HIV MID-YEAR MARKET MEMO

MAY 2022

Introducing the sixth edition of CHAI's **HIV Mid-Year Market Memo**, a brief covering the latest trends in the HIV space in LMICs since the publication of CHAI's annual HIV Market Report in October 2021.

For questions, reach out to Zack Panos (zpanos@clintonhealthaccess.org)

TEST SMART

US $0.95 EXW

Per test for the WHO-prequalified **SD Biosensor STANDARD Q HIV/Syphilis Combo test** made possible by a volume guarantee.

139 countries covered in this pricing agreement account for:

98% of the global burden of congenital syphilis

93% of the global HIV burden

US $1.50 EXW

Per test for **Abbott's blood-based CheckNOW HIV self-test**, WHO-prequalified in April 2022.

→ This is the lowest-cost HIV self-test currently on the market

→ **6** HIV self-tests now available with WHO PQ or GF ERPD

WHO Toolkit to Optimize HIV Testing Algorithms: this recently released toolkit provides countries with guidance to effectively conduct a local verification assessment to update national HIV testing algorithms

TREAT RIGHT *Advanced HIV Disease*

CD4 Testing

Scale-up of the **VISITECT CD4 Advanced Disease test, a device-free same-day CD4 test,** is ongoing across LMICs.

→ Available at a price of US $3.98 EXW/test in over 130 LMICs

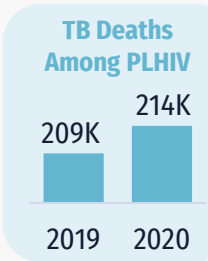
309K tests ordered as of April 2022

34 countries with tests delivered

Tuberculosis

→ For the first time in over a decade, TB deaths among people living with HIV increased in 2020

→ It is more important than ever to ensure access to short-course treatment regimens



Isoniazid/Rifapentine (INH/RPT) – 3HP

→ Macleods is scaling up production capacity and will continue the US $15 per pack access price through 2023

→ Lupin's INH/RPT (300/300 mg) tablets were recommended for use by the GF ERP in May 2022

The WHO released updated consolidated guidelines for the management of TB in children and adolescents

→ Major updates include the expansion of diagnostic testing to include **non-invasive specimens** and recommending new models of **decentralized and integrated care** that will improve access

Cryptococcal Meningitis

Flucytosine (5FC)

→ Viatris anticipated to receive approval for new API source and reinitiate supply in Q2 or Q3 2022

→ Strides has commercialized 5FC for LMICs with the first batches available from June 2022

5FC

104%

Increase in order volumes seen by APWG (2020-2021)

Liposomal Amphotericin B (L-AmB)

→ Sun Pharma received US FDA approval and work is ongoing to develop an LMIC pricing and access strategy

→ WHO issued rapid advice on use of single high dose of L-AmB based on AMBITION trial results, with new guidelines expected soon

L-AmB

672%

Increase in order volumes seen by APWG (2020-2021)

TREAT RIGHT *Adults*

TLD and DTG (50 mg)

>18M patients on TLD/DTG in 1L and 2L in LMICs

Access to **DTG in 2L** should be a priority, including **switching existing stable 2L patients** on protease inhibitors (PIs).

Countries Implementing Active Switching from PIs to DTG in 2L *(as of Q1 2022)*

Botswana *Eswatini* *India* *Malawi* *RSA* *Uganda* *Zambia*

Not Exhaustive

VISEND Trial 144-Week Results: TDF/3TC or TAF/FTC with DTG in 2L is non-inferior to AZT/3TC/PI-based standard of care, which could have implications for 2L sequencing

→ WHO guidelines on ARV backbone recycling have not been updated yet

NADIA Trial 96-Week Results: Reconfirms DTG or DRV/r equally effective in 2L and TDF/3TC can be recycled in 2L

→ Re-emphasizes the importance of 2L switching to DTG or DRV/r (for those unable to take DTG)

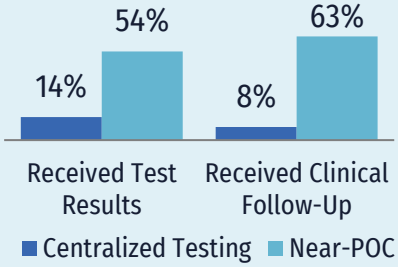
→ Southern African HIV Clinicians Society (SAHCS) endorses TDF/3TC backbone recycling in 2L

Near-POC Viral Load (VL) Monitoring in Pregnant Women

The results of a CHAI-supported study in Zimbabwe demonstrated that pregnant women tested on near-point-of-care (POC) VL platforms at the facility were:

4x more likely to receive their results within 30 days of testing

8x more likely to receive clinical follow-up action within 30 days of testing



These results support WHO Guidelines, which indicate **pregnant women are a priority population for POC VL testing**

DRV/r (400/50 mg)

Darunavir (DRV), an optimal protease inhibitor widely used in high-income countries, is now available as an affordable, fixed-dose combination with ritonavir (DRV/r 400/50 mg) thanks to a CHAI-Unitaid incentive program.

Unitaid

DRV/r (400/50 mg) from Hetero Labs is WHO-prequalified and available for

US $17.50 per pack EXW

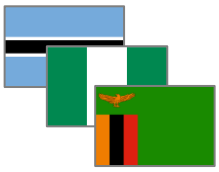
Benefits of DRV/r

- High barrier to resistance
- Improved viral suppression over LPV/r
- Better tolerability than LPV/r or ATV/r
- Less expensive than LPV/r
- Can be reused in 3L at a higher dose

DRV/r (400/50 mg) is for use by PLHIV who are PI-naïve, have not previously experienced treatment failure on a PI, or who do not have DRV-associated resistance mutations. Given the benefits and lower cost compared to LPV/r, **DRV/r does not need to be saved for third-line**.

PEPFAR

> "In the rare instances in which a patient cannot take TLD because of failure or intolerance, a regimen with DRV/r is preferred, provided DRV/r is reliably available at an affordable price."
>
> *– PEPFAR 2022 COP Guidance*



Botswana, Nigeria, and **Zambia** are introducing DRV/r (400/50 mg), initially for patients experiencing treatment failure on DTG, with early data expected later in 2022.

The CHAI HIV New Product Introduction Toolkit has numerous resources supporting DRV/r adoption and introduction

TREAT RIGHT *Adults*

Pipeline and Newly Approved Adult Products

Cabotegravir (CAB) + Rilpivirine (RPV) for Treatment

→ Injectable CAB+RPV approved by the US FDA for monthly treatment of HIV in Jan. 2021, with dosing schedule updated to every 8 weeks in Feb. 2022

→ ATLAS-2M: Injectable CAB+RPV dosed every 8 weeks is non-inferior to dosing every 4 weeks

Lenacapavir (LEN) for Prevention and Treatment

→ CAPELLA/CALIBRATE: Injectable LEN dosed every 6-months produces sufficient viral suppression

→ Injectable 6-month LEN also being studied for PrEP

→ Status: The US FDA lifted a clinical hold on injectable LEN in May 2022 following a resolution over concerns related to the compatibility of LEN and borosilicate vials

Islatravir (ISL) for Prevention and Treatment

→ ILLUMINATE SWITCH A&B: Daily oral ISL/DOR produced a viral response comparable to existing ART regimens

→ ISL also being studied in oral and implant formulations for PrEP

→ Status: The US FDA placed a partial clinical hold in Dec. 2021 based on decreases in total lymphocyte and CD4+ T-cell counts in some participants receiving ISL in studies

ISL + LEN for Treatment

→ Active trial of weekly oral formulation for treatment-experienced virologically-suppressed adult PLHIV in the US

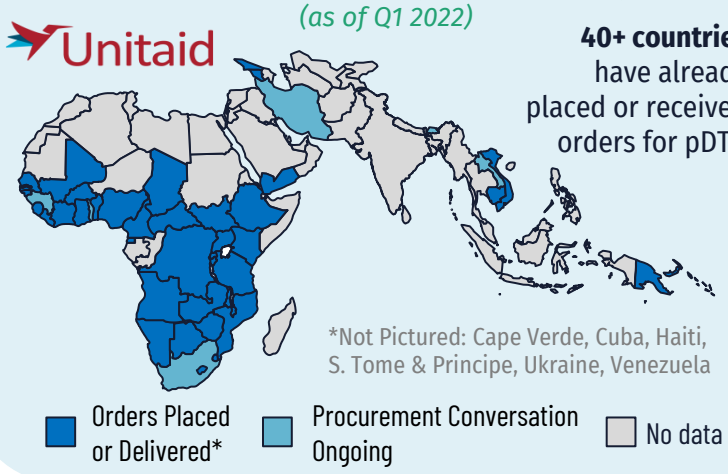
→ Status: Enrollment paused based on ISL clinical hold

TREAT RIGHT *Pediatrics*

Pediatric Dolutegravir (pDTG)

Current DTG (10 mg) Disp. Scored Adoption

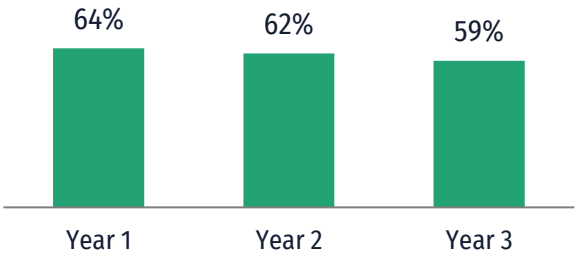
(as of Q1 2022)



Persistent low viral suppression among children following ART initiation reinforces the importance of rapidly initiating and transitioning CLHIV to pDTG.

Viral Suppression Following ART Initiation

Children <18 years old



Slow uptake of pDTG seen in some countries due to VL requirements.

→ According to the WHO, VL monitoring remains a good practice, but should not be considered a precondition to pDTG transitions

> "Children should not have their transition to DTG delayed due to lack of documented viral load."
> *– 2021 WHO Optimal Formulary*

94% of 2021 pediatric product procurement as seen by the APWG considered 'optimal' under the 2021 WHO Optimal Formulary and Limited-Use List.

Community and facility-level resources to support pDTG introduction can be accessed on the CHAI HIV New Product Introduction Toolkit

Pipeline Pediatric Treatment Products

pALD (60/30/5 mg): In March 2022 the US FDA approved ViiV's dispersible tablet formulation. CHAI & Unitaid are working to bring a generic version to market.

Development of generic **pDRV/r** and **pTAF** is also underway, further improving treatment options for children.

STAY NEGATIVE

Major Product Development and Regulatory Updates

Cabotegravir Long-Acting (CAB-LA)

→ In December 2021, the US FDA approved CAB-LA for HIV PrEP in at-risk adults and adolescents weighing at least 35 kg

→ Administered every 8 weeks (after first two doses), CAB-LA is a highly effective, injectable option for HIV PrEP, which may improve adherence

→ On May 27, 2022, ViiV committed to voluntarily license CAB-LA, a critical first step in enabling widespread, affordable access

Research & Evidence Generation

1. To inform further evidence generation, Unitaid and USAID are planning implementation science projects
2. Laboratory analysis of the HPTN 083 trial found that use of an RNA assay at screening may help identify HIV infections earlier and reduce the risk of INSTI resistance
   → However, HPTN researchers highlight that lack of RNA screening should not limit access

Key Steps for CAB-LA Introduction

WHO is reviewing evidence to inform CAB-LA guidance, which is expected mid-2022

Coordinated planning between communities, donors, and governments will be critical

Implementation tools to support efficient delivery need to be developed

Dapivirine Vaginal Ring (DVR)

In December 2021, the International Partnership for Microbicides voluntarily withdrew its application to the US FDA based on feedback that approval was unlikely based on current data and given the context of the HIV prevention landscape for women in the US.

The WHO conditionally recommends the ring alongside oral PrEP as a choice for women who do not want or are unable to take a daily oral tablet.

The DVR has received national regulatory approval in Zimbabwe and South Africa. It will also be offered in introduction studies in LMICs.

Dual Prevention Pill (DPP)

→ Bioequivalence (BE) studies are ongoing. Based on current timelines, US FDA submission is estimated for late 2023

→ CHAI is engaged in advanced planning for introduction of DPP as part of the broader pipeline of multipurpose prevention technologies (MPTs) introduction

Islatravir & Lenacapavir

The US FDA placed clinical holds on treatment and prevention trials involving both of these products in late 2021. The hold on LEN has since been lifted although the hold on ISL remains. See the *Treat Right* section for more information.

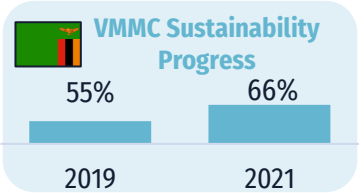
Funding and Sustainability Planning

→ Funding for HIV prevention research and development decreased 4.4% in 2020

→ Prevention funding focused on access will be critical to support new product introduction

VMMC

Progress toward country-defined VMMC sustainability targets increased in Zambia between 2019 and 2021 despite ongoing COVID impact.



DATA SOURCES

1. CHAI's annual data request to 25+ LMICs
2. Articles from journals and news outlets
3. Supplier and partner market intelligence
4. Major conferences and meetings
5. WHO guidelines and PEPFAR technical guidance

ACRONYMS USED

1L: First-line
2L: Second-line
3L: Third-line
3TC: Lamivudine
ALD: ABC/3TC/DTG
API: Active Pharmaceutical Ingredient
APWG: ARV Procurement Working Group
ART: Antiretroviral therapy
ARV: Antiretroviral
ATV/r: Atazanavir/ritonavir
AZT: Zidovudine
CAB: Cabotegravir
CLHIV: Children living with HIV
COP: Country Operational Plan
DOR: Doravirine
DRV/r: Darunavir/ritonavir
DTG: Dolutegravir
DVR: Dapivirine Vaginal Ring
EMAV: Early Market Access Vehicle
ERPD: Expert Review Panel for Diagnostics
EXW: Ex works
FTC: Emtricitabine
GF: Global Fund
HPTN: HIV Prevention Trials Network
INSTI: Integrase strand transfer inhibitor
ISL: Islatravir
LEN: Lenacapavir
LMIC: Low- and middle-income country
LPV/r: Lopinavir/ritonavir
PEP: Post-exposure prophylaxis
PI: Protease Inhibitor
PLHIV: People living with HIV
POC: Point of care
PrEP: Pre-exposure prophylaxis
RPV: Rilpivirine
TAF: Tenofovir alafenamide fumarate
TDF: Tenofovir disoproxil fumarate
TLD: TDF/3TC/DTG
VL: Viral load
WHO: World Health Organization

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