provided

Trials dates

Anticipated Start Date

Not provided

Actual Start Date

2012-07-24

Anticipated Date of Last Follow-up

Not provided

Estimated Primary Completion Date

Not provided

Estimated Completion Date

Not provided

Actual Primary Completion Date

2015-07-03

Actual Completion Date

2015-12-01

Studied populations

Age Cohort

- Adults

Genders

- Cisgender female

Accepts pregnant individuals

No

Accepts lactating individuals

No

Accepts healthy individuals

Yes

Comments about the studied populations

Women aged 18-45 years inclusive.

Health status

Negative to : HIV

Study type

Interventional (clinical trial)

Enrollment

2629

Allocation

Randomized

Intervention model

Parallel Assignment

Intervention model description

Not provided

Masking

Double-blind masking

Masking description

Double (Participant, Investigator)

Frequency of administration

Other(s) : "Rings inserted once every 28 days for twelve consecutive months "

Studied LA-formulation(s)

Non-Implantable Device

Studied route(s) of administration

Topical (Vaginal)

Use case

PrEP

Key results

Type of key results	Title	Website link
Article	Patterns of Adherence to a Dapivirine Vaginal Ring for HIV-1 Prevention Among South African Women in a Phase III Randomized Controlled Trial	https://doi.org/10.1097/qai.0000000000
Article	Experiences with simultaneous use of contraception and the vaginal ring for HIV prevention in sub-Saharan Africa	https://doi.org/10.1186/s12905-021-01321-5

Type of key results	Title	Website link
Article	Acceptability of the Dapivirine Vaginal Ring for HIV-1 Prevention and Association with Adherence in a Phase III Trial	https://doi.org/10.1007/s10461-021-03205-z
Article	Risk of HIV-1 acquisition among South African women using a variety of contraceptive methods in a prospective study	https://doi.org/10.1097/qad.000000000
Article	Acquisition of Sexually Transmitted Infections among Women Using a Variety of Contraceptive Options: A prospective Study among High-risk African Women	https://doi.org/10.1002/jia2.25257
Article	Clinical and Virologic Outcomes Following Initiation of Antiretroviral Therapy Among Seroconverters in the Microbicide Trials Network-020 Phase III Trial of the Dapivirine Vaginal Ring	https://doi.org/10.1093/cid/ciy909
Article	Vaginal Ring Use in a Phase 3 Microbicide Trial: A Comparison of Objective Measures and Self-reports of Non-adherence in ASPIRE	https://doi.org/10.1007/s10461-018-2261-8
Article	Use of a Vaginal Ring Containing Dapivirine for HIV-1 Prevention in Women	https://doi.org/10.1056/nejmoa150611

MTN-034

Identifier

NCT03593655

Link

https://clinicaltrials.gov/ct2/show/NCT03593655

Phase

Phase II

Status

Completed

Sponsor

National Institute of Allergy and Infectious Diseases (NIAID)

More details

Not provided

Purpose

Evaluate the adherence and safety of a Dapivirine vaginal ring with oral emtricitabine/tenofovir disoproxil fumarate (FTC/TDF) in adolescent and young adult females.

Interventions

Intervention 1

Device: Dapivirine Vaginal Ring

Intervention 2

Drug: FTC/TDF

Countries

South Africa

Uganda

Zimbabwe

Sites / Institutions

Not provided

Trials dates

Anticipated Start Date

Not provided

Actual Start Date

2019-01-14

Anticipated Date of Last Follow-up

Not provided

Estimated Primary Completion Date

Not provided

Estimated Completion Date

Not provided

Actual Primary Completion Date

2021-09-09

Actual Completion Date

2021-09-09

Studied populations

Age Cohort

Adolescents

- Adults

Genders

- Cisgender female

Accepts pregnant individuals

No

Accepts lactating individuals

No

Accepts healthy individuals

Yes

Comments about the studied populations

Women aged 16-21 inclusive.

Health status

Negative to : HIV, HBV

Study type

Interventional (clinical trial)

Enrollment

247

Allocation

Randomized

Intervention model

Cross-over assignment

Intervention model description

Not provided

Masking

Open label

Masking description

None (Open Label)

Frequency of administration

Monthly

Studied LA-formulation(s)

Non-Implantable Device

Studied route(s) of administration

Topical (Vaginal)

Use case

PrEP

Key results

Not provided

HOPE

Identifier

NCT02858037

Link

https://clinicaltrials.gov/ct2/show/NCT02858037

Phase

Phase III

Status

Completed

Sponsor

International Partnership for Microbicides, Inc.

More details

Not provided

Purpose

A follow-on, open label trial to assess adherence to and the continued safety of a Dapivirine vaginal ring in HIV-uninfected women.

Interventions

Intervention 1

Combination Product: Dapivirine Vaginal Ring

Countries

Malawi

South Africa

Uganda

Zimbabwe

Sites / Institutions

Not provided

Trials dates

Anticipated Start Date

Not provided

Actual Start Date

2016-07-18

Anticipated Date of Last Follow-up

Not provided

Estimated Primary Completion Date

Not provided

Estimated Completion Date

Not provided

Actual Primary Completion Date

2018-10-10

Actual Completion Date

2018-10-10

Studied populations

Age Cohort

- Adults

Genders

Cisgender female

Accepts pregnant individuals

No

Accepts lactating individuals

No

Accepts healthy individuals

Yes

Comments about the studied populations

Women aged 18-40 previously enrolled in MTN-020 (ASPIRE).

Health status

Negative to : HIV

Study type

Interventional (clinical trial)

Enrollment

1456

Allocation

Not provided

Intervention model

Single group assignment

Intervention model description

Participants will receive a silicone elastomer vaginal matrix ring containing 25 mg of Dapivirine to be replaced each month for a total period of 12 months of use.

Masking

Open label

Masking description

None (Open Label)

Frequency of administration

Monthly

Studied LA-formulation(s)

Non-Implantable Device

Studied route(s) of administration

Topical (Vaginal)

Use case

PrEP

Key results

Type of key results	Title	Website link
Article	Safety, uptake, and use of a dapivirine vaginal ring for HIV-1 prevention in African women (HOPE): an open-label, extension study	https://doi.org/10.1016/s2352-3018(20)30304-0
Article	Sharing Objective Measures of Adherence to a Vaginal Microbicide Promotes Candor About Actual Use and Bolsters Motivation to Prevent HIV	https://doi.org/10.1007/s10461-020-03026-6

MTN-042

Identifier

NCT03965923

Link

https://clinicaltrials.gov/ct2/show/NCT03965923

Phase

Phase III

Status

Active, not recruiting

Sponsor

National Institute of Allergy and Infectious Diseases (NIAID)

More details

Not provided

Purpose

Evaluate infant and maternal safety of the Dapivirine vaginal ring and daily oral Truvada in HIV-uninfected pregnant women.

Interventions

Intervention 1

Drug: Dapivirine Vaginal Ring

Intervention 2

Drug: Truvada Tablet

Countries

Malawi
South Africa
Uganda
Zimbabwe

Sites / Institutions

Not provided

Trials dates

Anticipated Start Date

Not provided

Actual Start Date

2020-01-09

Anticipated Date of Last Follow-up

Not provided

Estimated Primary Completion Date

2024-06-30

Estimated Completion Date

2024-06-30

Actual Primary Completion Date

Not provided

Actual Completion Date

Not provided

Studied populations

Age Cohort

- Adults

Genders

- Cisgender female

Accepts pregnant individuals

Yes

Accepts lactating individuals

No

Accepts healthy individuals

Yes

Comments about the studied populations

Women aged 18-40 years inclusive.

Health status

Negative to : HIV, HBV

Study type

Interventional (clinical trial)

Enrollment

Not provided

Allocation

Randomized

Intervention model

Sequential assignment

Intervention model description

Not provided

Masking

Open label

Masking description

None (Open Label)

Frequency of administration

Monthly

Studied LA-formulation(s)

Non-Implantable Device

Studied route(s) of administration

Topical (Vaginal)

Use case

PrEP

Key results

Not provided

IPM 024

Identifier

NCT02920827

Link

https://clinicaltrials.gov/ct2/show/NCT02920827

Phase

Phase I

Status

Completed

Sponsor

International Partnership for Microbicides, Inc.

More details

Not provided

Purpose

Evaluate the tolerability and safety of the dapivirine ring as compared to a placebo ring when inserted for four weeks in HIV-uninfected women.

Interventions

Intervention 1

Combination Product: Dapivirine Vaginal Ring

Intervention 2

Combination Product: Placebo Vaginal Ring

Countries

Belgium

Sites / Institutions

Not provided

Trials dates

Anticipated Start Date

Not provided

Actual Start Date

2009-08-01

Anticipated Date of Last Follow-up

Not provided

Estimated Primary Completion Date

Not provided

Estimated Completion Date

Not provided

Actual Primary Completion Date

2010-04-01

Actual Completion Date

2010-04-01

Studied populations

Age Cohort

- Adults

Genders

- Cisgender female

Accepts pregnant individuals

No

Accepts lactating individuals

No

Accepts healthy individuals

Yes

Comments about the studied populations

Women aged 18-40 years inclusive.

Health status

Negative to : HIV, HBV, HCV

Study type

Interventional (clinical trial)

Enrollment

16

Allocation

Randomized

Intervention model

Parallel Assignment

Intervention model description

Not provided

Masking

Double-blind masking

Masking description

Double (Participant, Investigator)

Frequency of administration

Other(s) : "Ring used continuously for 28 days "

Studied LA-formulation(s)

Non-Implantable Device

Studied route(s) of administration

Topical (Vaginal)

Use case

PrEP

Key results

Not provided

IPM 027

Identifier

NCT01539226

Link

https://clinicaltrials.gov/ct2/show/NCT01539226

Phase

Phase III

Status

Completed

Sponsor

International Partnership for Microbicides, Inc.

More details

Not provided

Purpose

Evalute the efficacy and safety of a Dapivirine vaginal matrix ring in healthy HIV-uninfected women.

Interventions

Intervention 1

Combination Product: 25 mg Dapivirine Vaginal Ring

Intervention 2

Combination Product: Placebo Vaginal Ring

Countries

South Africa

Uganda

Sites / Institutions

Not provided

Trials dates

Anticipated Start Date

Not provided

Actual Start Date

2012-03-27

Anticipated Date of Last Follow-up

Not provided

Estimated Primary Completion Date

Not provided

Estimated Completion Date

Not provided

Actual Primary Completion Date

2016-12-13

Actual Completion Date

2016-12-13

Studied populations

Age Cohort

- Adults

Genders

Cisgender female

Accepts pregnant individuals

No

Accepts lactating individuals

No

Accepts healthy individuals

Yes

Comments about the studied populations

Women participants aged 18-45.

Health status

Negative to : HIV

Study type

Interventional (clinical trial)

Enrollment

1959

Allocation

Randomized

Intervention model

Parallel Assignment

Intervention model description

Not provided

Masking

Double-blind masking

Masking description

Double (Participant, Investigator)

Frequency of administration

Other(s) : "Participants self-administered the rings every 4 weeks for up to 24 months "

Studied LA-formulation(s)

Non-Implantable Device

Studied route(s) of administration

Topical (Vaginal)

Use case

PrEP

Key results

Type of key results	Title	Website link
Article	Safety and Efficacy of a Dapivirine Vaginal Ring for HIV Prevention in Women	https://doi.org/10.1056/nejmoa1602046
Article	Assessment of risk compensation following use of the dapivirine vaginal ring in southwestern Uganda	https://doi.org/10.1136/sextrans-2020-054718

MTN-023/IPM 030

Identifier

NCT02028338

Link

https://clinicaltrials.gov/ct2/show/NCT02028338

Phase

Phase II

Status

Completed

Sponsor

International Partnership for Microbicides, Inc.

More details

Not provided

Purpose

Evalute the safety of a 25mg dapivirine vaginal ring in HIV-uninfected adolescent females, when inserted once every 28 days for 24-weeks.

Interventions

Intervention 1

Combination Product: Dapivirine Vaginal Ring

Intervention 2

Combination Product: Placebo Vaginal Ring

Countries

United States of America

Sites / Institutions

Not provided

Trials dates

Anticipated Start Date

Not provided

Actual Start Date

2014-07-27

Anticipated Date of Last Follow-up

Not provided

Estimated Primary Completion Date

Not provided

Estimated Completion Date

Not provided

Actual Primary Completion Date

2016-07-05

Actual Completion Date

2018-06-08

Studied populations

Age Cohort

- Adolescents

Genders

- Cisgender female

Accepts pregnant individuals

No

Accepts lactating individuals

No

Accepts healthy individuals

Unspecified

Comments about the studied populations

Participants aged 15-17 inclusive at enrollment.

Health status

Negative to : HIV

Study type

Interventional (clinical trial)

Enrollment

96

Allocation

Randomized

Intervention model

Parallel Assignment

Intervention model description

Not provided

Masking

Quadruple-blind masking

Masking description

Quadruple (Participant, Care Provider, Investigator, Outcomes Assessor)

Frequency of administration

Other(s) : "25mg Dapivirine vaginal ring inserted once every 28 days for 24 weeks "

Studied LA-formulation(s)

Non-Implantable Device

Studied route(s) of administration

Topical (Vaginal)

Use case

PrEP

Key results

Type of key results	Title	Website link
Article	Outline Images Download Cite Share Favorites Permissions PREVENTION RESEARCH Brief Report: Phase IIa Safety Study of a Vaginal Ring Containing Dapivirine in Adolescent Young Women	https://doi.org/10.1097/qai.0000000000

IPM 015

Identifier

NCT01071174

Link

https://clinicaltrials.gov/ct2/show/NCT01071174

Phase

Phase I/II

Status

Completed

Sponsor

International Partnership for Microbicides, Inc.

More details

Not provided

Purpose

Evaluate the safety profile of a Dapivirine intravaginal matrix ring in HIV-uninfected women.

Interventions

Intervention 1

Drug: Dapivirine Vaginal Ring

Intervention 2

Drug: Placebo Vaginal Ring

Countries

Kenya
Malawi
South Africa
Tanzania, United Republic of

Sites / Institutions

Not provided

Trials dates

Anticipated Start Date

Not provided

Actual Start Date

2010-04-01

Anticipated Date of Last Follow-up

Not provided

Estimated Primary Completion Date

Not provided

Estimated Completion Date

Not provided

Actual Primary Completion Date

2011-05-01

Actual Completion Date

2011-07-01

Studied populations

Age Cohort

- Adults

Genders

- Cisgender female

Accepts pregnant individuals

No

Accepts lactating individuals

No

Accepts healthy individuals

Yes

Comments about the studied populations

Women aged between 18-45 years inclusive.

Health status

Negative to : HIV

Study type

Interventional (clinical trial)

Enrollment

280

Allocation

Randomized

Intervention model

Parallel Assignment

Intervention model description

Not provided

Masking

Triple-blind masking

Masking description

Triple (Participant, Care Provider, Investigator)

Frequency of administration

Other(s) : "25mg dapivirine vaginal ring inserted every 28 days for 84 days total "

Studied LA-formulation(s)

Non-Implantable Device

Studied route(s) of administration

Topical (Vaginal)

Use case

PrEP

Key results

Not provided

IPM 034

Identifier

NCT01952561

Link

https://clinicaltrials.gov/ct2/show/NCT01952561

Phase

Phase I

Status

Completed

Sponsor

International Partnership for Microbicides, Inc.

More details

Not provided

Purpose

Evaluate the blood and vaginal pharmacokinetics of a 25mg Dapivirine vaginal ring worn for 1, 2, 4, 8 or 12 months.

Interventions

Intervention 1

Drug: Dapivirine Vaginal Ring

Countries

Not provided

Sites / Institutions

Not provided

Trials dates

Anticipated Start Date

Not provided

Actual Start Date

2013-11-01

Anticipated Date of Last Follow-up

Not provided

Estimated Primary Completion Date

Not provided

Estimated Completion Date

Not provided

Actual Primary Completion Date

2014-03-01

Actual Completion Date

2014-05-01

Studied populations

Age Cohort

- Adults

Genders

- Cisgender female

Accepts pregnant individuals

No

Accepts lactating individuals

No

Accepts healthy individuals

Yes

Comments about the studied populations

Women between 18-40 years of age.

Health status

Negative to : HIV, HBV, HCV

Study type

Interventional (clinical trial)

Enrollment

40

Allocation

Randomized

Intervention model

Parallel Assignment

Intervention model description

Not provided

Masking

Open label

Masking description

None (Open Label)

Frequency of administration

Other(s) : "25mg dapivirine vaginal ring usage over a time period of 1, 2, 4, 8 or 12 months. "

Studied LA-formulation(s)

Non-Implantable Device

Studied route(s) of administration

Topical (Vaginal)

Use case

PrEP

Key results

Not provided

IPM 009B

Identifier

NCT01337583

Link

https://clinicaltrials.gov/ct2/show/NCT01337583

Phase

Phase III

Status

Withdrawn

Sponsor

International Partnership for Microbicides, Inc.

More details

Not provided

Purpose

Evaluate the efficacy and safety of a Dapivirine vaginal matrix ring for HIV-1 PrEP in women.

Interventions

Intervention 1

Drug: Dapivirine Vaginal Ring

Intervention 2

Drug: Placebo Vaginal Ring

Countries

Kenya

Malawi

South Africa

Sites / Institutions

Not provided

Trials dates

Anticipated Start Date

Not provided

Actual Start Date

2011-07-01

Anticipated Date of Last Follow-up

Not provided

Estimated Primary Completion Date

Not provided

Estimated Completion Date

Not provided

Actual Primary Completion Date

2014-07-01

Actual Completion Date

2014-07-01

Studied populations

Age Cohort

- Adults

Genders

- Cisgender female

Accepts pregnant individuals

No

Accepts lactating individuals

No

Accepts healthy individuals

Yes

Comments about the studied populations

Women aged between 18-40 years.

Health status

Negative to : HIV

Study type

Interventional (clinical trial)

Enrollment

Not provided

Allocation

Randomized

Intervention model

Parallel Assignment

Intervention model description

Not provided

Masking

Double-blind masking

Masking description

Double (Participant, Investigator)

Frequency of administration

Other(s) : "25mg dapivirine vaginal ring inserted every 28 days for at least 15 months
"

Studied LA-formulation(s)

Non-Implantable Device

Studied route(s) of administration

Topical (Vaginal)

Use case

PrEP

Key results

Not provided

IPM 018

Identifier

NCT00469768

Link

https://clinicaltrials.gov/ct2/show/NCT00469768

Phase

Phase I

Status

Completed

Sponsor

International Partnership for Microbicides, Inc.

More details

Not provided

Purpose

Evaluate the pharmacokinetics and safety of a 25 mg of Dapivirine intravaginal ring in HIV-uninfected women to determine the release of Dapivirine from the reservoir and matrix.

Interventions

Intervention 1

Drug: Dapivirine Reservoir Intravaginal Ring

Intervention 2

Drug: Dapivirine Matrix Intravaginal Ring

Intervention 3

Drug: Placebo Vaginal Ring

Countries

Belgium

Sites / Institutions

Not provided

Trials dates

Anticipated Start Date

Not provided

Actual Start Date

2007-05-01

Anticipated Date of Last Follow-up

Not provided

Estimated Primary Completion Date

Not provided

Estimated Completion Date

Not provided

Actual Primary Completion Date

2007-08-01

Actual Completion Date

2007-08-01

Studied populations

Age Cohort

Adults

Genders

- Cisgender female

Accepts pregnant individuals

No

Accepts lactating individuals

No

Accepts healthy individuals

Yes

Comments about the studied populations

Women aged between 18-35 years.

Health status

Negative to : HIV

Study type

Interventional (clinical trial)

Enrollment

24

Allocation

Randomized

Intervention model

Parallel Assignment

Intervention model description

Not provided

Masking

Double-blind masking

Masking description

Double (Participant, Investigator)

Frequency of administration

Other(s) : "Intravaginal ring used continuously for 28 days "

Studied LA-formulation(s)

Non-Implantable Device

Studied route(s) of administration

Topical (Vaginal)

Use case

PrEP

Key results

Not provided

IPM 013

Identifier

NCT01144676

Link

https://clinicaltrials.gov/ct2/show/NCT01144676

Phase

Phase I

Status

Completed

Sponsor

International Partnership for Microbicides, Inc.

More details

Not provided

Purpose

Evaluate the delivery of dapivirine from matrix intravaginal rings to assess the safety in comparison to placebo intravaginal rings in HIV-uninfected sexually active women.

Interventions

Intervention 1

Drug: Dapivirine Vaginal Ring

Intervention 2

Drug: Placebo Vaginal Ring

Countries

Belgium

Sites / Institutions

Not provided

Trials dates

Anticipated Start Date

Not provided

Actual Start Date

2010-04-01

Anticipated Date of Last Follow-up

Not provided

Estimated Primary Completion Date

Not provided

Estimated Completion Date

Not provided

Actual Primary Completion Date

2010-09-01

Actual Completion Date

2010-09-01

Studied populations

Age Cohort

- Adults

Genders

- Cisgender female

Accepts pregnant individuals

No

Accepts lactating individuals

No

Accepts healthy individuals

Yes

Comments about the studied populations

Women aged between 18-40 years.

Health status

Negative to : HIV, HBV, HCV

Study type

Interventional (clinical trial)

Enrollment

45

Allocation

Randomized

Intervention model

Parallel Assignment

Intervention model description

Not provided

Masking

Double-blind masking

Masking description

Double (Participant, Investigator)

Frequency of administration

Other(s) : "Two or three intravaginal rings used over a period of 56 and 57 days for varying durations depending on experimental group "

Studied LA-formulation(s)

Non-Implantable Device

Studied route(s) of administration

Topical (Vaginal)

Use case

PrEP

Key results

Not provided

IPM 001

Identifier

NCT00700284

Link

https://clinicaltrials.gov/ct2/show/NCT00700284

Phase

Phase I

Status

Completed

Sponsor

International Partnership for Microbicides, Inc.

More details

Not provided

Purpose

Evaluate the feasibility, safety and tolerability of utilising a vaginal ring delivery system to administer TMC120 (dapivirine).

Interventions

Intervention 1

Drug: TMC120 (Dapivirine) Vaginal Ring

Intervention 2

Drug: Placebo Vaginal Ring

Countries

Belgium

Sites / Institutions

Not provided

Trials dates

Anticipated Start Date

Not provided

Actual Start Date

2004-10-01

Anticipated Date of Last Follow-up

Not provided

Estimated Primary Completion Date

Not provided

Estimated Completion Date

Not provided

Actual Primary Completion Date

2005-01-01

Actual Completion Date

2005-01-01

Studied populations

Age Cohort

- Adults

Genders

- Cisgender female

Accepts pregnant individuals

No

Accepts lactating individuals

No

Accepts healthy individuals

Yes

Comments about the studied populations

Women aged between 18-50 years.

Health status

Negative to : HIV

Study type

Interventional (clinical trial)

Enrollment

12

Allocation

Non-randomized

Intervention model

Cross-over assignment

Intervention model description

Not provided

Masking

Open label

Masking description

None (Open Label)

Frequency of administration

Weekly
Other(s) : "Placebo intravaginal ring used for an initial one week period followed by intravaginal ring containing 120 mg of TMC120 (dapivirine) for an additional week. "

Studied LA-formulation(s)

Non-Implantable Device

Studied route(s) of administration

Topical (Vaginal)

Use case

PrEP

Key results

Not provided

IPM 008

Identifier

NCT00332995

Link

https://clinicaltrials.gov/ct2/show/NCT00332995

Phase

Phase I

Status

Completed

Sponsor

International Partnership for Microbicides, Inc.

More details

Not provided

Purpose

Evaluate the systemic availability, safety and tolerability of a vaginal ring for the delivery of TMC120 (dapivirine).

Interventions

Intervention 1

Drug: TMC120 (Dapivirine) Vaginal Ring

Countries

Belgium

Sites / Institutions

Not provided

Trials dates

Anticipated Start Date

Not provided

Actual Start Date

2005-07-01

Anticipated Date of Last Follow-up

Not provided

Estimated Primary Completion Date

Not provided

Estimated Completion Date

Not provided

Actual Primary Completion Date

2005-08-01

Actual Completion Date

2005-08-01

Studied populations

Age Cohort

- Adults

Genders

- Cisgender female

Accepts pregnant individuals

No

Accepts lactating individuals

No

Accepts healthy individuals

Yes

Comments about the studied populations

Women aged 18-50 years.

Health status

Negative to : HIV

Study type

Interventional (clinical trial)

Enrollment

13

Allocation

Randomized

Intervention model

Parallel Assignment

Intervention model description

Not provided

Masking

Double-blind masking

Masking description

Not provided

Frequency of administration

Weekly
Other(s) : "Intravaginal ring containing 120 mg of TMC120 (dapivirine) used for seven days. "

Studied LA-formulation(s)

Non-Implantable Device

Studied route(s) of administration

Topical (Vaginal)

Use case

PrEP

Key results

Not provided

Excipients

Proprietary excipients used

DDU-4870 is a silicon elastomer product manufactured by NuSil™ Technology Inc. (Carpinteria, CA, USA). In 2016, NuSil Technology, Inc. merged with Avantor.

Novel excipients or existing excipients at a concentration above Inactive Ingredients Database (IID) for the specified route of administration

The novel excipient DDU-4870 is used in the final Ring-004 product formulation. DDU-4870 is contained and packaged within food-grade certified polyethylene pails, which have no effect on excipient quality. At room temperature (25ºC) DDU-4870 is estimated to maintain chemical stability for 12 months.

Residual solvents used

No residual solvent used

Patent info

Description

Dapivirine and analogues topical use for the prevention of HIV infection

Brief description

The invention concerns the microbicidal activity of certain pyrimidine or triazine containing non-nucleoside reverse transcriptase inhibitors. The compounds of the present invention inhibit the systemic infection of a human being with HIV, in particular, the present compounds prevent sexual HIV transmission in humans.

Representative patent

WO03094920

Category

Composition ; Use

Patent holder

Tibotec

Exclusivity

Not provided

Expiration date

May 13, 2023

Status

Expired

Description

Dapivirine compounds and analogues (Markush structure)

Brief description

The invention is concerned with pyrimidine derivatives having HIV replication inhibiting properties. The invention further relates to methods for their preparation and pharmaceutical compositions comprising them. The invention also relates to the use of said compounds in the manufacture of a medicament useful for the treatment of subjects suffering from HIV infection

Representative patent

WO9950250

Category

compound

Patent holder

Janssen

Exclusivity

Not provided

Expiration date

March 24, 2019

Status

Expired

Supporting material

Publications

Welsh, N. R., Malcolm, R. K., Devlin, B., & Boyd, P. (2019). Dapivirine-releasing vaginal rings produced by plastic freeforming additive manufacturing. International Journal of Pharmaceutics. https://doi.org/10.1016/j.ijpharm.2019.118725

Here we report the first use of an additive manufacturing (AM) technique based on high pressure material jetting of molten thermoplastic for the fabrication of dapivirine (DPV) loaded vaginal rings (VRs). The VRs are compared to those produced conventionally using injection molding (IM). VRs (outer diameter 54.0 mm, cross-sectional diameter 4.0 mm) were manufactured by either injection molding or Arburg Plastic Freeforming (APF) - a proprietary droplet deposition modelling (DDM) process, using medical grade thermoplastic polyurethanes (TPUs) loaded with 10% w/w DPV. This unique DDM process was used to produce rings of 100, 50 and 10% matrix infill density. DDM printed VRs with 10% density (57-62 mg drug load) exhibited up to seven-fold increase in DPV release compared to injection molded rings containing 190-194 mg DPV. This work has shown that DDM using the APF technique can be used to manufacture drug delivery devices of varying geometries, densities and surface areas to give precise levels of control over the drug release kinetics. This work presents a new opportunity to increase the release of poorly watersoluble compounds or to achieve desired dosing levels using lower drug loadings than those required using conventional thermoplastic processing techniques.

Malcolm RK, Woolfson AD, Toner CF, Morrow RJ, McCullagh SD. Long-term, controlled release of the HIV microbicide TMC120 from silicone elastomer vaginal rings. J Antimicrob Chemother. 2005 Nov;56(5):954-6. www.doi.org/10.1093/jac/dki326. Epub 2005 Sep 9. PMID: 16155060.

Objectives: The feasibility of providing prolonged and controlled release of the experimental non-nucleoside reverse transcriptase inhibitor TMC120 from a silicone vaginal ring in quantities sufficient to maintain a vaginal concentration offering

protection against heterosexual HIV transmission was investigated.

Methods: Core-type, silicone elastomer vaginal rings containing TMC120 were manufactured, and *in vitro* release studies performed under sink conditions. The experimental release data, as determined by HPLC, were correlated with estimates of vaginal TMC120 concentrations required to inhibit HIV replication.

Results: Continuous, zero-order release of TMC120 from core-type vaginal rings was observed *in vitro* over a 71 day period, equivalent to 136 µg/day. The release rate is predicted to maintain vaginal concentrations of the antiretroviral in the range of several orders of magnitude in excess of reported HIV inhibitory concentration values.

Conclusions: Continuous and prolonged zero-order release of TMC120 from a silicone vaginal ring device at quantities predicted to prevent HIV infection was observed.

Diarylaniline Derivatives as a Distinct Class of HIV-1 Non-nucleoside Reverse Transcriptase Inhibitors. Bingjie Qin, Xingkai Jiang, Hong Lu, Xingtao Tian, Florent Barbault, Li Huang, Keduo Qian, Chin-Ho Chen, Rong Huang, Shibo Jiang, Kuo-Hsiung Lee, and Lan Xie. Journal of Medicinal Chemistry, 2010**,** *53* (13), 4906-4916. www.doi.org/10.1021/jm1002952

By using structure-based drug design and isosteric replacement, diarylaniline and 1,5-diarylbenzene-1,2-diamine derivatives were synthesized and evaluated against wild type HIV-1 and drug-resistant viral strains, resulting in the discovery of diarylaniline derivatives as a distinct class of next-generation HIV-1 non-nucleoside reverse transcriptase inhibitor (NNRTI) agents. The most promising compound **37** showed significant EC50 values of 0.003−0.032 µM against HIV-1 wild-type strains and of 0.005−0.604 µM against several drug-resistant strains. Current results also revealed important structure−activity relationship (SAR) conclusions for diarylanilines and strongly support our hypothesis that an NH2 group on the central benzene ring *ortho* to the aniline moiety is crucial for interaction with K101 of the NNRTI binding site in HIV-1 RT, likely by forming H-bonds with K101. Furthermore, molecular modeling studies with molecular mechanism/general Born surface area (MM/GBSA) technology demonstrated the rationality of our hypothesis.

Additional documents

No documents were uploaded

Useful links

- Dapivirine Vaginal Ring 25 mg: Opinion on medicine for use outside EU
- WHO recommends the dapivirine vaginal ring as a new choice for HIV prevention for women
- Dapivirine Vaginal Ring for HIV Prevention

Access principles

Collaborate for development

Consider on a case by case basis, collaborating on developing long acting products with potential significant public health impact, especially for low- and middle-income countries (LMICs), utilising the referred to long-acting technology

Not provided

Share technical information for match-making assessment

Provide necessary technical information to a potential partner, under confidentiality agreement, to enable preliminary assessment of whether specific medicines of public health importance in LMICs might be compatible with the referred to long-acting technology to achieve a public health benefit

Not provided

Work with MPP to expand access in LMICs

In the event that a product using the referred to long-acting technology is successfully developed, the technology IP holder(s) will work with the Medicines Patent Pool towards putting in place the most appropriate strategy for timely and affordable access in low and middle-income countries, including through licensing

Not provided

Comment & Information

Not provided