HIV testing for CAB-LA

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WHO

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Long-acting injectable cabotegravir (CAB-LA)

- Injectable PrEP formulation (600mg cabotegravir) administered as an intramuscular gluteal injection

- Dosing :
  - First two injections (initiation) 1 month apart (+/- 7 days)
  - Following injections every 2 months (+/- 7 days)

- Efficacy:
  - Phase III trials (HPTN 083 and 084) showed high efficacy with a combined effect size of about 80% relative risk reduction (66% MSM and TG, 89% Women) compared with TDF/FTC*

WHO guidance: HIV testing for CAB- LA

- HIV testing is required before offering CAB-LA and should also be done before each injection while using CAB-LA and, ideally, regularly after CAB-LA discontinuation.

- It is important for programmes to select a testing strategy and algorithm that promotes access to CAB-LA among those who would benefit most.

- Programmes can employ the current national **HIV testing strategy and algorithm,** using a combination of RDTs and enzyme immunoassays according to WHO recommendations.

- Individuals with one or more reactive test results prior to initiating CAB-LA or while taking CAB-LA need further testing to confirm their HIV diagnosis.

- Anyone with inconclusive results should be referred to return for further testing to confirm HIV status after 14 days.

WHO Guidance: Using NAT with CAB-LA

- Some countries and programmes may include **NAT where feasible**, in addition to the national algorithm, particularly at **initiation,**

- Where NAT is implemented, it is important to have the necessary assays, resources, regulatory approvals and a clear testing strategy for resolving discrepant results and establishing HIV infection before initiating life-long ART.

- Countries need to consider **the feasibility of** using NAT before CAB-LA initiation, and while taking CAB-LA.
  - While NAT before CAB-LA initiation, and while taking CAB-LA, **might** prevent a small number of cases of drug resistance, countries need to consider the **feasibility** of NAT.
  - There are also uncertainties as to what impact these mutations will have on subsequent ART.

- Ongoing monitoring of implementation is needed to further optimize HIV testing approaches for CAB-LA.

HIV infections in people in the CAB-LA continuum

Even when used as prescribed, both CAB-LA and HIV tests are not perfect, and a minority of people in CAB-LA programmes may acquire HIV.

Possible clinical scenarios:

Scenario 1: Missed infections – Acquire HIV before CAB-LA initiation and who are undiagnosed due to inherent limitations of HIV tests (e.g. too soon to detect) or test performance

Scenario 2: Breakthrough infections –Acquire HIV during CAB-LA use. This can occur before CAB-LA has reached protective levels (~ 7 days), due to missed injections and, in rare cases, when injections are not missed

Scenario 3: Tail infections – Acquire HIV more than 2 months after CAB-LA discontinuation and drug concentration has decreased below protective levels

Testing diagnostics

- 3rd generation RDTs: expected to be negative for approx. 21 days post infection due to lack of an antibody response during acute or early HIV infection.
- 4th generation RDTs are highly sensitive but no evidence showing ability to pick up acute infection
- 4th generation EIA can identify new HIV infections, but will be negative in the eclipse period and before the window period
- NAT may be able to identify these recent HIV infections if viral loads are high, but if the infection is too recent they may also be negative such as testing in the eclipse period
    - NAT is not widely available and carryover or contamination can be an issue when implementing in low-capacity sites and turn around times in LMICs can be 35+ days
    - NAT **may detect HIV infection at 7 days post infection** (depending of limit of detection method)

What is WHO doing to address this?

- Ongoing review of existing and emerging evidence to characterise issues in the intersection between CAB-LA and HIV testing
- Mapping of the HIV testing algorithms used in programmes and implementation studies delivering CAB-LA
- Provision of technical assistance and support to countries, partners and programmes
- Provide implementation guidance and clear terminology
- Focused work on CAB-LA and testing for future guidance

Program/Project	CAB LA (initiation)	CAB LA (continuation)
Axis – South Africa	**RDT** - enroll clients based on RDT result following national algorithm. Sample taken for baseline resistance testing	**RDT** before each injection
PrEPared to Choose - SA	**RDT, followed by RNA** - enroll clients based on RDT results & take a sample to test for RNA at a later point	**RDT** before each injection **RNA done at Weeks 0, 4 and 24**
Project PrEP – SA	**RDT, followed by RNA** - enroll clients based on RDT results & take a sample to test for RNA at a later point	**RDT** before each injection
CATALYST – Kenya, Lesotho, Uganda, SA, Zim	**RDT, followed by RNA** - enroll clients based on RDT results & take a sample to test for RNA at a later point	**RDT** before each injection RNA done retrospectively on stored
Path to Scale- Malawi	**RDT** - enroll clients based on RDT result following national algorithm	**RDT** before each injection
ImPrEP Study - Brazil	**RDT & RNA** – enrol clients bases on RDT and RNA results	**RDT** before each injection RNA collected and stored
Tshireletso - Botswana	**RDT** - enroll clients based on RDT result following national algorithm, Samples stored for potential seroconversions	**RDT** before each injection
Zambia MoH	**RDT, followed by RNA** - enroll clients based on RDT results & take a sample to test for RNA at a later point	**RDT and RNA** before each injection
Zimbabwe MOH	**RDT** - enroll clients based on RDT result following national algorithm	**RDT** before each injection

Discussion

- **Questions? Clarifications ?**

- What **HTS algorithms** are other countries planning for their own CAB-LA roll-out and **why?**