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Foreword

As we look to the 2030 goal of ending AIDS as a public health threat, the Kingdom of Lesotho stands not just as a participant in the global HIV response, but as a beacon of innovation and a model of decisive leadership. The nation's remarkable achievement in surpassing the global 95-95-95 targets ahead of schedule is a testament to the unwavering commitment of its government, healthcare workers, and communities. This success, however, is not an endpoint. It is a powerful platform from which to launch the next, more complex phase of the journey: securing sustainable, equitable epidemic control for all.

This **Addendum to the National Guidelines on the use of ART for HIV Prevention and Treatment (2026)** is a critical piece of that forward momentum. It represents a bold, strategic pivot—moving from scaling foundational treatment to implementing a sophisticated, patient-centered, and technologically advanced arsenal against HIV. The updates contained within are not mere incremental changes; they are transformative shifts designed to close the most persistent gaps and protect the nation's hard-won gains.

Key among these advancements is the proactive introduction of **long-acting injectable PrEP, particularly Lenacapavir.** By embracing this twice-yearly prevention option, Lesotho is directly addressing the critical barriers of adherence, stigma, and access that have historically left key populations vulnerable. Becoming an early adopter country for this technology, with the support of partners like The Global Fund, demonstrates a visionary approach to prevention—one that prioritizes choice, dignity, and long-term efficiency in a changing funding landscape.

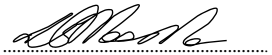
Furthermore, this document takes vital strides in fortifying the treatment cascade. It provides much-needed, updated guidance on **HIV Drug Resistance (HIVDR)** management, establishing a robust framework for surveillance, diagnosis, and response. This is essential for preserving the efficacy of our core antiretroviral regimens. Concurrently, it introduces an **optimized, fixed-dose pediatric formulation,** a compassionate and practical intervention that will dramatically improve the quality of life and treatment outcomes for children living with HIV. The adoption of a **simplified, high-dose regimen for Cryptococcal Meningitis** will save lives by reducing toxicity and complexity in the management of Advanced HIV Disease.

Perhaps most holistically, the integration of **Mental Health screening** and care into the HIV service continuum acknowledges a fundamental truth: there is no health without mental health. By systematically addressing the

co-morbidities of depression, anxiety, and substance use, we directly impact adherence, retention, and overall well-being, creating a more resilient and supported community of people living with and affected by HIV.
The development of this addendum has been a collaborative triumph. The Ministry of Health extends its deepest gratitude to the dedicated members of Lesotho's National HIV Technical Working group We are profoundly thankful for the invaluable technical partnership and support from the U.S. Centers for Disease Control and Prevention (CDC), the World Health Organization (WHO), , PEPFAR, The Global Fund, and the U.S. Department of State. The contributions of implementing partners—Solidarmed Lesotho, EGPAF, Baylor Lesotho, AIDS Healthcare Foundation Lesotho, mothers2mothers Lesotho, Population Services International, ICAP at Columbia University in Lesotho, Lenephwa, The People's Matrix Lesotho, and KAPAL Lesotho—alongside the academic rigor of the University of Basel, have ensured these guidelines are both evidence-based and grounded in the reality of service delivery across Lesotho.

This document is more than a set of clinical protocols; it is a declaration of intent. It underscores Lesotho's commitment to implementing the highest, most preferred standards of care as recommended by the WHO. It equips our heroic healthcare workers with the practical tools needed to translate policy into practice at the clinic and community level.

As we disseminate and implement this 2026 Addendum, let us do so with the same unity of purpose that brought us here. Let us embrace these innovations to protect the vulnerable, eliminate new infections, and ensure every Mosotho can live a long, healthy, and productive life. Together, we will sustain the progress and continue leading the path to an AIDS-free generation.



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Executive Summary: Advancing Lesotho's HIV Response Through Innovation and Patient Centered Approaches

Lesotho stands at a pivotal moment in its HIV response. Building on foundational successes in treatment coverage and viral suppression, the nation is now transitioning to a bold, forward-looking strategy that prioritizes cutting-edge prevention and comprehensive care. A critical pillar of this new phase is dedicated focus on closing the gap in Advanced HIV Disease (AHD) care and establishing a robust system of HIV Drug Resistance (HIVDR) screening, diagnosis and response. This document, an addendum to the 2022 ART guidelines, provides updated clinical guidance under the leadership of the Ministry of Health. It consolidates the latest evidence from global and local sources to equip healthcare workers with practical tools for implementation.

Key priorities outlined in this update include:

- Introducing novel biomedical prevention technologies, with a specific focus on the long-acting injectable PrEP.
- Enhancing the management of Cryptococcal Meningitis (CM) among persons with Advanced HIV Disease (AHD).
- Revised and refined guidance on viral load category definitions, HIV Drug Resistance (HIVDR) screening, diagnosis, use of genotypic resistance testing (GRT), regimen selection after confirmation of treatment failure and program monitoring indicators.
- Integrating Mental Health (MH) screening and diagnosis into routine HIV care.
- Introducing optimized, fixed-dose treatment formulations for pediatric patients.

A Paradigm Shift in Prevention: The Role of long acting injectables

The introduction of long-acting injectable PrEP, Lenacapavir (LEN), represents a HIV prevention game-changer for Lesotho. These powerful addresses critical adherence and access barriers faced by populations most vulnerable to acquiring HIV, including adolescent girls, young people, women, men and key populations.

Lenacapavir is administered just twice per year, offers individuals a choice of long-acting options that provide unprecedented convenience, discretion, and freedom from the challenges of daily pill-taking. This innovation is strategically aligned with Lesotho's differentiated service delivery models, making them ideal for reaching underserved communities through community outreach and mobile platforms.

The arrival of this injectable is particularly timely as Lesotho navigates a shifting funding landscape. Its selection as an early adopter country by The Global Fund affirms national readiness and provides a strategic opportunity to build a resilient, efficient HIV prevention program. By incorporating LEN into the national strategy, Lesotho is making a bold investment in choice, equity, and long-term epidemic control. This move is not merely an addition to the toolkit but a reaffirmation of Lesotho's leadership in the global effort to end AIDS as a public health threat.

This addendum ultimately underscores a commitment to implementing preferred, evidence-based, and WHO-recommended standards of care, positioning Lesotho to protect its most vulnerable, reduce new infections, AIDS related mortality, accelerating progress toward its national HIV goals.

Acronyms and Definition of Terms

3HP: Rifapentine -Isoniazid
AAC: ART Advisory Committee
ADR: Adverse Drug Reaction
AFAB: Assigned Female sex At Birth
AGYW : Adolescent Girls and Young Women
AHD: Advanced HIV Disease
AHI: Acute HIV Infection
AMBITION : AMBIsome Therapy Induction OptimisatioN
ANI: Asymptomatic Neurocognitive Impairment
ART: Antiretroviral Therapy
ASPIRE : A Study to Prevent Infection with a Ring for Extended Use
AVAC: AIDS Vaccine Advocacy Coalition
CAB -LA: Cabotegravir Long -Acting Injectable
CBT: Cognitive Behavioural Therapy
CD4: Cluster of Differentiation 4
CI: Confidence Interval
CIFF: Children's Investment Fund Foundation
CMD: Common Mental Disorder
CNS: Central Nervous System
CrAG: Cryptococcal Antigen
CSF: Cerebrospinal Fluid
CT: Computerised Tomography
CYP3A: Cytochrome P450 3A Family of Enzymes
DREAM: Dapivirine Ring Extended Access and Monitoring
DVR: Dapivirine Vaginal Ring
ED -PrEP: Event Driven Pre -Exposure Prophylaxis
eGFR: estimated Glomerular Filtration Rate
ESRD: End Stage Renal Disease
FBC: Full Blood Count
FDA: Food and Drug Administration
FTC: Emtricitabine
GAD7: General Anxiety Disorder (Screening tool)
GDG: Guideline Development Group
GRT: Genotypic Resistance Testing
HAD: HIV -Associated Dementia
HAND: HIV -Associated Neurocognitive Disorder
HCW: Health Care Worker
HIV: Human Immunodeficiency Virus
HIVDB: Standard HIV Drug Resistance Database
HIVST: HIV Self Testing
HOPE: Health Outcomes around Pregnancy and Exposure to HIV/Antiretrovirals
HOPE: Health Outcomes around Pregnancy and Exposure to HIV/Antiretrovirals
HPTN: HIV Prevention Trials Network
INSTI: Integrase strand transfer inhibitor
ISR: Injection Site Reaction
L-AmB: Liposomal Amphotericin B
LEN: Lenacapavir
LePHIA: Lesotho Population - Based HIV Impact Assessment
LFT: Liver Function Test
M&E: Monitoring and Evaluation
MDD: Major Depressive Disorder
MND: Major Neurocognitive Disorder
MMD: Multi -Month Dispensing
MOH: Ministry of Health
MSM: Men having Sex with Men
NAT: Nucleic Acid Test
OD: Once Daily
pALD: Pediatric Abacavir, Lamivudine, Dolutegravir
PCR: Polymerase Chain Reaction
PEP: Post Exposure Prophylaxis
PHQ9: Patient Health Questionnaire
PLHIV: People Living with Human Immunodeficiency Virus
PO: Per Os (Oral)
PrEP: Pre -Exposure Prophylaxis
PURPOSE:
RDT: Rapid Diagnostic Test
SASH: South Africa Stress Health
SC: Sub -Cutaneous
SD: Standard Diagnostic
SMD: Severe Mental Disorder
SSRI: Selective Serotonin Reuptake Inhibitor
TAF: Tenofovir Alafenamide
TB: Tuberculosis
TCA: Tricyclic Antidepressant
TDF: Tenofovir disoproxil fumarate
TLD: Tenofovir, Lamivudine, Dolutegravir
TPT: Tuberculosis Preventive Therapy
TSH: Thyroid Stimulating Hormone
UNAIDS: Joint United Nations Programme on HIV/AIDS
UTI: Urinary Tract Infection
VL: Viral Load
VMMC: Voluntary Medical Male Circumcision
WHO: World Health Organization

Background

Lesotho has made commendable progress achieving a public health triumph toward controlling the HIV epidemic. According to the 2025 National HIV Estimates Report, the country has surpassed the National and Global 95%, 95%, 95% targets by 2025. Ninety-seven percent % of Basotho living with HIV know their status; 97% of those who know their status are on life-saving treatment; and a world-leading 99% of those on treatment are virally suppressed. Between 2010 and 2024, Lesotho incredibly reduced new HIV infections by 83% from approximately 19,000 to approximately 3,200 new infections, respectively. During the same period, AIDS-related deaths dropped by half. This achievement places Lesotho in a unique position, among nations, on the cusp of epidemic control and on the path to ending AIDS by 2030.

However, some critical gaps threaten sustainable epidemic control. Significant disparities persist in the treatment cascade, with paediatric performance (99-77-75) severely lagging due to challenges in availability of optimized pediatric ART formulations, linkage and adherence. New HIV infections, and AIDS related deaths remain unacceptably high as the strategic target is to have zero new infections and AIDS related by 2030. These critical programmatic gaps include children not being on optimized ART regimen, sub optimal Advance HIV Disease care and limited up to date HIV drug resistance surveillance, monitoring and response persist.

Sustaining and improving the progress in the national HIV response demands programmatic innovations, such rapid introduction and effective scale up of novel HIV prevention choices, closing paediatric and male gaps, addressing and improving the quality and delivery of Advanced HIV Disease care, HIVDR management, integrating HIV services with other chronic care, for long-term sustainability.

This addendum builds on the Lesotho national guidelines on the use of antiretroviral therapy for HIV prevention and treatment, sixth edition, January 2022. It serves as a clinical reference tool designed to reinvigorate Lesotho's HIV program efforts to play a leading role in the region and globally in innovating and implementing the highest standards of patient-centered evidence driven comprehensive HIV care for individuals living in Lesotho.

Through this addendum, Basotho and all who dwell in Lesotho will have access to the 1st in class game changing, twice-yearly long acting Lenacapavir HIV prevention prophylactic injection. Children living with HIV on treatment will receive high quality optimized fixed dose ART reducing their pill burden. Individuals diagnosed with life threatening cryptococcal meningitis will no longer have to be exposed to daily doses of the potentially nephrotoxic L-amphotericin B in the induction phase instead will receive only one single high dose of L-amphotericin B minimizing and even potentially eradicating nephrotoxic exposure to the drug.

In addition, this addendum catalyzes all efforts to mitigate against the emergence of DTG related HIV Drug Resistance, achieving a critical programmatic goal of establishing HIVDR surveillance and response, effectively this will significantly contribute to the reduction in HIV.

Section I: Prevention

Objectives.

1. Use of HIVST for initiation, re-initiation and continuation of oral Pre-exposure prophylaxis (PrEP) and Post exposure prophylaxis (PEP).

2. Introduction and operationalization of long-acting injectable Pre-exposure prophylaxis (PrEP) :Cabotegravir-Long Acting (CAB_LA) and Lenacapavir (LEN).

3. Provision of new guidance on managing HIV seroconversion among individuals receiving PrEP.

4. Establishing protocols for switching between different PrEP methods.

5. Defining and addressing the challenges of Long Acting Early Viral Inhibition (LEVI) syndrome

Introduction

Prevention of HIV/STI's plays a critical role in supporting Lesotho's efforts to end AIDS as a public health threat by 2030.

Prevention strategies must be comprehensive, evidence-based, and tailored to the unique epidemiological and social context of individuals that dwell in Lesotho. This requires addressing structural, behavioural, and biomedical factors that drive transmission, while ensuring equitable access to services for all populations.

This section of the addendum emphasizes a combination HIV prevention approach, with introduction to the newly adopted PrEP methods (CAB-LA and LEN), with an emphasis on integrating:

- **Behavioural strategies**: abstinence from sexual activity, reduction of multiple and concurrent partnerships, and consistent condom use.
- **Biomedical interventions**: condom distribution, HIV testing, STI sensitivity testing, pre-exposure prophylaxis (PrEP), and treatment as prevention.
- **Social and Behaviour Change Communication (SBCC)**: targeted messaging and community engagement to promote safer sexual practices, reduce stigma, and empower individuals to make informed choices.
- **Structural interventions**: stigma reduction, gender-based violence prevention, and addressing social determinants of health.
- **Pre-exposure prophylaxis-PrEP** is the use of antiretroviral drugs by HIV negative individuals before a potential exposure to prevent acquisition of HIV. It is one of several HIV prevention strategies and is recommended for use in combination with other prevention methods. Some of the PrEP methods being deployed in Lesotho include: oral PrEP, long-acting injectable Cabotegravir (CAB-LA), and long-acting injectable Lenacapavir (LEN) to be introduced.

HIV Testing

HIV self-test for Oral PrEP

Lesotho has adopted the use of HIVST for initiation, reinitiation and continuation of oral PrEP to ease testing barriers. Healthcare workers should verify the same day HIVST negative status of the client prior to PrEP initiation to rule out HIV infection. HIVST and Rapid diagnostic testing (RDT) are both valid options for initiating, re-initiating and continuation of PrEP.

The use of HIVST shouldn't replace the use of RDT, rather, any of the two can safely be used for clients on Oral PrEP.

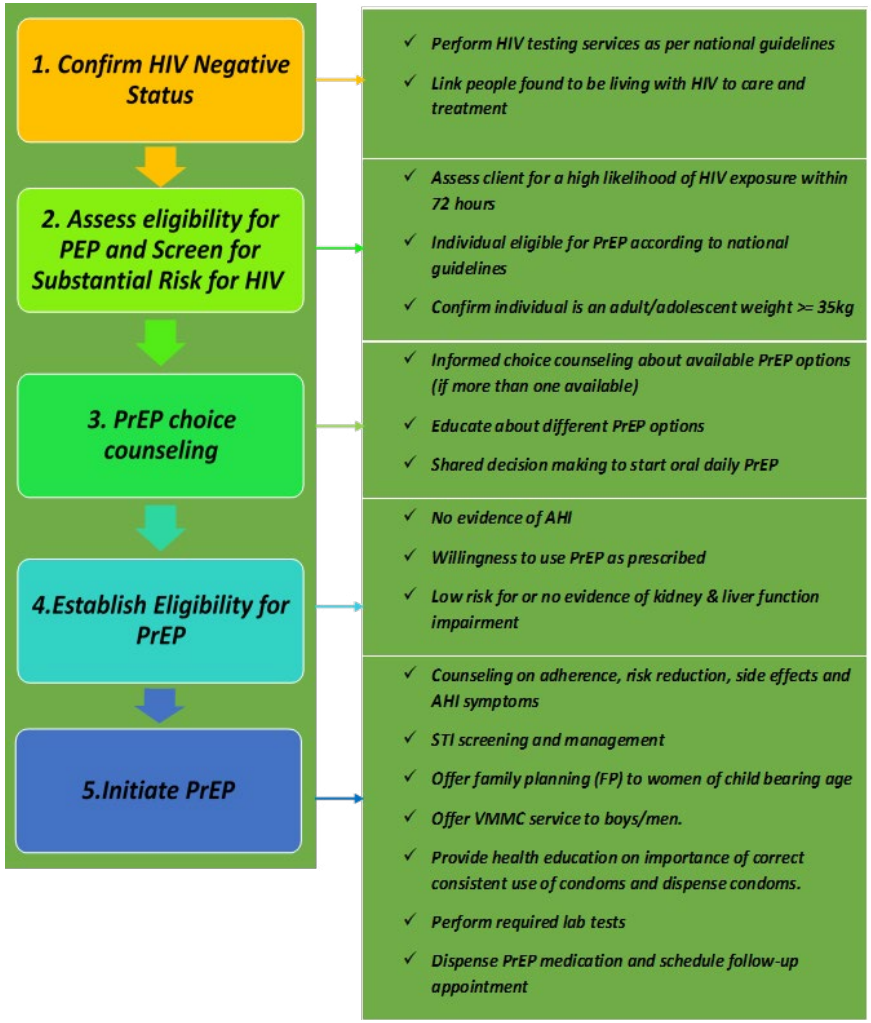
HIV Testing for Injectable PrEP

Injectable PrEP initiation, reinitiation, continuation and the discontinuation, should follow HIV testing using the nationally approved Rapid Diagnostic Testing Kits (RDTK) according to Lesotho's national HIV testing algorithm.

Only clients with confirmed HIV negative status should be started on injectable PrEP.

For inconclusive results, do not give PrEP but use other HIV prevention methods whilst awaiting DNA-PCR results.

Algorithm for PrEP eligibility assessment and initiation.



- Clinicians should consider any client who requests PrEP as being at risk and should provide PrEP after confirming the client's understanding of its use, benefits, and adherence requirements.

Contraindication

- HIV positive test result, or unknown status
- Risky potential exposure to HIV <72 hours prior to this visit.
- Suspicion of acute HIV infection (AHI
- History of allergies or hypersensitivity

PrEP Methods available in Lesotho

Table 1: PrEP Method Comparison for Lesotho

Feature	*Oral PrEP (TDF/3TC)*	*Cabotegravir (CAB-LA)*	*Lenacapavir (LEN)*
Dosing	Daily or Infrequent dosing	Injection every 2 months	Injection every 6months
Eligibility	Adults & adolescents ≥35kg	Adults & adolescents ≥35kg	Adults & adolescents ≥35kg
Key Contraindications	Severe renal impairment	Use of rifampin/ rifapentine, weight <35kg	Use of strong CYP3A inducers, weight <35kg
HIV testing	HIV test 3-monthly	HIV test before every injection	HIV test before every injection
Common Side effects	Nause and vomiting	Injection site reactions	Injection site reactions

PrEP METHODS

1. Oral PrEP

1.1. Description and Dosing

Oral PrEP is safe and effective for preventing HIV acquisition from sexual exposure. When used as directed, it can reduce the risk of HIV transmission by >90%. There are two dosing regimens:

- Daily Oral PrEP: One tablet taken once a day. (Refer to the 2022 National ART Guidelines for more details).
- Infrequent dosing: See Table 2 below

Table 2: Infrequent Dosing

Regimen	Description	Eligible Group
Infrequent dosing	• **Start**: Take two doses 2-24 hours before sex. Ideally, you should take it closer to 24 hours before. • **Continue**: Take one dose per day for as long as protection is desired, and for at least two days after the last potential exposure.	• Cisgender men (AMAB) • Trans and gender diverse people assigned male at birth (including transgender women) not taking exogenous estradiol-based hormones,

Note:

1. Infrequent dosing can transition to daily oral PrEP simply by extending the duration of use; there is no difference with oral PrEP on how to stop infrequent dosing.

2. Infrequent dosing is not recommended for people assigned female at birth due to different tissue pharmacology.

1.2. Infrequent Dosing PrEP.

Infrequent dosing oral PrEP users should be provided 30 pills bottle to support their choice to continue on daily oral PrEP, and to provide continued coverage should there be more than planned sexual exposures.

- **Infrequent dosing PrEP** is primarily recommended for **cisgender men who are not on gender affirming hormones.** The evidence for its effectiveness is strongest in this group.

- Ideal user profile: Individuals who can plan for sex **at least 2 hours in advance** and whose sexual activity is episodic or not frequent (e.g., fewer than 3 times per week on average).

(2-1-1 Infrequent Dosing-PrEP regimen)

The dosing follows a simple "2-1-1" pattern:

1. Dose 1: Take 2 pills 2 to 24 hours BEFORE anticipated sex.
2. Dose 2: Take 1 pill 24 hours after the first dose (i.e., 1 day later).
3. Dose 3: Take 1 pill 48 hours after the first dose (i.e., 2 days later)

Infrequent Dosing -PrEP is NOT! RECOMMENDED for:

- o **People who inject drugs**: Daily PrEP is the recommended regimen for this group.
- o Cisgender women and transgender men

Important considerations for Infrequent Dosing-PrEP

- **Adherence is Critical**: Missing a dose in the sequence significantly reduces protection. The "2 pills before" (loading dose) is essential to build protective drug levels rapidly.
- **Requires Planning**: Needs anticipation of sex 2-24 hours beforehand.
- **Not for Frequent Sex**: If you have sex more than 3 times a week on average, daily PrEP becomes simpler and is generally recommended.
- **Limited Population**: As highlighted it is not the first-line recommendation for all genders and exposure routes.
- **Infrequent Dosing-PrEP** users should be asked to come back for HIV test 1 month after starting the intervention for the first time or restarting. This visit should be recommended even if the client still has pills remaining. Similarly, HIV tests should be repeated at month three and every three months thereafter as recommended for daily oral PrEP.

1.3 Important considerations-switching & stopping Oral PrEP.

- A client on infrequent dosing can easily switch to Daily PrEP by continuing to take one pill every day.
- Upon stopping any oral PrEP, reinforce the use of other HIV prevention methods.
- The choice between Daily and infrequent dosing PrEP should be made in consultation with a healthcare provider. Healthcare providers should assess HIV individual risk, frequencyof sex, ability to adhere to the schedule, and what regimen is safest and most effective for individuals being provided PrEP.

2. Long acting injectable PrEP

2.1. Cabotegravir long acting injectable-(CAB-LA)

Description

CAB-LA is a highly effective long-acting PrEP method that belongs to a class of ARVs called integrase strand transfer inhibitors (INSTI), that prevents individuals from acquiring HIV.

It is an extended-release injectable suspension, does not require cold chain, thus can be stored at room temperature. Due to its extended-release properties, it allows individuals high levels of privacy and less frequent facility visits.

CAB-LA offers a protective effect after 7 days post initiation. During this lead in time the user should be counselled to use other prevention methods such as condoms.

Eligibility & Contraindications

Eligible:

- Confirmed HIV negative individuals weighing ≥35 kg and are at risk of HIV.

Contraindications:

- Co-administration with the following drugs is contraindicated: Rifampin, rifapentine, carbamazepine, phenytoin, phenobarbital.
- Weight <35 kg.

Dosing and administration of CAB-LA

The currently available formulation in Lesotho is 600mg /3 ml administered intramuscular injection in the gluteal muscle (IM).

IM Site: ***Ventrogluteal*** or ***dorsogluteal*** area is recommended.

Injection in the deltoid is currently NOT recommended for CAB-LA PrEP.

Practice: Alternate between left and right gluteal muscles for successive injections.

- **Initiation** -two initiation injections administered one month apart; healthcare workers should consider the date of initiation injection 1 as Day 0
- **Continuation** – after the initial doses, CAB-LA is given every 2 months.

There is a +/- 7-day window for receiving initiation injection 2 and continuation injections (re-injections).

N.B: **In the context of CAB_LA dosing period, a month refers to 30 days.**

Potential Side Effects of CAB-LA

Side effects are usually mild to moderate that usually decrease over time, rarely severe including:

- Local (injection site)- pain/soreness, redness, swelling or induration(firmness), warmth, bruising, small hematoma.
- Systemic general- mild fever, headache, fatigue/malaise, muscle aches.
- Less common/rare severe side effects- infection or abscess at site of injection, nerve injury (radiating pain, weakness, numbness) if injection is misplaced, local tissue necrosis , allergic reaction at the injection site and anaphylaxis (very rare, but a medical emergency). Initiation Steps

Monitoring & Follow-up

HIV test before every injection using the national algorithm. ***HIV self-testing (HIVST) is not recommended for use with injectable PrEP.***

Assess client for Liver disease and perform LFTs (AST, ALT) biannually.

Special considerations

Individuals on methadone or rifabutin may require dose adjustments. Clients on anticoagulants may have increased risk of bruising/bleeding therefore should be monitored closely.

TB Prophylaxis and treatment Considerations.

If an individual is using CAB-LA and is diagnosed with tuberculosis (TB), they will need to temporarily discontinue CAB-LA and receive treatment with a standard Rifampicin-based regimen.

In the interim, the individual may use another PrEP method or HIV prevention intervention. If the client completes TB therapy and wishes to continue with CAB-LA, they should be assessed for CAB-LA use and can restart CAB-LA with initiation injection 1. CAB-LA can be started two weeks after a client completes TB therapy. Individuals who receive TB preventative treatment with once-weekly rifapentine-isoniazid for 12 weeks (also known as 3HP) should temporarily discontinue CAB-LA for the duration of their rifapentine use. They may restart CAB-LA two weeks after completing 3HP.

For information on concurrent use of CAB-LA with other PrEP products, see the Switching Between PrEP Methods and Simultaneous Use (see section 5, page 25).

Liver disease

It is important to rule out liver disease which may be exacerbated by CAB-LA. Before initiation, all clients should have history taken, physical examination and baseline LFTs (AST, ALT) done to rule out liver disease. However, the absence of baseline tests shouldn't be a barrier to CAB-LA initiation, where there are no clear signs of liver disease.

***If active liver disease is suspected, offer other PrEP alternatives such as Oral TDF based PrEP and LEN, and refer for further management.

Pregnant and Breastfeeding women

Pregnant and breastfeeding women are at increased risk of HIV acquisition. Thus, they should be offered effective HIV prevention options including PrEP. Cabotegravir (CAB LA) is safe, well tolerated and effective for use during pregnancy and breastfeeding. CAB-LA has no increased risk of adverse pregnancy or birth outcomes compared to the normal population. There is also minimal transfer of CAB-LA to infants through breast milk supporting its use as convenient HIV prevention options for pregnant and lactating people at risk of HIV.

CAB-LA **should not** be discontinued during pregnancy or breastfeeding for women at risk of HIV exposure. **No dose adjustment is required** for pregnant and breastfeeding women or those who fall pregnant while on long acting injectable.

For pregnant and breastfeeding women (PBFW) using injectable PrEP, HIV testing should be conducted with a rapid HIV test at baseline and during follow-up visits. HIV self-testing (HIVST) is currently not recommended in this context.

Managing Missed Doses & Interruptions

CAB-LA injections can be given up to 7 days before, or after the scheduled dosing date without being classed as "missed" injections.

If the missed CAB-LA injection is initiation injection 2, and the client comes within 60 days post initiation injection 1, administer the injection and schedule for subsequent 2 monthly dosing.

If the missed CAB-LA injection is initiation injection 2, and the client comes after 60 days post initiation injection 1, restart with administration of injection 1, and schedule for initiation injection 2 in 1 month.

If the missed CAB-LA injection is a re-injection, and the client comes within 90days, administer the injection and continue the 2 monthly follow up dosing:

If the missed CAB-LA injection is a re-injection and the client comes beyond 90 days, restart with initiation injection 1 followed by injection 2, one month later

CAB-LA Bridging

Bridging is defined as a temporary use of oral PrEP during a short interruption of CAB-LA re-injections. **Only re-injections may be bridged using oral TDF.**

Bridging should be considered when a client knows in advance that they will not be available to return on time for the 2 months follow-up reinjection, they may postpone the reinjection visit by starting oral TDF PrEP on day 61 post the last reinjection visit.

Following the interruption of the 2- month CAB-LA dosing, if the time since their last CAB-LA injection is less than 3 months (90 days) continue with re-injection. If interruption is longer than 3 months (90 days), then they should follow the re-initiation protocol by restarting the CAB-LA initiation injections 1 and 2 respectively.

Planning for Cessation of CAB-LA PrEP

There are circumstances in which CAB-LA must be stopped, these include; client choice, liver diseases, TB treatment/ TPT, hypersensitivity, severe adverse reaction, drug-drug interaction and HIV sero-conversion.

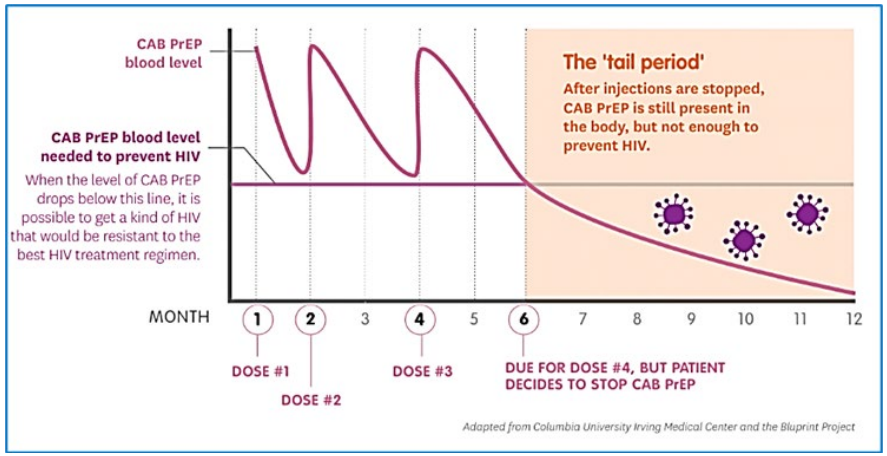
Clients who cease CAB-LA PrEP use should be reminded of the long pharmacokinetic tail of CAB-LA, and hence the risk of developing INSTI resistance if they acquire HIV during the twelve months after their last injection.

Clients should be advised to use other prevention methods during the twelve months following their last CAB-LA injection if they have ongoing risk of HIV acquisition.

Tail Period (Pharmacokinetic Tail): The extended period after the last CAB-LA injection when the drug is still present in the body at declining sub-protective concentrations. If the client acquires HIV infection during this period, the RDT may be unable to detect antibodies resulting in false negative or discordant result. The condition is referred to as LEVI Syndrome (Long-acting Early Viral Inhibition). HIV acquisition during this time carries a high risk of drug resistance (figure 3).

Figure 1: CAB-LA “tail period”

The “tail period” can last up to a year, but this time frame varies for people based on sex assigned at birth. Data on HIV acquisition during the tail period are limited. For those who do acquire HIV during this time, delayed diagnosis of HIV may be possible and could result in HIV drug resistance.



As with all PrEP methods, if a client discontinues CAB-LA, they should be offered other PrEP methods or HIV prevention strategy during the tail period if exposure to HIV is possible.

Clients must receive quarterly HIV testing for 12 months. If a client has potential exposure to HIV during the tail period while not using an HIV prevention strategy, they should speak to a health care worker as soon as possible because PEP may be appropriate. Ideally it should be started as soon as possible within 72 hours of potential exposure.

All clients who discontinue CAB-LA should receive the following services:

1. Quarterly Post-Discontinuation Monitoring Visits for a year
2. Rule-out HIV seroconversion. Refer for treatment if client seroconverts and **DO HIV RESISTANCE TEST.**
3. Offer alternative PrEP methods (oral TDF, LEN)
4. Counsel on other risk reduction strategies, (Abstinence, Being faithful, Condoms, VMMC)
5. Screen for the following:
    - Pregnancy and offer suitable contraception methods where applicable
    - Sexually transmitted infections and manage

Restarting CAB-LA PrEP

When clients who may have been on CAB-LA PrEP at some point before stopping and wish to receive it again, healthcare workers should use the guidance on managing **missed doses and interruption section above.**

Essential Instructions for Front-Line Healthcare Workers

1. **Adhere to the dosing schedule strictly:** Initiate with two loading doses one month apart, then continue with injections every two months. All doses have a ±7-day window.
2. **Test for HIV before every injection,** using the national testing algorithm. HIV self-tests are not acceptable for this purpose.
3. **When stopping CAB-LA, immediately offer an alternative PrEP method** and counsel the client that the protective "tail period" lasts up to a year. Schedule quarterly HIV tests for 12 months due to the high risk of drug-resistant HIV if seroconversion occurs.
4. **If a client is more than 3 months late for an injection, restart the two-dose initiation schedule.** Do not simply resume the 2-monthly cycle.
5. **Contraindication: Do not co-administer with rifampin/rifapentine.** Clients on these TB drugs must temporarily discontinue CAB-LA. Rule out active liver disease with baseline history and LFTs before initiation.

2.2. Lenacapavir long-acting PrEP injection (LEN)

Description

LEN is a highly effective long-acting PrEP method that belongs to a class of ARVs called Capsid inhibitor, that prevents individuals from acquiring HIV.

It is an extended-release injectable suspension, does not require cold chain, thus can be stored at room temperature. Due to its extended-release properties, it allows individuals high levels of privacy and less frequent facility visits.

LEN offers full protection from day 3, i.e, after completion of injections and the day 1 and 2 loading dose tablets are taken. The day 2 loading dose tablets must be taken for full protection. During this lead-in time the user should be counselled to use other prevention methods.

Eligibility & Contraindications

a. Eligibility;

- LEN is indicated for PrEP to reduce the risk of sexually acquired HIV in individuals weighing >35 kg who are at risk of HIV acquisition.
- Individuals must have a confirmed HIV negative test result on the day of LEN initiation.

b. Contraindications:

- Confirmed or unknown HIV-positive status.
- Use of strong CYP3A inducers: Rifampicin, rifapentine, carbamazepine, phenytoin, efavirenz.
- Weight <35 kg.

LEN dosing and administration.

LEN is available as tablets and the long-acting injectable formulations. The tablets are available as 300mg while the injection is 463.5mg/1.5ml vial.

The dosing schedule includes an initiation phase subcutaneous (SC) injections and oral tablets, followed by continuation dosing every 26 weeks (±2 weeks) via subcutaneous injection (Table 4, Figure 2). **LEN oral tablets may be taken with or without food.**

Table 4: LEN Dosing Schedule: Initiation and Continuation

Time	Dosage of LEN
Day 1	927 mg subcutaneously (2 injections × 1.5 mL LEN) + 600 mg orally (2 × 300 mg tablets)
Day 2	600 mg orally (2 × 300 mg tablets)
Every 26 weeks (±2 weeks)	927 mg subcutaneously (2 × 1.5 mL injections)

* DO NOT use one single dose of 3ml in one syringe because 3ml is too large a volume for a subcutaneous injection at once and would be very painful during administration. See annex 1 for information on components of the LEN kit and administration

Subcutaneous-SC site: Abdominal wall only

- o Aseptic technique, wash hands, clean the skin with alcohol, and use sterile, single use needle/syringe.
- o Always inject At least ~5 cm away from the umbilicus, avoid skin scars, bruises, indurations or irritated skin sites.
- o Avoid areas with scars, moles, bruising, induration, or lipodystrophy
- o Correct needle length and angle, use appropriate needle (usually short, 4-8mm), inject at a 45-90-degree angle as recommended per device instruction.
- o Inject LEN SLOWLY and apply GENTLE pressure (NO vigorous rubbing as this can cause irritation and erratic absorption). Apply gentle pressure if bleeding.
- o **Other subcutaneous sites (e.g., arm, thigh) are currently NOT recommended for lenacapavir PrEP injections. In addition, LEN should also NOT be administered intradermally.**

Practice: Systematic site rotation of LEN injection sites between doses, inject different quadrants of the abdomen to prevent lipodystrophy and to ensure consistent absorption; DO NOT inject into the exact same spot each time.

Proper LEN SC injection practices/techniques as explained above are crucial to prevent most complications

Potential Side Effects of Lenacapavir.

- Side effects are usually mild to moderate but usually decrease over time, and are rarely severe including:
- Local (injection site)- pain/soreness, itchiness, redness, swelling or induration (firmness), warmth or cellulitis.
- Systemic general- mild fever, headache, fatigue/malaise, muscle aches, abdominal discomfort- (nausea or diarrhoea).
- Less common/rare severe side effects - sterile abscess at site of injection, local tissue necrosis, site haemorrhage/hematoma, allergic reaction anaphylaxis (very rare, but a medical emergency).

Management of LEN side effects

For symptom relief at home:

- Use cold compresses initially for swelling and redness.
- After 24 hours, use warm compresses for muscle irritation.
- Take "Over The Counter" (OTC) pain relievers (e.g.,acetaminophen, ibuprofen) for pain and swelling.
- Use OTC anti-itch medications (e.g., antihistamines) for itching.
- Inject at a different area each time to encourage blood flow.
- Avoid scratching or rubbing the site.

Advice to clients to seek healthcare workers' intervention if:

- Severe, persistent, or worsening side effect symptoms.
- Signs of serious/severe side effects like infection, skin discoloration, blistering, or tissue damage (necrosis).
- Symptoms of a systematic allergic reaction/anaphylaxis (hives away from site, swelling of face/lips/tongues, difficulty breathing, dizziness)
- A persistent, painful warm tender lump or any concerning change are injection site
- Any changes in overall health

In summary, while subcutaneous LEN injections are generally very safe, the most frequent side effects are localized pain, redness and swelling

Monitoring and follow up of clients on LEN.

- HIV testing is mandatory before every injection.
- Discontinue LEN and initiate full ART immediately if HIV infection is confirmed.
- LEN injection used for PrEP represents incomplete treatment for HIV. If initiated in someone with an undiagnosed HIV infection, drug resistance mutations may develop. Healthcare workers should also monitor clients for and manage Injection Site Reactions (ISRs).
- LEN must be administered subcutaneously, not intradermally.

Lenacapavir special considerations.

a. Managing Missed Doses & Bridging;

Missed Oral Dose: If Day 2 oral initiation dose is missed, it should be taken as soon as possible.

Anticipated Delay in Injections: If a continuation dose is expected to be delayed beyond two weeks, LEN tablets (300 mg once weekly) may be used for up to six months until injections resume. This is termed "bridging".

Bridging: is the use of 300mg once-weekly oral LEN tablets to maintain protection if the next continuation injection is delayed beyond the 2-week grace period (up to 6 months).

Before restarting injections, the last tablet dose should be followed by a 7-day gap, after which the injection is given; this gap should not be exceeded, though giving the injection earlier is acceptable.

Due to limited access to oral LEN, bridging should only be done in consultation with the supply chain unit at the MOH. However, we encourage healthcare workers to work with clients to adhere to the 26-week visits and avoid bridging.

Table 5: Weekly Oral Dosing Schedule During Anticipated Delays

Time Since Last Injection	Dosage of LEN
26–28 weeks	300 orally once weekly, resume injection within 7 days after last oral dose

Missed Injection (>28 weeks without oral coverage): Reinitiate LEN using the full initiation protocol (Table 6).

Table 6: Re-initiation After Missed Injection

Time Since Last Injection	Dosage of LEN
>28 weeks (no oral coverage)	Restart initiation dosing (Table 4), then resume continuation dosing

b. Monitoring & Follow-up at LEN discontinuation.

LEN remains in the body for up to 12 months post-injection. This period is called Pharmacokinetic (PK) Tail. It is the period after a final injection where the drug remains in the body at levels too low to reliably prevent HIV but high enough to potentially select for resistance if HIV infection occurs. This prolonged exposure can increase risk of HIV acquisition and resistance if injections are missed or delayed.
To minimize the emergence of HIV drug resistance risk:

Test quarterly for HIV.
After stopping LEN, transition to another PrEP method within 26 weeks if ongoing HIV risk remains.

c. LEN drug-drug Interactions

LEN is a substrate of the cytochrome P450 enzyme CYP3A, P-glycoprotein (P-gp), and UGT1A1, making it susceptible to interactions with drugs that induce or inhibit these pathways. Table 7 provides more details on drug interactions with LEN.

Table 7: LEN Drug Interactions Summary Table

Drug Class	Drugs	Interaction with LEN	Clinical Recommendation
*CYP3A Inducers (Strong/Moderate)	Rifampicin, Carbamazepine, Phenytoin, Efavirenz, Rifapentine	LEN concentrations efficacy	Avoid co-administration For those diagnosed after injection add an alternative, e.g. oral PrEP
CYP3A Inhibitors (Strong)	Ketoconazole, Itraconazole, Clarithromycin, Ritonavir	LEN concentrations toxicity risk	**Avoid co-administration**
P-gp/UGT1A1/ CYP3A Inhibitors	Cobicistat, Ritonavir, Verapamil	LEN concentrations	Avoid use or proceed with **caution and monitoring**
CYP3A Substrates (Sensitive)	Midazolam, Triazolam, Fentanyl, Simvastatin	LEN substrate concentrations risk of adverse effects	Adjust substrate dose and **monitor for toxicity**
P-gp Substrates (Sensitive)	Digoxin, Dabigatran, Colchicine	LEN substrate concentrations	Monitor levels/ toxicity of substrates
Statins (Minimal Interaction)	Atorvastatin, Pitavastatin, Rosuvastatin	No clinically significant interaction	No adjustment needed
Others with No Significant Interaction	Famotidine, Voriconazole, Tenofovir alafenamide	No significant change in exposure	No adjustment needed

***Common CYP3A4 inducers can be remembered with the mnemonic COPPER: Carbamazepine, Oxcarbazepine, Phenobarbital (and primidone), Phenytoin, Enzalutamide, and Rifampin**

CYP3A Inducer Considerations
Supplemental dosing is required when initiating LEN in individuals who are also starting strong or moderate CYP3A inducers.

Use of LEN in Special Populations (Access Data FDA, 2025)

Table 8 provides vital information to consider for initiation special populations on LEN.

Table 8: Summary of LEN Use in Special Populations

Population	Key Considerations	Recommendation
Pregnancy	- No increased risk of birth defects or adverse outcomes observed. - Higher HIV acquisition risk during pregnancy.	- Continue or initiate LEN PrEP if clinically indicated.
Breastfeeding	- LEN is present in human milk with low levels detected in breastfed infants. - No adverse effects observed in breastfed infants.	LEN can be used during lactation because the benefit of preventing maternal HIV acquisition outweighs the potential, yet unknown, risk to the infant.
Adolescents ≥35 kg	- Safety and efficacy established. - HIV testing is required before initiation and every injection	Extra adherence support may be needed.
Children <35kg	- Not studied	Not recommended
Older Adults (65+)	- Limited data - Consider comorbidities and organ function	Use with caution
Renal Impairment	- No adjustment needed for eGFR ≥15 mL/min - Not studied in ESRD (eGFR <15 mL/min)	Use with caution in ESRD
Hepatic Impairment	- No adjustment needed for mild/ moderate (Child-Pugh A/B) - Not studied in severe (Child-Pugh C)	Avoid use in people with severe hepatic impairment unless necessary

***ESRD- End-Stage Renal Disease**

Pregnant and Breastfeeding women.

Pregnant and breastfeeding women remain at increased risk of HIV acquisition. Thus, they should be offered effective HIV prevention options including PrEP. Lenacapavir (LEN) is safe, well tolerated and effective for use during pregnancy and breastfeeding. LEN showed minimal transfer to infants through breast milk and no increase in adverse pregnancy or birth outcomes compared to the normal population, supporting their use as convenient HIV prevention options for pregnant and lactating people at risk of HIV.

LEN “should not be discontinued” during pregnancy or breastfeeding for women at risk of HIV exposure, no dose adjustment required for pregnant and breastfeeding women for those who fall pregnant while on long acting injectable. Ongoing monitoring is essential, as lenacapavir (LEN) has a prolonged pharmacological tail lasting up to 12 months after the last dose. Transitioning to oral PrEP or monitoring the HIV status during the tail period is essential.

For pregnant and breastfeeding women (PBFW) using injectable PrEP, HIV testing should be conducted with a rapid HIV test at baseline and during follow-up visits. HIV self-testing (HIVST) is not currently recommended in this context.

LEN essential instructions for Front-Line Healthcare Workers

- **Verify a Negative HIV Status Immediately Before Every Injection.** This is non-negotiable. Administering LEN to an HIV-positive individual can lead to the development of drug-resistant HIV due to the drug's prolonged presence in the body.
- **Follow the Exact 2-Day Initiation Protocol.** For new clients, the first dose must be: **Day 1:** 927 mg subcutaneously (two 1.5 mL injections) **PLUS** 600 mg orally (two tablets); **Day 2:** 600 mg orally (two tablets). Do not deviate from this sequence.
- **Screen for and Avoid Concurrent Use of Strong CYP3A Inducers.** Drugs like rifampin, carbamazepine, and phenytoin significantly reduce LEN levels, rendering it ineffective for prevention. These are contraindicated.
- **Administer Subcutaneously in the Abdomen and Counsel on Injection Site Reactions (ISRs).** Use two separate 1.5 mL injections. Educate clients that ISRs (pain, nodules, redness) are common, typically mild, and manageable with simple self-care measures, but to report severe or worsening symptoms.
- **Implement the "Bridging" Protocol for Late Injections.** If a continuation injection will be delayed beyond 28 weeks, initiate a bridging regimen with **once-weekly oral LEN tablets** (300 mg) to maintain protection until the injection can be rescheduled (must be given within 7 days of the last oral dose).
- **Encourage/offer partners of individuals accessing Lenacapavir who are eligible to receive LEN.**
- Always offer FP to all child bearing age women.
- Always offer VMMC to boys and men eligible.
- Screen, diagnose and manage any STI’s among individuals requesting Lenacapavir
- Always offer health education on importance of correct, consistent use of condoms and dispense condoms and lubrication

Switching Between PrEP Methods

Key Instructions for Switching PrEP Methods

- **Ensure no gaps in protection** during the transition between methods.
- **Follow the specific switching protocol** for the original and new PrEP product.
- **Always conduct a HIV test** before initiating the new method.
- **Counsel clients on the “PK tail”** risk after stopping injectables like CAB-LA or LEN.
- **Schedule the switch on time** to prevent unprotected periods.

Clients starting a particular PrEP product may decide to switch to another option later, for any number of reasons that may be related to their preferences or product characteristics. Therefore, switching between pre-exposure prophylaxis (PrEP) methods is common and should be done under a healthcare worker’s supervision to ensure continuous protection. Safe switching protocols vary depending on the PrEP methods involved, with some requiring overlap to maintain drug levels and others having a “pharmacokinetic (PK) tail” that requires special care.

Considerations when switching PrEP methods

- **Maintain continuous protection.** The core principle of switching is to prevent any lapse in HIV prevention. This may involve overlapping dosages for a short period.
- **Reasons for switching.** People change PrEP methods for many reasons, including a desire for fewer pills, changes in sexual activity, or to address side effects.
- **Method-specific requirements.** Each type of switch has its own set of instructions and considerations.
- **The injection (CAB-LA, LEN) “tail.”** If you are stopping the long-acting injectable PrEP the drug remains in your body for a long time at levels too low to prevent HIV. This period is known as the «PK tail» and carries a risk of developing drug-resistant HIV if infection occurs.
- Key universal steps for assessing client, testing for HIV, and counselling clients apply before switching to new choice. Provide information on newly selected PrEP choice to inform client`s choice.

Key Definitions

- **Switching (Transitioning)**: The process of changing from one Pre-Exposure Prophylaxis (PrEP) method (e.g., oral pills, injectable, ring) to another. This must be a supervised, planned process to ensure no gap in HIV protection.
- **Continuous Protection**: The fundamental goal of switching PrEP methods. It means always maintaining effective drug levels in the body to prevent HIV infection, with no lapses during the transition from one method to another.
- **Overlap (Overlapping Dosages)**: A switching strategy where two PrEP methods are used simultaneously for a short period (e.g., 2-7 days). This ensures protective drug levels from the new method are established before discontinuing the old method. This is used when

switching *to* CAB-LA, the DVR, or LEN.

- **Pharmacokinetic (PK) Tail**: The extended period *after* the final dose of a long-acting injectable PrEP (like Lenacapavir or CAB-LA) where the drug remains in the body at levels too low to reliably prevent HIV, but high enough to potentially select for drug-resistant virus if a person becomes infected with HIV during this time.
- **Switching Protocol**: A specific, method-dependent set of instructions that guides how to safely transition from one PrEP product to another. The correct protocol depends on which method a client is switching *from* and which they are switching *to*.

Table 9: Summary Table for Switching between PrEP Choices

Original PrEP Option	New PrEP Option	Switching Protocol
From Oral PrEP	To CAB-LA	1. Get the first CAB-LA injection. 2. Continue oral PrEP for 7 days after starting the new method.
	To LEN (Lenacapavir)	1. Receive the LEN initiation regimen (over two days – oral doses and injection). 2. Continue oral PrEP daily throughout the two days of the LEN initiation.
From DVR (ring)	To CAB-LA or Oral PrEP	1. Get the first CAB-LA injection or take the first oral PrEP dose. 2. Continue wearing the DVR for 7 days after starting the new method.
	To LEN (Lenacapavir)	1. Receive the LEN initiation regimen – oral doses and injection. 2. Continue wearing the DVR throughout the 2 days of LEN initiation.
From CAB-LA	To DVR, Oral PrEP, or LEN	• If switching soon after starting: Start the new method 1 month after Initiation Injection 1. • If switching later: Start the new method 2 months after your last injection (Initiation 2 or Follow-up).
From LEN	To DVR, CAB-LA, or Oral PrEP	Start the new method 26 weeks after your last LEN injection.

- Do not administer CAB-LA and LEN concurrently.
- NB: Healthcare workers must ensure a client who plans to switch PrEP option returns before or on the next scheduled appointment date. Clients who delay presenting risk becoming unprotected during the switch period***

Key Instructions for Switching PrEP Methods

- **Ensure no gaps in protection** during the transition between methods.
- **Follow the specific switching protocol** for the original and new PrEP product.
- **Always conduct a HIV test** before initiating the new method.
- **Counsel clients on the "PK tail"** risk after stopping injectables like CAB-LA or LEN.
- **Schedule the switch on time** to prevent unprotected periods.

HIV Seroconversion on PrEP

Managing HIV Seroconversion during PrEP provision.

Key Definitions.

- **Seroconversion**: The period during which a person develops antibodies to a specific pathogen; in this context, it refers to a person acquiring HIV infection while on or after using PrEP.
- **LEVI Syndrome (Long-acting Early Viral Inhibition)**: A condition where residual levels of a long-acting drug (like CAB-LA) suppress viral replication enough to cause a false-negative or discordant result on standard HIV tests, delaying diagnosis and increasing the risk of resistance.
- **Drug Resistance**: When HIV mutates and becomes less susceptible to the effects of a drug, making that drug less effective or ineffective.
- **Genotypic Resistance Testing (GRT)**: A laboratory test to identify specific mutations in the HIV virus's genetic code that confer resistance to antiretroviral drugs. It is essential for guiding ART selection after seroconversion on PrEP.

While HIV PrEP is highly effective when used correctly, rare cases of seroconversion (HIV infection) can occur. These instances are typically linked to two primary scenarios: undiagnosed, pre-existing HIV infection at the time of PrEP initiation, or a breakthrough infection due to ineffective PrEP use.

A significant concern in these cases is the potential development of HIV drug resistance, which, though rare, has been documented with all PrEP modalities, including oral PrEP, LEN), and cabotegravir long-acting (CAB-LA)

Continued use of PrEP by someone with HIV may lead to the development of HIV drug resistance. Though rare, this has been observed for users of oral PrEP, CAB-LA, and LEN.

6.2. Managing Seroconversion on Oral PrEP or DVR

If an individual seroconverts while on oral PrEP (daily or intermittent) or the DVR, first-line antiretroviral therapy (ART) with TLD can be started immediately. The risk of developing significant HIV drug resistance with these modalities is low.

6.3. Challenges of CAB-LA and LEN

The situation is more complex with CAB-LA and LEN due to their long-acting nature. Seroconversion can occur in three scenarios:

1. Undiagnosed HIV infection at the time of CAB-LA initiation.
2. Breakthrough HIV infection while receiving CAB-LA injections.
3. HIV infection acquired after the last injection, while drug levels are waning during the 12-month "tail period."

A critical complication is Long-acting Early Viral Inhibition (LEVI) syndrome (Landovitz, 2024), where the ongoing presence of CAB-LA can suppress viral replication enough to cause false-negative results on standard HIV tests. This delays diagnosis, and if CAB-LA injections continue, the client effectively receives monotherapy, creating high pressure for the selection of INSTI-resistant virus (since both cabotegravir and dolutegravir in TLD are INSTIs).

6.4. Recommended Clinical Response to Seroconversion on PrEP

When HIV seroconversion is confirmed in a client on PrEP, the following steps are critical:

1. **Immediately discontinue** all forms of PrEP.
2. **Initiate ART (TLD)** without a treatment gap to suppress the virus and reduce the risk of secondary transmission.
3. **Collect a sample** for genotypic resistance testing (GRT) before or at the time of ART initiation.
4. **Consult with an experienced HIV clinician** to review resistance results and tailor the ART regimen accordingly.
5. Document and report all cases of HIV seroconversion in HIV M&E registers, inform AAC committee, district clinical mentor and national HIV program PrEP focal person and program manager.

Post Exposure Prophylaxis (PEP)

PEP regimens, for both adults and children, remains unchanged and consistent with 2022 Lesotho National guideline on, but the models for delivery have been expanded (WHO, 2025).

Testing for PEP

Before starting PEP, people should be tested for HIV, using the national HIV testing algorithm as specified in the Lesotho 2025 national testing guidelines. Testing options include a rapid test by healthcare workers or a healthcare workers verified HIV self-test. If the HIV test is non-reactive (negative), PEP can be started immediately. **If HIV tests are unavailable but the person is suspected to have been exposed to HIV, PEP should be started regardless**. If the HIV test is reactive, the person should seek further testing following the national HIV testing strategy and be linked to ART if confirmed to have HIV. After completing the 28-day PEP course, follow-up HIV testing should be done. Again, this can be done with a rapid test or an HIV self-test. If the result is reactive, the person should seek further testing.

Differentiated PEP service delivery models

To enhance accessibility and ensure timely initiation of PEP, service delivery has been expanded beyond fixed facility-based setting. PEP may be offered through the following community-based models:

- Community Based Service Delivery Models
- Drop in centers
- Mobile clinics
- Health posts.

Referral and Linkage post PEP initiation

All PEP services delivery points must maintain community to facility referral pathways to ensure continuity of care. This includes:

- Referral for HIV testing post completion of 28-day PEP regimens.
- Documentation and communication between the initiating sites and receiving facility to support effective follow-ups.
- Ensure individuals completing PEP are linked to appropriate HIV prevention, treatment and support services post testing.

Section II: Advanced HIV Disease

Key Highlights:

- Introduction of high-dose Liposomal Amphotericin B (L-AMB) regimen.

1. Introduction

Advanced HIV Disease (AHD) is defined as adults, adolescents, and children older than 5 years with a CD4 cell count <200 cells/mm3 or a WHO stage 3 or 4 condition. All children <5 years old presenting with HIV and not on effective ART for more than one year are defined as having AHD.

Targeted CD4 testing is recommended for AHD identification for the following categories of people:

1. Newly initiated ART
2. Suspected treatment failure (VL >1000 copies)
3. Re-engaging in care following treatment interruption for >90 days (3 months)
4. Hospitalized or critically ill or considered clinically unstable
5. Clients with WHO clinical stage 3 and 4

Use of Point of care VISITECT® CD4 testing

VISITECT CD4 is a semi-quantitative point-of-care test that is used as the primary tool for Advanced HIV Disease (AHD) screening. When the VISITECT® result indicates a CD4 count below 200 cells/mm^3, **there is no requirement for confirmatory laboratory-based quantitative CD4 testing**, as this threshold is sufficient to classify a client as having AHD and to initiate the appropriate clinical management package, including cotrimoxazole (CTX) prophylaxis.

However, a confirmatory quantitative CD4 test would be required for clients offered AHD screening using VISITECT® ***with a CD4 above 200 cells/mm^3*** to identify those eligible for CTX prophylaxis—CD4 below 350 cells/mm^3.

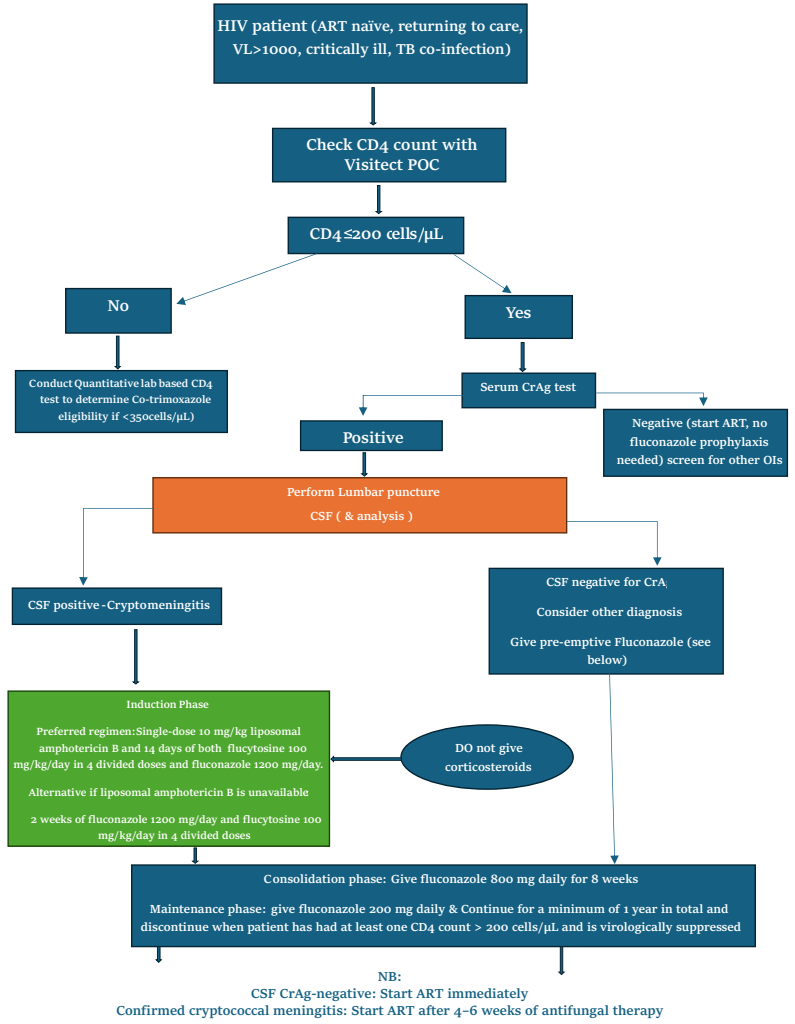
This approach enables rapid decision-making at the point of care, particularly for determining eligibility to CTX prophylaxis. All clients with a CD4 count below 350 cells/mm^3—whether newly diagnosed, returning to care, unsuppressed (>1000 copies/ml)—should be initiated on CTX and remain on it until their CD4 has risen above this benchmark. The VISITECT platform therefore streamlines AHD identification, reduces delays in care, and ensures timely initiation of prophylaxis and other essential interventions while also recognizing the value for quantitative laboratory-based platforms.

*CD4 monitoring should continue **every 6 months** or until the CD4>350 cells/mm3 using **Quantitative CD4 testing NOT** VISITECT® CD4, (whichever is earlier) and viral load is <1000 copies/ml.

7.1. Cryptococcal Meningitis

Cryptococcal Meningitis (CM) is one of the most common opportunistic infections among people living with HIV (PLHIV) with Advanced HIV Disease (AHD). With an estimated 3-month mortality rate of 70% in routine care settings, it accounts for about a fifth of all AIDS-related deaths. Access to essential antifungal drugs remains limited due to the lack of generic manufacturer and high prices, thus posing a critical barrier to care. Furthermore, drug toxicity, admission, and laboratory monitoring costs constitute additional barriers.

The previous WHO-recommended first-line treatment regimen for the management of cryptococcal meningitis, which is currently the preferred regimen in Lesotho as per the 2022 Lesotho ART guidelines, entails the administration of Amphotericin B (AmB) and Flucytosine (5FC) for one week followed by a week of high-dose fluconazole. (Lawrence, 2022) However, treatment with AmB has been shown to be associated with substantial drug-related adverse events with resultant long-term hospital stays and high healthcare costs.



Screening and Management of Cryptococcal Meningitis Flow Chart

Liposomal Amphotericin B

Liposomal amphotericin B is a safer, preferred treatment for fungal infections. The AMBITION trial showed that a single high dose, combined with other drugs, is as effective as and safer than standard care, while also being easier to administer and more cost-efficient. (Jarvis, 2022)

All PLHIV with AHD diagnosed with CM using CSF CrAg or other approved diagnostic tests should be managed using the protocol below:

Cryptococcal Meningitis Treatment Protocol

Below (Table 10) is a description of how healthcare workers can manage patients with

cryptococcal meningitis.

Table 10: Cryptococcal Meningitis Treatment Protocol

Induction Phase (2 weeks)	
Preferred regimen	Alternative regimen
A single **high dose (10 mg/kg)** of **liposomal amphotericin B** with 14 days of flucytosine (100 mg/kg per day divided into four doses per day) and fluconazole (1200 mg/daily for adults; 12 mg/kg per day for children and adolescents up to a maximum of 800 mg daily) should be used as the preferred induction regimen for treating people with cryptococcal meningitis	If no amphotericin B formulations are available: 14 days of fluconazole (1200 mg daily, 12 mg/kg per day for children and adolescents) + flucytosine (100 mg/kg per day, divided into four doses per day). If flucytosine is not available: 14 days of liposomal amphotericin (3-4 mg/kg per day) + fluconazole (1200 mg daily, 12 mg/kg per day for children and adolescents up to a maximum of 800 mg daily).
Consolidation Phase (8 weeks)	
Fluconazole 800mg/day for adults (or 6-12mg/kg/day for children and adolescents up to a maximum of 800mg daily)	
Maintenance Phase (>52 Weeks)	
Fluconazole (200 mg daily for adults, 6 mg/kg per day for adolescents and children) until the client reaches immune reconstitution (CD4 >200 cells/mm3) and suppression of viral loads on ART.	

CM dosing charts

Preferred Regimen

Phase	Adults >19 years	Pediatrics <19 years
Induction phase 14 days	Liposomal Amphotericin B **(High Dose) STAT** 10mg/kg + Flucytosine 100mg/kg per day (divided into 4 doses/day i.e., 6 hourly) X 14 days. + Fluconazole 1200mg per day X 14 days	Liposomal Amphotericin B (high dose) STAT 10mg/kg + Flucytosine 100mg/kg per day (divided into 4 doses/day i.e., 6 hourly) max 800mg X 14 days. + Fluconazole 12mg/kg per day max 800mg X 14 days
Consolidation phase (8 Weeks)	Fluconazole 800mg per day for 8 weeks	Fluconazole 6-12mg/kg/day max 800mg for 8 weeks
Maintenance phase (>52 weeks)	Fluconazole 200mg per day (Until CD4>200 cells/mm^3) and virally suppressed	Fluconazole 6mg/kg per day (Until CD4>200 cells/mm^3) and virally suppressed

Alternative regimen for Induction phase

Adults	Pediatrics
If liposomal Amphotericin is NOT available	
Flucytosine 100mg/kg per day (divided into 4 doses/day) X 14 days. + Fluconazole 1200mg per day X 14 days	Flucytosine 100mg/kg per day (divided into 4 doses/day) X 14 days. + Fluconazole 12mg per day X 14 days
If Flucytosine is not available	
Liposomal Amphotericin 3-4mg/kg per day X 14 days + Fluconazole 1200mg per day X 14 days	Liposomal Amphotericin 3-4mg/kg per day X 14 days + Fluconazole 12mg per day max 800mg X 14 days

NOTE: *flucytosine-containing regimens are superior, and steps should be taken to ensure access to this drug.*

Preparation of Liposomal Amphotericin B

1. Based on the patient's weight, calculate how many mg and how many vials are needed in total.

2. Inject 12ml of water for injection in each vial and shake vigorously for 30 sec until all powder

is dissolved and the solution is clear.

3. The solution in each vial will contain 4mg /ml

4. Calculate the total volume (ml of solution) needed for the total dose to be given.

5. Remove the equivalent volume of dextrose 5% or 10% from the infusion bag to make room for the total Liposomal Amphotericin B solution to be added.

6. Do not use saline or Ringer's lactate instead of dextrose solution because the Liposomal Amphotericin B solution may clot.

7. Attach a needle to the filter included with the Liposomal Amphotericin B and inject the solution through the filter into the dextrose bag. Use a new filter for each vial of Liposomal Amphotericin B solution.

8. Shake the dextrose bag gently to mix when all Liposomal Amphotericin B has been added.

Table 11: Product Description - Cryptococcal Meningitis Medicines

Drug	Class	Mechanism of action	Formulation
Liposomal Amphotericin B	Polyene	Fungistatic or fungicidal, depending on the concentration in body fluids and the fungus's susceptibility. The drug binds to sterols in the cell membrane, allowing leakage of intracellular contents and cell death.	Injection: 50mg/ vial
Flucytosine	Antimetabolite	It is converted to 5-fluorouracil in the fungus, which is extensively incorporated into fungal RNA. Thus, it inhibits DNA and RNA synthesis and ultimately leads to unbalanced growth and cell death.	Capsules: 500/250mg Injection: 10mg/ mL
Fluconazole	Azole	It selectively inhibits the fungal cytochrome P450-dependent enzyme that converts lanosterol to ergosterol, which is necessary for fungal cell wall synthesis. Subsequently, this disrupts the fungal membrane and halts its growth.	Tablets: 50, 100, 150, & 200mg Suspension: 50mg/5ml Injection: 2mg/mL

Table 12: Monitoring Amphotericin B-related Toxicity

Day	1	2	3	4	5	6	7	8	9	10	11	12	13	14
Single high-dose liposomal amphotericin B														
Pre-emptive hydration and electrolyte supplementation (adults and adolescents)														
1 litre of normal saline solution with 20 mEq KCl over two hours before infusion	X													
8-mEq KCl tablets orally (twice daily)	X	X	X											
Magnesium supplementation if available[a]	X	X	X											
Monitoring (adults, adolescents, and children)														
Serum potassium	X		X											

Serum creatinine	X		X											
FBC	X						X[b]							X[b]
2 times 8-mEq KCl tablet (twice daily)	X	X	X	X	X	X	X							
Magnesium supplementation (*250-mg tablet(s) of magnesium trisilicate or glycerophosphate twice daily or magnesium chloride 4mEq twice daily*. If available)[a]	X	X	X	X	X	X	X							

a Absence of magnesium trisilicate should not hinder treatment with Liposomal Amphotericin B.

b As long as still on Flucytosine.

Additional Notes

-Amphotericin B is incompatible with normal saline. Administer with 5% dextrose solution.

- Potassium replacement should NOT be given to people with pre-existing renal impairment or hyperkalaemia.

- Careful attention should be given to monitoring the intake and output of fluid and daily weight, especially among children.

- Flucytosine: because of concerns about bone marrow suppression, regular monitoring of full blood counts should be considered; guidelines from the Southern African HIV Clinicians Society recommend monitoring full blood counts at baseline and at least weekly for as long as the person takes flucytosine.

*If the standard dose of liposomal amphotericin B is given for 14 days with fluconazole, the incidence of renal dysfunction and electrolyte disturbance is lower than with amphotericin B deoxycholate, but renal function and electrolytes still need to be monitored. However, unavailability of Laboratory monitoring should **NO**T be a deterrent to initiating Liposomal Amphotericin B, in settings with limited monitoring, clinical presentation of the patient, hydration status and the use of a single High dose will take precedence.*

Table 13: Management of Amphotericin B-related Toxicity

	Single 10 mg/kg liposomal amphotericin B
Hypokalaemia	If hypokalaemia is significant (K <3.3 mol/l), increase potassium supplementation to 40 mEq KCl by intravenous infusion and/or one to two 8-mEq KCl tablets orally three times daily. Monitor potassium daily.
Elevated creatinine	Ensure adequate hydration and discontinue concurrent nephrotoxic drugs if possible. If renal impairment is significant, adjust fluconazole and flucytosine doses appropriately. Note that renal function often improves initially following rehydration.
Severe anaemia	Transfusion, if possible, for severe (grade 4 and clinically symptomatic) liposomal amphotericin B–related anaemia

Flucytosine (5-FC) Toxicity

Because of concerns about bone marrow suppression, regular monitoring of full blood count should be considered for the duration of the treatment to monitor for associated anemia, neutropenia, and thrombocytopenia. (Refer to Table 13 above)

Drug Interactions

Drug interactions in the context of concurrent use of amphotericin, flucytosine and fluconazole alongside ART regimens have not been well documented. However, the following guidance is provided to healthcare workers.

- **Amphotericin B & TDF**: Patients on tenofovir disoproxil fumarate (TDF) require close kidney monitoring due to a heightened risk of nephrotoxicity when given amphotericin B, even the safer liposomal form. TDF dosage must be adjusted for any pre-existing renal impairment.
- **Flucytosine**: Its metabolism can lead to blood toxicity, requiring regular monitoring of blood counts (Hb, WCC, platelets). Its dose must also be adjusted in patients with reduced kidney function.
- **Fluconazole**: No antiretroviral therapy (ART) dose adjustments are needed despite its effects on certain enzymes.

Treatment for Pregnant Women

Amphotericin B can be used in pregnancy if the benefits justify the risks. The other common antifungal drugs, flucytosine and fluconazole, carry a risk of birth defects and should only be considered on a case-by-case basis.

Adjunctive Corticosteroids in Treating HIV-Associated Cryptococcal Meningitis

Routine use of adjunctive corticosteroid therapy during the induction phase **is not recommended** in treating adults, adolescents and children who have HIV-associated cryptococcal meningitis. A clinical trial found no difference in mortality but increased disability and serious adverse events among people receiving dexamethasone. Furthermore, the rate of fungal clearance in the CSF in the first two weeks of treatment was slower in the dexamethasone group than in the placebo group.

Planning for discharge and follow-up care

Recommendation for improving re-engagement and reducing readmissions: Hospitalized patients with HIV may be provided interventions to support referrals to outpatient care and reduce avoidable readmissions, and these include:

- Follow-up schedule
- Medication review
- Bi-directional referral (transitional care planning)
- Telephone follow-up
- Home visits by healthcare workers and/or peer supporters
- Individualized support

Refer to the 2022 National ART Treatment Guidelines, pg. 120 for more details.

Section III: HIV-Drug Resistance Management

2. INTRODUCTION

This amendment provides updated national guidance on HIV drug resistance (HIVDR), including definitions, epidemiology, diagnosis, use of genotypic resistance testing (GRT), interpretation principles, regimen selection after confirmed treatment failure, and programme monitoring indicators. The guidance complements the national ART guidelines and aims to support consistent, programmatic,

context-adapted, evidence-based decision-making across facilities and districts.
The guidance is intended for healthcare workers

Objectives of this section include:

1. Strengthening early detection of treatment failure.
2. Ensuring appropriate use and interpretation of GRT.
3. Guiding selection of effective second-line and third-line regimens.
4. Supporting Lesotho's national response to emerging DTG resistance.
5. Clarifying roles of facility staff and ART Advisory Committees (AAC) in managing HIVDR.

Key points for front-line health-care workers

- This section guides recognition, diagnostic steps, and referral pathways for HIVDR.
- Facility staff do not change ART regimens based on GRT results; all treatment switch requests must be submitted to the respective AAC.
- HCWs ro main roles are early detection of virological failure, timely enhanced adherence counselling (EAC), complete documentation, timely submission of requests for GRT to the AAC's and regimen switch, and consistent follow-up.

WHAT IS HIV DRUG RESISTANCE AND WHEN DOES IT OCCUR?

8.1. Definition and Mechanism

HIV drug resistance occurs when HIV continues to replicate in the presence of antiretroviral (ARV) drugs, leading to the selection of viral mutations that reduce susceptibility to one or more medicines (WHO). Resistance may be:

- **Acquired resistance,** arising during treatment, usually when drug levels are insufficient to suppress replication.
- **Pre-treatment resistance**, present before treatment start (either transmitted resistance or from previous interrupted drug exposure).

HIVDR typically develops when ART exposure is present but not sufficient to fully suppress viral replication. This is most often caused by:

- **Suboptimal adherence**, including missed doses or treatment interruptions (Barth).
- **Inadequate drug concentrations** due to malabsorption, vomiting, or drug–drug interactions (e.g., rifampicin) (Doodley, 2008).
- **Prolonged viraemia** on partially active regimens (Gupta, 2012).

When the replicating virus is exposed to drug pressure, viral variants with survival advantages under drug pressure (resistance mutations) gradually dominate the viral population.

Types of Resistance Relevant to Lesotho

Driven by the drugs prescribed in Lesotho's national ART programme, the mutations most frequently encountered include: (Tschumi, 2024)

- **NRTI mutations**: M184V, K65R, thymidine analogue mutations (TAMs).
- **NNRTI mutations**: K103N, Y181C (mainly among individuals previously on efavirenz/nevirapine-based regimens).
- **INSTI mutations**: G118R, R263K, Q148H/K/R, N155H — rare but increasingly reported after prolonged viraemia on DTG (Tzou, 2020).
- **PI mutations**: uncommon due to the high genetic barrier of boosted PIs; when present, they indicate prolonged unaddressed viraemia.

Key points for front-line health-care workers

- HIVDR develops when HIV replicates under insufficient ART pressure.
- Good adherence prevents the majority of resistance cases.
- Once extensive resistance has emerged (especially to the core agent), good adherence usually will not lead to re-suppression and a change in ART regimen might be needed.

Key points for front-line health-care workers

- Most HIVDR in Lesotho arises from delayed action on high viral load results.
- DTG resistance is rare but can occur when high viral load persists for long periods.
- Early EAC and timely repeat viral load are the strongest interventions to prevent HIVDR.

8.3. DEFINITIONS AND DIAGNOSTIC CRITERIA

Viral Load Categories

Lesotho follows WHO categories for interpreting viral-load results:

- Viral load ≤1000 copies/Ml[3]: suppressed.
- Viral load ≥1000 copies/mL[3]: high viral load unsuppressed.
- Viral load 51 – 999 copies/mL[3]: low-level viraemia.
- Viral load < 50 copies/mL[3]: undetectable

Confirmed Virological Failure

Virological failure is defined as:

- An individual on ART for ≥ 6months with.
  - o two consecutive viral loads ≥ 1000 copies/mL≥ 3 months apart,
  - o after at least three sessions (3 months) of enhanced adherence counselling,
  - o while the person is still on the same regimen and shows ≥95% adherence.

Both, viral load-unsuppressed and low-level viraemia require.

1. Immediate provision of Enhanced Adherence Counselling (EAC).
2. Address All Correctable Causes of Unsuppression.
3. Repeat Viral Load in 3 Months after EAC
   a) If VL is undetectable continue routine ART care,
   b) If VL > 50 copies/mL[3] continue EACs and ensure all correctable causes of unsuppression are addressed and repeat Viral Load in 3 Months after 3 EAC.
   c) If an individual has been on ART for over 2 years with 2 VL drawn 3 months apart each remain ≥ 1000 copies/mL[3], with continued EAC, all causes of unsuppression are ruled out and adherence has been successively > 95% - **this is defined as Virological Failure - Immediately document and send for GRT request through the AAC**
   d) If an individual has been on ART for ≥ 6months; with 3 VL drawn 3 months apart each remain between 51-999 copies/mL[3], with continued EAC, all causes of suppression are ruled out and adherence has been successively > 95% **this is defined as very low level viremia- Closely monitor conduct EACs and repeat VL at every 6 month clinical visit.**

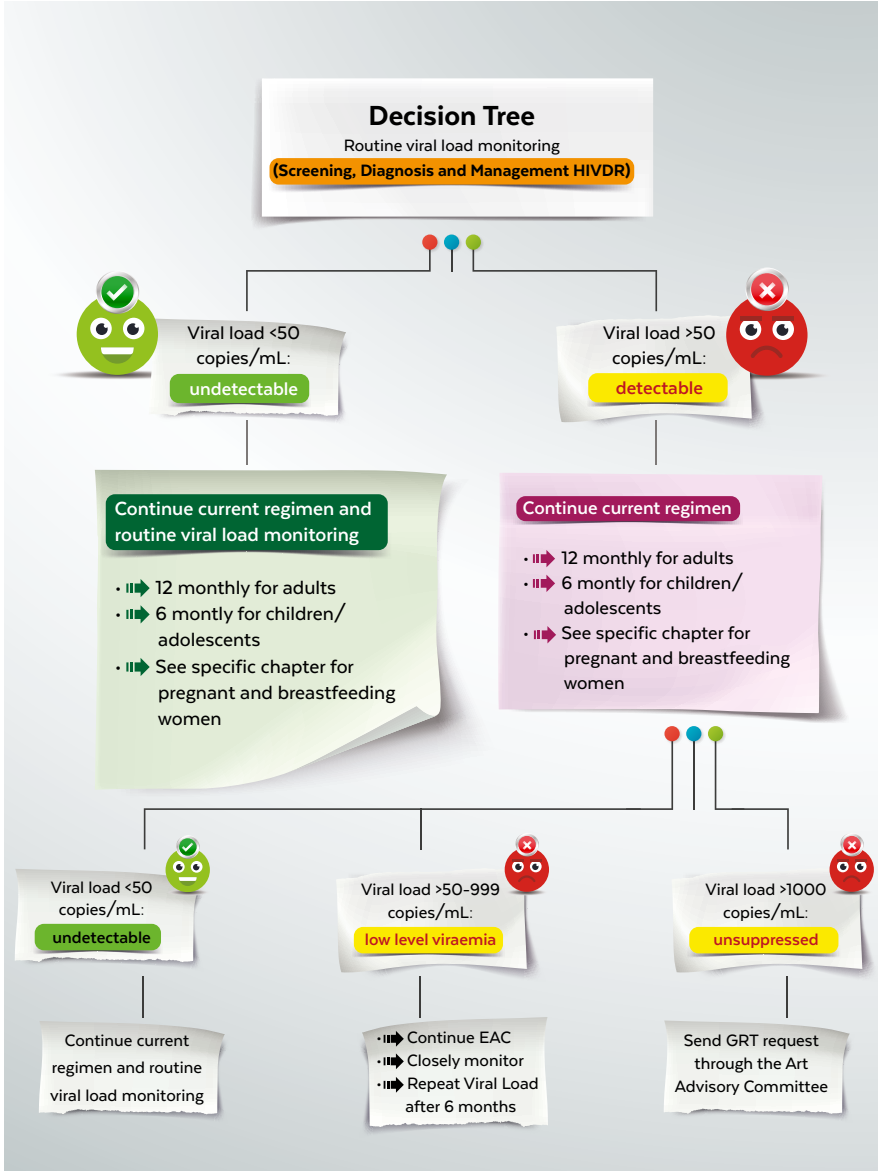


Figure 2:Routine Viral Load Monitoring Decision Tree

Definition of HIV Drug Resistance

HIVDR is defined as the presence of one or more resistance-associated mutations detected on a genotypic resistance test (GRT) in a person with confirmed virological failure.

Important considerations:

- GRT can only detect mutations present in a sufficient proportion of circulating viruses.
- Mutations may no longer be detected if the selective drug pressure is removed (e.g., stopping ART before testing), even though archived resistance remains and will reemerge under drug pressure (e.g. M184V). This means that in the GRT a resistance mutation may "disappear". However, it remains archived and viruses with the resistance mutation will reemerge in case the respective drug is taken again.
- GRT results must therefore always be interpreted in the context of recent drug exposure and viral load history.

When to Request Genotypic Resistance Testing

A GRT should be requested as soon as possible after confirmed virological failure. It makes only sense to request a GRT if one is confident that the adherence during the last 4 weeks before blood draw was ≥95%. In some cases, directly observed therapy (daily pill-take under supervision) may be an approach to be more certain about adherence.

Priority populations include:

- Children and adolescents,
- Pregnant or breastfeeding women,
- People failing INSTI-based regimens or PI-based regimens people with clinical or immunological deterioration,

Important: **Facility staff must never stop ART while awaiting GRT results.**

How to request a GRT

Performing GRT is resource - and labour-intensive; therefore, it should only be requested when appropriately justified and aproved by AAC.

If adherence cannot be confidently assured, the healthcare worker should consider directly observed therapy followed by repeat viral load testing before requesting GRT.

GRT is requested using the National Reference Laboratory (NRL) GRT Request Form. All required fields must be completed accurately and in full.

Sample collection and transport:

Good sample integrity is key for successful GRT. Thus, drawing enough blood, sending it for centrifugation and freezing rapidly is key!

- Draw at least 5mL blood in an EDTA tube (same as for viral load)
- Send the EDTA blood sample to the nearest district hospital or laboratory for immediate

centrifugation and freezing (plasma separation).
- The frozen plasma, together with the completed GRT Request Form, will then be transported to the NRL following the established cold-chain procedures.

What GRT Can and Cannot Do

What GRT can do:

- Identify mutations that reduce susceptibility to specific ARVs.
- Support AAC decision-making on selecting effective second-line or third-line regimens.
- Provide insight into underlying causes of treatment failure.

What GRT cannot do:

- Identify historical or archived resistance after mutation reversion.
- Identify mutations that occur only in a small proportion of viruses.
- Assess adherence directly.
- Predict regimen success without clinical and viral load context.

Because of these limitations, GRT interpretation is performed by experts and should always consider:

- the person's full viral load history,
- current and all previous ART regimens,
- adherence patterns,
- co-treatments such as rifampicin.

Key points for front-line health-care workers

- Request a GRT as soon as possible after confirmed treatment failure and if you are confident that adherence is ≥95% through the AAC.
- Carefully complete the GRT request form and ensure you send a large enough blood sample of good quality to your laboratory
- At the laboratory the sample must be centrifuged and plasma frozen the same-day
- Never stop ART while awaiting results.
- Resistance testing has limitations — AAC interprets the results.
- Early identification of high viral load and timely repeat viral load are critical to prevent resistance.
- Your role is to ensure timely viral load follow-up, request GRT in case of confirmed virological failure and then submission of complete, accurate documentation to AAC.

ACTIONS AFTER RECEIVING GENOTYPIC RESISTANCE TEST (GRT) RESULTS

Once GRT results are received, health-care workers must prepare a complete referral to the ART Advisory Committee (AAC). The AAC makes all decisions regarding regimen changes.

Required Documentation for AAC Submission

A complete AAC referral must contain:

1. Viral-load (VL) history
    - List all VL results, including dates and corresponding regimens taken at the time of each VL.
2. The GRT report
    - Upload or attach the full report.
3. ART treatment history
    - All previous ART regimens and dates.
    - PMTCT or maternal ART for people with vertically acquired HIV.
    - Information on PrEP and PEP if previously taken.
    - Include any treatment interruptions or restarts.
    - Include recent or ongoing TB treatment or other drug–drug interactions (e.g., anticonvulsants), and any dosing adjustments to ART (e.g. DTG 50 mg should be taken twice daily if taking TB treatment).
4. Adherence assessment
   Provide a brief, structured summary:
    - Self-reported adherence
    - Pharmacy refill patterns
    - Barriers (stigma, travel, side-effects, mental health, alcohol use)
    - Interventions already provided (e.g., EAC sessions)
5. Clinical information
    - Pregnancy or breastfeeding status
    - Significant weight loss or gastrointestinal illness
    - Co-morbidities or opportunistic infections
    - Social factors affecting adherence
6. Facility and contact information
    - Name and phone number of submitting health-care worker
    - Health facility name and district

What Not to Do

- Do **not** switch ART regimens at facility level based on GRT without approval by AAC.
- Do **not** stop ART while waiting for the AAC decision.
- Do **not** delay sending results; prompt AAC review prevents further resistance.

Key points for front-line health-care workers

- Do not ignore treatment failure! Submit GRT request and once you have the GRT, submit all information to AAC.
- Your documentation enables AAC decision quality — incomplete submissions cause delays.
- Continue ART and strengthen adherence while waiting for the AAC decision.
- Never switch ART based on GRT without AAC approval.

How GRT Results Are Interpreted

GRT results should be submitted to AACs for interpretation. This section explains, for awareness, what the AAC does with the GRT results. The AAC uses the **Stanford HIV Drug Resistance Database (HIVDB)** as the primary reference tool for mutation-based interpretation: https://hivdb.stanford.edu

HIVDB provides internationally standardised scoring for each detected mutation and categorises antiretroviral drugs as susceptible, low-level resistance, intermediate resistance, or high-level resistance.

In the Stanford HIVDB, the AAC enters the list of relevant mutations detected on the GRT report. The system then automatically generates a standardised interpretation that classifies each antiretroviral as susceptible, low-level, intermediate, or high-level resistance.

Here is an illustrative example on how this may look like:
Resistance mutations provided in the GRT report from the laboratory: M184V, K65R (NRTI); K103N (NNRTI); G118R (INSTI)

HIVDB interpretation (summary):

- **NRTIs**:
  - 3TC/FTC: High-level resistance
  - TDF, ABC: Intermediate resistance
  - AZT: Susceptible / potential low-level resistance
- **NNRTIs**:
  - EFV/NVP: High-level resistance
- **INSTIs**:
  - DTG, BIC: Intermediate resistance (due to G118R)
  - RAL: High-level resistance

This example illustrates how HIVDB identifies which drugs remain fully active (e.g., AZT), which retain partial activity (e.g., TDF, ABC, DTG), and which are no longer effective (e.g., 3TC, EFV). The AAC then integrates this technical output with viral-load history, ART history, and adherence to guide regimen decisions. As a reminder again: If the person is currently not taking AZT, it may be that relevant AZT mutations are not detected even though they are archived and would reemerge in case of AZT exposure.

Key points for front-line health-care workers

- The AAC enters the resistance mutations detected into the Stanford HIV Drug Resistance Database
- This database then provides predicted activity for each ARV
- The AAC takes then the predicted ARV activity into account when deciding on the new regimen

8.4. PRINCIPLES FOR MANAGING HIV DRUG RESISTANCE

Management of HIVDR in Lesotho is based on available evidence and consistent with WHO recommendations and major regional trials.

The Core Agent + Backbone Concept

Antiretroviral regimens consist of:

- a core drug (dolutegravir or a boosted protease inhibitor), and
- an NRTI backbone (e.g., TDF/3TC, ABC/3TC or AZT/3TC).

Core drugs
DTG and boosted PIs (ATV/r, LPV/r, DRV/r) have high genetic barriers to resistance and provide the main antiviral potency. In future new core drugs may emerge, such as capsid inhibitors, modern NNRTIs, 3rd generation INSTIs and NRTTIs.

Backbone NRTIs
NRTIs may retain partial activity even when resistance is present.
This partial activity is clinically meaningful when paired with a potent core drug.

Viral Fitness, Partial Activity, and Why Some Drugs Are Maintained

Some resistance mutations reduce viral fitness, meaning the virus becomes less efficient at replicating. A key example is M184V, which:

- causes high-level resistance to lamivudine (3TC) and emtricitabine (FTC),
- increases susceptibility to TDF and AZT, and
- significantly decreases viral fitness.

Because of this fitness cost, continuing 3TC in a regimen even when M184V is present remains beneficial and is standard practice internationally and in Lesotho.

Also because of this fitness cost, in the absence of drug pressure from 3TC or FTC, viral variants without the M184V mutation become dominant again. However, if M184V has ever been present in an individual, the person still carries HIV with the mutation (archived resistance) even if it is no longer visible in a GRT result (see section 0).

Not all resistance mutations eliminate drug activity completely. Some confer low or intermediate-level resistance, which may still allow partial antiretroviral activity, especially when combined with a potent core agent such as DTG or a boosted PI.

Evidence Supporting NRTI Re-use

Findings from the NADIA and EARNEST trials demonstrate that:

- Potent core agents (DTG or boosted PI) can achieve high suppression rates even when NRTI resistance is present.
- Strategic re-use of NRTIs is safe and effective if adherence is addressed.

DTG Resistance

DTG has a high barrier to resistance; however, resistance can occur in the presence of:

- prolonged unaddressed high VL,
- significant NRTI resistance compromising the backbone,
- poor adherence over time.

Common DTG-associated mutations reported in Southern Africa include R263K, G118R, N155H, and Q148 variant patterns. These mutations differ in their clinical impact, and some remain under study.

Because clinical implications are complex, DTG resistance must always be evaluated by AAC experts.

Protease Inhibitor (PI) Resistance

Boosted PIs also have a very high resistance barrier.
Most people with high viral load on PI-based therapy do not have PI resistance; rather, non-adherence is the major contributor.

When major PI mutations are detected, this indicates advanced HIVDR requiring third-line or individualised regimens, always decided by National ART Advisory Committee.

Multi-Class Resistance and the Role of Newer Agents

Rarely, a person may develop resistance to NRTIs, NNRTIs, INSTIs, and PIs simultaneously.

This multi-class resistance requires expert review and may need:

- dual-core combinations (e.g., DRV/r + DTG),
- in exceptional cases and where accessible, newer agents approved for use can be considered.

Key points for front-line health-care workers

- Potent core drugs (DTG or boosted PI) are central to treatment success.
- NRTIs may be re-used even with resistance — AAC decides this.
- Lamivudine is always kept due to M184V's viral fitness cost.
- DTG or PI resistance is uncommon but serious.
- Await AAC advice to construct new treatment regimen for individuals with resistance

REGIMEN SELECTION AFTER CONFIRMED HIVDR

Regimen selection is determined by the AAC, based on:

- GRT results,
- VL history,
- ART history,
- adherence assessment,
- comorbidities (e.g., pregnancy, TB treatment),
- drug availability.

Below are the national principles underpinning AAC decisions.

First-Line Failure Without DTG Resistance

This is the most common failure pattern.

Typical GRT findings:

- M184V (common)
- ± K65R
- No DTG resistance

AAC actions:

- DTG remains the core drug.
- Choose an optimised NRTI backbone:
    - TDF + 3TC may be retained if residual activity is expected
- Reinforce adherence counselling and social support.

Treatment Failure with DTG Resistance

DTG resistance must be confirmed through GRT interpretation.

AAC actions:

- Switch to a boosted PI-based regimen.
- Options include:
    - TDF/3TC + DRV/r (ABC/3TC or AZT/3TC + DRV/r)
    - In selected cases, DRV/r + DTG (dual-core)
- Select NRTIs based on residual activity and tolerability.
- Intensify adherence support.

Treatment Failure PI-Based Regimens with history of INSTI failure

If no PI resistance:

- Continue the same regimen.
- Address adherence barriers.
- Repeat VL in three months.

If PI resistance is present [multi-class resistance to PI and INSTI]:

- AAC conducts expert review.
- Potential options include:
    - DRV/r + DTG dual-core regimen
    - Regimens with optimised NRTIs
    - If accessible, lenacapavir for salvage therapy

Special Populations

People on TB treatment

- Rifampicin reduces DTG levels — use DTG twice daily during TB treatment.
- If DTG resistance or drug interactions prevent its use, AAC may recommend a PI-based regimen using super-boosted LPV/r.
- Darunavir may NOT be used concurrently with rifampicin.

Key points for front-line health-care workers

- Facility staff do not switch ART regimens without directives from AAC.
- Provide close adherence support before and after switching.
- Schedule follow-up VL testing after a regimen change. Escalate concerns (pregnancy, TB, severe illness) urgently.

8.5. KEY MONITORING & EVALUATION (M&E) INDICATORS

Monitoring and evaluation of HIV drug resistance (HIVDR) is essential for identifying gaps in viral load (VL) monitoring, adherence support, and regimen-switch processes. These indicators guide programme improvement at facility, district, and national levels.

Core Indicators for Facilities and Districts

1. Viral Load Coverage

Definition: Proportion of people on ART who had at least one VL test within the past 12 months.
Purpose: Ensures appropriate monitoring and early identification of viraemia.
Target: ≥95%.

2. Viral Load <1000 copies/mL Rate

Definition: Proportion of people on ART with a most recent VL <1000 copies/mL.
Purpose: Measures programme effectiveness and identifies populations at risk of failure.
Target: ≥95% suppression among people retained on ART.

3. High Viral Load Rate

Definition: Proportion of people on ART with VL >1000 copies/mL at most recent measurement.
Purpose: Helps quantify the burden of potential treatment failure and triage EAC needs.

4. Timely Repeat VL After High Viral Load

Definition: Proportion of people with an initial VL ≥1000 copies/mL who received a repeat VL at 3 months after EAC.
Purpose: Tracks adherence to national guidelines; delays increase risk of HIVDR.
Target: ≥90%.

5. Confirmed Virological Failure Rate

Definition: Proportion of individuals receiving confirmatory VL testing 3 months after a first VL ≥1000 copies/mL and EAC who have another VL ≥1000 copies/mL.
Purpose: Identifies the subset potentially requiring GRT and potential regimen change.

6. Timely GRT Completion After Confirmed Failure

Definition: Proportion of individuals with confirmed virological failure for whom a GRT sample was successfully collected and submitted to the national laboratory within 3 months after confirmed virologic failure.
Purpose: Ensures appropriate diagnosis of HIVDR.
Target: ≥90%.

7. Timely AAC Submission After Receiving GRT Results

Definition: Proportion of cases where facilities submit complete AAC referral files within two weeks of receiving GRT results.
Purpose: Prevents prolonged viraemia and the emergence of further resistance.

Target: ≥90%.

8. Time to Regimen Switch After AAC Decision

Definition: Median number of days between transmission of AAC decision and initiation of the recommended regimen.
Purpose: Identifies operational delays in drug availability, documentation, or patient follow-up.

Target: <30 days.

9. Suppression After Regimen Switch

Definition: Proportion of individuals who achieve VL ≤1000 copies/mL six months after switching to a new regimen.
Purpose: Measures effectiveness of AAC-recommended regimens and post-switch adherence support.

Key points for front-line health-care workers

- Monitor VL results closely and acts early when VL ≥50 copies/mL.
- Ensure you repeat VL after EAC at three months without delay.
- GRT must be collected promptly after confirmed failure.
- Complete AAC submissions ensure timely, effective regimen switching.
- Following up after AAC decisions timely.

Section IV: Optimized Pediatrics ART

9. Introduction of Fixed Dose Pediatric Abacavir, Lamivudine and Dolutegravir (pALD):

Background and Rationale

Lesotho continues to make remarkable progress in scaling up access to lifesaving antiretroviral therapy (ART) for children living with HIV (CLHIV). However, despite these gains, achieving and sustaining optimal viral suppression among children remains a persistent challenge—driven largely by complex treatment regimens, high pill burdens, and caregiver fatigue. Recognising these barriers, the Ministry of Health, in alignment with the World Health Organisation (WHO) 2024 guidance and the Paediatric ARV Working Group (PAWG) recommendations, is introducing the paediatric ABC/3TC/DTG (60/30/5mg) fixed-dose combination (pALD) dispersible tablet.

This transition from the use of separate loose pills—paediatric dolutegravir (pDTG) and paediatric abacavir/lamivudine (pABC/3TC), to a single fixed-dose combination marks a major milestone in Lesotho's paediatric HIV treatment program. The pALD formulation offers a child-friendly, once-daily dispersible tablet designed to simplify treatment, enhance adherence, and improve overall health outcomes. Its introduction supports Lesotho's national goal of achieving 99% viral suppression among children on ART and contributes to the global commitment to end AIDS in children by 2030.

The addendum therefore seeks to:

- **Simplify ART regimens** by consolidating three active ingredients into a single, weight-based, once-daily tablet that is easier for both clinicians to prescribe and caregivers to administer.
- **Reduce pill burden and improve adherence**, particularly among younger children who struggle with multiple tablets or unpleasant-tasting formulations.
- **Enhance treatment continuity and caregiver confidence** through a more palatable and easily dispersible formulation that can be administered with minimal effort.
- **Improve therapeutic outcomes**, ensuring consistent viral suppression, reduced risk of treatment failure, and alignment with global best practices for paediatric HIV care.

By adopting pALD, Lesotho reinforces its leadership within the region in implementing optimised paediatric HIV regimens. This step not only simplifies care delivery but also strengthens the continuum of treatment, from diagnosis to sustained viral suppression, ensuring that every child living with HIV receives safe, effective, and age-appropriate therapy.

Table 14: Product Specifications

Tablet Strength	ABC/3TC/DTG 60/30/5mg
Formulation	Dispersible tablets (not scored)
Administration	Dispersed in water, taken orally once daily
Taste	Strawberry cream flavoured
Target Population	Children 3–24.9kg, ≥4 weeks of age

Table 15: Weight-based Pediatric ART Dosing Guidelines

Weight Band	New Regimen (pALD FDC) ABC/3TC/DTG 60/30/5mg
3–5.9kg	1 tablet
6–9.9kg	3 tablets
10–13.9kg	4 tablets
14–19.9kg	5 tablets
20–24.9kg	6 tablets

Note: *Children ≥25kg should transition to adult formulations (ABC/3TC 600/300 + DTG 50mg). Once 35kg, may transition to TLD.*

Administration Guidelines

Preparation (Annex 3):

1. Add the appropriate pALD dose to 15–20mL of clean, safe drinking water.
2. Stir until tablets dissolve completely (no lumps).
3. Ensure the child consumes the entire mixture within 30 minutes.
4. If any medicine remains, add a small amount of water, swirl, and ensure full consumption.
5. Can be taken with or without food.

Infant treatment

pALD formulation is appropriate for treatment in infants at least 4 weeks of age and at least 3kg body weight. Neonates and infants below 3 kg body weight will receive AZT/3TC/NVP for treatment (Table 17).

Once the infant is at least four weeks of age and weighs at least 3kg, standard paediatric treatment with weight-appropriate ABC/3TC/DTG is recommended.

Neonatal dosing

Neonatal dosing recommendations change after four weeks due to the rapid maturation of renal and hepatic functions.

- Treatment is given twice daily (with exceptions as noted for NVP – Table 16).
- Nevirapine is administered once daily for the first two weeks of treatment and twice daily thereafter.

Notify Pediatric HIV Specialist for treatment in pre-term infants.

Table 16: ART for infants younger than four weeks of age

	2 - <3 kg	3 - <4 kg	4 - <5 kg
AZT 10mg/ml syrup	1 ml BD	1.5 ml BD	2 ml BD
3TC 10mg/ml syrup	0.5 ml BD	0.8 ml BD	1 ml BD
NVP 10mg/ml syrup	1.5 ml BD*	2 ml BD*	3 ml BD*
*NVP is given once daily for two weeks of treatment and twice daily thereafter			

Table 17: ART for Infants over Four Weeks of Age but Weight Below Kg

Drug	Strength	2 kg to < 3 kg	
		AM	PM
AZT/3TC	60/30 mg	0.5 tab	0.5 tab
NVP	10 mg/ml	1.5 ml	1.5 ml*
*NVP is only given once daily during first two weeks of treatment			

Alternative regimen

Abacavir/lamivudine/dolutegravir is the preferred ART regimen for children. Children who have abacavir hypersensitivity or are otherwise unable to receive abacavir should receive AZT/3TC backbone until weight is appropriate for TDF/3TC backbone. Children with sensitivity to dolutegravir should receive a PI-based regimen with darunavir.

9.1. Recognition of Advanced HIV Disease

Immune system health is what determines opportunistic infection risk. Immunosuppression, as determined by CD4 testing, places individuals at risk for OIs, regardless of the viral load. Therefore, CD4 testing is crucial to early recognition of advanced HIV disease.

Immunological Staging: Immunologic (CD4) Monitoring:

CD4% is the preferred monitoring test for infants and young children as they naturally have higher CD4 values than adults. Children below 5 years of age with a CD4% in the advanced or Severe suppression range, should have CD4/CD4% repeated every 6 months along with routine VL until the CD4% reaches mild or no significant immunodeficiency. As the absolute CD4 does not reach adult levels until around age 5 years, children identified to be living with HIV prior to the age of 5 years, should have one routine CD4 taken between 5-6 years of age (Table 19).

Table 18: Immunological Staging of HIV

Classification Of Immune Deficiency	< 12 Months (CD4%)	12-35 Months (CD4%)	36-59 Months (CD4%)	>5 Years (CD4 Count)	Adolescents & Adults
Not Significant	>35%	>30%	>25%	>500	>500
Mild	30-35%	25-30%	20-25%	350-499	350-499
Advanced	25-30%	20-25%	15-20%	200-349	<200-249
Severe	<25% or <1500 cells/mm^3	<20%, or <750 cells/mm^3	<15%, or <350 cells/mm^3	<15%, or <350 cells/mm^3	<15%, or <350 cells/mm^3

9.2. Infant Prophylaxis

The most important determiner of risk for HIV-exposed infants is maternal viral load. All efforts should continue to ensure support to pregnant and breastfeeding women, their infants and families. Regular consultation, viral load monitoring and adherence support are needed to ensure that mothers achieve treatment success and viral load suppression (Table 20).

Infants born to mothers living with HIV are at risk for HIV infection and need review of risk at follow-up appointments. Risk is not static and those infants with low risk of HIV transmission at birth may have higher risk during the breastfeeding period if mother is not adequately supported and followed.

Table 19: ARV Prophylaxis Recommendations Based on Risk of HIV Infection

Infant risk	Prophylaxis
Low risk infant Mother was on ART for ≥12 weeks prior to delivery Mother VL<1000 copies in 3rd trimester	Give infant NVP syrup until the infant is 6 weeks old for both breastfeeding and non-breastfeeding infants
High risk infants - Mother was not started on ART until <12 weeks before delivery or in early postpartum period - Mother VL of ≥ 1000c/ml in 3rd trimester or no VL result - Mother refuses to start ART, has defaulted ART, or has poor adherence on ART - Mother seroconverts during breastfeeding period	Breastfeeding • Give infant AZT syrup + NVP syrup for 6 weeks then additional 6 weeks of NVP syrup alone • Continue NVP prophylaxis until maternal viral load is suppressed Non-breastfeeding AZT syrup + NVP syrup for 6 weeks only

9.3. Tuberculosis Prevention Therapy (TPT)

Children living with HIV are at higher risk of tuberculosis infection and disease. All PLHIV above 1 year of age without signs or symptoms of active TB should be provided with TB preventive therapy (TPT). Children who are exposed to TB through household contacts should also receive TPT, including infants below 1 year of age. Standard options for TPT include rifapentine and isoniazid for 12 weekly doses – 3HP, daily rifampicin and isoniazid for 3 months – 3HR, and daily isoniazid for 6 months – 6H. Children on DTG-based regimens do NOT require boosted dosing for DTG for 3HP (Table 21).

Children receiving rifampicin as a component of either TB prevention or TB treatment require dose-adjustment of dolutegravir. DTG is given twice daily for those on rifampicin.

Table 20: Standard 3HP Dosing

	Isoniazid 100mg (dispersible)	Rifapentine 150mg (dispersible)	Rifapentine 300mg/ Isoniazid 300mg FDC
3-5.9 kg (below 3 months)	6 ml (1 tablet in 10ml water)	5 ml (1 tablet in 10ml water)	
3-5.9kg (above 3 months)	7 ml (1 tablet in 10ml water)	7 ml (1 tablet in 10ml water)	
6-9.9 kg	1.5 tablets	1.5 tablets	
10-14.9kg	2.5 tablets	2 tablets	
15-19.9kg	3 tablets	3 tablets	1 tablet
20-24.9kg	4.5 tablets	4 tablets	1.5 tablets
25-29.9kg			2 tablets
30-34.9kg			2.5 tablets
>35kg			3 tablets

Section V: Protease Inhibitor Optimization

Darunavir is highly potent and has a high genetic barrier to resistance. It also has relatively less metabolic side effects than other protease inhibitors. Darunavir/r will be the preferred alternative for those individuals who are unable to be treated with dolutegravir due to treatment failure or adverse reactions. NRTI backbones are similar to those receiving dolutegravir therapy. ABC/3TC is the preferred backbone for children and adolescents below 35kg. TDF/3TC is the preferred backbone for adults and adolescents above 35kg. ABC/3TC is an alternative for adults with renal insufficiency. (Table 18)

Table 21: Recommended ART regimen

	Preferred ART Regimen	**Alternative ART Regimens**
Adolescents and Adults ≥35 kg (including pregnant and breastfeeding women)	TDF + 3TC + DTG	ABC+3TC+DTG AZT+3TC+DTG TDF+3TC+ DRV/r or ATV/r
Children (≥ 4 weeks and ≥3 kg) and Adolescents	ABC + 3TC + DTG	AZT+3TC+ DRV/r + ATV/r [1]
Infants < 4 weeks and < 3kg	AZT + 3TC + NVP	ABC + 3TC + DTG

Table 22: Recommended Second line ART Regimen

Age Group	Failed 1st-Line ART Regimen	Recommended 2nd-line ART regimen
Adults and adolescents ≥35kg	TDF/3TC + LPV/r (or ATV/r)	TDF (or ABC or AZT) + 3TC + DTG
	ABC/3TC + LPV/r (or ATV/r)	
	AZT/3TC+ LPV/r (or (ATV/r)	
	TDF/3TC + DTG	TDF/3TC + DRV/r If contraindicated use ABC/3TC + ATV/r (or LPV/r) (e.g., in TB patients on rifampicin)
	ABC/3TC + DTG	
	AZT/3TC + DTG	
Children and adolescents <35kg	ABC/3TC + LPV/r (or ATV/r)	ABC/3TC + DTG If contraindication to ABC - AZT/3TC + DTG
	AZT/3TC+ LPV/r (or ATV/r)	
	ABC/3TC + DTG	ABC/3TC + DRV/r If contraindicated use TDF - ABC/3TC + ATV/r (or LPV/r) (e.g., in TB patients on rifampicin)
	AZT/3TC + DTG	
*PLHIV currently (2021) on PI-based 2nd-line therapy are eligible for transition to DTG-based regimens. See Section 6.7 for details. **Change AZT/3TC to TDF/3TC once 35kg if no contraindications to TDF		

NB: All clients who fail first-line regimens should be reviewed by the ART Advisory Committee before being switched to second-line regimens.

Table 23: Fixed dose Darunavir/ritonavir Dosing Chart

Strength of dosage(mg)	Number of tablets						
	10.0 - 13.9 kg		14.0 - 24.9kg		25.0 - 34.9		≥35.0
	AM	PM	AM	PM	AM	PM	Daily
120/20 mg tablet	2	2	3	3	4	4	-
800/100mg tablet	-	-	-	_-	_-	-	1

Darunavir may NOT be administered concurrently with rifampicin. Therefore, temporary drug substitution is required for individuals with HIV/TB co-infection on darunavir. Lopinavir/r with super-boosting will be used during TB treatment. Individuals will resume darunavir therapy two weeks after the completion of TB treatment.

PI based regimens monitoring: Fasting blood glucose (FBSL) and lipid profile should be done at initiation and annually thereafter.

Section VI: Mental Health in HIV Care

10. Management of Mental Health Conditions in People Living with HIV

Key Highlights:

- Mandatory Integration of Mental Health Screening into the HIV Service Continuum
- Explicit Principles for HIV Testing in People with Mental Health Conditions, Challenging
- Structured, Stepwise Management for HIV-Associated Neurocognitive Disorder (HAND) with a Simple Screening Tool

10.1 Introduction

'There is no health without mental health.' (Freeman, 2005) The WHO constitution states: "Health is a state of complete physical, mental, and social well-being and not merely the absence of disease or infirmity." It is a state of well-being in which an individual realizes their abilities, can cope with the stresses of life, be productive and contribute to their community. (WHO, 2013) Despite their prevalence in PLHIV, mental health conditions are often disregarded, underdiagnosed or inadequately managed in PLHIV. Thus, comprehensive HIV management approaches must include mental health and psychosocial support of people living with HIV at its core.

Objectives of this section:

1. To integrate systematic screening for common mental health conditions (e.g., depression, anxiety, substance use) into the standard HIV service continuum for all people living with HIV.
2. To ensure all patients with mental health conditions are offered HIV testing, prevention education, and access to condoms, with consent assessed on an individual basis.
3. To establish a stepwise protocol for the diagnosis and management of depression and anxiety disorders in PLHIV, prioritizing psychosocial interventions and using safe, monitored pharmacotherapy when indicated.
4. To implement routine screening for HIV-associated neurocognitive disorders (HAND) at key clinical milestones (pre-ART, initiation, and during stable treatment) to enable early detection and management.

Key notes for frontline healthcare workers:

- Actively screen all people living with HIV for common mental disorders, particularly depression, anxiety, and substance use, during routine visits, as they are highly prevalent and impact HIV outcomes.
- Always assess suicide risk by directly asking about thoughts, plans, and acts of self-harm in any patient presenting with depressive or distressing symptoms.
- For patients with mental health conditions, offer HIV testing and prevention education, and remember that the presence of a mental illness does not automatically mean they cannot consent.
- Use a "start low, go slow" approach when prescribing psychotropic medications (like antidepressants) to PLHIV, as they are often more sensitive to side effects and drug interactions.

10.2 Bidirectional Links Between Mental Illness and HIV

Mental health conditions are highly prevalent among people living with HIV, with major depressive disorder (MDD) occurring almost twice as frequently among this group than in the general population. (Ciesla, 2001) There is a strong bidirectional relationship between HIV and mental illness. There is a bi-directional relationship between mental health and HIV with poor mental health being a risk factor for HIV exposure, while living with HIV is a significant risk factor for a decline of an individual's mental health and development of mental illness. (Nakimuli-Mpungu, 2021)The impact of untreated mental disorders on health outcomes is substantial. Clinicians must care for PLHIV actively screen for, diagnose and manage mental disorders in this population. (Thom, 2009)

In addition to the treatment of specific mental health conditions, tailored psychological, behavioral and social interventions can significantly contribute to prevention and improved treatment adherence and outcomes.

10.3 Model of Integration

The HIV service continuum provides multiple entry points for the integration of mental health services. The following must be included (Figure 6):

- HIV testing in all people with mental health conditions
- Screening all PLHIV for common mental health conditions such as depression, anxiety and alcohol use disorder
- Diagnosis and management of common mental disorders
- Ongoing psychological interventions and social support
- Appropriate referrals to higher levels of care where needed

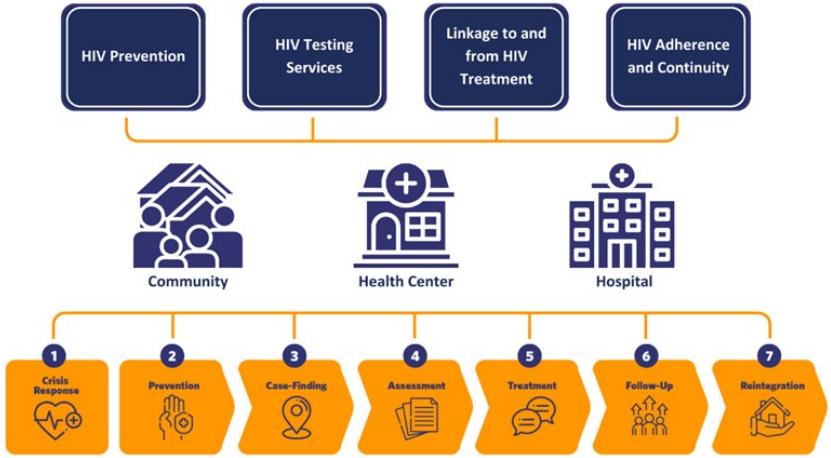


Figure 3: Integration of HIV service and Mental Health Services

1. **Principles of HIV testing in people with mental health conditions**
   - All patients with mental health conditions (in-/out-patients, voluntary/involuntary patients admitted under the Mental Health Care Act) should be offered HIV testing, HIV-prevention/ risk-reduction education and access to condoms
   - The presence of a mental illness does not automatically equal incapacity to consent to HIV testing
   - Capacity to consent to HIV testing must therefore be assessed on an individual basis, particularly in patients with severe mental disorders (SMD)
   - For capacity to consent, patients should be able to:
     - Understand why they are being tested
     - Understand and report on the consequences of a negative or positive test result
     - Report on how they are likely to respond to either result
   - Patients should be included in decision-making about their HIV testing, as far as possible in all cases
   - If the patient is assessed as being incapable of giving informed voluntary consent (e.g. active psychosis, dementia), then proxy consent may be sought

2. **Assessment and diagnosis of common mental disorders**:

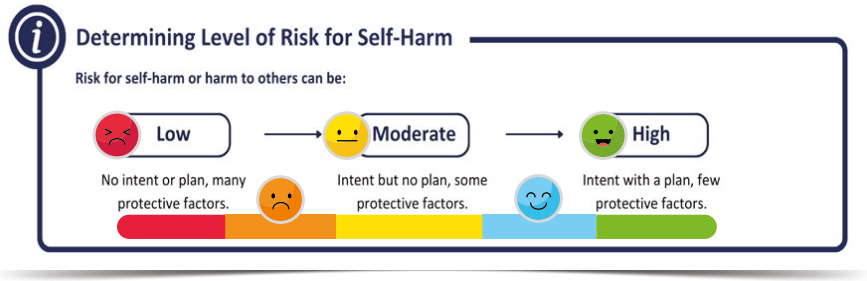
The term 'common mental disorder', used to describe disorders that are highly prevalent in the general population (usually occurring at rates >10%), typically includes:

- Depressive disorders
- Anxiety disorders
- Substance use disorders

10.4 Risk Assessment

Suicide is the act of deliberately killing oneself. Self-harm is a broader term referring to intentional self-inflicted poisoning or injury, which may or may not have a fatal intent or outcome. Evaluate for thoughts, plans and acts of self-harm during the initial assessment and periodically thereafter, as required. Attend to the person's mental state and emotional distress. It is important to assess suicide risk. Clinicians should always ask about suicidal ideation in patients with depressive symptoms.

High risk is indicated by:



- A clear plan for ending life
    - An identified lethal method
    - A previous suicide attempt
    - A lack of social support
    - Severe (psychotic) depressive disorder
    - Concurrent substance use
    - No protective factors

Management:

- Place the person in a secure and supportive environment with constant to ensure safety at all times.
- Remove access to means of self-harm.
- Consult a mental health specialist, if available.
- Mobilize carers and social networks to monitor and support the person during the imminent risk period, with the person's consent.
- Treat people who have self-harmed with the same care, respect and privacy given to other people, and be sensitive to the emotional distress associated with self-harm.
- Instill hope and elicit protective factors.
- Provide emotional support and education to carers/family members if they need it.
- Ensure continuity of care.
- Not all patients with suicidal ideation require hospitalization, first determine the degree of risk.
- Refer for hospitalization to mental health facility in persons who are at high risk.
- If prescribing medication, use medicines that are the least hazardous in case of intentional overdose and give prescriptions as short courses (e.g. one week at a time)

10.5 Mental Conditions in HIV

10.5.1 Depression in PLHIV

Around 30% of PLHIV in Lesotho may suffer from some form of depression during the course of the illness (Hayes-Larson, 2017). The overall prevalence estimates of depressive disorders and probable major depressive disorders were 36.5% and 14.9% respectively in Africa for PLHIV (Bigna, 2019). Severe depression is also known as major depressive disorder (MDD). Even mild depression can lead to erratic adherence, poor care engagement and ultimately to more serious outcomes.

Diagnosing Depression:

A Major Depressive Episode is characterized by five or more of the following occurring together in a two-week period:

- EITHER: depressed mood almost all day every day
- OR: loss of interest or enjoyment of usually pleasurable activities for most of the day
- Plus (occurring nearly every day):
    - Significant unintentional weight loss not due to medical illness, or weight, or decreased/increased appetite
    - Insomnia or hypersomnia
    - Psychomotor agitation or retardation observable by others\Fatigue or loss of energy
    - Feelings of worthlessness or excessive or inappropriate guilt (which may be delusional) – not merely self-reproach or guilt about being sick
    - Diminished ability to think or concentrate, or indecisiveness (either by subjective account or as observed by others)
    - Recurrent thoughts of death (not just fear of dying), recurrent suicidal ideation without a specific plan, or a suicide attempt or a specific plan for committing suicide.

Management of Depression

a) Provide psychoeducation to the person and their carers:

- **On Stigma and Misconceptions**
    - Depression and anxiety are common medical conditions, not signs of weakness, laziness, or a lack of willpower.
    - Because symptoms are often invisible, others may misunderstand, offering unhelpful advice like "snap out of it" or "just be stronger."
    - Recovery is not simply a matter of willpower; it often requires professional support and treatment.
- **On Stigma and Misconceptions**
    - Depression and anxiety are common medical conditions, not signs of weakness, laziness, or a lack of willpower.
    - Because symptoms are often invisible, others may misunderstand, offering unhelpful advice like "snap out of it" or "just be stronger."
    - Recovery is not simply a matter of willpower; it often requires professional support and treatment.

- **On Stigma and Misconceptions**
    - Depression and anxiety are common medical conditions, not signs of weakness, laziness, or a lack of willpower.
    - Because symptoms are often invisible, others may misunderstand, offering unhelpful advice like "snap out of it" or "just be stronger."
    - Recovery is not simply a matter of willpower; it often requires professional support and treatment.

b) Hospitalization - patient requires hospitalization:

- If there is a high suicide risk
- In complex cases: the presence of psychosis and/or minimal social support and/or a poor response to out-patient treatment and/or a diagnostic dilemma
- In complex medical comorbidity (to monitor antidepressant medication)
- In the event of severe psychomotor retardation or no eating/drinking.

c) Psychotherapy

The first line of treatment for Common Mental Disorders (CMDs) is evidence-based therapeutic interventions which may be delivered via a one-on-one approach or in a group setting, including:

- Stress reduction techniques: relaxation and deep breathing exercises
- Meditation and mindfulness
- Strengthening coping skills

- Improving problem-solving skills
- Behavioral activation to encourage the person to be more active
- Cognitive-behavioral therapy (CBT): a form of psychotherapy addressing dysfunctional emotions and maladaptive ideas through cognitive restructuring

It is important to share with patients that regular sleep, being physically active, good nutrition, spending quality time with loved ones can all help improve mood. Peer support groups are vital to help people share experiences, better understand and cope with their illness, for both HIV and mental health conditions. People will also benefit from building livelihood skills and linkage to social support in their journey to recovery and mental wellbeing. Key determinants of successful therapy include the motivation of patients to attend multiple sessions and the access to facilities.

d) Antidepressants

The initiation of antidepressant therapy in patients with MDD is based on a stepwise approach, using the PHQ-9 (Annexe 5.3) as a guide to diagnosis, management and follow-up. It is essential to remember that one 'starts low and goes slow' as patients with HIV/AIDS are often more sensitive to side-effects of medication.

Introducing an Antidepressant

"Start low and go slow":

1) Prior to initiating medication, provide psychoeducation on the drug, expected response and potential side-effects.
   - Selective Serotonin Reuptake Inhibitors (SSRIs) are the drug of coice for depression and anxiety
   - Fluoxetine can take up to 2-4 weeks to start acting.
2) Initiate 20 mg of fluoxetine (or similar) at the lowest available dose and refer to psychosocial support services where available.
3) Reassess using the PHQ-9 at 2-4 weeks and for side-effects (e.g. irritability, nausea, headache, disturbed sleep patterns).
   - Most side-effects settle within 2-weeks.
4) If after a total of 6-8 weeks there is no/minimal improvement, then increase the dose and reassess with the PHQ-9 in 4-6 weeks.
5) If after reassessment there is still no improvement, then refer-up.

Deep Breathing Exercise

Breathe
- Breathe in slowly through your nose for 3 seconds: 1-Phuthiatsana, 2-Phuthiatsana, 3-Phuthiatsana.
- Silently and gently say to yourself "calm down" in Sesotho "theola maikutlo."
- Breathe out slowly through your mouth for 3 seconds: 1-Phuthiatsana, 2-Phuthiatsana, 3-Phuthiatsana.
- Silently and gently say to yourself "release stress" in Sesotho "ke ntša stress"

Reflect
- How did the breaths feel?
- What did you notice when you were breathing this way?

Repeat
- Try to take at least three deep breaths using this strategy when you are experiencing overwhelming stress.
- Practice the three deep breaths at least twice a day, or as many times as necessary.

10.5.2 Anxiety Disorders in PLHIV

Anxiety disorders in PLHIV are common. The most recent general population study of the prevalence of mental disorders in SA was the SASH study, which reported a combined 12-month prevalence of depressive and anxiety disorders of 12.6%. (Thom, 2012) It is important to recognize and treat anxiety disorders as they have been associated with increased rates of poor treatment adherence and high-risk behaviour. Quality of life is also adversely affected by anxiety disorders. Tables 22 and 23 show key features of common and stress-related anxiety disorders, and drug interactions.

Table 24: Management of Common Anxiety and Stress Related Disorders

Disorder	Key Features	First-Line Treatment Approaches
Generalized Anxiety Disorder (GAD)	• **Persistent anxiety** that interferes with daily functioning (work, social life, activities). • Physical symptoms (restlessness, fatigue) and psychological worry are pervasive and distressing.	**Psychotherapy**: Cognitive Behavioral Therapy (CBT), psychoeducation, stress management. **Medication**: SSRIs (same dosing as for MDD). Short-term benzodiazepines (e.g., Clonazepam) may be used cautiously for 2–4 weeks.
Panic Disorder (PD)	• **Recurrent, unexpected panic attacks** (intense fear with physical symptoms: palpitations, choking sensation, doom). • Often leads to anticipatory anxiety and avoidance (e.g., agoraphobia). • Commonly co-occurs with substance use or other mood disorders.	**Psychotherapy**: CBT (including exposure therapy), psychoeducation, stress management. **Medication**: SSRIs are first-line. Short-term benzodiazepines may be used during initial SSRI titration.
Post-Traumatic Stress Disorder (PTSD)	• **Follows exposure to severe trauma.** Symptoms include: 1. **Re-experiencing** (flashbacks, nightmares). 2. **Avoidance** of trauma reminders. 3. **Hyperarousal** (startle response, hypervigilance). • *Caution:* Single-session debriefing or immediate benzodiazepines post-trauma may increase PTSD risk.	**Psychotherapy**: Trauma-focused CBT, EMDR, structured trauma counselling. **Medication**: SSRIs/SNRIs are first-line pharmacotherapy.
Obsessive-Compulsive Disorder (OCD)	• **Obsessions**: Intrusive, irrational thoughts/fears (e.g., contamination, harm). • **Compulsions**: Repetitive behaviors or mental acts (e.g., washing, checking) performed to neutralize anxiety.	**Psychotherapy**: CBT with Exposure and Response Prevention (ERP) is gold standard. **Medication**: SSRIs, typically at higher doses than for MDD or other anxiety disorders.

Table 25: Commonly Used Drugs and Their Interactions

Class and Drug	Dosage	Possible Side Effects	Possible Drug Interactions
Selective Serotonin Inhibitors (SSRIs)			
Fluoxetine	20 - 60 daily	· Headache, nausea, vomiting, irritability (initially), sexual dysfunction.	· EFV: potential increase in EFV levels. · Monitor for worsening of neuropsychiatric conditions.
Citalopram	10 - 20/5 - 10 mg daily	· Headache, nausea, vomiting, irritability (initially), sexual dysfunction.	· Generally nil clinically significant drug interactions. · PIs: potential for decrease citalopram dose.
Tricyclic Antidepressants (TCAs)			
Amitriptyline	25 - 100 mg nocte	· Sedation, anticholinergic side-effects – urinary retention, worsening confusion in older patients, constipation Fatal in overdose	· Amitriptyline and PIs may increase the concentration of amitriptyline; potential cardiac arrhythmia abnormalities due to increased dose of amitriptyline
Mood Stabilizers			
Sodium Valproate	200 - 800 mg	· Sedation, thrombocytopenia, toxic valproate levels if not monitored regularly.	· Interaction with AZT (increased AZT levels). · PI/r may decrease valproate and increase PI. · Monitor levels closely.
Carbamazepine	100 - 200 mg bd	· Sedation, syndrome of inappropriate ADH, skin rash, cognitive dulling, decreased white cell count.	· NVP and EFV: decreased carbamazepine, decreased EFV. · PI/r: increased carbamazepine, decreased PI.
Lamotrigine	25 - 200 mg	· SJS	· Possible interactions with PIs; decreased dose of lamotrigine.
Benzodiazepines			
Diazepam	5-30 mg/ day	· Sedation, respiratory depression and ataxia.	· PIs increase diazepam level.

Note on special populations:

- **For adolescents aged 12 and older with treatment-resistant depression**: Fluoxetine is the preferred pharmacologic option; other SSRIs and TCAs are not recommended. Initiate fluoxetine only with a plan for **weekly safety monitoring** during the first month to assess for emergence or worsening of suicidal thoughts.
- **For patients who are pregnant or breastfeeding**: Specialist consultation is advised. Psychotropic medications are contraindicated where possible. If treatment is necessary, employ the **lowest effective dose** with **close monitoring of both the patient and the child**.
- **For older adult patients**: Employ a conservative prescribing strategy: **avoid** non-essential medications, **minimize** doses, and **reduce** polypharmacy to lower the risk of adverse events.
- **For patients with cardiac, hepatic, or renal disease**: Exercise **caution** with all medications. Select agents to avoid exacerbating the underlying condition. Implement **enhanced monitoring** of organ function and utilize **dose-adjusted** regimens.
- **For adults presenting with active suicidal ideation**: Select an SSRI as first-line therapy. **Avoid tricyclic antidepressants (e.g., amitriptyline)** in this population due to their **high potential for fatal overdose**.

1.1.3 Substance use Disorders

Substance use disorders, particularly alcohol use disorders, are very prevalent in PLHIV and can affect other risk behaviors and adherence to treatment.

Screening and diagnosis

- **Acute Intoxication**: A transient state of impaired consciousness, cognition, perception, mood, or behavior caused by recent substance intake.
- **Overdose**: The ingestion of a substance in quantities high enough to produce acute, adverse physical or mental effects.
- **Withdrawal**: A set of unpleasant symptoms occurring after the abrupt cessation or reduction of a substance, typically experienced after prolonged or heavy use that has led to physical or mental dependence.
- **Harmful Use**: A pattern of substance use that causes physical (e.g., liver disease) or mental (e.g., depression) health damage, often with negative social consequences.
- **Dependence**: A condition where substance use becomes a central priority, characterized by a strong craving, loss of control over use, and often, physical withdrawal upon cessation.

Management of alcohol dependence

The management of alcohol dependency is outlined below:

1. **Assessment & Engagement**
   - Provide clear psychoeducation linking their substance use pattern to specific harms.
   - Explore their motivations for use and readiness for change using a collaborative approach.
2. **Intervention Planning**
   - Conduct motivational interviewing to build intrinsic motivation.
   - Collaboratively explore harm reduction strategies and treatment goals (prioritizing abstinence while supporting reduction).
   - If the patient is ready, develop a specific change plan and strategy.
3. **Implementation & Support**
   - Provide and arrange for ongoing psychosocial support
   - **For Alcohol Use**:
     - **Safety First**: Warn that sudden cessation can cause seizures/delirium. Facilitate a

medically managed detox if they choose to stop.
- **Protect Health**: Prescribe Thiamine (100mg/day) and Folate (5mg/day).
- **Prevent Relapse**: Consider pharmacologic aids like acamprosate or naltrexone to support reduction or abstinence.

Alcohol withdrawal and management

Table 26: Common Features and Management of Alcohol Withdrawal

Features of Alcohol Withdrawal		
Syndrome	**Clinical Findings**	**Onset After Last Drink**
Minor withdrawal	Tremulousness, mild anxiety, headache, diaphoresis, palpitations, anorexia, gastrointestinal upset; normal mental status.	**6-36 hours**
Seizures	Single or brief flurry of generalized tonic-clonic seizures, short postictal period; status epilepticus rare.	**6-48 hours**
Alcoholic Hallucinosis	Visual, auditory, and / or tactile hallucinations with intact orientation and normal vital signs.	**12-48 hours**
Delirium Tremens	Delirium, agitation, tachycardia, hypertension, fever, diaphoresis.	**48-96 hours**
Management of Alcohol Withdrawal		
Class/Indication	Benzodiazepines: to treat alcohol withdrawal, stimulant intoxication, and psychosis	
Medication	Diazepam	
Dosing	· 10-20 mg for observable features of alcohol withdrawal or stimulant intoxication every 2 hours until features of alcohol withdrawal/stimulant intoxication are no longer observable or the person is lightly sedated. Lower doses (up to 10 mg four times a day) for alcohol withdrawal in an outpatient setting.	
Side Effects	· Sedation and respiratory depression which can be life threatening. Prolonged use can lead to dependence.	
Contraindications / Cautions	· Do NOT use in people who are sedated. · Beware of combining with other sedatives. · Patients should not drive. · Duration of effect may be prolonged in persons with severe liver disease. · Supervise dosing to minimize risk of diversion (i.e. selling the medication to someone else).	

Preventing and Treating Wernicke's Encephalopathy

Chronic and heavy users or alcohol are at risk for Wernicke's encephalopathy, a thiamine deficiency syndrome characterized by confusion, nystagmus, ophthalmoplegia (trouble with eye movements), and ataxia (uncoordinated movements).

Prevention of Wernicke's Encephalopathy	• All persons with a history of chronic alcohol us should be given thiamine 100 mg p.o. per day. • Give thiamine prior to administering glucose to avoid precipitating Wernicke's encephalopathy.

1.1.4 HIV-associated neurocognitive disorders (HAND)

Screening and Management: Clinical Presentation

HIV-associated neurocognitive disorder (HAND) typically presents with a subcortical pattern of deficits, including:

- Psychomotor slowing
- Impaired memory, attention, and language
- Executive dysfunction
- Behavioral apathy

Classification

HAND is categorized based on the severity of neurocognitive and functional impairment:

- **Asymptomatic Neurocognitive Impairment (ANI)**
- **Mild Neurocognitive Disorder (MND)**
- **HIV-Associated Dementia (HAD)**

The Importance of Screening

Without systematic screening, many individuals with gradual neurodegenerative changes remain undiagnosed. Patients often do not self-report functional decline, and milder forms of HAND may only become apparent during hospital presentations for confusional states or psychosis. Early detection is critical because:

- Mild HAND may progress to more severe neurodegeneration.
- Initiation or optimization of antiretroviral therapy (ART) may prevent further decline.

Screening Recommendations

- **Pre-ART**: Screen approximately annually. Patients with identified neurocognitive impairment should be encouraged to start ART.
- **At ART Initiation**: Conduct a baseline cognitive assessment to monitor progress or recovery over time. Those with cognitive problems may require additional treatment and adherence support.
- **On Stable ART**: Screening may be offered annually, integrated into adherence support visits, or prioritized for patients with:
    - Treatment failure or poor adherence
    - Ongoing depression
    - Self-reported functional impairment
    - Other clinical concerns

Screening Tool: **Simioni Neurocognitive Symptom Questions**

Ask the patient the following. Responses are: *Never, Hardly Ever,* or *Yes, definitely.* **One answer of "Yes, definitely" constitutes a positive screen.**			
Question	**Never**	**Hardly Ever**	**Yes, definitely**
Do you experience frequent memory loss (e.g., forgetting special events, appointments)?			
Do you feel slower when reasoning, planning activities, or solving problems?			
Do you have difficulties paying attention (e.g., to conversations, books, or movies)?			

Next Steps After a Positive Screen

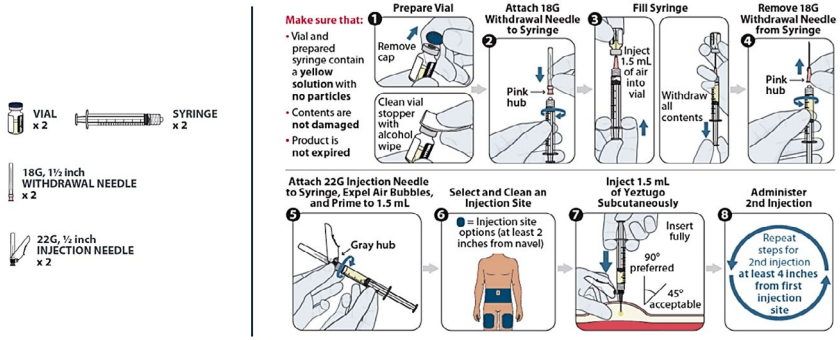
1. **Refer for formal neurocognitive testing.**
2. **Rule out confounding conditions** that may contribute to symptoms, such as:
    a. Depression
    b. Alcohol or substance abuse
    c. Head injury
    d. Epilepsy
    e. Nutritional deficiencies
    f. CNS opportunistic infections
    g. Neurosyphilis
3. **Assess functional impairment** in both basic and complex daily activities (e.g., medication management, cooking, shopping, driving, work tasks).

Note: Neurocognitive impairment in people living with HIV can significantly affect ART adherence and overall health outcomes. Early recognition of symptoms ensures timely evaluation, appropriate psychosocial support, and optimized clinical management.

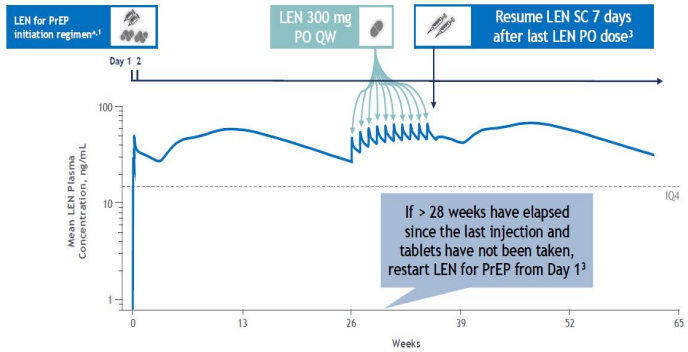
Table 27: Simioni Neurocognitive Symptom Questionnaire

Annexure

Annexe 1: Components of Injection Kits and Steps for Administering LEN (Access Data FDA, 2025)



Weekly LEN PO Maintains LEN at Target Concentration Until LEN SC Can Be Resumed[1,2]



Individuals who anticipate a missing/delayed LEN SC injection should take LEN PO 300 mg once every 7 days starting 26-28 weeks after the last LEN SC injection, for up to 6 months if needed, before resuming LEN SC[3]

Annex 2: Lenacapavir Bridging Protocol (Jogiraju V, 2022)

Annexe 3: Instructions on Use of pALD

INSTRUCTIONS FOR USE of PALD

This Instructions for use contains information on how to take peadiatric abacavir, lamivudine and dolutegravir (pALD). These tablets are strawberry cream flavored.

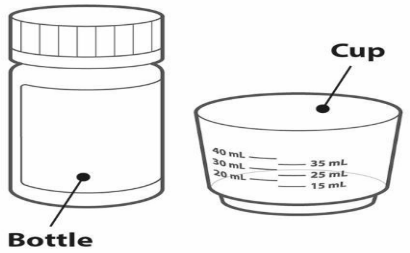
Important information

pALD may be given with OR without food.

Do not chew, cut, or crush the tablets. Dissolve in water or swallow tablet whole.

If you forget to give a dose of pALD, give it as soon as you remember as long as it is closer to your missed dose than your next dose. Do not give 2 doses at the same time or give more than your health-care worker has prescribed.

Your pack contains:



- A bottle containing pALD tablets for oral suspension

- Dosing cup

- Pour 15 mL or 20 mL clean drinking water into the cup.

See Figure A.

Use drinking water only.

Do not use any other drink or food to prepare the dose.

Figure A

Step 2. Prepare the medicine

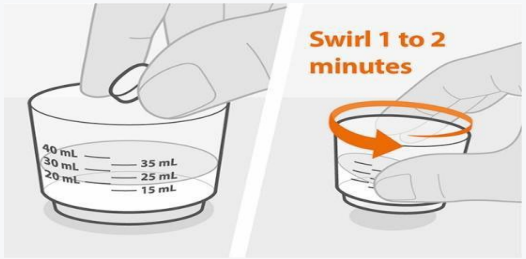


Figure B Figure C

- Add the prescribed number of tablet(s) to the water. See **Figure B.**

- Swirl the cup gently for 1 to 2 minutes to disperse the tablet(s). The medicine will become cloudy. Take care not to spill any of the medicine. See Figure C

- Check that the tablet is dissolved. If there are any lumps of tablet, swirl the cup until they are gone.

If you spill any medicine, clean up the spill.

Throw away the rest of the prepared medicine and make a new dose.
You must give the dose of medicine within 30 minutes of preparing the dose. If it has been more than 30 minutes, wash away all the dose in the cup using water and prepare a new dose of medicine.

Giving the medicine using either a cup, a syringe or the older child may swallow the tablets whole.

Step 3. Give the medicine

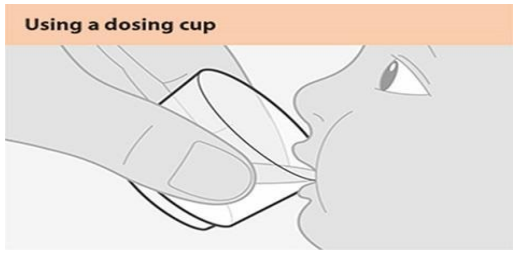


Figure D

- Make sure that the child is upright. Give all the prepared medicine to the child. **See Figure D.**

- Add another 15 mL of drinking water to the cup, swirl, and give it all to the child.

- Repeat if any medicine remains in the cup to make sure the child gets the full dose.

Clean

Step 4. Clean the dosing cup

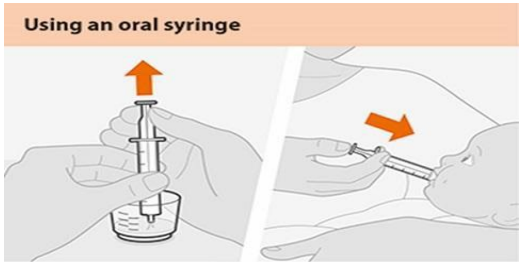


Figure E

- Wash the cup with water. See **Figure E.**

- The cup will need to be clean before preparing the next dose.

Annex 4: Weight-Based Dosing Charts for Antiretroviral Drugs

Ministry of Health – Lesotho: Weight-Based Dosing Charts for Antiretroviral Drugs (except neonates) Monitoring

Once Daily

	Strength	Medication dosages by weight band					Strength	Weight band	Strength	Weight band
		3-5.9 kg	6-9.9 kg	10-13.9 kg	14-19.9 kg	20-24.9 kg		25-34.9 kg		>35 kg
ABC/3TC	120/60 mg	1	1.5	2	2.5	3	600/300 mg	1	600/300 mg	1
DTGa	10 mg	0.5	1.5	2	2.5	3	50 mg	1	50 mg	1
ABC/3TC/ DTGb	60/30/5 mg	-	3	4	5	6	adult tabs	use above adult doses		to TLD
TDF/3TC		-	-	-	-	-		-	300/300 mg	1
TDF/3TC/ DTG		-	-	-	-	-		-	300/300 /50 mg	1
ATV or ATV/rc	200 mg	-	-	1	1	1	300/100 mg	1	300/100 mg	1
DRVc	150 mg	-	-	-	4	4	600 mg	1	800 mg	1
DRVc	600 mg	-	-	-	1	1				
Ritonavird	100 mg	-	-	1	1	1	100 mg	1	100 mg	1

Twice Daily

Medication	Strength	3-5.9 kg		6-9.9 kg		10-13.9 kg		14-19.9 kg		20-24.9 kg		Strength	25-34.9 kg		Strength	>35 kg	
		AM	PM	AM	PM	AM	PM	AM	PM	AM	PM		AM	PM		AM	PM
LPV/re	40/10 mg	2	2	3	3	4	4	5	5	6	6	100/25 mg	3	3	200/50 mg	2	2
LPV/r	100/25 mg	-	-	-	-	2	1	2	2	2	2						
LPV/r	200/50 mg	-	-	-	-	-	-	1	1	1	1	200/50 mg	2	1			
AZT/3TC	60/30 mg	1	1	1.5	1.5	2	2	2.5	2.5	3	3	300/150 mg	1	1	300/150 mg	1	1
DRVc	75 mg	-	-	-	-	-	-	5	5	5	5	400 mg	1	1	600 mg	1	1
Ritonavird	50 mg							1	1	1	1	100 mg	1	1	100 mg	1	1
ETR	25 mg 100 mg	-	-	-	-	-	-	100 mg	100 mg	125 mg	125 mg	25 mg 100 mg	150 mg	150 mg	200 mg	1	1

aDTG dispersible tablets and DTG film-coated tablets are not bioequivalent; That is, 5 x 10mg dispersible tablet is not equivalent to 1 x 50mg film-coated tablet. DTG 50mg dispersible is approximately equivalent to DTG 30mg film-coated. DTG 50 mg film-coated tablets are preferred for children who have reached 20 kg (unless they cannot swallow tablets).
bOnce a patient reaches 35 kg they should be transitioned to TDF.3TC.DTG if their last VL was < 1000 cps/ml
cAtazanavir and Darunavir should be taken with food. Darunavir once or twice daily dependent on PI mutations.
dRitonavir at this dose is used to boost Atazanavir and Darunavir which are currently not co-formulated. Refer to TB section for use of ritonavir to boost LPV/r for TB treatment. eLPV/r cannot be used for infants below 42wks corrected gestational age. LPV/r granules may be used then. LPV/r pellets should not be used until 3 months of age. Transition to LPV/r 100/25mg tablets is recommended as soon as the child can reliably swallow the tablets whole.

Annex 5: Mental Health Tools

1. *General Anxiety Disorder 2 (GAD-2)*

General Anxiety Disorder 2 (GAD-2):

Libekeng tse peli tse fetileng u kile oa ba le engoe ea tse latelang? Khetha karabo e nepahetseng ho uena / *Over the last 2 weeks, how often have you been bothered by the following problems? Circle or check the most appropriate answer.*				
Lipotso / Questions	**Ha ho letho** / 0 days	**Matsatsi a maloa** / 1-7 days	**Beke Kapa ho feta** / 8-10 days	**Matsatsi kaofela** / 11-14 days
1. **Ho ikutloa u na le letsoalo, u sena na botsitso?** / *Feeling nervous, anxious, or on edge?*	**0**	**1**	**2**	**3**
2. **Ho tšoenyeha hoo u sitoang ho ithiba?** / *Not being able to stop or control worrying?*	**0**	**1**	**2**	**3**
Total Score:				

2. *Patient Health Questionnaire 2 (PHQ-2)*

Patient Health Questionnaire 2 (PHQ-2):

Bekeng tse peli tse fetileng, ke ha kae u ileng oa ts'oengoa ke a mang a mats'oao a latelang? Khetha karabo e nepahetseng ho uena. / *Over the last 2 weeks, how often have you been bothered by the following problems? Circle or check the most appropriate answer.*				
Lipotso / Questions	**Hohang** / Not at all	**Ka seoelo** / Several days	**Hangata** / More than half the days	**Kamehla** / Nearly everyday
1. **Ho hloka thahasello linthong tse u li ratang kapa tse u tloaetseng ho li etsa?** / *Little interest or pleasure in doing things?*	**0**	**1**	**2**	**3**
2. **Ho sithabela maikutlo,moea o fats'e kapa ho hloka ts'epo?** / *Feeling down, depressed, or hopeless?*	**0**	**1**	**2**	**3**
Total Score:				

Patient Health Questionnaire 9 (PHQ-9)

Patient Health Questionnaire 9 (PHQ-9) – for patients who score >3 on PHQ2 of GAD7

Khetha karabo e nepahetseng ho uena / *Circle or check the most appropriate answer.*

Lipotso / Questions	Hohang / Not at all	Ka seo-elo / Several days	Hangata / More than half the days	Kamehla / Nearly everyday
1. **Ho hloka thahasello linthong tse u li ratang kapa tse u tloaetseng ho li etsa?** / *Little interest or pleasure in doing things?*	0	1	2	3
2. **Ho sithabela maikutlo,moea o fats'e kapa ho hloka ts'epo?** / *Feeling down, depressed, or hopeless?*	0	1	2	3
3. **Ho hlobaela kapa ho khaleha haholo?** / *Trouble failing or staying, or sleeping too much?*	0	1	2	3
4. **Mokhathala kapa ho hloka matla?** / *Feeling tired or having little energy?*	0	1	2	3
5. **Ho hloka takatso ea lijo kapa ho ja haholo?** / *Poor appetite or overeating?*	0	1	2	3
6. **Ho ikahlola,ho ipona u phoqile batho ba haufi le uena?** / *Feeling bad about yourself- or that you are a failure or have let yourself or your family down?*	0	1	2	3
7. **U na le bothata ba ho tsepamisa maikutlo, mesebetsing ea letsatsi le letsatsi**. / *Trouble concentrating on things, such as reading the newspaper or watching television.*	0	1	2	3
8. **Na hona le phetoho mokhoeng oa hau oa ho bua le ho tsamaea hoo batho ba seng ba hlokometse?** / *Moving or speaking so slowly that other people could have noticed. Or the opposite being so figety or restless that you have been moving a lot more than usual?*	0	1	2	3
9. **Ho ba le monahano oa ho ipolaea kapa ho itlhokofatsa** / *Thoughts that you would be better off dead, or of hurting yourself?*	0	1	2	3

Score Interpretation:		**Total Score**	
• 1 - 4 Minimal depression • 5 - 9 Mild depression • 10 - 14 Moderate depression	• 15 - 19 Moderately severe depression • 20 - 27 Severe depression		

Mats'oaong ao u a bolet seng ka holimo,a thatafatsa mosebetsi oa hau oa letsatsi le letsatsi, ho hlokomela lelapa le likamano tsa hau le batho ba bang? / *If you checked off any problems, how difficult have these problems made it for you to do your work, take care of things at home, or get along with other people?*		*Che ha ho thata*/Not difficult at all...
	Ho thatanyana/somewhat difficult...	
	Ho thata/ very difficult...	
	Ho thata haholo /Extremely difficult...	

4. *Generalized Anxiety Disorder Questions 7 (GAD-7)*

Generalized Anxiety Disorder Questions 7 (GAD-7)

Khetha karabo e nepahetseng ho uena / *Circle or check the most appropriate answer.*				
Lipotso / Questions	**Ha ho letho** / 0 days	**Matsatsi a maloa** / 1-7 days	**Beke Kapa ho feta** / 8-10 days	**Mat-satsi kaofe-la** / 11-14 days
1. **Ho ikutloa u na le letsoalo, u sena na botsitso?** / *Feeling nervous, anxious, or on edge?*	0	1	2	3
2. **Ho tšoenyeha hoo u sitoang ho ithiba?** / *Not being able to stop or control worrying?*	0	1	2	3
3. **Ho nahana haholo ka lintho tse ngata?** / *Worrying too much about different things?*	0	1	2	3
4. **Ho se phomole hantle?** / *Trouble relaxing?*	0	1	2	3
5. **Ho teneha kapa ho koata kapele?** / *Feeling afraid, as if something awful might happen?*	0	1	2	3
6. **Ho teneha kapa ho koata kapele?** / *Becoming easily annoyed or irritable?*	0	1	2	3
7. **Ho ikutloa u tsóhile eka ho na le ntho e mpe e tla etsahala?** / *Feeling afraid, as if something awful might happen?*	0	1	2	3

Score Interpretation:		**Total Score**	
• 1 - 4 Minimal anxiety • 5 - 9 Mild anxiety	• 10 - 14 Moderate Anxiety • > 15 Severe Anxiety		

Mats'oaong ao u a boletseng ka holimo,a thatafatsa mosebetsi oa hau oa letsatsi le letsatsi, ho hlokomela lelapa le likamano tsa hau le batho ba bang? / *If you checked off any problems, how difficult have these problems made it for you to do your work, take care of things at home, or get along with other people?*		**Che ha ho thata**/*Not difficult at all...*
	Ho thatanyana/*Somewhat difficult...*	
	Ho thata/ *Very difficult...*	
	Ho thata haholo / *Extremely difficult...*	

Sad Persons Scale

SAD PERSONS Scale

Letter	Risk	Yes	No
S: Sex	Male gender represents a higher risk.	1	0
A: Age	Extremes of age are at higher risk (e.g. <18 years, and >55 years).	1	0
D: Depression	Depression or other psychiatric comorbidity are at a higher risk.	1	0
P: Previous suicide attempts	Those with a history of suicide attempts are at a higher risk.	1	0
E: Ethanol or alcohol	Ethanol/alcohol or other substance use / abuse.	1	0
R: Rational thinking	Rational thinking loss (e.g. psychosis with command hallucinations).	1	0
S: Social support	No social support confers higher risk.	1	0
O: Organized plan	Organized plan.	1	0
N: No spouse	No spouse.	1	0
S: Sickness	Medical or psychiatric illness may confer a higher risk.	1	0
	Total Score:		

Score Interpretation	
0-2 Points	This Patient may be sent home but one needs to ensure follow-up in the future
3-4 Points	Close follow-up needs to be ensured, and hospitalization considered
5-6 Points	Hospitalization is strongly considered
7-10 Points	Ensure hospitalization and consider involuntary admission if necessary

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