CHAPTER FOUR:

CARE AND TREATMENT OF PEOPLE LIVING WITH HIV INFECTION

4.1. General Care Packages for PLHIV

It is critical for people living with HIV to initiate ART as early as possible. This enables to shorten the time between HIV diagnosis and ART initiation hence significantly reducing HIV related morbidities and mortality, and transmission of HIV.

As all PLHIV are eligible for ART, enrolment in care provides an opportunity for close clinical and laboratory monitoring, early assessment and timely prevention and management of opportunistic infections and other comorbidities. Many interventions are relevant across the full continuum of care, including care for HIV-exposed individuals and PLHIV before initiation of treatment. The following critical interventions need to be addressed at initial encounter with the client:

- Confirm HIV status by retesting and enrolling into HIV care (including recording into HIV positive tracking and pre-ART registers).
- Ensure any OI and other clinical problems that may delay ART initiation are ruled out or addressed.
- Ensure initiation of ART within two weeks after TB treatment is started except when signs and symptoms of meningitis (both TB and/or cryptococcal meningitis) are present.
- Ensure that barriers to adherence and treatment continuity are assessed and addressed accordingly.
- Ensure client is fully aware and makes informed decision for early initiation and continuation of treatment

Key elements of chronic HIV care include:

- Retesting for verification
- Complete clinical assessment (history taking, complete physical examination and relevant lab tests)
- WHO clinical staging
- Prevention, screening and management of opportunistic infections and co-morbidities (see chapter 5)
- Rapid ART initiation
- Patient monitoring and follow up
- Support for disclosure and assisted partner notification
- Risk reduction counseling and combination HIV prevention approaches

- Screening for and managing mental health problems and substance use
- Adherence and psychosocial counseling and support
- Nutritional assessment and counseling
- Screening for other STIs
- Prevention screening and treatment of cervical cancer.
- Management of pain and symptoms.
- Pregnancy status, family planning and contraception.
- Document all relevant client information

4.2. Advanced HIV Disease

Definition of advanced HIV disease

For adults and adolescents, and children older than five years, advanced HIV disease is defined as CD4 cell count <200cells/mm3 or WHO stage 3 or 4 event.

All children younger than five years old with HIV are considered as having advanced HIV disease.

Diagnosis of Advanced HIV Disease:

Diagnosis of advanced HIV disease is done through CD4 testing of clients at base line for those initiating treatment,(re-engaging with care after a period of interruption for >28 days) and targeting those who have interrupted ART treatment and with persistently unsuppressed VL (>1000 copies per ml). In addition to CD4 testing and when CD4 testing is unavailable, a clinical diagnosis of WHO stage 3 or 4 can also be used to diagnose advanced HIV disease.

Package of care for PLHIV with advanced disease

In Ethiopia among adults (ages 15-64 years) living with HIV, 35.8% (45.6% of men and 31.1% of women) had immunosuppression with CD4 count less than 350 cells per microliter (µL). Whereas among adults who reported that they were unaware of their HIV-positive status, 22.0% had severe immunosuppression which is a CD4 count less than 200 cells/µL (16.9% of men and 26.5% of women), (EPHIA 2017/2018). People with advanced HIV disease are at high risk of death, even after starting ART, the risk will increase with declining CD4 cell count. The most common causes of death are TB, severe bacterial infections and cryptococcal meningitis.

A package of interventions including screening, treatment and/or prophylaxis for major opportunistic infections, rapid ART initiation and intensified adherence support interventions should be offered to everyone presenting with advanced HIV disease including those

who are re-engaging with care after a period of interruption for >28 days. Baseline CD4 cell count testing for all PLHIV remains clinically important in order to identify those who have advanced HIV disease and who should be offered the package of care as presented in table 4.1.

Table 4.1: WHO recommendations for components of packages of care for people with advanced HIV disease.

Areas for the package	Intervention	CD4 cell count	Adults & Adolescents	Children
Diagnosis	Sputum Xpert ® MTB/ RIF as the first test for TB diagnosis among symptomatic PLHIV	Any	Yes	Yes
	LF-LAM for TB diagnosis among people with symptoms and signs of TB	≤200 cells/mm3 (inpatient) ≤100cells/mm3 (outpatient) Or any CD4 count with TB symptoms or if seriously ill.	Yes	Yes
	Cryptococcal antigen screening	<100 cells/mm3	Yes	No
Prophylaxis & preventive treatment	Co-trimoxazole prophylaxis	≤350 cells/ mm3 or clinical stage 3 or 4	Yes	Yesz
	TB preventive treatment [a]	Any	Yes	Yes[a]
	Fluconazole pre-emptive therapy for cryptococcal antigen– positive people without evidence of meningitis [b]	<100 cells/ mm3	Yes	NA
ART initiation	Rapid ART initiation as mentioned above[c]	Any	Yes	Yes
	Defer initiation if clinical symptoms suggest TB or cryptococcal meningitis	Any	Yes	Yes
Adapted adherence support	Tailored counselling to ensure optimal adherence to the advanced disease package, including home visits if feasible	<200 cells/mm3	Yes	Yes

a. TB preventive treatment should be provided in accordance with current guidance.

b. When cryptococcal antigen screening is not available, fluconazole primary prophylaxis should be given to adults and adolescents living with HIV who have a CD4 cell count of < 100 cells/mm3.

c. People receiving a positive WHO four-symptom screen should initiate ART while being evaluated for TB if clinical signs and symptoms of meningitis are absent.

4.3. Preparing People Living with HIV for ART

Before initiating people on ART, assess client's willingness and their readiness to initiate ART, discuss in detail about the ARV regimen, dosage, the likely benefits and possible adverse effects, and agree on the required follow-up and monitoring visits. For children with HIV, this conversation should directly involve the parent/legal guardian and include discussion about disclosing their HIV status. Initiation of ART in children should consider nutritional status, any co-morbidities and potentially interacting medications for possible contraindications or dose adjustment.

After going through detailed discussion, quickly assess the readiness and offer rapid ART initiation. Check the following issues to assess readiness of the clients:

- Patient understands the benefits of ART, adherence and need for lifelong commitment and appointment schedules.
- Patient understands possible side effects of ARVs.
- Patient understands the importance of disclosure and family support.

If clients or caregiver declines initiating ART as early as possible, address the following issues in the subsequent visits with the aim of initiating ART as soon as possible:

- Identify and address barriers for starting ART.
- Reiterate the benefits of ART for the client's own health and for reduced risk of transmission to partners
- Consequences of delaying initiation.
- Encourage disclosure to partners/family.
- Encourage engagement in peer and community support.

NB: Clients who declined initiation need to be seen repeatedly on a weekly bases for continued counseling and support to initiate ART.

If there is mental health problem, substance use or psychosocial problems that are major barriers to initiation, appropriate support should be provided, and readiness to initiate ART should be reassessed at regular intervals. Utilize a range of patient information materials as well as community and peer support to help the person's readiness and decision to start therapy.

People starting treatment and care givers should understand that the first ART regimen offers the best opportunity for effective virological suppression and immune recovery, and that successful ART requires them to take the medications exactly as prescribed. They should be advised that many adverse effects are temporary or may be treated, or that substitutions can often be made when necessary. People receiving ART and care givers should also be asked regularly about any other medications that are taken, including herbal remedies and nutritional supplements.

People receiving ART should understand that; they should continue practicing safer sex (including condom use) and avoidance of other high-risk activities, such as sharing of injecting equipment, to prevent transmitting HIV to other people.

In conclusion the following principles should be considered:

- ART should be started rapidly based on a client's informed decision.
- Interventions should be implemented to address barriers to ART.
- HIV programs should promote treatment literacy among all PLHIV, including providing information on the benefits of early treatment, the lifelong commitment required, the risks of delaying treatment and available adherence support.
- Care providers should support shared decision-making.

4.4. When to Start ART

All HIV positive individuals are eligible for ART. The ideal time for ART initiation is at time of HIV diagnosis. Understanding of clients about HIV and the importance of life long treatment adherence need to be emphasized. All adherence barriers should be exhaustively assessed and addressed while ART is initiated.

Rapid ART initiation is defined as initiation of ART within seven days of HIV diagnosis, if there are no contraindications. Rapid ART initiation should be offered to all PLHIV following a confirmed HIV diagnosis, clinical assessment, and assessment of client readiness except in the case of TB meningitis and cryptococcal meningitis. ART initiation should be offered on the same day (initiating ART on the date of HIV diagnosis), for people who are ready to start. Rapid ART initiation, including same-day increases the number of people starting ART, reduces mortality, and may further reduce both mother-to-child transmission and transmission to HIV-negative partners. This recommendation applies to all PLHIV at all age groups and is particularly important in people with very low CD4 cell counts who have an increased risk of death.

4.4.1. When to Start ART in Adults and Adolescents

Rapid treatment initiation is associated with clinical and HIV prevention benefits, improving survival, and reducing the incidence of HIV infection at the family and community level. Start ART rapidly, preferably same day, to all adults and adolescents with a confirmed HIV diagnosis who are ready and willing regardless of their WHO clinical stages and CD4 counts. Prenatally infected adolescents need special consideration and support as they may have readiness issues to accept HIV status and decision to start ART.

4.4.2. When to Start ART in Pregnant and Breast-feeding Women

Start ART rapidly, preferably same day, to all pregnant and breastfeeding women living with HIV regardless of their WHO clinical stages and CD4 counts. For women identified at labor and delivery, provide ART within the same hour of

HIV diagnosis with brief counseling and provide detailed counseling on ARV and adherence after delivery. Make sure to provide enhanced ARV prophylaxis for the infant immediately after birth.

4.4.3. When to Start ART in Children

Start ART rapidly, preferably same day, to all children living with HIV regardless of their WHO clinical stages and CD4 counts/percentage. Infants and young children infected with HIV have exceptionally higher morbidity and mortality. Up to 52% and 75% of children die before the age of two and five years respectively in the absence of any intervention.

For HIV infected infants diagnosed with the first DNA PCR result, initiate ART and take DBS specimen for confirmatory DNA PCR. Continue ART if the second DNA PCR confirms positive results; whereas if the second DNA PCR turns negative, without holding the ART, make the 3rd DNA PCR test. (Refer the algorithm, Figure 3.3)

For HIV infected infants and younger children who need particular care and support, ensure the readiness and understanding of their parents and care givers. Counseling on dosage and administration should be provided for parents/ care givers in case of HIV infected infants.

4.4.4. When to start ART in adults, adolescents, and children with TB

Start ART in all TB patients living with HIV as soon as possible within 2 weeks following initiation of anti-TB treatment regardless of their CD4 count except when there is TB meningitis. If a patient has TB meningitis, delay ART for at least 4 weeks and initiate within 8weeks after treatment of TB meningitis is initiated.

4.4.5. When to start ART in adults, adolescents, and children with drug resistant TB

Antiretroviral therapy is recommended for all patients with HIV and drug- resistant TB (both MDR/XDR-TB) requiring second-line anti-tuberculosis treatment, irrespective of CD4 cell count, as early as possible (within the first two weeks) following initiation of anti-tuberculosis treatment.

4.4.6. When to start ART in HIV/HBV co-infected patients

Start ART rapidly for all HIV/HBV co-infected patients regardless of their CD4 count.

4.4.7. When to start ART in HIV/ Cryptococcal meningitis co-infected patients

ART should be delayed by 4-6 weeks following initiation of treatment for cryptococcal meningitis. Earlier ART is associated with more severe adverse event and increased mortality with cryptococcal meningitis.

ART should be initiated for all individuals (children, adolescents, and adults) living with HIV rapidly, preferably same day, (within an hour for laboring mother) after confirming HIV diagnosis, regardless of WHO clinical stage and CD4 cell count except for TB and cryptococcal meningitis.

4.5. What ART regimen to start with (first-line ART)

Using simplified, less toxic, more effective, and convenient regimens as fixed-dose combination is recommended for first-line ART.

Table 4.2. Summary table for what ART regimen to start with (first-line ART)

Population	Preferred first-line regimens	Alternative first-line regimens	Special circumstances [a]
Adolescents(10 to 19 years OR weight ≥30 kg), adults, pregnant, childbearing and breast feeding women including those with TB/ HIV- co infection	TDF+3TC+DTG[b] (FDC)	TDF + 3TC + EFV AZT + 3TC + DTG AZT + 3TC + EFV	AZT+ 3TC + ATV/r TDF+ 3TC+ ATV/r ABC[c]+3TC+DTG
Children > 4weeks and ≥3kg but less than 10 years	ABC + 3TC + DTG[b*]	ABC+ 3TC+LPV/r AZT+3TC+DTG	ABC+3TC+EFV [d] AZT+3TC+EFV AZT+3TC+LPV/r[a]

[a] ABC or boosted PIs (ATV/r, LPV/r) can be used in special circumstances for those clients who could take neither DTG nor EFV due to contraindication and/or side effects.

[b] In case of TB-HIV co-infection, the dose of DTG should be 50mg BID.

[b*] In case of TB-HIV co-infection, the dose of DTG should be doubled depending on body weight of the child.

[c] For PLHIV with renal insufficiency and anemia

[d] EFV is for children 3 years and older.

4.5.1. First-line regimen for adults and adolescents

The preferred first-line regimen for adults and adolescents (>10 years of age or >30 kg body weight) including pregnant and breast feeding women is TDF+ 3TC+DTG as a once-daily dose.

4.5.2. First line ART for children

The preferred first-line regimen for children > 4weeks and ≥3kg but less than 10 years is ABC+3TC+DTG. Availability of a new generic formulation of 10mg DTG in 2021 has created the opportunity to use DTG based regimen for children living with HIV (CLHIV) who are at least 4weeks of age and weight 3kg or more.

4.5.3. Consideration for first line ART regimen for PLHIV on TB treatment

In case of TB-HIV coinfections in adults and adolescents, including pregnant/breast feeding women and children >20kg body weight, the dose of DTG should be 50mg BID. For children less than <20kg, the dose of DTG depends on the exact body weight of the child.
(Refer Annex 8)

4.5.4. Consideration for alternative and special circumstance first line ART regimens

If the preferred regimen is contraindicated or not available, alternative regimen is used. These regimens are effective and tolerable but have potential disadvantages when compared with the preferred regimens. An alternative regimen may be a preferred regimen for some clients.

Special circumstances may include situations where preferred or alternative regimens may not available or suitable because of significant toxicities, anticipated drug-drug interactions.

4.6. Monitoring response to ART

Monitoring of patients on ART should start from the day of initiation. Although taking ART is a lifelong commitment, the first six months of therapy are especially important.

4.6.1. What to expect in the first months of ART and how to manage them

Clinical and immunological improvement and virological suppression are expected when individuals adhere to ART, but care providers need to be alert as opportunistic infections and/or immune reconstitution inflammatory syndrome (IRIS) may develop, as well as early adverse drug events, such as drug hypersensitivity, in the first three months of ART.

ART significantly decreases mortality and HIV related illnesses; however, mortality can be higher in the first three to six months of ART initiation among people who started ART with advanced HIV disease with existing co-infections and/or co-morbidities, severely low hemoglobin, low body mass index (severe malnutrition) and/or very low CD4 counts.

In most adults and children, when ART is initiated, immune recovery starts and CD4 cell counts rise. Generally, this increase occurs during the first year of treatment, and then continues to rise further during the second year. However, severe immune-suppression may persist in some individuals who do not

experience a significant rise in CD4 cell count with treatment, especially those with a very low CD4 cell count at the time of ART initiation. Consideration should be given to continue prophylaxis for OI such as CPT till patients recover immunologically.

Immune Reconstitution Inflammatory Syndrome (IRIS)

Immune Reconstitution Inflammatory Syndrome (IRIS) is a spectrum of clinical signs and symptoms thought to be associated with immune recovery brought about by a response to ART. In patients with advanced HIV disease the risk of IRIS is high, it even goes higher when CD4 count gets below 50 cells/mm3. IRIS may present in two different ways: paradoxical IRIS, when an opportunistic infection or tumor diagnosed before ART initially responds to treatment but then deteriorates after ART starts; or unmasking IRIS, in which initiating ART triggers disease that is not clinically apparent before ART. It should be considered only when the presentation cannot be explained by a new infection, expected course of a known infection or drug toxicity.

The clinical spectrum is diverse, and IRIS has been reported for many different infections, tumors and non-infectious conditions. The most serious and life-threatening forms of paradoxical IRIS are due to TB, Cryptococcus, Kaposi's sarcoma and hepatitis. BCG vaccine–associated IRIS (localized and systemic) may occur in some HIV infected infants. IRIS is generally self-limiting, and interruption of ART is rarely indicated, but people may need to be reassured in the face of protracted symptoms to prevent discontinuation of or poor adherence to ART.

Timing of ART in people with opportunistic infections requires balancing a greater risk of IRIS after early initiation against continuing high mortality if ART is delayed.

Health care providers need to give due consideration for patients with signs and symptoms of TB meningitis and cryptococcus infection before initiating ART. Providers should give close attention to patients with risk factors for IRIS, including those presented with CD4 count <50 cells/mm3, disseminated opportunistic infections or tumors.

The most important steps to reduce the development of IRIS include:

- Earlier HIV diagnosis and rapid initiation of ART
- Improved screening and management of TB and Cryptococcus before ART
- Optimal management of opportunistic infections

The diagnosis of IRIS can be challenging, and typically has the following criteria:

- A low pretreatment CD4 count (often less than 100 cells/mm3) except in tuberculosis. IRIS secondary to preexisting M. tuberculosis infection may occur in individuals with CD4 counts >200 cells/mm3

- The absence of evidence of alternate diagnoses, including drug-resistant infection, bacterial super infection, drug allergy or other adverse drug reactions, and reduced drug levels due to non-adherence drug-drug interactions or mal-absorption. ;
- The presence of clinical manifestations consistent with an inflammatory condition; and
- A temporal association between antiretroviral therapy (ART) initiation and the onset of clinical features of illness- usually within the first 3 months.

Management of IRIS

- Patients should generally be treated for the underlying OI as soon as possible.
- Continuation of ART when IRIS occurs.

Role of anti-inflammatory agents:

Anti-inflammatory agents may be particularly helpful in the setting of obstructive mass lesions (e.g. expanding cervical lymph node). Use of anti-inflammatory agents, particularly corticosteroids, must be weighed against potential risks and side effects. When a decision is reached to treat with corticosteroids, initiate therapy with prednisone at a dose of 1 mg/kg/day (maximal dose 60 to 80 mg) followed by a rapid taper over a 10 to 14-day period. IRIS in closed spaces (e.g. CNS OI) should be managed promptly or referred to appropriate center to avert significant morbidity and mortality.

IRIS is not indicative of treatment failure or drug side effect. It is a transient phenomenon and is not a reason to stop ART or change regimen. The OI should be treated using standard guidelines and in critically sick patients short course of corticosteroid might be indicated to control severe symptoms.

4.6.2. Clinical and laboratory monitoring

Standardized clinical assessment of patients and, when available baseline CD4 count, are important to determine the severity of immunosuppression and decide on initiation of prophylactic therapies. Patients shall be thoroughly evaluated at baseline and at periodic follow up visits to monitor for response to treatment, IRIS, adverse effects, and treatment intolerance or non-adherence. Patient readiness before ART initiation and treatment adherence at subsequent visits should always be assessed, and necessary support should be provided when barriers are identified. Opportunistic infections including TB, cryptococcal infection, and other co-morbidities including non-communicable diseases (NCDs) should be regularly assessed and managed.

Table 4.3. Baseline and follow-up assessment

Baseline assessment, week 0 (First encounter) Objective: to conduct initial assessment.	
Assess	**Act**
■ Check/Assess if retesting for verification is done and documented. ■ Assess: socio-economic status, any HIV related illnesses in the past, advanced HIV disease, symptom screen for TB, other OI, co-morbidities, pregnancy, past and current medication. ■ Determine WHO staging. ■ Clinical records: fill intake form, follow up form and registers (positive tracking, pre ART or ART registers). ■ Counselling and education: adherence, treatment readiness, disclosure, and address adherence barriers. ■ BP and BMI	■ Do retesting for verification if not done Determine treatment readiness. ■ Start CPT and TPT if clinically indicated Consider provision of prophylaxis for other OIs (e.g. Fluconazole) ■ Treat OIs. ■ Manage co-morbidities ■ Start ART for those who are ready and have no adherence barriers; and give appointment to return after two weeks. If not, give appointment to return within one week. For those who still defer ART continue to counsel on benefit of rapid ART initiation and start them on ART as early as possible. (N.B. Continue follow up counselling sessions until the patient is initiated on ART). ■ Patients who are not initiated on ART due to meningitis (TB/cryptococcus), (Refer section 4.4.7.) ■ Continue ART for transfer-ins. ■ Screen for STI ■ Screen for cervical cancer for women between 15-49 ■ Refer if necessary.
2nd visit: 2 weeks after initiation Objective: To determine toxicity/intolerance, adherence, and IRIS	
■ Clinical assessment for: IRIS, toxicity etc. ■ Assess and support adherence, addressing adherence barriers. ■ Provide counseling and education including prevention of HIV transmission. ■ Lab tests if necessary. ■ Support disclosure if not done. ■ BP and BMI	■ Manage toxicity as indicated. ■ Treat OI if diagnosed. ■ Gtive appointment to return in 2 weeks. ■ Screen for cervical cancer for women between 15-49 if not done ■ Screen for STI ■ Refer if necessary.

3rd visit: 4 weeks after initiation
Objective: Same as second visit

- Same as 3rd visit.
- Hgb if patient is on AZT.
- BP and BMI

- Refill ART and other medicines as necessary for one month.
- Treatment of OI and comorbidities if identified.
- Manage drug toxicity and intolerance.
- Assess and provide adherence support and patient education including HIV prevention.
- Do other lab tests as indicated
- Screen for STI
- Screen for cervical cancer for women between 15-49 if not done
- Refer if necessary.
- Appointment to return after 4 weeks.

4th visit: 8 weeks after initiation
Objective: same as 3rd visit

- Same as 4th visit.
- BMI and BP

- Refill ART and other drugs as necessary for 1 month.
- Treatment of OI and co-morbidities.
- Manage toxicity and intolerance.
- Provide adherence support and patient education including HIV prevention.
- Screen for STI
- Screen for cervical cancer for women between 15-49 if not done
- Refer if necessary.
- Appointment to return after 4 weeks.

5th visit: 12 weeks after initiation
Objective: Same as 4th visit.

- Same as 5th visit.
- BP and BMI

- Refill ART and other drugs as necessary for 1 month.
- Treatment of OI and other co-morbidities.
- Manage toxicity and intolerance.
- Assess and provide adherence support and patient education including HIV prevention.
- Screen for STI
- Screen for cervical cancer for women between 15-49 if not done
- Refer if necessary.
- Appointment to return after 4 weeks

6th visit: 16weeks after initiation Objective: Same as 5th visit	
■ Same as 6thvisit. ■ BP and BMI	■ Refill ART and other drugs as necessary for 1 month. ■ Treatment of OI and other co-morbidities. ■ Manage toxicity and intolerance. ■ Assess and provide adherence support and patient education including HIV prevention. ■ Screen for STI ■ Screen for cervical cancer for women between 15-49 if not done ■ Refer if necessary. ■ Appointment to return after 4 weeks.
7th visit: 20 weeks after initiation Objective: Same as 6th visit	
■ Same as 6th visit. ■ BP and BMI	■ Refill ART and other drugs as necessary for 1 month. ■ Assess and provide adherence support and patient education including HIV prevention. ■ Treat OI and other co-morbidities. ■ Manage toxicity and intolerance. ■ Screen for STI ■ Screen for cervical cancer for women between 15-49 if not done ■ Refer if necessary. ■ Appointment to return after 4 weeks.
8th visit: 24 weeks after initiation Objective: Same as 7th visit	
■ Same as 6th visit. ■ BP and BMI	■ Assess and provide adherence support and patient education including HIV prevention. ■ Determine viral load. ■ Refill ART and other drugs as necessary for 3 months. ■ Treat OI and other co-morbidities. ■ Manage toxicity and intolerance. ■ Screen for STI ■ Screen for cervical cancer for women between 15-49 if not done ■ Refer if necessary. ■ Appointment to return after 3months.

Note:

- Newly started patients will be appointed every two weeks during the first month of treatment and every 4weeks (every month) then after until 24 weeks of treatment. After the 24th week of initiation of antiretroviral therapy patients will be scheduled to return every twelve weeks.
- OIs prophylaxis, treatment for co-morbidities and SRH services should be provided in the context of/integrated with ART multi month dispensing.
- Patients should be encouraged to come at any time if they have concerns and can be seen out of the above schedule whenever necessary.
- For follow up schedule during COVID19 pandemic, refer service delivery section (Chapter 6).

Table 4.4. Recommended tests for HIV treatment monitoring and approaches to screening for co-infections and non-communicable diseases.

Management	Recommended	Desirable (if feasible)
Baseline/ART initiation	■ CBC including hemoglobin[d] ■ CD4 cell count. ■ Cryptococcus antigen if CD4 cell count <100 cells/mm3. ■ FBS ■ Gene Xpert, LF-LAM if eligible	■ HBV (HBsAg)[a] serology. ■ HCV serology. ■ Pregnancy test. ■ HPV-DNA if available ■ Lab investigations for major non communicable chronic diseases and comorbidities[b] ■ Pregnancy test ■ Serum creatinine and estimated glomerular filtration rate (eGFR) for starting TDF[e]

Management	Recommended	Desirable (if feasible)
Receiving ART	■ HIV viral load at 6 and 12 months after initiating ART and every 12 months thereafter ■ Viral load testing for pregnant mothers: ■ Newly diagnosed mothers: Conduct a viral load by three months after ART initiation to ensure that there has been rapid viral suppression. If viral load testing is expected to be undertaken near the planned viral load at 34–36 weeks of gestation, the first viral load test can be delayed until weeks 34–36 of gestation. ■ For women already on ART, conduct VL testing at the first contact at ANC (VL result conducted in the last 3 months before the first contact can also be used), at 34-36 weeks of gestational age or delivery at the latest, followed by three months after delivery and then every 6months. ■ For those who are already on ART with previous VL test conducted more than three months back repeat VL test at first ANC contact / PMTCT visit, at 34-36 weeks of gestational age (or at the latest at delivery) and 3 months after delivery and every six months thereafter until MTCT risk ends. ■ For all pregnant women, regardless of ART initiation timing: conduct viral load testing at 34–36 weeks of gestation (or at the latest at delivery) to identify women who may be at risk of treatment failure and/or may deliver infants at higher risk of perinatal transmission ■ For all breastfeeding women, regardless of when ART was initiated: conduct a viral load test three months after delivery and every six months thereafter to detect viremic episodes during the postnatal period ■ FBS at 6 months after ART and every 12 months annually.	■ Serum creatinine and eGFR for TDFc ■ Pregnancy test, especially for women of childbearing age not receiving family planning. ■ CD4 cell count if indicated ■ HPV-DNA if available

[a] If feasible, HBsAg testing should be performed at baseline to identify people with HIV and HBV coinfection and who should therefore initiate TDF-containing ART.

[b] Consider assessing for the presence of chronic conditions that can influence ART management, such as hypertension, other cardiovascular diseases, diabetes and TB according to the WHO Package of Essential NCD interventions (PEN), mental health Gap Action Program (mhGAP) or national standard protocols

[c] Monitoring may include a range of tests, including serum creatinine and estimated glomerular filtration rate (eGFR), serum phosphate and urine dipsticks for proteinuria and glycosuria. eGFR = 140– age (years) × body weight (kg)/(72 × serum Cr in mg/dL) for male and eGFR = 140– age (years) × body weight (kg) × 0.85/(72 × serum Cr in mg/dL) for female.

[d] Among children and adults with a high risk of adverse events associated with AZT (low CD4 or low BMI).

[e] Among people with a high risk of adverse events associated with TDF: underlying renal disease, older age group, low body mass index (BMI), diabetes, hypertension and concomitant use of a boosted PI or potential nephrotoxic drugs.

N.B. If the recommended baseline tests are not available, it should not delay ART initiation

4.6.3. Monitoring drug toxicities and substitution of ARV

Guiding principles

- Establish whether the clinical condition is due to ARV toxicities, other drugs, or other illness including new OIs.
- Try to identify the responsible ARV drug.
- Assess the severity using toxicity grading matrix (Annex 10 and 11)

Major types of ARV toxicities

The major causes of drug discontinuation in the first 3-6 months after initiating ART are due to drug toxicities; and hence, they must be closely monitored.

They typically occur from few weeks to months after ART initiation or change. The most common side effects related to the ARV drugs recommended in these national guidelines are provided in the table below.

Table 4.5. Types of toxicities associated with first, second and third-line ARV drugs

ARV Drug	Major types of toxicity	Risk factors	Suggested management	Remark
ABC	Hypersensitivity reaction		Substitute with TDF or AZT	
ATV/r	Electrocardiographic Abnormalities (PR and QRS interval prolongation)	Pre-existing conduction system disease. concomitant use of other drugs that may prolong the PR interval	Use with caution in people with preexisting conduction disease or who are on concomitant drugs they may prolong the PR or QRS interval	
	Indirect hyperbilirubinemia (clinical jaundice)	Underlying hepatic disease, HBV and HCV co-infection Concomitant use of hepatotoxic drugs	This phenomenon is clinically benign; however, can be associated with social and personal discomfort and in some circumstances with stigma. Substitute with LPV/r only if adherence compromised	Strongly advice the client not to seek traditional healers and herbal medications
	Renal stone	History of renal stone.	Substitute with LPV/r	
AZT	Anemia, neutropenia	Baseline anemia or neutropenia CD4 count ≤200 cells/mm3.	Avoid use of AZT for people with HIV and severe anemia at baseline (hemoglobin <7.0 g/dl) as first-line therapy. Substitute with TDF or ABC	
DRV/r	Hepatotoxicity	Underlying hepatic disease; Coinfection with HBV or HCV; Concomitant use of hepatotoxic drugs.	Substitute with ATV/r or LPV/r. When it is used in third-line ART, limited options are available.	
	Severe skin and hypersensitivity reactions.	Sulfonamide allergy.	For hypersensitivity reactions, substitute with another therapeutic class	
DTG*	Hepatotoxicity Hypersensitivity reactions	Coinfection with Hepatitis B or C, Liver disease.	Substitute another therapeutic class: EFV or boosted PIs	

ARV Drug	Major types of toxicity	Risk factors	Suggested management	Remark
	Insomnia Body weight gain or obesity	Older than 60 years Low CD4 or high viral load Female African ethnicity	Consider morning dose or substitute EFV, boosted PI Monitor body weight and promote anti-obesity measures (Such as diet and physical exercise). If significant increase despite measures, consider substituting EFV or boosted PI	
LPV/r	Electrocardiographic abnormalities (PR and QT interval prolongation, torsade's de pointes).	People with pre-existing conduction system disease; concomitant use of other drugs that may prolong the PR interval, Congenital long QT syndrome, Hypokalemia Concomitant use of drugs that may prolong the QT interval	Use with caution in people with pre-existing conduction disease or those on concomitant drugs that may prolong the PR or QRS intervals	
	Hepatotoxicity	Underlying hepatic disease HBV and HCV co-infection Concomitant use of hepatotoxic drug	If LPV/r is used in children, substitute with DTG or EFV according to age. ATV can be used for children older than 6 years. If LPV/r is used in second-line ART for adults, use ATV/r. If boosted PIs are contraindicated and the person has failed an NNRTI based first line ART use DTG or consult specialist	
	Pancreatitis	Advanced HIV disease, Alcohol class (INSTIs)	Substitute another therapeutic class (INSTIs)	
	Dyslipidemia	Cardiovascular risk factors such as obesity and diabetes	Substitute another therapeutic class (INSTIs)	
	Diarrhea	Risk factor unknown	Substitute with ATV/r or DTG	

ARV Drug	Major types of toxicity	Risk factors	Suggested management	Remark
NVP (For HEIs prophylaxis)	There are rare reports of Hypersensitivity and hepatotoxicity		Use AZT only	
EFV	Persistent central nervous system toxicity (such as abnormal dreams, depression or mentalconfusion)**	Depression or other mental disorder (previous or at baseline) Daytime dosing	DTG or boosted PI	
	Hepatotoxicity	Underlying hepatic disease – HBV and HCV co-infection Concomitant use of hepatotoxic drug		
	Convulsions	History of seizure		
	Severe skin Hypersensitivity reaction.	Risk factors unknown.	Use DTG or boosted PI	
	Gynecomastia	Risk factor unknown.	Use DTG or boosted PI	
TDF	Chronic kidney disease, acute renal injury, Fanconi syndrome.	Underlying renal disease; older age; BMI <18.5 (or body weight <50 kg); untreated diabetes mellitus; untreated hypertension; Concomitant use of nephrotoxic drugs or boosted PI.	Substitute with AZT or ABC. Do not initiate TDF at eGFR <50 mL/ min, uncontrolled hypertension, untreated diabetes, or presence of renal failure. It is recommended to monitor growth in children taking TDF containing regimen.	
	Decreases in bone mineral Density.	History of osteomalacia and pathological fracture; risk factors for osteoporosis or bone loss.		
	Lactic acidosis or severe hepatomegaly with steatosis.	Prolonged exposure to nucleoside analogues; Obesity.		

*Hyperglycemia has been reported from different sites in Ethiopia and small-scale studies from other countries.

**Most CNS side effects will improve within 2-4 weeks after initiation

NB:

- For those patients with HBV and HIV co-infection suffering from TDF toxicity, consult or refer national viral hepatitis guideline.
- The clinical manifestations due to hypersensitivity reactions for some ARVs may be confused with IRIS

Drug substitutions for ARV drug toxicity

Drug regimen or single agent substitutions may be required for drug toxicity and to avoid drug interactions.

Clinical considerations

- Delaying substitutions or switches when there are severe adverse drug effects may cause harm and may affect adherence, leading to drug resistance and treatment failure.
- When drug interruptions are required, it is important to consider the various half-lives of ARV drugs. For example, when a NNRTI needs to be discontinued, a staggered approach should be used by prolonging the use of the NRTI backbone for two weeks except life threatening conditions (grade 4 conditions) where you have to discontinue all ARV drugs (see annexes 10 and 11 for details).

Strategies for managing adverse drug reactions:

Step 1: Establish whether the problem is due to antiretroviral drugs, other medications, OIs, non HIV related problems or clinical condition.

Step 2: Try to identify the responsible ARV drug.

Step 3: Assess the degree/severity of the Adverse Event using the ACTG/PACTG adverse events grading system.

Step 4: Manage the adverse event according to severity and decide whether to substitute or discontinue ARV drug based on common adverse events clinical grading system. Annexes 10 and 11.

Step 5: Report Adverse event through appropriate tools and channels (Refer chapter 6)

4.6.4. Drug interactions

Providers should be aware of all drugs that people with HIV are taking when ART is initiated and new drugs that are added during treatment maintenance.

Table 4.6. Key ARV drug interactions and suggested management

ARV drugs	Key interactions	Effect	Suggested management
AZT	Ribavirin and pegylated interferonalpha-2a		Substitute with TDF
EFV	Bedaquiline		Avoid the combination
	Amodiaquine, DHA/ piperaquine		Use an alternative antimalarial agent or substitute EFV for DTG
	Artemisinin or lumefantrine		Use an alternative antimalarial agent or substitute EFV for DTG
			Risk of QT prolongation with ATV/r and LPV/r
	Methadone		Adjust the methadone dose as appropriate
	Hormonal contraceptives		Use alternative or additional contraceptive methods
	Amlodipine		Adjust the amlodipine dose as appropriate
	Simvastatin and atorvastatin		Adjust the statin dose as appropriate
	Low-dose dexamethasone (COVID-19)		Double dose of dexamethasone
Boosted PI (ATV/r, DRV/r, LPV/r)	Rifampicin		Adjust the PI dose or substitute with DTG
	Lovastatin and simvastatin	Increase concentration	Use an alternative dyslipidemia agent (for example pravastatin)
	Halofantrine and lumefantrine		Use an alternative antimalarial agent
	Estrogen-based hormonal contraception		Use alternative or additional contraceptive methods
	Methadone and Buprenorphine		Adjust methadone and buprenorphine doses as appropriate
	Astemizole and terfenadine		Use alternative antihistamine agent
	Rifapentine	Reduce serum level	Do not provide 3HP with protease inhibitors and consider 6H in this case
TDF	nephrotoxic drugs [e.g. aminoglycosides, amphotericin B, ganciclovir, pentamidine, vancomycin or interleukin-2]	Exacerbate nephrotoxicity	Avoid concurrent use

ARV drugs	Key interactions	Effect	Suggested management
	ritonavir boosted PIs		Closely monitor renal function
	Ledipasvir- or velpatasvir-containing Regimens		Monitor for TDF-associated adverse effects, including renal dysfunction, particularly when TDF is coprescribed with boosted HIV PIs
	Lithium		TDF: monitor renal function closely
DTG	Carbamazepine, Phenobarbital, and phenytoin		Use alternative anticonvulsant agent,(such as valproic acid or gabapentin) or if not possible substitute DTG with EFV and for children below 3 years substitute with boosted PIs
	Polyvalent Cation products containing Mg, Al, Fe, Ca, and Zn	Absorption of DTG is affected/ reduced	Use DTG at least 2 hours before or at least 6 hours after supplements containing polyvalent cations, including but not limited to – Fe-, Ca-, Mg-, or Zn-multivitamin supplements; mineral supplements, cation containing laxatives and Al-, Ca- or Mg- containing antacids. Monitor for virological efficacy.
	Rifampicin,	Increases metabolism of DTG, and hence reduces concentration of DTG in the blood.	DTG 50mg BID. For pediatrics DTG BID by weight band. Continue with twice daily dosing of DTG in children for 2 weeks after use of rifampicin has ended based on their weight band
	Rifapentine		No evidence that changes of dose of rifapentine or DTG is needed to achieve adequate exposures of DTG
	Metformin	DTG increases metformin levels, which may lead to hypoglycemia.	Start metformin at lowest dose and titrate based on glycemic control. Monitor for adverse events of metformin Or adjust metformin dosing if already on metformin When starting or stopping DTG in patients on metformin dose adjustment of metformin may be necessary to maintain optimal glycemic control and/or minimize adverse events of metformin.

Table 4.7: Drug-drug interactions (ARVs and anti-TB drugs for treatment of DR-TB).

Clinical Condition	Responsible ARV drug/s	Responsible anti TB drug/s	Recommendations
Bone marrow suppression	AZT	Lzd, R, H	Monitor blood counts regularly. Replace AZT if bone marrow suppression occurs. Consider suspension of Lzd. Also consider cotrimoxazole, if patient is taking.
Hepatotoxicity	EFV protease inhibitors, NRTIs	H, R, E, Z, Bdq, PAS, Eto/ Pto, FQ	When severe, stop both the ART and TB medications, and restart the TB medications first. Consider cotrimoxazole, if patient is taking. Also rule out viral hepatitis (Hepatitis A, B, C & Cytomegalovirus(CMV)).
Renal toxicity	TDF	Amino-glycosides, amikacin	TDF may cause renal injury. If possible, avoid TDF in patients receiving aminoglycosides or amikacin. If TDF is absolutely indicated, serum creatinine and electrolytes should be monitored (at least every two weeks). Even without the concurrent use of TDF, PLHIV have increased risk of renal toxicity secondary to aminoglycosides and amikacin. In the presence of renal insufficiency, ARV and anti-TB medications need to have their doses adjusted.
Central nervous system (CNS) toxicity	EFV	Cs, H, Eto/Pto, FQ	EFV has a high rate of CNS side effects in the first 2–3 weeks of use, but typically self-limited and resolves. At present, there are limited data on the use of EFV with Cs; concurrent use is the accepted practice with frequent monitoring for central nervous system toxicity. Psychosis can occur with Cs, but is rare with EFV alone; other causes should always be ruled out.
QTc Prolongation	Protease inhibitors (PIs) LPV/r	Bdq, Dlm, Mfx, Gfx, Cfz, Lfx, Ofx	PIs may result QTc prolongation. The additive effects of combining ART with known second-line anti-TB drugs on QTc prolongation is not known. Close monitoring is indicated.

Dysglycaemia (disturbed blood sugar regulation)	Protease inhibitors (PIs)	Gfx, Eto/Pto	Protease inhibitors tend to cause insulin resistance and hyperglycemia. Eto/Pto tends to make insulin control in diabetics more difficult, and can result in hypoglycemia and poor glucose regulation.
For patients who are co-infected with HIV and MDR/XDR-TB, there is limited information on interactions of ARV drugs with new drugs such as bedaquiline and delamanid. Concomitant use of EFV and PIs with bedaquiline may interfere with drug concentrations and require close clinical monitoring; alternative ARV options should be considered, if possible. N.B. For details of ARVs and anti-TB drugs for treatment of DR-TB interactions, please refer the latest TB guideline			

4.7. Re-engaging with care after ART interruption

Interruption in treatment is defined as client has missed appointment for greater than 28 days from the last appointment date. People who interrupted their treatment need to be re-evaluated for possible adherence barriers and advanced clinical conditions.

For reengaged clients after missing appointment for greater than 28 days (interrupted treatment), the following essential elements should be part of the care.

- Exhaust all possible adherence barriers and provide an ongoing Enhanced Adherence Support (EAS).
- Resume the same (previous) ART regimen they used before interruption.
- People interrupting treatment on NNRTI –containing regimen are at higher risk of drug resistance and should restart ART using a DTG-containing regimen if not contraindicated to DTG.
- Maintain close or frequent follow-up schedule.
- Monitor the viral load closely and determine the VL at 3 and 6 months after resuming ART. If the viral load is >1000copies/ml in the two consecutive measurements, switch to second or third line regimen and continue adherence support
- Those with low level viraemia, (50 –1000 copies/ml) need to be provided with enhanced adherence counselling and viral load testing after 3 months to promote more viral suppression.(see figure 4.1)

*For clients who missed their appointments less than 28 days, assess for the cause and strengthen adherence support. In addition, ensure the clients are on optimized regimen (DTG based treatment for those who are on first line).

4.8. Diagnosis and management of antiretroviral treatment failure

Monitoring individuals receiving ART is important to ensure successful treatment, identify adherence problems and determine whether and which ART regimens should be switched in case of treatment failure. Routine viral load testing is a more sensitive and

earlier indicator of treatment failure. Routine viral load testing should be done at 6 and 12 months of initiating ART and then every 12 months thereafter to detect treatment failure proactively. Aside from the routine viral load testing schedule, viral load testing should be used whenever there is clinical or immunologic suspicion of treatment failure.

Table 4.8: Definitions of clinical, immunological and virological failure for the decision to switch ART regimens

Failure	Definition	Remark
Clinical failure	Adults and adolescents New or recurrent clinical event indicating severe immunodeficiency (WHO clinical stage 4 condition and certain WHO clinical stage 3 conditions (pulmonary TB and severe bacterial infections) may also indicate treatment failure) after 6 months of optimal adherence to appropriate ART regimen. Children New or recurrent clinical event indicating advanced or severe immune deficiency (WHO clinical stage 3 and 4 clinical condition with exception of TB) after 6 months of effective treatment.	The condition must be differentiated from immune reconstitution inflammatory syndrome occurring after initiating ART.
Immunologic failure	Adults and adolescents ■ CD4 count at or below 250 cells/mm3 following clinical failure or ■ Persistent CD4 levels below 100 cells/mm3.	Without concomitant or recent infection to cause a transient decline in the CD4 cell count. Persistent is to mean at least 2 CD4 measurements below the threshold. Current WHO clinical and immunological criteria have low sensitivity and positive predictive value for identifying individuals with virological failure.
	Children Younger than 5 years Persistent CD4 level below 200 cells/mm3or <10% Older than 5 years Persistent CD4 levels below 100 cells/mm3.	
Virologic failure	Viral load above 1000 copies/ml based on two consecutive viral load measurements 3 months apart with enhanced adherence support following the first viral load test	An individual must be taking ART for at least 6 months before it can be determined that a regimen has failed. VL testing should not be done when there is an acute infection/fever. (Refer algorithm on Figure 4.1.)

NB:

1. Viral suppression: is a viral load that is undetectable, equal to or less than 50 copies/ml.

2. Low-level viraemia: is any viral load results that are detectable (more than 50 copies/ml) but equal to or less than 1000 copies/ml.

3. Virological failure Viral load above 1000 copies/ml based on two consecutive viral load measurements in 3 months, apart with enhanced adherence support following the first viral load test.

Treatment failure threshold should remain at 1000 copies/ml. Viral suppression or undetectability, however, are defined as viral load equal to or less than 50 copies/ml. PLHIVs should be supported with adherence counselling to achieve viral suppression .However, treatment failure should be considered for those with a repeat viral load result >1000 copies/ml after three months of EAS following the first viral load. Those with low-level viraemia at the first viral load test (50–1000 copies/ml) need to be provided with enhanced adherence support (EAS) and repeat viral load test after 3 months to promote viral suppression. If viral load is still 50-1000 copies/ml, maintain ARV drug regimen and continue viral load test every six months. In addition, continue the routine follow up support and link to community-based adherence support services.

Enhanced Adherence Support (EAS)

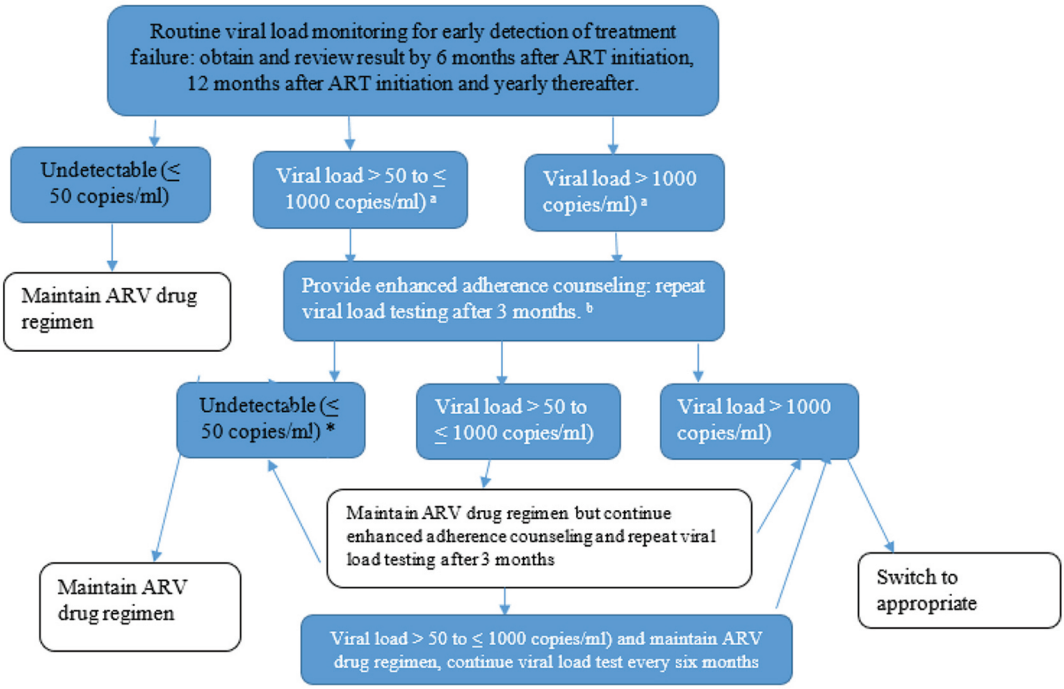
Enhanced adherence support is important for patients that have unsuppressed VL, persisted or new immunosuppression, developing new OI or have multiple adherence barriers. It shall be systematic and with documenting the interventions provided during the EAS period.

Table 4.9: Summary of components of EAS.

Enhanced adherence support sessions overview	
First Session (When the viral load result >50 is received; Day 0)	■ Review cognitive, behavioral, emotional, and socio-economic barriers to adherence: ■ Treatment literacy ■ Medications: dosage, timing, storage ■ Side effects ■ Motivation ■ Mental health screening (screen for depression and other common mental problems using national Mental Health Assessment tool (Annex 20) **Action:** ■ Discuss risk reduction (e.g. for substance abuse) ■ Discuss patient's support systems ■ Assist patient to develop adherence plan to address the identified issues. ■ Referrals and networking when necessary

Second Session (30days after the first session)	■ Review adherence plan from the first session and discuss any challenge. ■ Identify other possible gaps and emerging issues. **Action** ■ Assist patient to modify the adherence plan to address the identified issues ■ Referrals and networking when necessary.
Third Session (60 days after the first session)	■ Review adherence plan from the first and second session and discuss any challenges. ■ Identify other possible gaps and emerging issues. **Action** ■ Assist patient to modify the adherence plan to address the identified issues. ■ Decision on repeat VL based on current adherence: ■ If the adherence is good, plan repeat VL testing after a month and explain possible ways forward, emphasizing the role of the patient and the health facility in terms of strengthening adherence. ■ If adherence challenges persist, link to appropriate client centered care.
Fourth Session (90 days from the first session)	■ Take the second VL sample. ■ All efforts should be employed to get the VL result as soon as possible. ■ As soon as the VL result is received, discuss the result with the client. **Action** 1.If VL is < 50 copies/ml, maintain the current regimen and encourage adherence 2.If VL is 50-1000 copies/ml, continue the current regimen and the monthly EAS for the next 3months then repeat the viral load testing. If the low-level viremia (50–1000 copies/ml) persists, maintain ARV drug regimen and continue viral load test every six months. In addition, continue the routine follow up support and link to community-based adherence support services. If VL is > 1000 copies/ml, switch to appropriate regiment (second or third line).

Figure 4.1. Treatment monitoring algorithm



a. Unsuppressed viral load results should be immediately communicated

b Conduct same-day testing using point-of-care viral load testing for a repeat viral load test, where available, to expedite the return of results. If not available, viral load specimens and results for a repeat viral load should be given priority across the laboratory referral process (including specimen collection, testing and return of results).

Implementation considerations for treatment monitoring of pregnant and breastfeeding women

Whenever possible, use same-day point-of-care testing for viral load testing of pregnant and breastfeeding women to expedite the return of results and clinical decision-making. If this is not available, viral load specimens and results for pregnant and breastfeeding women should be given priority across the laboratory referral process (including specimen collection, testing and return of results).

For all pregnant women, regardless of ART initiation timing:

Conduct viral load testing at 34–36 weeks of gestation (or at the latest at delivery) to identify women who may be at risk of treatment failure and/or may deliver infants at higher risk of perinatal transmission.

In addition:

a) For pregnant women receiving ART before conception:

Conduct a viral load test at the first antenatal care visit (or when first presenting) to identify women at increased risk of in utero transmission.

- For women already on ART, conduct VL testing at the first contact at ANC (VL result conducted in the last 3 months before the first contact can also be used), at 34-36 weeks of gestational age or delivery at the latest, followed by three months after delivery and then every 6months.
- For those who are already on ART with previous VL test conducted more than three months back repeat VL test at first ANC contact /PMTCT visit, at 34-36 weeks of gestational age (or at the latest at delivery) and 3 months after delivery and every six months thereafter until MTCT risk ends.

b) For pregnant women starting ART during pregnancy:

Conduct a viral load by three months after ART initiation to ensure that there has been rapid viral suppression. If viral load testing is expected to be undertaken near the planned viral load at 34–36 weeks of gestation, the first viral load test can be delayed until weeks 34–36 of gestation

For all breastfeeding women, regardless of when ART was initiated:

Conduct viral load test three months after delivery and every six months thereafter to detect viremic episodes during the postnatal period.

4.9. Management of treatment failure

4.9.1. Management of first-line treatment failure (switching to second-line ART)

Using a boosted PI + two NRTI combinations is recommended as the preferred strategy for second-line ART for adults, adolescents, and children. Two NRTI + DTG can be used as second line regimen if it is not used in the first line.

Guidance for changing ARV regimens for treatment failure

- Ensure diagnosis of treatment failure to avoid premature switching.
- Assess adherence and address barriers.
- Assess for and address drug interaction issues.
- Do not add one drug to a failing regimen.
- Consider resistance and cross resistance patterns.
- Get advice from experienced clinicians.
- At least two new drugs.
- Preferably one new drug class.

Once it is decided and patients are switched to second-line regimen, strong adherence support should be continued and viral load monitoring should be started after 6 months of second-line treatment and then every 12 month.

4.9.2. Management of second-line treatment failure (switching to third line ART)

Patients who are on second-line regimen and have high viral load level (>1000copies/ml) after 6 months of treatment need to go through the algorithm as described for first line treatment failure with enhanced adherence support and repeat test after three months to decide second line treatment failure. Once patients are confirmed to have second line failure, they should be referred to hospitals selected for third line ART service.

Treatment failure is indicated by virological non-suppression with or without immunologic and/or clinical deterioration. Before switching to third-line regimen, the issue should be discussed with experienced physician in HIV care and treatment. Treatment failure while on a second line PI regimen is often due to non-adherence.

Doctors and nurses should participate directly in the adherence assessments, and do not delegate the assessment to the adherence counselor alone (see enhanced adherence counseling section for detailed steps of adherence counseling for patients with adherence problems).

Before switching to third line regimen, health care providers should ensure the following.

- Two consecutive viral load measurements > 1000 copies/ml at least 3 months apart.
- First viral load measurement done at least 6 months after switching to second-line regimen.
- The repeat VL test should be done after 3 months of enhanced adherence support.

The approach in switching to third line should follow the guiding principles listed out for switching to second line drugs.

Table 4.10: Summary of sequencing options for first line, second line and third line ART regimens for adults, adolescents, and children

Population	1st line regimens		2nd line regimens	3rd line regimens a,b
Adults and adolescents 10 years & older	Preferred	TDF + 3TC + DTG	AZT+3TC+ATV/r or LPV/r	DRV/rC+TDF+3TC+EFV DRV/r+TDF+3TC+DTGe
	Alternative	TDF+3TC+EFV	AZT+3TC+DTG or ATV/r or LPV/r	DRV/r+TDF+3TC +DTGf
		AZT+3TC+ EFV	TDF+3TC+DTG or ATV/r or LPV/r	DRV/r+AZT+3TC+DTG
		AZT+3TC+DTG	TDF+3TC+ ATV/r or LPV/r	DRV/r+AZT+3TC +EFV
	Special Circumstances	ABC+3TC+EFV	AZT+3TC+ DTG or ATV/r or LPV/r	DRV/r+TDF+3TC +DTG
		ABC+3TC+DTG	AZT+3TC+ATV/r or LPV/r	DRV/r+TDF+3TC +EFV
		TDF+3TC+ATVr or LPV/r	AZT+3TC+DTG	DRV/r+TDF+3TC +EFV
		AZT+3TC+ATVr or LPV/r	TDF+3TC+DTG	DRV/r+AZT+3TC +EFV
Children 4weeks to 10 years and >3kg	Preferred	ABC+3TC+DTG	AZT+3TC+LPV/r	For those <3 years, maintain second line regimens till they become 3years. For children 3-10 Years, switch to DRV/rd+DTGg+ABC+3TC
	Alternative	ABC+3TC+LPV/r	AZT+3TC +DTG	For those <3 years, maintain second line regimens till they become 3years. For children 3-10 Years, switch to DRV/r +ABC+3TC+ EFV
		AZT+3TC+DTG	ABC+3TC+LPV/r	For those <3 years, maintain second line regimens till they become 3years. For children 3-10 Years, switch to DRV/r +AZT+3TC+EFV or DRV/r+DTG+AZT+3TC

	Special circumstances	ABC+3TC+EFV	AZT+3TC+DTG	For those <3 years, maintain second line regimens till they become 3years. For children 3-10 Years, switch to DRV/r +ABC+3TC+EFV
		AZT+3TC+EFV	ABC+3TC+DTG or LPV/r	For those <3 years, maintain second line regimens till they become 3years. For children 3-10 Years, switch to DRV/r +AZT+3TC+EFV or DRV/r+DTG+AZT+3TC
		AZT+3TC+LPV/r	ABC+3TC+DTG or EFV	For those <3 years, maintain second line regimens till they become 3years. For children 3-10 Years, switch to DRV/r+AZT+3TC+EFV or DRV/r+DTG+AZT+3TC

a. Consider genotyping before constructing a third line regimen whenever accessible, however switching to third line should not be delayed while waiting for the result, if the TAT is prolonged.

b. When constructing third line regimens for special circumstances in the absence of genotyping please consult senior experts on HIV

c. In PI-experienced patients, the recommended DRV/r dose should be 600mg/100 mg twice daily; refer the weight band for pediatrics

d. DRV/r should not be used in children younger than three years of age.

e. DTG based 3rd line following use of INSTI must be administered with DTG BD.

4.9.3. Second line ART service in health centers

Patients who have treatment failure on first line ARV regimens in health centers can be switched to second line ART in the same facility based on the below mentioned criteria; also patients who were switched to second line ART in hospitals can be transferred to selected health centers for follow-up.

Eligible health centers to provide second line ART service

Second line ART service is available at health centers that have a patient load of 200 or more. That is a reasonably adequate patient load which could give rise to viable number of prospective clients who might need to be switched to a second line ART.

Eligible patients for second line ART service at health centers

The following criteria should be used to sort out treatment failure patients who will be switched to second line ART or will have follow up at the health centers:

a. Patients who fulfill the criteria of treatment failure and with no signs of clinical failure

b. Patients who are initiated on second line ART at hospital and became stable with no signs of OI or drug toxicity and transferred out to health centers having second line ART.