ZAMBIA CONSOLIDATED GUIDELINES
for Prevention and Treatment of HIV Infection
2018
Zambia Consolidated Guidelines

for Treatment and Prevention of HIV Infection
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<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Full Form</th>
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<tbody>
<tr>
<td>DR TB</td>
<td>Drug Resistant Tuberculosis</td>
</tr>
<tr>
<td>DRV</td>
<td>Darunavir</td>
</tr>
<tr>
<td>DST</td>
<td>Drug Susceptibility Testing</td>
</tr>
<tr>
<td>DTG</td>
<td>Dolutegravir</td>
</tr>
<tr>
<td>E</td>
<td>Ethambutol</td>
</tr>
<tr>
<td>EFV</td>
<td>Efavirenz</td>
</tr>
<tr>
<td>EMTCT</td>
<td>Elimination of Mother-to-Child Transmission (of HIV)</td>
</tr>
<tr>
<td>EPI</td>
<td>Expanded Program for Immunization</td>
</tr>
<tr>
<td>ETR</td>
<td>Etravirine</td>
</tr>
<tr>
<td>ETV</td>
<td>Entecavir</td>
</tr>
<tr>
<td>FDC</td>
<td>Fixed-Dose Combination</td>
</tr>
<tr>
<td>FP</td>
<td>Family Planning</td>
</tr>
<tr>
<td>FTC</td>
<td>Emtricitabine</td>
</tr>
<tr>
<td>GRZ</td>
<td>Government of Republic of Zambia</td>
</tr>
<tr>
<td>Hb</td>
<td>Haemoglobin</td>
</tr>
<tr>
<td>HBeAg</td>
<td>Hepatitis B E-Antigen</td>
</tr>
<tr>
<td>HBsAg</td>
<td>Hepatitis B Virus Surface Antigen</td>
</tr>
<tr>
<td>HBV</td>
<td>Hepatitis B Virus</td>
</tr>
<tr>
<td>HCW</td>
<td>Health Care Worker</td>
</tr>
<tr>
<td>PrEP</td>
<td>Pre-Exposure Prophylaxis</td>
</tr>
<tr>
<td>R</td>
<td>Rifampicin</td>
</tr>
<tr>
<td>RR</td>
<td>Rifampicin Resistance</td>
</tr>
<tr>
<td>-r</td>
<td>Ritonavir (Low-Dose)</td>
</tr>
<tr>
<td>RNA</td>
<td>Ribonucleic Acid</td>
</tr>
<tr>
<td>R</td>
<td>Rifampicin</td>
</tr>
<tr>
<td>RAL</td>
<td>Raltegravir</td>
</tr>
<tr>
<td>sd-NVP</td>
<td>Single-Dose Nevirapine</td>
</tr>
<tr>
<td>TAF</td>
<td>Tenofovir Alafenamide</td>
</tr>
<tr>
<td>FBC</td>
<td>Full Blood Count</td>
</tr>
<tr>
<td>TAT</td>
<td>Toxoplasmosis Antigen Test</td>
</tr>
<tr>
<td>TB</td>
<td>Tuberculosis</td>
</tr>
<tr>
<td>TDF</td>
<td>Tenofovir Disoproxil Fumarate</td>
</tr>
<tr>
<td>UNAIDS</td>
<td>Joint United Nations Programme on HIV/AIDS</td>
</tr>
<tr>
<td>UNICEF</td>
<td>United Nations Children’s Fund</td>
</tr>
<tr>
<td>VIA</td>
<td>Visual Inspection with Acetic Acid</td>
</tr>
<tr>
<td>XDR - TB</td>
<td>Extensively Drug – Resistant Tuberculosis</td>
</tr>
<tr>
<td>XTC</td>
<td>Lamivudine or Emtricitabine</td>
</tr>
<tr>
<td>FTC</td>
<td>Emtricitabine</td>
</tr>
<tr>
<td>Z</td>
<td>Pyrazinamide</td>
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</table>
FOREWORD

With this publication, the Ministry of Health issues the first guidelines on universal routine HIV testing, counselling and treatment, HIV self testing and use of better tolerated drugs such as Dolutegravir, Efavirenz-400mg and Tenofovir alafenamide. These ambitious guidelines have followed the recent trends and global approach of fast-tracking towards HIV epidemic control. This will be achieved through, counselling leading to more individuals being tested, implementation of the universal routine HIV testing, improved linkage to care and retention through adoption of the decentralised service delivery models and better tolerated regimens leading to increased HIV treatment coverage and better virological outcomes with virological suppression and eventual reduction in new HIV infections.

A key way to accelerate progress towards HIV epidemic control is to test all consenting individuals, initiate therapy the same day an individual is tested HIV positive, as recommended in these guidelines. This will bring the dual advantage of keeping people healthier longer and reducing the risk of virus transmission to others. These guidelines have also defined individuals at high risk of acquiring HIV and providing those who test HIV negative within these high risk categories with pre exposure prophylaxis (PrEP).

These new guidelines will therefore provide a reference tool to health care providers and support staff on the new trends that do reflect the changes in the diagnosis, care and management of all people living with HIV in Zambia.

The Ministry of Health expects implementation of these guidelines to help fast-track towards HIV epidemic control. I therefore call on all health care workers to take advantage of these new guidelines to accelerate scale up of HIV prevention, treatment and care services to all people living with HIV.

Dr Jabbir Mulwanda
Permanent Secretary Technical Services
Ministry of Health
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INTRODUCTION

In July 2017, the World Health Organization released the technical update on transitioning to new antiretroviral drugs and guidelines on managing advanced HIV disease. This version of the Zambia Consolidated Guidelines for Treatment and Prevention of HIV Infection provides simplified guidance on a country transition plan, the continued approach that positively affects the continuum of HIV care, while adding to innovative methods that will reduce transmission rates and increase life span for those on treatment. This is all to further accelerate efforts to meet the ambitious Fast-Track target for 2020, including achieving major reductions in the number of people dying from HIV-related causes and the 90–90–90 treatment target: ensuring that 90% of the people living with HIV know their HIV status; 90% of the people living with HIV who know their HIV status are accessing treatment; and 90% of people living with HIV who are receiving treatment have suppressed viral load.

Besides the recommendation to provide lifelong cART to all HIV infected populations, regardless of CD4 cell count these guidelines present several new recommendations, including universal routine HIV testing, counselling and treatment in all public and private health facilities in Zambia. The approach of offering Universal Routine HIV Testing gives a window to provide immediate treatment and care to all HIV infected individuals through the “test and treat” strategy. This will accelerate our strides towards HIV epidemic control. Additionally, these guidelines provide the use of better and safer antiretroviral agents such as Dolutegravir, Tenofovir alafenamide, and Efavirenz-400mg and how to transition patients who are on the older regimens.

Our 2016 guidelines have also adopted the recommendations to offer PrEP to selected people at substantial risk of acquiring HIV. Alternative treatment regimens are recommended, including an integrase inhibitor as an option in resource-limited settings and reduced dosage of a key recommended first-line drug. Importantly, there has been introduction of Raltegravir, an integrase inhibitor, as a part of the second-line regimen for children failing Lopinavir-ritonavir-based first-line therapy. These guidelines also highlight the management of patients failing second-line cART with third-line cART, who should be managed at higher-level health facilities called Advanced Treatment Centres (ATCs). All of the recommendations have been adopted because of their anticipated public health effect.

Several significant recommendations from the previous guidelines remain a priority, namely providing lifelong cART regardless of CD4 cell count to all pregnant and breastfeeding women and moving toward viral load testing as the preferred means of monitoring people on cART. Newer developments aim to complement and improve the service delivery of HIV services to our population. Importantly, the guidance WHO emphasizes the need for differentiated approaches to care for people who are stable on cART, such as reducing the frequency of clinic visits and community ART distribution. Such efficiencies are essential if countries with a high burden of HIV infection are to manage their growing numbers of people receiving cART and reduce the burden on people receiving treatment and on health facilities.

There will be continued concerted efforts required toward implementing these guidelines at district and health facility levels; the 2016 Consolidated Guidelines represent an important step toward achieving the goal of universal access to ARV drugs, treating and preventing HIV, and ultimately ending the HIV epidemic by 2030.
HIV Testing Services (HTS) refers to the full range of services that should be provided with HIV testing, including counseling (pre-test information and post-test counseling). HTS is a gateway to appropriate HIV prevention, treatment, and care, and other clinical services; and coordination with laboratory services to support quality assurance (QA) and the delivery of accurate results.

HTS is primarily conducted by healthcare workers as well as trained, certified and supervised lay providers that can conduct safe and effective HIV testing using recommended test kits.

HTS should be done at all service delivery points (see Table 1) within the facility, as well as in the community, as an efficient and effective way to identify people with HIV, bearing in mind the priority and key populations. Community-based testing embraces a family-centered approach based on the index-patient model and leads to early diagnosis of HIV infection and prompt linkage to care and treatment. Every individual in the index-patient’s home and network, regardless of age and risk factors, should be tested with a serological test (also known as antibody test or rapid test), or given an opportunity to self-test (see Figure 1). All individuals testing negative should re-test after 3 months to account for the window period.

**Universal Routine HIV Testing**

Universal Routine HIV Testing gives an opportunity to provide immediate treatment and care to all HIV infected individuals through the “test and treat” strategy without using CD4 as eligibility criteria for HIV treatment.

Health care workers are therefore mandated to offer routine HIV testing to all individuals presenting to health facilities (in the inpatient department, routine testing should be extended to the caregivers). Routine HIV testing should be offered with the following considerations:

- Provide information in a confidential manner - those who opt out should continue to be counseled and offered an HIV test at each interaction with health care providers, including the opportunity to self-test
- Provide counselling on benefits of HIV testing and other services available for HIV negative and positive individuals
- Provide correct results following the HIV testing algorithms
- Provide linkage or connection to preventive and treatment and care services by issuance of a National Unique Patient Number (NUPN), regardless of test result.

**Recommendations**

- Universal Routine HIV Testing and Linkage to Services
- HIV Self-testing for increased access to testing Services
- Partner Notification Services and HIV Self Testing (HIV-ST) to complement conventional testing
- POC Technologies for early diagnosis of HIV-infected infants and children
Therefore, *Universal Routine HIV testing*, counselling and treatment should be implemented in all health facilities (public and private) to all without discrimination.

**HIV SELF-TESTING (HIV-ST)**

HIVST is a process in which a person collects their own oral fluid or blood and then performs an HIV rapid test and interprets the result. An HIV self-test is a screening test which requires further testing and confirmation for any reactive result. Health care providers should ensure that users receive clear information on:

- How to perform the test and interpret the result correctly
- Where to access HTS and further support services
- How to safely dispose of the used test-kits
- The ethical and legal obligations (no one should test a third party without their consent)

**Figure 1: HIV Self Testing Algorithm**

![HIV Self-Testing Algorithm](image)

- **If Reactive/Positive:**
  - Confirm result at clinic with trained provider using validated algorithm.

- **If Non-reactive/Negative:**
  - If there was possible exposure to HIV in the preceding 6 weeks or with ongoing risk of HIV infection, repeat test after 3 months.
  - Recommend comprehensive prevention services.

- **If confirmed HIV-positive:**
  - Refer for treatment

- **Recommend comprehensive prevention services**
**PARTNER NOTIFICATION SERVICES THROUGH INDEX CLIENTS**

HIV Partner notification is a voluntary process where trained health providers (including lay providers) ask index clients (people diagnosed HIV positive) about their sexual or drug injecting partners (including children under 12 years) and with the consent of the HIV positive client to offer HIV testing to these partners/children who may have been exposed to HIV within the past 12 months.

Partner notification is provided using passive or assisted approaches. (It is recommended to use the best approach for each index client at that time).

Passive HIV partner notification services is where HIV positive clients are encouraged by health care providers to disclose their status to their sexual/drug injecting partners by themselves, and to suggest HTS to the partner(s) given their potential exposure to HIV infection. Being at the discretion of the index client to encourage their contacts to test, this approach is less effective.

Assisted HIV partner notification services is where consenting HIV positive clients are assisted by health care providers to disclose their status or to anonymously notify their sexual/drug injecting partner(s) of their potential exposure to HIV infection. The provider then offers testing to these partner(s).

Assisted partner notification is done using provider contract or dual referral approaches.

Provider contract is where HIV positive clients enter into a contract with a trained provider and agree to disclose their status (and the potential HIV exposure to their partners) by themselves and to refer their partner(s) to HTS within a specific time period. If the partner(s) of the HIV-positive individual do not access HTS or contact the health provider within that period, then the provider will contact the partner(s) directly and offer voluntary HTS.

Provider referral is when the health care provider confidentially contacts the person's partner(s) directly and offers the partner(s) voluntary HTS.

Dual referral is when a health care provider accompanies and provides support to HIV positive clients when they disclose their status and the potential exposure to HIV infection to their partner(s). The provider also offers HTS to the partner(s).

In partner and family-based index testing, it is critically important to ensure that sexual partners and children under the age of 12 years also offered an opportunity to test for HIV.
**Figure 2: Partner Notification Services Algorithm**

**Engaging the Index Client**

**Step 1:** Introduce Partner Notification Services to the Index Client and obtain concurrence

**Step 2:** Obtain a list of all partners who may be at risk for HIV infection

**Step 3:** For each listed partner, record contact information, screen for intimate partner violence (IPV), and determine the preferred notification method

**Notifying the Partner(s)**

**Step 4:** Contact each named partner using the selected approach; notify and offer HTS

**Step 5:** Record outcomes on Partner Notification Worksheet

**Step 6:** Record all data in PNS Register

- **Client self-Referral:** Coach client on disclosure; provide “Tips for Telling Your Partner about HIV” and referral

- **Provider Contract Referral:** Coach client on disclosure; provide “Tips for Telling Your Partner about HIV” and referral slip. Agree that client will refer partner for HTS within 30 days

- **Provider Referral:** Initiate partner contact attempts using telephone, SMS, and home visit scripts.

- **Dual Referral:** Coach client on joint disclosure process and develop plan for provider and client to disclose to partner together; provider offers HTS to partner.
**EARLY INFANT DIAGNOSIS**

For children <24 months old who are breastfeeding, the mother should be tested first. If she is HIV-positive, perform a Nucleic Acid Test (NAT) which can be done using either a Dried Blood Spot-DBS (by being sent to a central testing lab) or a Point-of-care machine (POC) on the HIV-exposed infant (HEI), regardless of age. The advantage of new POC technologies is that they are done at the point of service delivery and offer same-day results. Infants who have HIV detectable by NAT at birth are likely infected in utero, will progress to disease rapidly, and, in the absence of treatment, will experience high mortality in the first few months of life. Infants infected at or around delivery may not have virus detectable by NAT for several days to weeks. The ability of NAT to detect the virus in the blood may be affected by ARV drugs taken by the mother or infant for postnatal prophylaxis, resulting in false-negative results. This includes drugs present in breast milk as a result of maternal ART during breastfeeding.

The rationale behind this recommendation is that infants who are first identified as HIV-exposed postpartum have a high cumulative risk of already having acquired HIV by the time prophylaxis is initiated; thus NAT should be performed around the time of initiating prophylaxis, which would be at birth. This will help to minimize the risk of development of resistance because of extended prophylaxis in infected infants and help to promote linkage to timely initiation of cART.

**LINKAGE TO HIV TREATMENT AND SUPPORT SERVICES**

Linkage to care is a process of actions and activities that support people testing for HIV and those diagnosed with HIV to engage with prevention, treatment, and care services as appropriate for their HIV status. Linkage to care and treatment is the period beginning with HIV diagnosis and ends when a person enters into HIV care and/or initiates cART.

For clients who test HIV negative, it is necessary to link them to prevention services including condoms, VMMC, PrEP, and others depending on their individual risk factors. Linkage to treatment is a vital bridge between the first 90 (diagnosis) and the second 90 (treatment initiation).

**QUALITY ASSURANCE/IMPROVEMENT**

All testing sites should participate in HIV proficiency testing at least twice per year. If testing is performed in the community by community health workers, every 10th sample (10%) should be retested at the nearest health facility.
**Table 1: Timing of HIV Testing Services for Specific Populations**

<table>
<thead>
<tr>
<th>Specific populations</th>
<th>Whom to test</th>
<th>When to test</th>
<th>HIV testing</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Pregnant women, breastfeeding women (and their sexual partners)</strong></td>
<td>All</td>
<td>During antenatal care (ANC): at first ANC visit and repeat test every 3 months if negative. In labour and delivery (L&amp;D): test if last test &gt;6 weeks ago. During postnatal care (PNC): test at first contact if unknown status. Serologic test at 6 weeks if negative. If breastfeeding: repeat test every 3 months if negative until cessation of breastfeeding. Partner testing: same time points.</td>
<td>Serologic test</td>
</tr>
<tr>
<td><strong>Well, never-breasted HIV Exposed Infant (HEI)</strong></td>
<td>At birth/first week of life or at first contact.</td>
<td><strong>NAT</strong>&lt;sup&gt;+&lt;/sup&gt;</td>
<td><strong>Serologic test</strong></td>
</tr>
<tr>
<td></td>
<td>6 weeks old</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>18 months old</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Well, breastfed HEI</td>
<td>At birth/first week of life or at first contact.</td>
<td><strong>NAT</strong>&lt;sup&gt;+&lt;/sup&gt;</td>
<td>Serologic test. If positive, follow with NAT. If negative, follow up with serologic test at 18 months.</td>
</tr>
<tr>
<td></td>
<td>6 weeks old</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>6 months old</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>9 months old</td>
<td>Serologic test. If positive, follow with NAT. If negative, follow up with serologic test at 18 months.</td>
<td></td>
</tr>
<tr>
<td></td>
<td>12 months old</td>
<td>Serologic test; if positive, follow up with NAT. If negative, follow up with serologic test at 18 months.</td>
<td></td>
</tr>
<tr>
<td></td>
<td>18 months old</td>
<td>Serologic test; if positive, follow up with NAT.</td>
<td></td>
</tr>
<tr>
<td></td>
<td>24 months old</td>
<td>Serologic test; if positive, follow up with NAT.</td>
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</tr>
<tr>
<td>Infant or child who has completely stopped breastfeeding</td>
<td>≥6 weeks after breastfeeding cessation.</td>
<td>Serologic test; if positive, follow up with NAT.</td>
<td><strong>Serologic test</strong></td>
</tr>
<tr>
<td></td>
<td>≥18 months old</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Asymptomatic infant with unknown HIV exposure</td>
<td>At first contact.</td>
<td>Maternal serologic test and/or infant serologic test; follow with NAT for positive serologic child &lt;18 months old.</td>
<td></td>
</tr>
<tr>
<td>Infant or child symptomatic for HIV infection</td>
<td>Immediately regardless of age.</td>
<td>Serologic test; follow with NAT for positive serologic child &lt;18 months old.</td>
<td></td>
</tr>
<tr>
<td>Positive serologic child &lt;18 months old</td>
<td>At first contact.</td>
<td>NAT.</td>
<td></td>
</tr>
<tr>
<td>All infants and children with unknown HIV status admitted for inpatient care, attending malnutrition clinic, outpatient care or immunization clinics</td>
<td>Routine HIV testing.</td>
<td>Age-appropriate tests.</td>
<td></td>
</tr>
<tr>
<td><strong>Adolescents (10 – 19 years) and adults</strong></td>
<td>All sexually active persons with their partners and any person of unknown HIV status</td>
<td>At first contact, 3 months if negative and every 6 months.</td>
<td>Serologic test.</td>
</tr>
</tbody>
</table>

*Where there is no POC NAT a DBS should be sent for HIV PCR. Where NAT is positive, a repeat test should be done to rule out false-positive results. cART should be initiated without waiting for the receipt of the second test result because of the high risk of mortality with in utero infection; if the second specimen tests negative, a third NAT should be performed before interrupting cART. Although plasma remains the gold standard sample for NAT, DBS will be the preferred mode of sample transportation for both DNA and RNA testing.*
**Figure 3: HIV Serologic Testing Algorithm**

Universal Routine Testing (Screening Test) by healthcare provider.

- Test-1

**Results - Reactive. Proceed to test 2**
- Confirmatory and HIV-2 differentiation

Every individual in the index patient’s* home, regardless of age and risk factors should be tested

- HIV 1
- HIV 2

Both tests 1 & 2 are reactive
- Report as positive

Both tests 1 & 2 are non-reactive
- Report as negative

Test 2 - Reactive
- Report as HIV Positive

Test 2 - Non-reactive
- Report as HIV negative

Self -Testing
- If Self-Testing results Reactive

Results - Non reactive
- Report as HIV negative

Test 2 - Non-reactive
- Repeat Testing Using the same specimen (Test 1 & 2)

Discordant results
- Repeat after 14 days Using same tests

- HIV testing for those <18 months, NAT is gold standard. Although plasma remains the gold standard sample for NAT, DBS will be the preferred mode of sample transportation for both DNA and RNA testing
- Index patient refers to the client being tested and identified HIV positive, whether child, adolescent or adult
- Determine is used as a screening test and Bioline as confirmatory test (discriminates between HIV-1 and HIV-2)
Summary/Key Points

- HIV testing services (HTS) include HIV testing, pre-test information, post-test counselling, linkage to appropriate HIV prevention, treatment, care, other clinical services, and coordination with laboratory services to support quality assurance (QA) and delivery of accurate results.
- HTS should be done at all service delivery points within the facility, as well as in the community, as an efficient and effective way to identify people with HIV.
- HIV testing is the gateway to HIV prevention, treatment, care, and other support and clinical services, and Universal Routine HIV Testing, Counselling and Treatment (HTCT) should be offered to all clients and in all service points.
- HIV testing is primarily conducted by health care workers. Lay providers who are trained, certified by MOH, and supervised can conduct safe and effective HIV testing using recommended diagnostic tests.
- All mothers of breastfeeding children <24 months old should be tested. If she tests HIV positive, a Nucleic Acid Test (NAT) should be performed on the HIV-exposed infant (HEI), regardless of age.
- Where NAT is positive, a repeat test should be done to rule out false-positive results at 18 months with serological test. cART should be initiated without waiting for the receipt of the second test result because of the high risk of mortality with in utero infection; if the second specimen tests negative, a third NAT should be performed before interrupting cART.
- Where NAT is negative, a repeat test should be done at 6 weeks, 6 months, 9 months, 12 months and serological tests at 18 and 24 months if the HEI infant is being breast fed.
- Community-based testing embraces a family-centred approach based on the index-patient model and leads to early diagnosis of HIV infection and prompt linkage to care and treatment.
PRE-EXPOSURE PROPHYLAXIS (PrEP)

Pre-exposure prophylaxis, or PrEP, is when people at high risk for HIV take two HIV medicines daily to lower chances of getting infected. When someone is exposed to HIV through sex or injection drug use, these medicines can work to keep the virus from establishing a permanent infection.

PrEP involves the use of antiretroviral (ARV) drugs before HIV exposure by people who are not infected with HIV to block the acquisition of HIV. Twelve trials on the effectiveness of oral PrEP have been conducted among serodiscordant couples, heterosexual men, women, men who have sex with men, people who inject drugs, transgender men and women. Where adherence has been high, significant levels of efficacy have been achieved, showing the value of this intervention as part of combination prevention approaches. WHO recommends oral PrEP containing Tenofovir (TDF) with either Emtricitabine (FTC) or Lamivudine (3TC) to be offered as an additional prevention choice for people at substantial risk of HIV infection as part of combination HIV prevention approaches.

Considerations for PrEP

- The combination of TDF+XTC (Emtricitabine or Lamivudine) is active against Hepatitis B infection thus discontinuation of TDF+XTC requires close monitoring in those infected with Hepatitis B due to the concern for rebound viremia.
- Persons with osteopenia/osteomalacia/osteoporosis may be at risk of bone loss associated with TDF.
- PrEP efficacy has not yet been established in pregnancy and breastfeeding, therefore its use in this population is NOT recommended.
- TDF should not be co-administered with other nephrotoxic drugs, e.g. aminoglycosides.
- Standard TB medication does not interact with PrEP drugs and there is no need for dose adjustments.
- Clients on MDR-TB medications may have increased risk of renal side effects. PrEP should therefore be avoided.
- Other prevention methods should be recommended and PrEP screening should be delayed until the end of MDR-treatment.
- Standard hormonal contraception does not affect PrEP effectiveness, nor does PrEP affect contraceptive effectiveness.
- PrEP clients must be routinely tested for HIV infection, and cART offered immediately if the PrEP user seroconverts.
- PrEP is not 100% effective at preventing HIV and clients need to be counselled that they should use other prevention methods as well.
Eligibility Criteria

- No suspicion of acute HIV infection
- Test HIV negative at health facility
- Interested in PrEP and willing to be adherent
- Able to attend regular 3 month reviews and HIV testing
- Able to concomitantly apply other prevention methods such as barriers to prevent the transmission of other STIs
- Willing to stop taking PrEP when no longer eligible

And: at substantial risk for HIV infection, defined as engaging in one or more of the following activities within the last six months:

- Vaginal/anal intercourse without condoms with more than one partner
- Sexually active with a partner who is known to be HIV positive or at substantial risk of being HIV positive
- Sexually active with an HIV-positive partner who is not on effective treatment (defined as on cART for > 6 months and virally suppressed)
- History of STI
- History of PEP use
- Sharing injection material or equipment

PrEP may also be considered for key populations (as defined by the 2017 NASF) or by persons self-selected as high-risk for HIV acquisition. Such persons should meet the eligibility criteria above.

Recommendations

- PrEP should be taken for a minimum of 7 days in men, 21 days in women to achieve maximal protection from HIV acquisition before engaging in high risk sexual exposure and must be continued as long as risky exposure persists or one remains negative

HIV testing is required before PrEP is offered

- Repeat HIV testing every 3 months is mandatory while a client is on PrEP
- The frequent HIV testing during PrEP use should also ideally become an opportunity for STI screening and management.
- Those who seroconvert while on PrEP should be immediately switched to a standard first line regimen
- PrEP should be provided as part of the combination prevention package (condom use, HTS, family planning, STI screening, etc.)

Lab Tests before PrEP

- HIV test (only HIV-negative partners should be on PrEP)
- Creatinine (or urinalysis if creatinine not available)
- ALT
- RPR/RST
- Repeat HIV testing is recommended while PrEP is taken every three months
- Hepatitis B (those with positive results should be on lifelong TDF+XTC to treat HBV)

ARV regimen to be used for oral PrEP

- Tenofovir in combination with Emtricitabine (TDF+FTC) is preferred for PrEP
- However, if Emtricitabine is not available, Lamivudine in combination with Tenofovir (TDF+3TC) may be used for PrEP

Lab Monitoring while on PrEP

- Creatinine at 1 month, 2 months, every 3 months for first 12 months then annually thereafter
- ALT every 3 months for first 12 months then annually thereafter
Adherence Support on PrEP

- Support for adherence should include information that PrEP is highly effective when used with strict adherence.
- PrEP users should be advised that **PrEP only becomes effective after 7 days (21 days in women)** and must be continued as long as risky exposure persists or one remains negative.
- Brief client-centred counseling that links daily medication use with a daily habit (such as waking up, going to sleep, or a regular meal) may be helpful.
- Special programmes to facilitate adherence among particular groups—such as young people and women—may be needed.
- Support groups for PrEP users, including social media groups (for example, https://www.facebook.com/groups/PrEPFacts) may be helpful for peer-to-peer sharing of experience and challenges.
- People who start PrEP may report side effects in the first few weeks of use. These side effects include nausea, abdominal cramping, or headache, are typically mild and self-limited, and do not require discontinuation of PrEP. People starting PrEP who are advised of this start-up syndrome may be more adherent.

When to Stop PrEP

- PrEP can be discontinued if a person taking PrEP is no longer at risk and when this situation is likely to be sustained (i.e., no longer engaging in any high-risk behaviors as defined above).
- PrEP can be discontinued after 4 weeks of elimination of the risk exposure.
- Significant side effects or if the creatinine clearance decreases to <50mL/min.
- If in a serodiscordant relationship, the HIV positive partner has been on cART for more than 6 months, is known to be virally suppressed, and there are not other partners, then the HIV negative partner on PrEP may discontinue therapy.
**FIGURE 4: PrEP Flow Chart**

1. **Perform HIV testing and screening (TB, STI)**
   - HIV Testing as per National Algorithm

2. **HIV Negative**
   - Potentially eligible for PrEP
   - Risk reduction counselling and confirm interest in PrEP
   - Creatinine (or UA) and Hepatitis B Screening
   - Pregnancy test for women
   - Same day Initiation of PrEP
   - Provide one month PrEP prescription
   - Provide ongoing PrEP educational and counselling
   - Book a follow up appointment within 28 days and Repeat HIV Test

3. **HIV Positive**
   - Refer all for immediate cART initiation, as per guidelines

4. **HIV positive: Refer to the National Consolidated Guidelines**
   - Use rapid tests as per guidelines and availability
   - Treat any present STIs
   - Clients with acute or chronic hepatitis B can be safely initiated onto PrEP but require liver function test (LFT) monitoring
   - If creatinine clearance results are <50mL/min, contact client to stop PrEP and return for repeat creatinine test in 2 weeks
**Post-Exposure Prophylaxis (PEP)**

Post-exposure prophylaxis is the use of cART to prevent HIV transmission. Non-occupational exposure to HIV in children is mostly due to sexual abuse. In adults, exposure to HIV is mostly associated with occupational injuries. The risk of acquiring HIV infection after occupational exposure to HIV-infected blood is low (1:300 after percutaneous exposure to <1:1000 after mucocutaneous exposure).

There is no risk of transmission when the skin is intact. Factors associated with an increased risk include: deep injury, visible blood on the device that caused the injury, injury with a large bore needle from artery or vein, and unsuppressed HIV viral load in source patient. Body fluids and materials that pose a risk of HIV transmission are amniotic fluid, cerebrospinal fluid, human breast milk, pericardial fluid, peritoneal fluid, pleural fluid, saliva in association with dentistry, synovial fluid, unfixed human tissues and organs, vaginal secretions, semen, any other visibly blood-stained fluid, and fluid from burns or skin lesions. Other blood-borne infections are hepatitis B and hepatitis C viruses. Thus all HCWs should receive HBV vaccination.

Management of occupational exposure to infectious substances includes the following steps:

Immediately after exposure:

- Clean the site: wash skin wounds with soap and running water. DO NOT squeeze, allow wound to freely bleed. If the exposed area is an eye or mucous membrane, flush with copious amounts of clean water. DO NOT USE BLEACH or other caustic agents/disinfectants to clean the skin.
- Contact your In-Charge or supervisor.
- Consult the clinical officer or medical officer, who does the following:
  - Determine the need for post-exposure prophylaxis (PEP) based on the risk of transmission and risks and benefits of taking (or not taking) cART.

### Table 3: Post Exposure Prophylaxis Recommendations by Risk Category

<table>
<thead>
<tr>
<th>Risk category</th>
<th>cART</th>
<th>Duration</th>
</tr>
</thead>
<tbody>
<tr>
<td>No risk: intact skin</td>
<td>Not recommended</td>
<td></td>
</tr>
<tr>
<td>Medium risk: invasive injury, no blood visible on needle</td>
<td>Preferred: TDF**+XTC+DTG** Alternative: TDF + XTC + ATV-r** AZT + 3TC + LPV-r (children &lt;10 years)</td>
<td>28 days</td>
</tr>
<tr>
<td>High risk: large volume of blood/liquid, known HIV-infected patient, large bored needle, deep extensive injury</td>
<td>* For patients with CrCl &lt;50mL/min, replace TDF with AZT **DTG is effective against both HIV 1 and 2 and prevents integration of the viral DNA into the host DNA. It should be avoided in pregnancy and for HIV/TB patients on Rifampicin, the dose of DTG should be 50mg twice daily instead of the regular 50mg once daily. For intolerance to DTG (such, insomnia, anxiety, depression), use a recommended PI **For patients who intolerant to ATV-r or if source is HIV-2 infected and cannot tolerate DTG, LPV-r should be used.</td>
<td></td>
</tr>
<tr>
<td>Penetrative sexual abuse</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* For patients with CrCl <50mL/min, replace TDF with AZT
**DTG is effective against both HIV 1 and 2 and prevents integration of the viral DNA into the host DNA. It should be avoided in pregnancy and for HIV/TB patients on Rifampicin, the dose of DTG should be 50mg twice daily instead of the regular 50mg once daily. For intolerance to DTG (such, insomnia, anxiety, depression), use a recommended PI
**For patients who intolerant to ATV-r or if source is HIV-2 infected and cannot tolerate DTG, LPV-r should be used.
Management of non-occupational exposure to infectious substances should be managed as shown in Figure 5 below:

**Figure 5: Algorithm for Evaluation and Treatment of Possible Non-Occupational HIV Exposure**

- **Substantial Exposure Risk**
  - ≤ 72 hours since exposure
  - Source patient known to be HIV positive or of unknown HIV status
    - nPEP recommended
  - > 72 hours since exposure
    - Case by case determination

- **Negligible Exposure Risk**
  - nPEP NOT recommended

---

**Substantial risk for HIV exposure of:**
Vagina, rectum, eye, mouth, or other mucous membrane, non-intact skin, or percutaneous contact;
With:
  - Blood, semen, vaginal secretions, rectal secretions, breast milk, or any body fluid that is visibly contaminated with blood;
When:
  - The source is known to be HIV–infected or source’s status is unknown

**Negligible risk for HIV exposure with:**
Urine, nasal secretions, saliva, sweat, or tears if NOT visibly contaminated with blood;
Regardless: of the known or suspected HIV status of the source
Prong 1: Primary HIV Prevention

The drivers of the HIV epidemic include low rates of HIV testing, multiple concurrent sexual partners, low rates of male circumcision, MTCT, commercial sex workers, and migrant workers. Adolescents, especially young female adolescents, are vulnerable to HIV infection. The following interventions should be done in the health facilities and community:

- Counsel regarding STIs and HIV prevention, including post-test information on how to remain HIV negative or to live positively based on the outcome of the HIV test result
- Provide condoms or information on where to access condoms, including female condoms
- Refer to youth friendly services for more comprehensive sexual information, including HIV prevention
- Treatment of discordant couples
- Provide adherence support for adolescents on cART (prevention with positives)
Prong 2: Prevention of Unintended Pregnancies

Prevention of unintended pregnancies in HIV-infected women contributes to elimination of mother-to-child transmission. It includes counseling and provision of a variety of family planning (FP) methods. With timely initiation of cART and adherence to cART in HIV-infected non-pregnant women, planning for pregnancy is encouraged

- Refer patients to Family Planning clinics for further counseling and alternative methods if needed
- Promote mixed methods, also known as dual protection, because condoms alone or hormonal methods alone when the woman is on cART have been associated with unintended pregnancies
- Offer condoms to all men and women ≥15 years old
- Offer long-term FP methods to all women ≥15 years old
- Depot medroxyprogesterone acetate (DMPA) 150mg (1 vial) IM injection in deltoid muscle every 3 months
- Noristerat 200mg IM injection in deltoid or gluteal muscle, every 2 months
- Hormonal implant
- Intrauterine contraceptive device (IUCD)
- Sterilization (male or female) if child-bearing is complete
- Patients have the right to choose their FP method, including declining all method

Prong 3: Prevention of Mother-to-Child Transmission of HIV Using ARVs

In pregnant and breastfeeding women of unknown HIV status should be offered: HIV test & counseling (and depending on the result follow the guidelines) and routine antepartum, intrapartum, and postpartum obstetric care

- For mothers testing positive, immediately initiate cART among all pregnant or breastfeeding women diagnosed with HIV within MNCH under the key steps of:
  - Treatment preparation and adherence counseling should be accelerated so that it is completed on the same day where feasible
  - Initiation may be done by ART trained HNPs, nurses/midwives within MNCH
  - Where there is NO adequate capacity within MNCH to initiate the pregnant woman on cART, she should be fast-tracked through the ART clinic
  - Start CTX among all HIV-infected pregnant and breastfeeding women, regardless of CD4 count or WHO stage or gestational age
  - Viral load should be performed 1 to 4 weeks before delivery to estimate risk of transmission for all mothers who are pregnant and on cART
  - At 6 weeks postnatally, check CD4 count and if >350 cells/µL CTX may be discontinued.
  - Continuous counseling
  - Positive health, dignity, and prevention
  - Promoting safer sex practices
Prong 4: Care and Support to HIV infected women and their infants/families

- Continued treatment and adherence support for HIV infected women on treatment. Both high and low risk infants should be provided with prophylaxis.

- Encourage counseling and provision of a variety of family planning (FP) methods.

- For HIV-positive partners, transfer the sexual partner after cART initiation to ART clinic for further management.

- Refer all HIV-uninfected male partners in serodiscordant relationships to medical male circumcision and encourage routine retesting every 3-6 months.
# MANAGEMENT OF HIV EXPOSED INFANTS AND HIV INFECTED POPULATIONS

## Recommendations

- **ARV Prophylaxis in High-risk Infants** = AZT/3TC + NVP for 12 weeks
- **Treat ALL regardless of CD4 count or WHO Clinical Stage**
- **TDF+XTC+DTG** as preferred first line in ART naïve or those on TDF+XTC+EFV and are virologically suppressed
- **AZT+3TC+RAL** for children failing ABC+3TC+LPV-r first line therapy
- **Routine Viral Load Monitoring**

### HIV Exposed Infants (HEIs)

**Table 4: HEI ARV Prophylaxis for Routine Cases**

<table>
<thead>
<tr>
<th>Case scenario</th>
<th>Management of the mother at delivery and in Postnatal Care (PNC)</th>
<th>Infant ARV prophylaxis and Nucleic acid test (NAT)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>High-Risk HIV-Exposed Infants</strong></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
| 1. Born to women with established HIV infection and having received less than 12 weeks of cART at the time of delivery; or:  
2. Born to women with established HIV infection with viral load >1000 copies/mL within four weeks before delivery, if viral load measurement available* | Start or continue cART immediately                              | All exposed infants to be put on AZT/3TC+NVP for 12 weeks |
| 1. Born to women with established HIV infection not on cART; or:  
2. Born to known HIV positive woman who refuses cART | Start or continue cART immediately  
Continue counseling for need to start therapy. Suggest to start cART with possibility of stopping after delivery (Option B) while counseling continues toward the mother accepting lifelong cART (Option B+) | Prophylactic ART (AZT/3TC+NVP) until confirmed final outcome HIV negative after complete cessation of breastfeeding |
| **Low-Risk HIV-Exposed Infants**                       |                                                                  |                                                     |
| Known HIV-positive women on cART for more than 12 weeks | Continue cART                                                   | All exposed infants to be put on AZT/3TC+NVP for 6 weeks |
| HIV-negative women with known positive partner         | Do NAT, if negative, continue PrEP (if woman was already on PrEP before pregnancy) and provide HTS every 3 months | If NAT on the mother is positive do NAT on the baby |

*ALL HIV POSITIVE PREGNANT WOMEN ON CART SHOULD HAVE A VIRAL LOAD DONE 1 TO 4 WEEKS BEFORE DELIVERY*
### Table 5: HEI ARV Prophylaxis in Complicated Cases

<table>
<thead>
<tr>
<th>Case scenario</th>
<th>Management of the mother at delivery and in Postnatal Care (PNC)</th>
<th>Infant ARV prophylaxis and Nucleic acid test (NAT)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Woman with an HIV positive test in ANC who starts cART in ANC and has been on cART for &gt;12 weeks. She has a home delivery. Infant does not receive AZT/3TC+NVP at birth, but presents &gt;72 hours after birth</td>
<td>Continue cART</td>
<td>Do NAT: If positive, start cART. If negative, start AZT/3TC+NVP for 6 weeks and repeat NAT at 6 weeks of age. *If NAT results are delayed, start AZT/3TC+NVP immediately</td>
</tr>
<tr>
<td>Woman with unknown antenatal HIV status who has a home delivery and has an HIV positive test in postnatal clinic &gt;72 hours after delivery</td>
<td>Start (or switch to) cART</td>
<td>AZT/3TC+NVP for 12 weeks NAT testing</td>
</tr>
<tr>
<td>Born to woman with established HIV infection who has received less than 12 weeks of cART at the time of delivery; or Birth to woman with established HIV infection with viral load &gt;1000 copies/mL in the four weeks before delivery, if viral load measurement available</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Woman with an HIV negative test in ANC and has an HIV positive test in L&amp;D or during breastfeeding period*</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### Table 6: Simplified Infant Prophylaxis Dosing

<table>
<thead>
<tr>
<th>Infant age</th>
<th>Dosing of NVP</th>
<th>Dosing of AZT/3TC</th>
</tr>
</thead>
<tbody>
<tr>
<td>Birth to &lt;6 weeks old</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Birth weight 2000g – 2499g**</td>
<td>10mg once daily (1mL of syrup once daily)</td>
<td>10mg/5mg twice daily (1mL of syrup twice daily)</td>
</tr>
<tr>
<td>Birth weight 2500g – 2999g</td>
<td>15mg once daily (1.5mL of syrup once daily)</td>
<td>15mg/7.5mg twice daily (1.5mL of syrup twice daily)</td>
</tr>
<tr>
<td>&gt; 6 weeks to 12 weeks</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3000g – 5900g</td>
<td>20mg once daily (2mL of syrup once daily or half a 50mg tablet once daily)</td>
<td>Use treatment dose 60mg/30mg twice daily (6mL syrup twice daily or a 60mg/30mg tablet twice daily)</td>
</tr>
</tbody>
</table>

**For infants weighing <2000g and older than 35 weeks of gestational age, the suggested doses are: NVP 2mg/kg per dose once daily and AZT 4mg/kg per dose twice daily. Premature infants younger than 35 weeks of gestation age should be dosed using expert guidance**
**FIGURE 6: ALGORITHM FOR HIV TESTING (NAT) IN CHILDREN < 24 MONTHS OLD**

**HIV-Exposed Infant or Child <24 Months**

- **Nucleic Acid Testing at birth/first week of life/first contact and at 6 weeks old, and if stops breastfeeding < 9 months old, at 6 weeks after complete cessation of breastfeeding**
  - Positive test result
    - Likely HIV infected
      - Repeat NAT immediately to confirm HIV
  - Negative test result
    - Monthly clinical monitoring
  - No NAT available
    - Likely HIV uninfected
    - Symptomatic
      - Screen for presumptive severe HIV disease
  - **NAT available**
    - Likely HIV uninfected
    - Symptomatic
      - Screen for presumptive severe HIV disease
    - Well
      - **Await NAT results and start cART if indicated**
    - Positive test result
      - **NAT immediately to confirm HIV**
    - **Serologic test at 9 months old and if stops breastfeeding <18 months old, at 6 weeks after cessation of breastfeeding**
      - **Positive test result**
        - Likely HIV infected
        - Symptomatic: remains HIV-exposed until cessation of breastfeeding
        - If confirmed severe HIV disease, initiate cART immediately and follow up results for NAT
      - **Negative test result**
        - Likely HIV uninfected
        - If >18 months old, go to algorithm for serologic testing
      - **Screen for presumptive severe HIV disease and proceed to initiate cART as you await NAT results**

*Presumptive clinical diagnosis of HIV infection is done in infants and children <18 months old where there is no access to Nucleic acid testing (NAT), or reporting of results is delayed, but the child has symptoms suggestive of HIV infection. The criteria for making a presumptive diagnosis of HIV infection are:

**HIV serologic test positive in infant or child AND**

Symptomatic with 2 or more of the following: oral thrush, severe pneumonia, severe sepsis, or has any Stage 4 condition

NAT available means unable to collect sample or the test cannot be run at the testing lab due to various logistical issues
**Figure 7: Testing Algorithm of HIV-Exposed Infants**

**HIV EXPOSED INFANT OR CHILD < 24 MONTHS OLD: UNDER 5 AND NUTRITION CLINICS, TB AND IN-PATIENT WARDS**

- **Never breastfed**
  - NAT done at birth/first week of life/first contact and at 6 weeks old
  - Positive test result:
    - Likely HIV infected
    - Repeat NAT immediately to confirm HIV
    - Refer for cART treatment, care, and support
  - Negative test result:
    - HIV uninfected

- **No longer breastfeeding**
  - Nucleic acid test at birth/first week of life/first contact, at 6 weeks, 6 months old and if stops breastfeeding < 9 months old, at 6 weeks after complete cessation of breastfeeding
  - Positive test result:
    - Likely HIV infected
    - Repeat NAT immediately to confirm HIV
  - Negative test result:
    - HIV uninfected

- **If breastfeeding: Remains HIV exposed until cessation of breastfeeding**
  - Positive test result:
    - Likely HIV infected
    - Repeat test at least 6 weeks after complete cessation of breastfeeding
  - Negative test result:
    - HIV uninfected

Testing should be done alongside immunization visits
### Table 7: ARV Prescribers and Corresponding Regimens for cART Initiation

<table>
<thead>
<tr>
<th>Cadre with specific training</th>
<th>Initiation of cART</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nurse/Midwife (registered, enrolled) certified with Integrated HIV Care Training*</td>
<td>1st line</td>
</tr>
<tr>
<td>Nurse Prescribers with Integrated HIV Care Training*</td>
<td>1st line, 2nd line**</td>
</tr>
<tr>
<td>Clinical Officers with Integrated HIV Care Training*</td>
<td>1st line, 2nd line**</td>
</tr>
<tr>
<td>Medical Licentiates with Integrated HIV Care Training*</td>
<td>1st line, 2nd line</td>
</tr>
<tr>
<td>Medical Officers with Integrated HIV Care Training*</td>
<td>1st line, 2nd line</td>
</tr>
<tr>
<td>Medical Specialists with relevant training and experience†</td>
<td>1st line, 2nd line, 3rd line</td>
</tr>
</tbody>
</table>

*Providers with Integrated HIV Care Training should satisfy requirements of competency-based training in the use of cART for treatment and prevention of HIV

**Initiation on second-line should only be done in consultation with a medical officer with appropriate training

†Relevant training and experience refers to management of advanced and complicated HIV, including second-line treatment failure

To improve cART initiation and adherence, counseling must be done so that the individual (or caregiver) understands its benefits. The benefits of starting cART earlier include:

- Reduced rates of HIV-related morbidity and mortality
- Reduced MTCT (in pregnant and breastfeeding women)
- Potential reductions in the incidence and severity of chronic conditions (e.g., renal disease, liver disease, certain cancers, and neurocognitive disorders)
- Reduction in infectious complications (e.g., TB)
- Reduced sexual transmission
- High levels of adherence to cART are needed to attain these objectives.
FIGURE 8: FLOW DIAGRAM FOR HIV CARE AND TREATMENT FROM HIV TESTING TO cART INITIATION

HIV testing services (with partner and/or family)

Assign National Unique Patient Number (NUPN) Link to MC and FP services, if desired

HIV-uninfected

- Provide HIV prevention messages and connect to VMMC/PrEP/PEP
- Establish partner status
- Retest after 3 months

HIV-infected

Start CTX if:
- Child < 5 years old
- Pregnant and breast feeding woman
- Child/Adolescent/Adult ≥ 5 years old with CD4 count <350 cells/µL

Screen for TB, Cryptococcal meningitis and renal insufficiency

TREAT ALL
- Start all patients tested HIV positive on cART regardless of CD4 count and WHO clinical stage
- Baseline tests still have to be done
### Table 8: WHO Clinical Staging of HIV Disease by Specific Populations

<table>
<thead>
<tr>
<th>Children (0 to &lt;10 years old)</th>
<th>Adolescents (15 to 19 years old)</th>
<th>Pregnant &amp; Breastfeeding Women</th>
<th>Adults</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Clinical Stage 1</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Asymptomatic</td>
<td>• Asymptomatic</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Persistent generalized lymphadenopathy</td>
<td>• Persistent generalized lymphadenopathy</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Clinical Stage 2</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Unexplained persistent hepatosplenomegaly</td>
<td>• Moderate unexplained weight loss (&lt;10% of presumed or measured body weight)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Recurrent or chronic upper respiratory tract infections (otitis media, otorrhea, sinusitis, tonsillitis)</td>
<td>• Recurrent respiratory tract infections (sinusitis, tonsillitis, otitis media, pharyngitis)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Herpes zoster</td>
<td>• Herpes zoster</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Lineal gingival erythema</td>
<td>• Angular cheilitis</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Recurrent oral ulceration</td>
<td>• Recurrent oral ulceration</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Papular pruritic eruption</td>
<td>• Papular pruritic eruption</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Fungal nail infections</td>
<td>• Fungal nail infections</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Extensive wart virus infection</td>
<td>• Seborrhoeic dermatitis</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Extensive molluscum contagiosum</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Unexplained persistent parotid enlargement</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Clinical Stage 3</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Unexplained moderate malnutrition not adequately responding to standard therapy</td>
<td>• Unexplained severe weight loss (&gt;10% of presumed or measured body weight)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Unexplained persistent diarrhoea (14 days or more)</td>
<td>• Unexplained chronic diarrhoea for longer than 1 month</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Unexplained persistent fever (above 37.5°C, intermittent or constant, for &gt;1 month)</td>
<td>• Unexplained persistent fever (intermittent or constant for &gt;1 month)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Persistent oral candidiasis (after 6 weeks old)</td>
<td>• Persistent oral candidiasis</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Oral hairy leukoplakia</td>
<td>• Oral hairy leukoplakia</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Lymph node tuberculosis</td>
<td>• Pulmonary tuberculosis</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Pulmonary tuberculosis</td>
<td>• Severe bacterial infections (such as pneumonia, empyema, pyomyositis, bone or joint infection, meningitis, bacteremia)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Severe recurrent bacterial pneumonia</td>
<td>• Acute necrotizing ulcerative stomatitis, gingivitis or periodontitis</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Acute necrotizing ulcerative gingivitis or periodontitis, Unexplained anaemia (&lt;8g/dL), neutropaenia (&lt;0.5 x 10^9/L) or chronic thrombocytopenia (&lt;50 x 10^9/L)</td>
<td>• Unexplained anaemia (&lt;8g/dL), neutropaenia (&lt;0.5 x 10^9/L) and/or chronic thrombocytopenia (&lt;50 x 10^9/L)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
### TABLE 9: ELIGIBILITY CRITERIA FOR CART INITIATION IN CHILDREN, ADOLESCENTS, PREGNANT AND BREASTFEEDING WOMEN, AND ADULTS

<table>
<thead>
<tr>
<th>Specific populations</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pregnant &amp; Breastfeeding Women</td>
<td>Treat irrespective of WHO clinical stage or CD4 count</td>
</tr>
<tr>
<td>Children (0 to &lt;10 years old)</td>
<td></td>
</tr>
<tr>
<td>Adolescents (10 to ≤19 years old)</td>
<td></td>
</tr>
<tr>
<td>Adults</td>
<td></td>
</tr>
</tbody>
</table>

Under these new guidelines: Treat ALL, the assessment through WHO Staging (Table 8) guides the evaluation and management of HIV; however initiating on ART does not require a CD4.
### Table 10: Pre-initiation Tasks

<table>
<thead>
<tr>
<th>Timeline/Specific populations</th>
<th>Clinical tasks</th>
<th>Laboratory tests*</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Visit 1 Enrollment/Initiate cART based on patient readiness</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Children</strong></td>
<td>Complete history &amp; examination Screen for TB and other opportunistic infections (OIs)</td>
<td>□ Creatinine (calculate CrCl) **□ ALT □ HBsAg (if not vaccinated)</td>
</tr>
<tr>
<td></td>
<td>□ Adherence counseling and PHDP† messages, including the caregiver: sessions 1 &amp; 2 □ WHO clinical assessment □ Initiate CTX for child &gt;6 weeks old □ HPV vaccine for girl &lt;10 years old</td>
<td>□ Pregnancy test (Adolescent or woman of reproductive age)</td>
</tr>
<tr>
<td></td>
<td>□ Screen for TB and other OIs □ WHO clinical assessment □ Initiate CTX for ALL adolescents □ Initiate CTX for adults if eligible (CD4 &lt;350 cells/µL, Pregnancy and breastfeeding) □ Adherence counseling and PHDP† messages □ Urinalysis</td>
<td>□ Syphilis test (adolescent or adult)</td>
</tr>
<tr>
<td></td>
<td>□ Complete history &amp; examination</td>
<td>□ Cholesterol, and triglycerides (especially if starting PI)</td>
</tr>
<tr>
<td></td>
<td>□ Screen for TB and other OIs □ WHO clinical assessment □ Initiate CTX (if eligible and not initiated at enrollment)</td>
<td>□ HPV test or visual inspection with acetic acid (VIA) in sexually active adolescent or woman</td>
</tr>
<tr>
<td><strong>Visit 2</strong></td>
<td>Targeted history and examination □ Screen for TB, Cryptococcus, and PCP</td>
<td>□ Urinalysis</td>
</tr>
<tr>
<td>1-2 weeks later</td>
<td>□ Review CTX adherence (if already started) □ Initiate CTX (if eligible and not initiated at enrollment)</td>
<td>□ Sputum AFB smear/GeneXpert MTB RIF in individuals with a positive Screening</td>
</tr>
<tr>
<td><strong>Initiate cART if not initiated at visit 1</strong></td>
<td>□ Review laboratory test results □ Initiate cART if not initiated at visit 1</td>
<td>□ Serum CRAG for adolescents and adults with CD4 count &lt; 100 cells/µL</td>
</tr>
<tr>
<td><strong>Children</strong></td>
<td>□ Adherence counseling and PHDP† messages, including the caregiver</td>
<td></td>
</tr>
<tr>
<td><strong>Adolescents</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Adults</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Visit 3</strong></td>
<td>Targeted history and examination □ Screen for TB and other OIs</td>
<td>□ Urinalysis</td>
</tr>
<tr>
<td>2-4 weeks from enrollment</td>
<td>□ And review CTX adherence</td>
<td>□ Sputum AFB</td>
</tr>
<tr>
<td><strong>Initiate cART if not initiated at visits 1 and 2</strong></td>
<td>□ Initiate cART if not yet started in the last two visits</td>
<td>□ Serum CRAG for adolescents and adults with CD4 count &lt; 100 cells/µL</td>
</tr>
<tr>
<td><strong>Children</strong></td>
<td>□ Adherence counseling and PHDP† messages</td>
<td></td>
</tr>
<tr>
<td><strong>Adolescents</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Adults</strong></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

† Positive Health Dignity and Prevention (PHDP) includes: risk reduction, ART adherence, correct condom use, family planning, STI screening, and partner HIV testing.

*If health facility is unable to perform a required laboratory test, refer sample or patient to higher level facility.

** Creatinine should be done in all patients initiating TDF based cART and Hb for all children initiating AZT based cART, according to the guidelines. CD4 should be done in all patients, but should not be used to determine eligibility.

TAT = Toxoplasmosis Antigen Test
**Brief Targeted Medical History:**
Ask about fever, weight loss, cough, persistent headache, h/o: Kidney Disease, Hypertension, Diabetes, Acute or Chronic Diarrhoea, use of NSAIDs (Ibuprofen, Diclofenac, Aspirin, Indomethacin), Herbal Medications

**Clinical Examination:**
Check BP, Weight, Height, BMI + Random Blood Sugar & Urinalysis (where glucostix & urine dipstix tests are available)

<table>
<thead>
<tr>
<th>Question</th>
<th>Answer</th>
</tr>
</thead>
<tbody>
<tr>
<td>BP &gt; 140/90</td>
<td>NO Evidence of above: Prepare patient for same day cART: Initiate the following ARVs: ● TDF or TAF + XTC + DTG ● If HIV/TB and on Rifampicin DTG 50mg twice daily ● If pregnant or DTG not available: TDF + XTC + EFV 400mg Provide adherence counselling</td>
</tr>
<tr>
<td>BMI &lt; 18.5</td>
<td>YES Evidence of above: Prepare patient for same day cART: ● Screen for TB and Cryptococcal meningitis ● If positive TREAT these OIs and defer cART ● If evidence of renal disease, replace TDF with TAF Or ABC ● If pregnant, avoid TAF</td>
</tr>
<tr>
<td>Severe acute illness</td>
<td></td>
</tr>
<tr>
<td>Chronic use of NSAIDs or Herbal medications</td>
<td></td>
</tr>
<tr>
<td>Proteinuria +3 (if urine dipstix test available)</td>
<td></td>
</tr>
<tr>
<td>RBS &gt;11.1 (if glucostix test available)</td>
<td></td>
</tr>
</tbody>
</table>

**For Patient's on TDF, Creatinine Clearance >50mL/min:**
For Patients on TDF, Creatinine Clearance >50mL/min: continue TDF or if <50mL/min, replace TDF with ABC and adjust dose of 3TC

**For Patients on TAF with Creatinine Clearance >50mL/min:**
For Patients on TAF with Creatinine Clearance >50mL/min, continue TAF and may need to adjust dose of 3TC

**Those previously exposed to cART:**
If history of Adverse Reaction to previous cART; DEFER cART and refer to clinician

**If Suspicion of TB or other OIs:** DEFER cART and refer to clinician

**If TB/HIV and on Rifampicin:**
TDF or TAF + XTC + DTG (DTG should be given 50mg twice daily)
If pregnant or DTG not available: TDF + XTC + EFV-400mg

**Patient not ready for cART?**
Discuss reasons why and schedule follow up appointment within 7 days

**Draw baseline labs (CD4, Creatinine, Hb, HBV, RPR, ALT), send them for testing and review patient within 14 days to discuss laboratory results:**

**Zambia Consolidated Guidelines for Treatment and Prevention of HIV Infection**
**FIRST LINE cART**

Providing optimized, fixed-dose cART regimens in all populations have consistently demonstrated that there are better clinical and laboratory outcomes if HIV treatment is initiated early. Reduce the time between HIV diagnosis and cART initiation. This is based on an assessment of the person’s readiness and must be done within 2 weeks.

**Table 11: Preferred First-Line cART and Alternative Regimens by Specific Populations**

<table>
<thead>
<tr>
<th>Specific Populations</th>
<th>Description</th>
<th>Preferred 1st line cART</th>
<th>Alternative regimen</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pregnant &amp; Breastfeeding</td>
<td>ARV naïve or Sure of tail coverage</td>
<td>TDF + XTC + EFV&lt;sub&gt;400&lt;/sub&gt;&lt;sup&gt;a&lt;/sup&gt;</td>
<td>TDF + XTC + ATV-r (or LPV-r) or ABC + 3TC + EFV</td>
</tr>
<tr>
<td>Women</td>
<td>Previous sdNVP exposure; or NVP monotherapy exposure (NVP without 7 days of AZT + 3TC cover); or unsure of tail coverage</td>
<td>TDF + XTC + LPV-r</td>
<td>ABC + XTC + LPV-r or ABC + XTC + ATV-r</td>
</tr>
<tr>
<td>Children (0-2 weeks)</td>
<td>All</td>
<td>AZT + 3TC + NVP</td>
<td>Consult or refer to expert opinion</td>
</tr>
<tr>
<td>Children (2 weeks to &lt; 5 years old)</td>
<td>HIV and TB co-infection</td>
<td>AZT + ABC + 3TC (if &lt; 3 months)</td>
<td>After completion of ATT, substitute to preferred 1st line with LPV-r</td>
</tr>
<tr>
<td>Children (5 to &lt;10 years old)</td>
<td>ARV naïve or Sure of tail coverage</td>
<td>ABC + 3TC + EFV</td>
<td>AZT + 3TC + EFV or ABC + 3TC + NVP</td>
</tr>
<tr>
<td>Adults</td>
<td>History of maternal sdNVP; maternal or infant NVP monotherapy; mother unsure of tail coverage</td>
<td>ABC + 3TC + LPV-r</td>
<td>AZT + 3TC + LPV-r or AZT + 3TC + ATV-r</td>
</tr>
<tr>
<td>Adolescents (10 to &lt;19 years old) weighing ≥35kg</td>
<td>NO history of maternal sdNVP; maternal or infant NVP monotherapy; mother unsure of tail coverage</td>
<td>TDF or TAF&lt;sup&gt;c&lt;/sup&gt; + XTC&lt;sup&gt;d&lt;/sup&gt; + DTG&lt;sup&gt;e&lt;/sup&gt;</td>
<td>TDF or TAF&lt;sup&gt;c&lt;/sup&gt; + XTC&lt;sup&gt;d&lt;/sup&gt; + EFV ABC + 3TC + EFV (weight-based dosing)</td>
</tr>
<tr>
<td></td>
<td>History of maternal sdNVP, unsure of tail coverage; maternal or infant NVP monotherapy</td>
<td>TDF or TAF&lt;sup&gt;c&lt;/sup&gt; + XTC&lt;sup&gt;d&lt;/sup&gt; + DTG&lt;sup&gt;e&lt;/sup&gt;</td>
<td>TDF or TAF&lt;sup&gt;c&lt;/sup&gt; + XTC&lt;sup&gt;d&lt;/sup&gt; + EFV ABC + 3TC + EFV (weight-based dosing)</td>
</tr>
<tr>
<td>Adults</td>
<td>All</td>
<td>TDF or TAF&lt;sup&gt;c&lt;/sup&gt; + XTC&lt;sup&gt;d&lt;/sup&gt; + DTG&lt;sup&gt;e&lt;/sup&gt;</td>
<td>TDF or TAF&lt;sup&gt;c&lt;/sup&gt; + XTC&lt;sup&gt;d&lt;/sup&gt; + EFV&lt;sub&gt;400&lt;/sub&gt; or ABC + 3TC + EFV</td>
</tr>
</tbody>
</table>

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<sup>a</sup> EFV<sub>400</sub> is lower dose EFV of 400-mg/day

<sup>b</sup> If NVP exposure, initiate on LPV-r based therapy

<sup>c</sup> TAF is Tenofovir alafenamide. Avoid in pregnancy and HIV/TB patients on Rifampicin

<sup>d</sup> Can either be 3TC or FTC

<sup>e</sup> DTG (Dolutegravir) to be given to cART naïve adolescents and adults. Avoid in pregnancy. For HIV/TB patients on Rifampicin, increase the frequency of DTG to 50mg twice daily instead of the usual 50mg once daily only if single tablet is available
NEWER ANTIRETROVIRAL AGENTS AND THEIR USE

1. Dolutegravir (DTG)

a. Dolutegravir (DTG) is a newer Integrase Inhibitor with a higher genetic barrier to resistance than Raltegravir (RAL) and Elvitegravir (EVG) and NNRTIs.

b. DTG is associated with the following mutations: F121Y, E138A/K, G140S/A, Q148 H/K/R, N155H, R263K.

c. Cross-resistance studies with RAL and EVG-resistant viruses indicate that G140S and Q148 H/K/R in combination with L74I/M, E92Q, T97A, E138A/K, G140A, or N155H are associated with 5-fold to 20-fold reduced DTG susceptibility and reduced virologic suppression in patients.

d. It is dosed as 50mg dosed as once daily EXCEPT as 50mg twice daily in patients on Rifampicin or those with integrase mutations.

e. It has no food requirements and has few drug interactions.

f. It has drug interactions with UDP glucuronyl transferase (UDP) inducers like Rifampicin, which leads to decreased plasma DTG levels.

g. It also has decreased absorption with aluminum, calcium or magnesium containing anti-acids.

h. There is also reported increase in serum creatinine with no true effect on the glomerular filtration rate (GFR).

i. There is no safety and efficacy data on the use of DTG in pregnant women and adolescents younger than 12 years of age.

Practical hints on use of DTG

- It should be used in the following populations:
  - Adults and adolescents with HIV-1 or HIV-2 or HIV-1/HIV-2 mixed infection who are being initiated on cART as part of combination ART as:
    - TDF or TAF + XTC + DTG
  - Adults and adolescents with HIV-1 who have an undetected viral load while on NNRTI based first line as:
    - TDF + XTC + EFV to TDF or TAF + XTC + DTG
    - TDF + XTC + NVP to TDF or TAF + XTC + DTG
    - ABC + 3TC + EFV to ABC or TAF + XTC + DTG
    - ABC + 3TC + NVP to ABC or TAF + XTC + DTG
  - Adults and adolescents with HIV-2 or HIV-1/HIV-2 mixed infection who have an undetected viral load while on PI based first-line as:
    - TDF + XTC + LPV-r to TDF or TAF + XTC + DTG
    - ABC + 3TC + LPV-r to ABC or TAF + XTC + DTG

- In HIV/TB infected populations on Rifampicin, increase the frequency of DTG to 50mg twice daily instead of the usual 50mg once daily. However, where the single 50mg tablet is not available, give:
  - TDF + XTC + EFV-400mg. This switch should be done if viral load is <20 copies/mL, if it is >20 copies/mL, give TDF + XTC + LPV-r

- It should not be used in HIV infected individuals who are pregnant.

- DTG significantly increases Metformin plasma levels, which can be partially explained by Organic Cation Transporter-2 inhibition. It is recommended that dose adjustments of Metformin be considered to maintain optimal glycaemic control when patients are starting/stop DTG while taking Metformin:
  - In patients taking DTG who are starting Metformin, begin with low Metformin dose and titrate up carefully. Recommended dose limit of Metformin 1000 mg daily. If patient is already on Metformin and initiating DTG, monitor glucose, haemoglobin a1c, and Metformin adverse effects and adjust dose as necessary.
2. Tenofovir alafenamide (TAF)

Tenofovir alafenamide is a phosphonoamidate prodrug of the nucleotide analog Tenofovir which belongs to a class of Nucleotide reverse transcriptase inhibitors. It is predominantly metabolized intracellularly to Tenofovir which undergoes subsequent phosphorylations to yield the active Tenofovir diphosphate (TFV-DP) metabolite which inhibits the activity of HIV reverse transcriptase by competing with natural substrates and causing DNA chain termination after being incorporated into viral DNA.

- TAF is dosed as 25mg once daily (when used without pharmaco-enhancers)
- TAF has also demonstrated IN VITRO and IN VIVO activity against HBV
- The median terminal half-life of TAF is 0.51 hours and the active metabolite, TFV-DP, has an intracellular half-life of 150 to 180 hours
- TAF is intracellularly metabolized in hepatocytes, peripheral blood mononuclear cells (PBMCs) and macrophages and less than 1% of the dose is excreted in the urine and 31.7% excreted in feces
- TAF has been associated with K65R and the K70E substitutions which lead to reduced susceptibility to Abacavir, Didanosine, Emtricitabine, Lamivudine, and TDF. HIV-1 containing multiple thymidine analog mutations (TAMs) (M41L, D67N, K70R, L210W, T215F/Y, K219Q/E/N/R) lead to resistance to TAF. In addition, multi-nucleoside resistant virus with a T69S doubles insertion mutation or with a Q151M mutation complex including K65R exhibit IN VITRO resistance to TAF
- Adverse events include diarrhea, fatigue, nausea, and rash
- TAF is associated with significantly less increase in proximal tubular proteinuria and less reduction in estimated glomerular filtration rate (eGFR) when compared to TDF
- TAF is associated with significantly less change in spine and hip bone mineral density (BMD) compared to TDF
- There is no safety and efficacy data on the use of TAF in pregnant women and people with HIV/TB co-infection

Practical hints on use of TAF

- It should be used in the following populations:
  - Adults and adolescents with HIV-1 or HIV-2 or HIV-1/HIV-2 mixed infection who are being initiated on cART as part of combination ART as
    - TAF + XTC + DTG
  - Adults and adolescents with HIV-1 who have an undetected viral load while on NNRTI based first-line as
    - TDF + XTC + EFV to TAF + XTC + DTG
    - TDF + XTC + NVP to TAF + XTC + DTG
    - ABC + 3TC + EFV to TAF + XTC + DTG
    - ABC + 3TC + NVP to TAF + XTC + DTG
  - Adults and adolescents with HIV-2 or HIV-1/HIV-2 mixed infection who have an undetected viral load while on PI based first-line as
    - TDF + XTC + LPV-r to TAF + XTC + DTG
    - ABC + 3TC + LPV-r to TAF + XTC + DTG
- It should NOT be used in HIV/TB infected populations
  - It is therefore recommended that such patients are on TDF or ABC containing regimen instead of TAF containing regimen
- It should not be used in HIV infected individuals who are pregnant
  - It is therefore recommended that such patients are on TDF or ABC containing regimen instead of TAF containing regimen
**Practical Hints for EFV initiation**

- EFV-400mg is the preferred NNRTI for first-line cART initiation in Pregnant and Breastfeeding Women
  - Consider using EFV at all times unless there are contraindications to its use, see Figure 10
- EFV-600mg is associated with central nervous system (CNS) side effects (e.g. dizziness, drowsiness, insomnia, abnormal dreams, and impaired concentration).
  - In systematic reviews, there is evidence showing that EFV-400mg is comparable to EFV-600mg in terms of viral suppression, but better in terms of CD4 cell count recovery and protective in terms of treatment discontinuation because of adverse events. When compared with the standard dose of EFV, EFV-400mg is also associated with lower toxicity, lower cost, and smaller pill size. It is also comparable to other treatment regimens with respect to morality or AIDS-defining illnesses and emergent serious adverse events.
  - EFV-400mg is recommended as part of the preferred first-line regimen
  - If CNS effects persist beyond 6-8 weeks on EFV-400mg substitute to PI-based regimen
  - Avoid fatty meals 4 hours before or after taking EFV. Recommend taking EFV before bedtime
  - EFV should not be used to treat patients with HIV-1/HIV-2 co-infections or HIV-2 mono-infection. See section on HIV-2 Treatment

**FIGURE 10: ALGORITHM FOR CHOOSING DTG OR EFV-400MG IN PATIENTS INITIATING cART**

```
Always use DTG unless there are contraindications

PRIMARY INSTI-DOLUTEGRAVIR (DTG)

Is there a contraindication to DTG?

NO

Select DTG

YES

Consider EFV-400mg as alternative

Lower toxicity, lower cost, and smaller pill size compared to EFV-600mg

Select EFV-400mg

Pregnant

Contraindications for DTG

Significant insomnia, anxiety, depression and hypersensitivity reactions

Co-infection of HIV with TB (DTG in this case is supposed to be dosed as 50mg twice daily for those on Rifampicin-based treatment)
```
HIV-2 Treatment

Clinicians should:

- Use the preferred standard first-line regimen TDF or TAF + XTC + DTG
  - If unable to tolerate DTG, substitute with a Lopinavir-ritonavir when prescribing cART for HIV-2 mono-infected or HIV-1/ HIV-2 co-infected individuals
- Not prescribe NNRTIs (NVP, EFV or RPV) or the PI Atazanavir-ritonavir as part of a cART regimen against HIV-2 mono-infection
- Consult with a provider with the ATCs in the management of HIV-2 where there doubts before initiating cART in HIV-2-infected patients
- Educate patients with confirmed HIV-2 infection about the types of drugs that can be used to treat it

No randomized clinical trials have been conducted to determine when to initiate cART in the setting of HIV-2 infection, and the best choices of therapy for HIV-2 infection remain under study. Because the optimal treatment strategy for HIV-2 infection has not been defined, the recommendations provided in this section are based on this committee's expert opinion with supporting evidence highlighted in Table 12 below.

Although HIV-2 is generally less aggressive, and progression to AIDS is less frequent, HIV-2 responds less predictably to cART when progression occurs, and response is more difficult to monitor. The standard methods and interpretation protocols that are used to monitor cART for HIV-1-infected patients may not apply for HIV-2-infected patients. Some cART regimens that are appropriate for HIV-1 infection may not be as effective for HIV-2. The following factors should be considered:

- The majority of HIV-2-infected patients are long-term non-progresses
- HIV-2 may confer more rapid resistance to cART agents because of wild-type genetic sequence that results in a significant increase in resistance to cART agents compared with HIV-1
- Pathways for the development of drug mutations may differ between HIV-1 and HIV-2

<table>
<thead>
<tr>
<th>Specific Populations</th>
<th>Description</th>
<th>Preferred 1st line cART</th>
<th>Alternative regimen</th>
</tr>
</thead>
<tbody>
<tr>
<td>HIV-1 / HIV-2 co-infected</td>
<td>First-line</td>
<td>TDF or TAF* + XTC + DTG**</td>
<td>TDF or TAF + XTC + LPV – r ** or ABC + 3TC + LPV-r</td>
</tr>
<tr>
<td>HIV-2 mono-infected</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* TAF should also be avoided in pregnancy and in HIV/TB patients on Rifampicin
** DTG is active against HIV 1 and 2. However, it should be avoided in pregnancy and in HIV/TB patients on Rifampicin
** *LVP-r is the only PI that actively works against HIV-2
Table 13: Efficacy of Antiretroviral Therapy against HIV-2 Infection

### Nucleoside Reverse Transcriptase Inhibitors (NRTIs)
- Although most in vitro studies have shown that similar concentrations of NRTIs are needed to block both HIV-1 and HIV-2 replication, data suggest that some NRTIs may not be as effective against HIV-2.
  - For example, HIV-1 more readily incorporates Zidovudine and is more susceptible to Zidovudine than HIV-2, and there is a lower barrier to resistance with HIV-2 than with HIV-1.
- Genotypic analysis of HIV-2-infected patients on cART has shown that many of the same amino acid substitutions that are associated with NRTI resistance in HIV-1 may be implicated in HIV-2. Some resistance mutations (K65R, Q151M, and M184V) in combination can confer class-wide NRTI resistance and cause rapid virologic failure.

### Non-Nucleoside Reverse Transcriptase Inhibitors (NNRTIs)
- NNRTIs block HIV-1 reverse transcription through a specific binding site that is not present in HIV-2; this class of drugs will not be effective against HIV-2.
- HIV-2 appears to be intrinsically resistant to NNRTIs; the Y188L polymorphism appears naturally in all HIV-2 isolates. Reversion to Y188 restores the reverse transcriptase sensitivity to some NNRTIs, including Efavirenz.
- In general, NNRTIs inhibit HIV-2 at effective concentrations that are at least 50-fold higher than those that inhibit HIV-1, making the use of these drugs for HIV-2 infection problematic.
- Etravirine appears to have limited activity against HIV-2, but this may not be clinically relevant because the mean 50% effective concentration in MT4 cells is 2500-fold higher than that observed for HIV-1.

### Protease Inhibitors (PIs)
- HIV-2 expresses natural polymorphisms in the protease that may be implicated in emergent drug resistance and accelerate time to development of PI resistance.
- One study noted that the pathways for HIV-2 protease drug resistance may differ from those for HIV-1.
- Saquinavir, Lopinavir, and Darunavir have shown comparable activity against HIV-1 and HIV-2.
- Atazanavir has lower and variable activity against HIV-2 in comparison with HIV-1. It should not be prescribed for HIV-2 and in HIV/TB patients on Rifampicin-based treatment.
- Lopinavir dose should be doubled for HIV/TB patients on Rifampicin-based treatment.

### Integrase Strand Transfer Inhibitors (INSTIs)
- Dolutegravir is safe for use in HIV-2.
- The integrase inhibitors Raltegravir and Elvitegravir have demonstrated activity in vitro. Clinical response to Raltegravir was reported in a patient with highly treatment-experienced HIV-2 infection but the emergence of mutations was reported in another patient.

### CCR5 co-receptor antagonists
- The activity of Maraviroc has been limited to patients with CCR5-tropic viruses.
- Primary HIV-2 isolates can utilize a broad range of co-receptors, including CXCR4, CCR5, CCT-5, GPR15, and CXCR6. This limits the therapeutic utility of Maraviroc in HIV-2 infection.

### Fusion inhibitors
- HIV-2 is intrinsically resistant to the fusion inhibitor Enfuvirtide.
**MONITORING HIV INFECTED POPULATIONS ON cART**

**CLINICAL AND LABORATORY MONITORING**

Monitoring consists of two components: clinical and laboratory

- Clinical monitoring includes history and examination, as well as evaluation of adherence, side effects, and relevant drug toxicities.

- Laboratory tests need to be conducted routinely and as needed (Table 14). It includes CD4 count, viral load, and toxicity monitoring.

The purpose of monitoring includes:

- Evaluation of treatment response and diagnose treatment failure early
- Evaluation of adherence
- Screening for Pulmonary tuberculosis
- Detection of toxicity to ARV drugs

Viral load is recommended as the preferred monitoring approach to determine the performance of cART in an individual. If viral load is not routinely available, CD4 count and clinical monitoring should be used.
**FIGURE 11: VIRAL LOAD MONITORING IN PATIENTS ON cART**

- **Patient on cART for ≥6 months**
  - **Viral Load at 6 months**
    - **VL: <1000 cp/mL**
      - Continue adherence support and cART
      - Repeat VL at 12 months then routine annual VL
    - **VL: >1000 cp/mL**
      - Enhanced adherence
        - Repeat VL within 3 months after last VL
          - If >1000cp/mL = Virologic Failure
          - If on 1\textsuperscript{st} line then switch to 2\textsuperscript{nd} line
          - If on 2\textsuperscript{nd} line then consult ATC

* Priority should be given to samples for Children when there are limitations to performing Routine Viral Load Testing
* Children may require more frequent viral load monitoring
### Table 14: Clinical and Laboratory Monitoring – General Population

<table>
<thead>
<tr>
<th>Timeline</th>
<th>Clinical tasks</th>
<th>Laboratory tests</th>
</tr>
</thead>
<tbody>
<tr>
<td>Enrollment and cART initiation</td>
<td>› History and examination</td>
<td>› Serum creatinine</td>
</tr>
<tr>
<td></td>
<td>› Screen for TB, Cryptococcus</td>
<td>› ALT</td>
</tr>
<tr>
<td></td>
<td>› Adherence counseling</td>
<td>› Hb or FBC</td>
</tr>
<tr>
<td></td>
<td>› PHDP† messages</td>
<td>› Blood glucose</td>
</tr>
<tr>
<td></td>
<td>› Initiate cART after adherence counselling</td>
<td>› CD4 count</td>
</tr>
<tr>
<td></td>
<td>› If no signs and symptoms of active TB disease, initiate IPT (i.e. after ruling out TB)</td>
<td>› HBsAg</td>
</tr>
<tr>
<td></td>
<td></td>
<td>› Syphilis test</td>
</tr>
<tr>
<td></td>
<td></td>
<td>› Urinalysis for protein and glucose, RBCs</td>
</tr>
<tr>
<td></td>
<td></td>
<td>› Cholesterol, and triglycerides (especially if starting PI)</td>
</tr>
<tr>
<td>Week 2 post-initiation</td>
<td>› Targeted history &amp; examination</td>
<td>› Serum creatinine (if on TDF)</td>
</tr>
<tr>
<td></td>
<td>› Screen for TB, Cryptococcus</td>
<td>› Urinalysis (if on TDF)</td>
</tr>
<tr>
<td></td>
<td>› Review adherence, side effects, toxicity</td>
<td></td>
</tr>
<tr>
<td></td>
<td>› Review laboratory tests</td>
<td></td>
</tr>
<tr>
<td></td>
<td>› Adherence counseling</td>
<td></td>
</tr>
<tr>
<td>Week 4 post-initiation</td>
<td>› Targeted history &amp; examination</td>
<td>› Serum creatinine (if on TDF)</td>
</tr>
<tr>
<td></td>
<td>› Screen for TB, Cryptococcus</td>
<td>› Urinalysis (if on TDF)</td>
</tr>
<tr>
<td></td>
<td>› Review adherence, side effects, toxicity</td>
<td></td>
</tr>
<tr>
<td></td>
<td>› Adherence counseling</td>
<td></td>
</tr>
<tr>
<td>Week 12 post-initiation</td>
<td>› Review adherence, side effects, toxicity*</td>
<td>› Serum creatinine (if on TDF)</td>
</tr>
<tr>
<td></td>
<td>› Adherence counseling</td>
<td>› Urinalysis (if on TDF)</td>
</tr>
<tr>
<td></td>
<td>› PHDP† messages</td>
<td></td>
</tr>
<tr>
<td></td>
<td>› Review laboratory tests</td>
<td></td>
</tr>
<tr>
<td></td>
<td>› Refill cART with enough supply to next visit (maximum: 3 months of supply)</td>
<td></td>
</tr>
<tr>
<td>6 months post-initiation</td>
<td>› Review adherence, side effects, toxicity*</td>
<td>› Viral load</td>
</tr>
<tr>
<td></td>
<td>› Adherence counseling</td>
<td>› CD4 cell count *</td>
</tr>
<tr>
<td></td>
<td>› PHDP† messages</td>
<td>› Serum creatinine (if on TDF)</td>
</tr>
<tr>
<td></td>
<td>› Review laboratory tests</td>
<td>› Urinalysis (if on TDF)</td>
</tr>
<tr>
<td></td>
<td>› Refill cART with enough supply to next visit (maximum: 3 months of supply)</td>
<td></td>
</tr>
<tr>
<td>12 months post-initiation</td>
<td>› Review adherence, side effects, toxicity*</td>
<td>› Viral load</td>
</tr>
<tr>
<td>and every 12 months</td>
<td>› Adherence counseling</td>
<td>› CD4 cell count *</td>
</tr>
<tr>
<td></td>
<td>› PHDP† messages</td>
<td>› Serum creatinine (if on TDF)</td>
</tr>
<tr>
<td></td>
<td>› Review laboratory tests</td>
<td>› Urinalysis (if on TDF)</td>
</tr>
<tr>
<td></td>
<td>› Refill cART with enough supply to next visit (maximum: 3 months of supply)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
### Table 15: Clinical and Laboratory Monitoring for HIV-Infected Pregnant and Breastfeeding Women

<table>
<thead>
<tr>
<th>Timeline</th>
<th>Clinical tasks</th>
<th>Laboratory tests</th>
</tr>
</thead>
<tbody>
<tr>
<td>Day 0: Enrollment &amp; cART initiation</td>
<td>‣ History and examination</td>
<td>‣ Serum creatinine</td>
</tr>
<tr>
<td></td>
<td>‣ If pregnant, focused ANC (FANC)</td>
<td>‣ ALT</td>
</tr>
<tr>
<td></td>
<td>‣ Screen for TB, Cryptococcus</td>
<td>‣ Hb or FBC Blood</td>
</tr>
<tr>
<td></td>
<td>‣ Adherence counseling</td>
<td>‣ CD4 count</td>
</tr>
<tr>
<td></td>
<td>‣ PHDP† messages</td>
<td>‣ HBsAg</td>
</tr>
<tr>
<td></td>
<td>‣ Initiate cART after adherence counselling</td>
<td>‣ Syphilis test</td>
</tr>
<tr>
<td></td>
<td>‣ If no signs and symptoms of active TB disease, initiate IPT (i.e. after ruling out TB)</td>
<td>‣ Viral load testing at baseline for known HIV positives</td>
</tr>
<tr>
<td></td>
<td></td>
<td>‣ Urinalysis for protein and glucose, RBCs</td>
</tr>
<tr>
<td></td>
<td></td>
<td>‣ Viral load testing at baseline for known HIV positives</td>
</tr>
<tr>
<td></td>
<td></td>
<td>‣ Cholesterol, and triglycerides (especially if starting PI)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Week 2 post-initiation</td>
<td>‣ Targeted history &amp; examination</td>
<td>‣ Serum creatinine</td>
</tr>
<tr>
<td></td>
<td></td>
<td>‣ Urinalysis</td>
</tr>
<tr>
<td>Week 4 post-initiation</td>
<td>‣ Screen for TB, Cryptococcus, and other OIs</td>
<td>‣ As needed</td>
</tr>
<tr>
<td>Subsequent visits to occur per:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>‣ FANC if pregnant</td>
<td>‣ If pregnant, FANC</td>
<td>HIV viral load to be done every 6 months during pregnancy and breastfeeding period</td>
</tr>
<tr>
<td>‣ HEI schedule if postnatal and breastfeeding</td>
<td>‣ Review adherence, side effects, toxicity*</td>
<td>‣ Serum creatinine and urinalysis at every FANC visit</td>
</tr>
<tr>
<td>‣ Adult cART schedule if postnatal and not breastfeeding</td>
<td>‣ Adherence counseling</td>
<td>Laboratory testing to occur per: FANC while pregnant except for viral load</td>
</tr>
<tr>
<td></td>
<td>‣ PHDP† messages</td>
<td>‣ VL 1 – 4 weeks before labour &amp; delivery</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>First postnatal visit</td>
<td>‣ CD4 cell count to determine need for continuation of Co-trimoxazole</td>
<td></td>
</tr>
<tr>
<td>24 months after delivery</td>
<td>‣ cART dispensed in MNCH until transferred</td>
<td></td>
</tr>
<tr>
<td></td>
<td>‣ Transfer to ART clinic for continuum of HIV care and treatment</td>
<td></td>
</tr>
<tr>
<td></td>
<td>‣ Earlier transfer or referral may be done for logistical reasons or complicated cases</td>
<td></td>
</tr>
</tbody>
</table>

† Positive Health Dignity and Prevention (PHDP) includes: risk reduction, cART adherence, correct condom use, family planning, STI screening, and partner HIV testing

* See Appendix 3 regarding WHO toxicity estimate
Monitoring Drug Side Effects and Toxicities

Changing an ARV drug should be done only after careful review of adherence. The indication for changing needs to be addressed. A specific ARV drug may be changed (substitution) because of:

- Toxicity, such as anaemia, peripheral neuropathy, lipodystrophy, liver or renal abnormalities
- Intolerance or unresolved and prolonged side effects
- Poor adherence: change indicated only to simplify dosing schedule and to improve adherence
- Occurrence of active TB (refer to section on TB-HIV co-infection)
- Failure (clinical, immunologic, or virologic)

When patients are substituted to alternative regimen (see Table 16), the goals are to achieve HIV viral suppression, avoid adverse events, and optimize adherence.

Table 16: Common cART Toxicities and Recommended Substitutes (for all populations)

<table>
<thead>
<tr>
<th>ARV drug</th>
<th>Common associated toxicity</th>
<th>Recommended ARV substitute</th>
</tr>
</thead>
<tbody>
<tr>
<td>ABC</td>
<td>Hypersensitivity reaction</td>
<td>TDF (if normal creatinine clearance) AZT (if child &lt;10 years old)</td>
</tr>
<tr>
<td>ATV-r</td>
<td>Hyperbilirubinaemia, icterus*</td>
<td>LPV-r</td>
</tr>
<tr>
<td>AZT**</td>
<td>Severe anaemia or neutropenia, severe gastrointestinal intolerance, lactic acidosis</td>
<td>TDF or ABC (if on 1st line cART regimen; rule out failure before substitution) d4T (if on 2nd line cART regimen for anaemia)</td>
</tr>
<tr>
<td>DTG</td>
<td>Insomnia, anxiety, depression and hypersensitivity reactions</td>
<td>ATV-r or LPV-r</td>
</tr>
<tr>
<td>EFV</td>
<td>Severe or persistent CNS side effects</td>
<td>ATV-r or LPV-r</td>
</tr>
<tr>
<td>LPV-r</td>
<td>Persistent diarrhoea, hyperlipidaemia</td>
<td>ATV-r</td>
</tr>
<tr>
<td>NVP (or EFV)</td>
<td>Rash, Stevens Johnson Syndrome, hepatitis</td>
<td>ATV-r or LPV-r</td>
</tr>
<tr>
<td>RAL</td>
<td>Rash and hypersensitivity reaction</td>
<td>ATV-r or LPV-r</td>
</tr>
<tr>
<td>TAF</td>
<td>Gastrointestinal symptoms, headache</td>
<td>Rarely causes significant side toxicities, if occurs consult expert advice</td>
</tr>
<tr>
<td>TDF</td>
<td>Renal toxicity (renal tubular dysfunction)</td>
<td>ABC or TAF</td>
</tr>
</tbody>
</table>

*Hyperbilirubinaemia and icterus do not reflect hepatic disease and are not contraindications to continued therapy. Only substitute ATV-r if the condition is intolerable to the patient.

**AZT should no longer be used in 1st line cART. Patients on AZT-based 1st line cART and are not failing treatment should be substituted to TDF- or ABC-based 1st line cART.
**FIGURE 12: ALGORITHM FOR DIAGNOSING TREATMENT FAILURE WITH ROUTINE VIRAL LOAD MONITORING**

**Diagnosing Treatment Failure with Routine Viral Load Monitoring**

**Order ROUTINE HIV Viral Load (HIV VL)**

- **HIV VL > 1000 copies/mL**
  - **VIROLOGICAL FAILURE**
    - Enrol patient in intensive adherence program
    - Switch to 2nd line cART and ensure adherence
    - Follow up:
      - Review in 2 weeks
      - Reassess adherence, side effects, toxicity
  - Repeat VL within 3 months

- **HIV VL <1000 copies/mL**
  - **NO TREATMENT FAILURE**
    - Reassess adherence
    - Continue current cART
    - Treat OIs
    - If patient still ill, examine and treat accordingly
  - Repeat VL within 3 months
SWITCHING cART REGIMENS

When patients are switched to second-line cART regimens, the goals are to achieve HIV viral suppression resulting in reconstitution of the clinical and immunologic status, avoid adverse events, and optimize adherence. LPV-r is the primary recommended second-line PI (see Figure 13).

**TABLE 17: RECOMMENDED SECOND-LINE cART REGIMENS BY SPECIFIC POPULATIONS**

<table>
<thead>
<tr>
<th>Specific populations</th>
<th>Initial 1st line category</th>
<th>Failing 1st line cART</th>
<th>2nd line cART</th>
</tr>
</thead>
<tbody>
<tr>
<td>Children &lt;5 years old</td>
<td>LPV-r-based first-line regimen</td>
<td>ABC + 3TC + LPV-r</td>
<td>AZT + 3TC + RAL</td>
</tr>
<tr>
<td></td>
<td></td>
<td>AZT + 3TC + LPV-r</td>
<td>ABC + 3TC + RAL</td>
</tr>
<tr>
<td>Children 5-10 years old</td>
<td>DTG and NNRTI -based first line regimen</td>
<td>TDF + XTC + DTG*</td>
<td>AZT + 3TC + LPV-r or ATV-r</td>
</tr>
<tr>
<td></td>
<td></td>
<td>ABC + 3TC + EFV**</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>TDF + XTC + EFV*</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>TAF + XTC + DTG*</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>TDF + XTC + NVP**</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>ABC + 3TC + NVP**</td>
<td></td>
</tr>
<tr>
<td>Adolescents and Adults</td>
<td>NNRTI-based first-line regimen</td>
<td>TDF + 3TC + EFV</td>
<td>AZT + XTC + LPV-r or ATV-r</td>
</tr>
<tr>
<td>Pregnant &amp; Breastfeeding Women</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* Represents newer regimens
**Represents older regimens

**TABLE 18: SUMMARY OF PREFERRED SECOND-LINE cART REGIMENS FOR ADULTS AND ADOLESCENTS**

<table>
<thead>
<tr>
<th>Specific populations</th>
<th>Preferred 2nd line cART</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adults and adolescents</td>
<td>If AZT was used in first-line cART TDF + XTC + LPV-r or ATV-r</td>
</tr>
<tr>
<td></td>
<td>If TDF or TAF was used in first-line cART AZT + 3TC + LPV-r or ATV-r</td>
</tr>
<tr>
<td>Pregnant or breastfeeding women</td>
<td>Same regimens as recommended for adults and adolescents as long as no previous NVP exposure without tail coverage</td>
</tr>
</tbody>
</table>

**HIV & TB Co-infection**

On Rifampicin based TB treatment

If AZT +3TC + EFV or NVP was used in first-line cART TDF or TAF + XTC + DTG (50mg twice daily) if DTG not available: Double dose LPV-r (LPV-r-800mg/200mg twice daily)

If TDF or ABC + XTC + EFV or NVP was used in first-line cART AZT + 3TC + DTG (50mg twice daily) if DTG not available: Double dose LPV-r (LPV-r-800mg/200mg twice daily)

On Rifabutin based TB treatment

If Rifabutin available use same PI regimens as recommended for adults and adolescents

**HIV and HBV co-infection**

AZT + TDF + XTC* + (LPV-r or ATV-r )

* TDF+XTC should always be part of the combination in HBV/HIV co-infections
### TABLE 19: RECOMMENDED SECOND-LINE cART REGIMENS FOR HIV-2

<table>
<thead>
<tr>
<th>Specific populations</th>
<th>Initial 1st line category</th>
<th>Failing 1st line cART</th>
<th>2nd line cART</th>
</tr>
</thead>
<tbody>
<tr>
<td>HIV-1 / HIV-2 Co-infected</td>
<td>DTG -based first-line regimen</td>
<td>TDF + XTC + DTG</td>
<td>AZT + 3TC + LPV-r*</td>
</tr>
<tr>
<td>HIV-2 mono-infected</td>
<td>ABC + 3TC + DTG</td>
<td>AZT + 3TC + LPV-r*</td>
<td></td>
</tr>
</tbody>
</table>

*a DO NOT substitute with Atazanavir in HIV-1/HIV-2 con-infection or HIV-2 mono-infection. Atazanavir is not active against HIV-2

### FIGURE 13: ALGORITHM FOR CHOOSING A PI IN SECOND-LINE

- **PRIMARY PI – Lopinavir-ritonavir (LPV-r)**
- **Is there a caution to use LPV-r?**
  - **NO** => **Select LPV-r**
  - **YES** => **Does the patient have TB or Hyperbilirubinaemia or Jaundice?**
    - **NO** => **Select ATV-r**
    - **YES** => **Cautions for LPV-r**
      - Porphyria
      - GI Intolerance
      - Hyperglycaemia
      - Hyperlipidaemia

- If TB & on Rifampicin and DTG not used before, use DTG 50mg twice daily
- If hyperbilirubinaemia & DTG not used before, use DTG 50mg once daily
**Clinical guidance on use of ATV-r**

**Administration**
- ATV-r is given once a day (300/100mg)
- Do not split or crush ATV-r tablets
- ATV-r should be used in children above 6 years and those weighing >25 kg or more and adults

**Patient Sensitization**
- ATV-r is safe for use in pregnancy
- Ensure patients on ATV-r drink plenty of fluids to reduce the risk of kidney stones
- A common side effect associated with ATV-r is jaundice, which is benign and in most cases, should resolve in a few weeks.
- Jaundice from unconjugated hyperbilirubinaemia is largely a cosmetic issue and not related to hepatitis or liver damage
- A liver function test, if available, should be conducted to help rule out other causes of jaundice
- If patient has symptomatic or profound jaundice, consult the UTH Advanced Treatment Centre

**Contraindications**
- **Do not use ATV-r** with Rifampicin-containing TB treatment. If patient is on ATV-r with no exposure to DTG in first line and they develop TB replace ATV-r with DTG 50 mg twice daily (see Figure 13).
- Do not use ATV-r with proton pump inhibitors (Omeprazole, Pantoprazole, Lansoprazole).
- Substitute PPIs (Omeprazole) with H2 receptor blockers (e.g. Cimetidine). It should be taken 2-3 hours apart with ATV-r
- Do not start patients with pre-existing jaundice or suspected hepatitis on ATV-r
MANAGEMENT OF PATIENTS PREVIOUSLY ON cART (INCLUDING DEFAULTERS)

Individuals who interrupt cART for any reason are at increased risk of resistance and treatment failure. Management in cART re-initiation is based on several factors, and a complete history to establish why the treatment was stopped is critical. For HIV-infected children, the caregivers must be questioned.

- If treatment failure or toxicity is not suspected as the reason for stopping cART, and previous good adherence is reported, reinitiate original cART in consultation with next level.
- If previous adherence is poor and there is treatment failure, these individuals (and caregivers of children) MUST be enrolled in intensive adherence counseling sessions until there is agreement among the patient, provider, and adherence counsellor that the patient is ready to commence second line cART. Use of treatment supporters for such patients is strongly recommended.
- If severe toxicity is the reason for stopping cART, refer to the next level and initiate cART using the appropriate drug substitution and counsel regarding adherence.
- Viral load testing should be done 6 months after re-initiation of the original regimen to document HIV viral suppression.

When to stop cART

Patients may choose to postpone or stop therapy, and providers, on a case-by-case basis, may elect to defer or stop therapy on the basis of clinical and/or psychosocial factors.

The following are indications for stopping cART:

- Patient’s inability to tolerate all available ARV medications
- Patient’s request to stop after appropriate counselling
- Non-adherence despite repeated counselling: treatment should be stopped to avoid continued toxicity, continued evolution of drug resistance, and transmitting drug resistant HIV
- Unreliable caregiver
- For children, the caregiver is instrumental in ART adherence. Any factors that affect the capability for the caregiver to give medications consistently may be an indication to stop cART in an HIV-infected child.
- Serious drug toxicity or interactions
- Intervening illness or surgery that precludes oral intake
- ARV non-availability

How to stop cART

- Stop ALL the drugs when discontinuing therapy
- Discontinue EFV or NVP; continue the NRTI components (backbone) for 1-2 additional weeks
- Preventive measures, such as condom use and safer sex practices, should be strongly emphasized for all patients, especially those discontinuing treatment

Treatment Failure with No Further Treatment Options

Continue the failing cART regimen unless there are intolerable toxicities or drug interactions. Even with treatment failure, the regimen is likely to have some residual antiviral activity. Stopping therapy in the setting of virologic failure can be associated with rapid falls in CD4 counts and development of OIs.
When to Consult or Refer to the Next Level

The following criteria are indications to consult or refer to the next level:

- Suspected hepatotoxicity not responding to standard management (e.g., TB/HIV co-infection treatment, ALT/AST >5-fold of upper limit of normal)
- Second line treatment failure or inability to tolerate second-line therapy
- Complications on PI-based regimen
- Severe or life-threatening adverse reactions
- Inability to tolerate therapy despite change in regimen
- HIV-HBV co-infection with renal insufficiency

Third-line cART: Second-Line Treatment Failure

Treatment failure is defined by a persistently detectable viral load >1,000 copies/mL. For adolescents and adults, failure is two consecutive viral load measurements within a three-month interval, with adherence support between measurements after at least six months of using triple combination ARV drugs. For children, viral load may still be detectable at 6-9 months after initiation and does not necessarily mean treatment failure. Viral blips or intermittent low-level viremia (20–1,000 copies/mL) can occur during effective treatment, but have not been associated with an increased risk of treatment failure unless low-level viremia is sustained. A repeat blip should be assessed further at the ATC. Additionally, clinical and epidemiological studies show that the risk of HIV transmission and disease progression is very low when the viral load is lower than 1,000 copies/mL.

Provision of third-line cART occurs in very rare circumstances and is beyond the scope of most cART providers. All patients being considered for third-line cART should have:

- Confirmed second-line cART failure (defined by a persistently detectable viral load exceeding 1,000 copies/mL [i.e., two consecutive viral load measurements within a three-month interval with enhanced adherence support between measurements] after at least six months of using second-line cART)
- Genotype (resistance) testing
- Refer (see Figure 14) to an HIV Specialist at an Advanced Treatment Centre (ATC) with a complete cART treatment history (i.e., all previous ARV drugs that the patient has taken with duration of use)
- Before starting third line, establish the reason for treatment failure (e.g., poor adherence, suboptimal dosing, drug-drug interactions) and conduct intensive adherence counseling sessions until there is agreement between the patient, provider, and adherence counselor that the patient is ready to commence third-line cART
- Use of treatment supporters for such patients is STRONGLY recommended
- The most likely ARVs to be successful in patients who have followed National Guidelines are Dolutegravir or Raltegravir (Integrase inhibitor) or Darunavir with ritonavir (Protease inhibitor) plus optimal nucleoside background (e.g. TDF+XTC or AZT+3TC)

Other considerations with major constraints:

- Etravirine: especially if genotype is available at time of 1st line NNRTI failure, although in some patients NNRTI mutations persist even after non-exposure to NNRTIs in second line
- Maraviroc: needs special tropism test before initiation, which is currently not available in Zambia

Before switching therapy in suspected treatment failure, HCWs need to rule out:

- Poor adherence: change therapy only after enhanced adherence counseling has been conducted
- Immune Reconstitution Inflammatory Syndrome (IRIS): treat underlying condition and continue cART if tolerated
- Untreated OIs: treat underlying condition and continue cART if tolerated
- Pharmacokinetics (e.g., Rifampicin reduces NVP or LPV-r blood levels): switch NVP to EFV or double the dose of LPV-r or switch Rifampicin to Rifabutin
  - Current infections causing transient decrease in CD4 count: treat infection, and if possible, repeat CD4 one month after resolution of illness to confirm immunologic failure
Figure 14: Information Pathways for Patients Needing ATC Services

- MOH - Ministry of Health
- ATC - Advanced Treatment Center
- PMO - Provincial Medical Office
- DCMO - District Community Medical Office

- Sample transportation (VL)
- Results delivery
- Reports – Feedback system
- Action – Feedback system
- ATC e-referral

Referral

Facility

ART

MOH

PMO

DMO
**NUTRITIONAL CARE**

**Nutrition in HIV-Infected Children**

Routine assessment is essential to identify malnutrition and growth faltering early. The following should be done for HIV-infected infants and children:

- Assess nutritional status, diet, and symptoms at every visit
- Laboratory monitoring includes: total cholesterol, triglycerides, glucose, and Hb
- Assess WHO clinical stage, ask about history of recent diseases such as persistent diarrhoea or OIs (associated with increased nutritional need), determine energy needs, and provide additional energy
- Measure weight and height at each visit and plot against national growth curves
  - Normal growth
  - Underweight (weight-for-age <3rd %)
  - Stunted (height-for-age <3rd %)
  - Wasted (weight-for-height <3rd %)
- If normal child growth, inform on healthy eating and avoidance of obesity
- If poor child growth
  - Full dietary assessment is needed
  - Assessment of drug adherence if the child is on cART
  - Mothers or caregivers should be asked about food availability and food types offered to the child, as well as who feeds the child, how much, and how often children should be examined for signs of OIs or wasting
  - Provide appropriate clinical interventions (e.g., food support programmes)
- If severe malnutrition
  - Stabilize the acute phase of malnutrition, similar to HIV-uninfected children with severe malnutrition, and initiate cART soon after
  - Immediately initiate cART if unexplained malnutrition (e.g., not associated with untreated Opportunistic Infection [OI]) and does not respond to standard nutritional therapy
  - If unknown HIV status, test for HIV and consider cART initiation as needed
- If on cART, reassess frequently to adjust dose as needed. Recurrence of growth failure and severe malnutrition may indicate treatment failure, poor cART adherence, or OIs.

**Nutrition supplementation**

- Give high-dose vitamin A supplementation every 6 months for children 6 to <60 months old
- Give Zinc supplementation for acute diarrhoea
- Mothers should exclusively breastfeed HIV-infected infants and young children for 6 months minimum and may continue up to 2 years old
Infant and Young Child Feeding
As a public health approach, all mothers should be encouraged to practice exclusive breastfeeding (EBF) for 6 months (Table 20). EBF is defined as giving a baby only breast milk and no other liquids or solids, not even water unless medically indicated. Thereafter, mothers should introduce nutritionally adequate complementary feeding while continuing breastfeeding up to at least 24 months old. Replacement feeding should only be considered if acceptable, feasible, affordable, sustainable, and safe (AFASS).

<table>
<thead>
<tr>
<th>Maternal HIV status</th>
<th>Infant HIV status</th>
<th>Recommended Feeding</th>
<th>Timing of Complementary feeding</th>
<th>Recommended Timing of Complete Cessation of Breastfeeding*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Positive on cART</td>
<td>Negative or unknown</td>
<td>Exclusive breastfeeding (EBF) for 6 months Replacement feeding</td>
<td>After 6 months</td>
<td>At 12 months if food security assured Up to 2 years if food security not assured</td>
</tr>
<tr>
<td>Positive</td>
<td>Positive</td>
<td>EBF for 6 months</td>
<td></td>
<td>Up to 2 years</td>
</tr>
<tr>
<td>Negative or unknown</td>
<td>N/A</td>
<td>EBF for 6 months</td>
<td></td>
<td>Up to 2 years</td>
</tr>
</tbody>
</table>

*HIV-infected women should stop breastfeeding (at any time) gradually within one month.

Nutrition in HIV Infected Adolescents, Breastfeeding Women and Adults
- Calculate the body mass index (BMI) = weight/height² to determine if the individual is underweight (<18.5kg/m²), normal (18.5 to 24.9kg/m²), overweight (25 to 29.9kg/m²), or obese (≥30kg/m²).
- If BMI <16kg/m² or anemia (Hb <10g/dL) or has TB, refer for nutrition support programmes. Observe closely for treatment complications, such as re-feeding syndrome, undiagnosed OIs, and IRIS.
- If BMI >25kg/m², provide nutrition counseling, including dietary advice and need for physical exercise.
- Table 19 lists some of the specific BMI-related ARV drug risks

<table>
<thead>
<tr>
<th>BMI</th>
<th>ARV drug</th>
<th>Associated Risks</th>
<th>Recommended Actions</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;1kg/m²</td>
<td>TDF</td>
<td>Tubular renal dysfunction Fanconi syndrome</td>
<td>Manage these patients with caution. Consult next level if necessary.</td>
</tr>
<tr>
<td>&gt;25kg/m²</td>
<td>AZT</td>
<td>Lactic acidosis Severe hepatomegaly with steatosis</td>
<td></td>
</tr>
<tr>
<td></td>
<td>d4T</td>
<td>Lactic acidosis Severe hepatomegaly with steatosis Acute pancreatitis</td>
<td></td>
</tr>
</tbody>
</table>
**Immune Reconstitution Inflammatory Syndrome and HIV**

Immune reconstitution inflammatory syndrome (IRIS) is an exaggerated inflammatory reaction from a re-invigorated immune system presenting as unmasking of previously sub-clinical opportunistic infections OR clinical deterioration of pre-existing opportunistic infections OR development of autoimmune disease.

- **Onset:** usually within 2-12 weeks after starting cART
- **Frequency:** 10% among all patients on cART, up to 25% when cART initiated with CD4 <50 cells/µL
- **Risk factors:**
  - Initiating cART close to diagnosis of an opportunistic infection
    - Initiating cART when CD4 is less than 50 cells/µL
    - Rapid initial fall in HIV-1 RNA level in response to cART in patients with low CD4 counts
    - Commonly seen with TB, cryptococcal disease, Kaposi’s sarcoma, and Mycobacterium avium complex infection
    - Patients initiated on DTG and with low cd4 counts have a higher risk of having IRIS

**Management of IRIS**

- Have high index of suspicion with early complications
- cART should be continued
- If cART continuation is impossible, temporarily interrupt the cART and restart same regimen after OI or IRIS is addressed
- Diagnose and treat OI or inflammatory condition
- Corticosteroid treatment in moderate to severe cases: Prednisolone 0.5-1.0mg/kg/day for 5-10 days
ART ADHERENCE

Provider-Related Strategies to Improve Adherence

- Establish trust and make sure the patient feels you are there to help manage and solve problems
  - Involve the patient in developing a plan for taking the drugs that is simple and works with the patient’s daily activities
  - Educate about goals of therapy, side effects, what will happen if the patient does not take all the drugs
- Treat depression or substance abuse issues
- Treat and manage side-effects
- Monitor adherence at each visit
- Reinforce importance of adherence at each follow-up visit

Ensure patients identify treatment supporters with whom they are comfortable (e.g., family members, buddies) and encourage treatment supporters to attend counselling sessions and clinic visits

Main Populations to be targeted for reinforced adherence

- Late - classified as late up to 60 days of missing scheduled appointment
- Lost to follow up (LTFU) - more than 60 days after last scheduled pharmacy pick up (all tracking efforts have been exhausted) and patient cannot be traced
- Defaulter - when a person who has been located as late or lost to follow up chooses not to return to care
- Unknown status - tracking measures not exhausted to determine enrolment status

Structured treatment preparation before cART initiation (Table 10 and Figure 8) should be conducted for all patients for successful HIV treatment and care. Take note that cART can be initiated during any of these sessions (all patients should be fast-tracked after looking at safety and also readiness):

- Session 1: Enrolment and Assessment, HIV education and cART initiation
- Session 2: cART support, preparation and cART initiation
- Session 3: cART education, preparation, and cART initiation

Adherence assessment should be done by all members of the health care team using:

- Clinical and laboratory parameters
- Patient reports
- Pill counts
- Pharmacy pick-ups
- Other tools of adherence
CO-MORBIDITIES

Recommendations

- cART should be started in all TB patients living with HIV regardless of CD4 count
- Xpert MTB/RIF is the preferred diagnostic test for HIV associated TB
- Assessment and management of Cardiovascular Diseases (CVDs) in all HIV patients

TUBERCULOSIS AND HIV

There is a high incidence of TB among HIV-infected persons. All HIV-infected individuals should be screened for TB and placed on TB treatment if found with TB. HIV-infected individuals with TB should begin anti-tuberculosis therapy (ATT) via directly observed therapy, short course (DOTS) as per National TB Guidelines. Persons who screen negative for TB should be given TB INH Preventive Therapy (TB-IPT).

Screening for Active Tuberculosis

**Figure 15: TB Screening Algorithm**

HIV-infected children (0 to <10 years old)*

- Screen for TB at every service delivery point every time
- Poor weight gain
- Reported weight loss or very low weight (weight for age less than -3 z-score)
- Underweight (weight less than -2 z-score)
- Confirmed weight loss (>5%) since the last visit
- Growth curve flattening
- Fever
- Current cough
- Contact history with a TB case

HIV-infected adolescents, pregnant & breastfeeding women, and adults

- Screen for TB at every service delivery point every time
- Current cough
- Fever
- Weight loss
- Night sweats

TB screening (as above)

Negative TB screening

Positive TB screening

Investigate for TB
Diagnostic Tools and Tests for TB

Tools and tests used for TB diagnosis provide either a definitive diagnosis (bacteriological confirmation of TB) or supportive information to aid diagnosis of tuberculosis.

**Key Messages**

- Xpert MTB/RIF is recommended as the initial diagnostic test in all presumptive TB patients
- Smear microscopy may continue being the initial test in settings where Xpert MTB/RIF is not yet available
- Smear microscopy --- and NOT Xpert MTB/RIF --- should be used for treatment monitoring
- All TB retreatment patients tested RIF negative on Xpert MTB/RIF should have FL LPA, Culture and DST
- All DR-TB and RIF positive on Xpert MTB/RIF patients should be tested with SL LPA, Culture and DST
- A negative laboratory test (i.e. smear, Xpert MTB/RIF, LPA and/or culture) in the setting of a TB-compatible clinical presentation does NOT definitively rule out TB. Such patients should be clinically evaluated for TB.
- Patients with strong clinical evidence of TB (especially PLHIV, Children, EPTB) should start TB treatment even if bacteriological tests are negative or not available (clinically diagnosed TB)

**Bacteriological Tests for TB Diagnoses**

**Xpert MTB/RIF**

Xpert MTB/RIF test * is a fully automated real time PCR based (molecular) test, disposable, cartridge-based nucleic acid amplification test.

- Highly sensitive and specific, more sensitive than smear microscopy.
- Rapid and simultaneous detection of tuberculosis and Rifampicin resistance (a reliable proxy for MDR-TB).
- Results are available within 2 hours.
- Xpert MTB/RIF should not be used for follow up (use smear microscopy instead)
- Collect one spot specimen (3-5 mL).
- Submit the specimen as soon as possible for testing. Samples must be stored at 2-8°C for maximum of 5 days or at room temperature for a maximum of 3 days if testing cannot be done on the same day.
- Xpert MTB/RIF is recommended as the first diagnostic test in all adults and children with signs and symptoms of TB where available (Algorithm 1).
- If not available, the samples from Priority* patients should be referred to facilities with GeneXpert machines (PLHIV, Children, EPTB, risk of DR-TB, HCW, miners, prisoners).

**Limitations:**

- Does not detect resistance to Isoniazid or other first- or second-line anti-tuberculosis medications
- Cannot be used for treatment monitoring (may remain positive even after treatment kills the bacteria because it detects TB DNA and not live bacteria).
Smear Microscopy

Smear microscopy is the first diagnostic test in facilities where Xpert MTB/RIF is not available. Smear microscopy is recommended to monitor treatment response (follow up). Results should be reported according to Tables 22-23.

Limitations:

It is often negative in PLHIV, children and EPTB samples and cannot detect rifampin resistance.

- Two spot specimens should be collected for smear microscopy at the time of request (at least 15 to 30 minutes apart).
- Should be used for treatment monitoring.
- LED microscopy has a sensitivity gain of 10% over ZN and should be used in place of ZN.
- The results of positive sputum examination should be recorded in red ink in the register for easy identification.
- Sputum results must be reported within 24 hours.

Reporting Xpert MTB RIF Results

Reporting Xpert positive results must also include the results from Rifampicin resistance testing

- MTB detected, RR+ve (MTB detected with Rifampicin resistance detected)
- MTB Detected, RR-ve (MTB detected with no Rifampicin resistance detected)
- MTB detected, RRI (MTB detected Rifampicin resistance indeterminate)

Xpert Negative results must be reported:

- MTB not detected

In rare cases, where the only result that is available for Xpert MTB RIF is error, invalid or no result- this result should be captured as below and a repeat sample collected for testing:

- Err, Inv, No result

*Operational problems associated with this test include: the shelf-life of the cartridges is only 18 months, a very stable electricity supply is required, the machine needs to be calibrated annually, and the temperature ceiling is critical
The following WHO recommended method of reporting of smear microscopy results should be used.

**TABLE 22: REPORTING FOR FLUORESCENCE MICROSCOPY (FM) RESULTS**

<table>
<thead>
<tr>
<th>200x</th>
<th>400x</th>
<th>Result Reported</th>
</tr>
</thead>
<tbody>
<tr>
<td>No AFB in one length</td>
<td>No AFB in one length</td>
<td>No AFB Seen</td>
</tr>
<tr>
<td>1– 4 AFB in one length</td>
<td>1 – 2 AFB in one length</td>
<td>Report actual number *</td>
</tr>
<tr>
<td>5 – 49 AFB in one length</td>
<td>3 – 24 AFB in one length</td>
<td>Scanty Positive</td>
</tr>
<tr>
<td>3 – 24 in one field</td>
<td>1 – 6 AFB in one field</td>
<td>1+</td>
</tr>
<tr>
<td>25 – 250 AFB in one field</td>
<td>7 – 60 AFB in one field</td>
<td>2+</td>
</tr>
<tr>
<td>&gt;250 AFB in one field</td>
<td>&gt;60 AFB in one field</td>
<td>3+</td>
</tr>
</tbody>
</table>

*Confirmation required by another technician or prepare another smear, stain and read. Report as positive (actual number only if the result is confirmed by a second reader of a repeat smear)
### Table 23: Reporting of Ziehl–Neelsen (ZN) Results

<table>
<thead>
<tr>
<th>Number of bacilli seen in smear</th>
<th>Results</th>
<th>Result Reported</th>
</tr>
</thead>
<tbody>
<tr>
<td>No AFB in 100 fields</td>
<td>Negative</td>
<td>No AFB Seen</td>
</tr>
<tr>
<td>1 – 9 AFB in 100 fields</td>
<td>Positive</td>
<td>Record exact number of bacilli</td>
</tr>
<tr>
<td>10 – 99 AFB in 100 fields</td>
<td>Positive</td>
<td>1+</td>
</tr>
<tr>
<td>1 – 10 AFB per fields, check 50 fields</td>
<td>Positive</td>
<td>2+</td>
</tr>
<tr>
<td>&gt;10 AFB per field, check 20 fields</td>
<td>Positive</td>
<td>3+</td>
</tr>
</tbody>
</table>

### Line Probe Assay (LPA)

LPA is based on polymerase chain reaction (PCR) and the DNA strip technology. LPA does not eliminate the need for conventional culture and phenotypic drug susceptibility testing. LPA is available in Zambia at referral Mycobacterial culture laboratories. Line Probe Assay can be performed directly using a processed sputum sample or indirectly using DNA isolated and amplified from a culture of *M. tuberculosis*.

First-line LPA is recommended for the rapid detection of resistance to rifampicin and isoniazid in sputum specimens and cultures of *Mycobacterium tuberculosis*. It is recommended on DR –TB suspected patients with MTB detected and RIF negative on Xpert.

Second-line drugs Line probe assay (SL LPA) is recommended for patients with confirmed Rifampicin resistance (RR-TB) or multi drug resistant tuberculosis (MDR-TB);

### Table 24: Interpretation of Results for LPA

<table>
<thead>
<tr>
<th>Result</th>
<th>Interpretation</th>
</tr>
</thead>
<tbody>
<tr>
<td>MTB complex detected</td>
<td>MTB was isolated from the specimen therefore the patient has bacteriologically confirmed TB</td>
</tr>
<tr>
<td>MTB complex not detected</td>
<td>MTB was not isolated from the specimen</td>
</tr>
<tr>
<td>Rifampicin and Isoniazid susceptible</td>
<td>Patient has drug susceptible TB</td>
</tr>
<tr>
<td>Rifampicin and Isoniazid resistant</td>
<td>Patient has multi drug resistant TB (MDR-TB)</td>
</tr>
<tr>
<td>Rifampicin resistant and Isoniazid susceptible*</td>
<td>Patient has Rifampicin resistance (RR-TB)</td>
</tr>
<tr>
<td>Rifampicin susceptible and Isoniazid resistant</td>
<td>Patient has Isoniazid resistance</td>
</tr>
</tbody>
</table>
Mycobacterial Culture

Culture is the gold standard for TB Diagnosis.

- Highly sensitive and specific method.
- There are two culture methods available, namely solid and liquid. If liquid culture is used, sensitivity gain is +10% compared with Löwenstein-Jensen solid culture.
- Refrigerate culture specimens at 2-8°C until ready for transport to the laboratory.
- If a refrigerator is not available, specimens must be held in coolers with ice packs.
- Specimens must be delivered as soon as possible, but no later than 48 hours from time of collection.

Limitations:

- Long turnaround time of the results (Liquid 21 days, Solid 48 days to inform a negative result)
- Expensive

Positive Liquid Culture

Positive LJ Culture

Genotype Results

GenoType MTBDRplus (Hain Lifescience GmbH, Nehren, Germany)

- A line probe hybridization assay.
- Detection of rifampin and isoniazid resistance
- GenoType MTBDRplus assay

Culture is recommended for:

- All previously treated TB patients (loss to follow up, retreatment, failure)
- Smear-positive after 2 months of first line treatment
- Drug resistant TB contacts
- RR TB patients by Xpert MTB/RIF
- Patients who develop active PTB during or after IPT
- Health care worker, miners, prisoners
- Extra-pulmonary specimens
- Specimens from Children
- Diagnostic uncertainty
### Table 25: Interpretation of Results for Culture

<table>
<thead>
<tr>
<th>Result</th>
<th>Meaning</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mycobacterium tuberculosis isolated</td>
<td>Positive</td>
</tr>
<tr>
<td>Mycobacterium tuberculosis not isolated</td>
<td>Negative</td>
</tr>
<tr>
<td>Contaminated</td>
<td>Specimen not properly handled (repeat specimen collection)</td>
</tr>
<tr>
<td>Not Done</td>
<td>The test was not performed due to many reasons such leaked specimen, mismatch information on the sample and request form and insufficient specimen etc.</td>
</tr>
<tr>
<td>Mycobacteria’s other than Mycobacterium tuberculosis isolated (MOTT)</td>
<td>Non Tuberculous Mycobacterium (NTM) which may or may not be clinically significant</td>
</tr>
</tbody>
</table>

**Notes:** A practical description of all the procedures for sputum smear microscopy, culture and DST and Xpert MTB/RIF are detailed in the relevant TB laboratory Manuals.

### Phenotypic Drug Susceptibility Test (DST)

Phenotypic, culture methods are based on assessment of the ability of *M. tuberculosis* to grow in culture media (solid or liquid) containing a critical concentration of specific anti-TB agents (which indicates resistance) or, conversely, its inability to grow in the same media (which indicates susceptibility).

- Phenotypic DST for first-line agents (Isoniazid, Rifampicin Ethambutol and Streptomycin), and selected second-line anti-TB drugs (Kanamycin, Amikacin, Ofloxacin, Levofloxacin) is generally reliable and reproducible.
- Other anti-TB agents such as the later generation fluoroquinolones (Moxifloxacin and Gatifloxacin), Capreomycin, Thioamides, Cycloserine and Pyrazinamide are becoming increasingly important in the treatment of DR-TB and there is a need for their critical concentrations to be re-evaluated.
- DST methods for new and repurposed drugs for the treatment of MDR-TB such as Bedaquiline, Delamanid, Linezolid, Clofazimine need validation.

### Lateral Flow Urine Lipoarabinomannan (LF-LAM)

- Tests based on the detection of LAM antigen in urine. LAM antigen is released from metabolically active or degenerating bacteria.
- A positive results is diagnostic of active TB disease
- A negative results does not rule out TB
- Urine is easy to collect and the test can be performed at bed side, and lacks the infection control risks associated with sputum collection.
- Is recommended for HIV-positive persons with low CD4 (<100 cell/µL) counts and signs and symptoms of TB (pulmonary and/or extrapulmonary) OR who are seriously ill/ hospitalized regardless of CD4 count or without a known CD4 count.
- Can be used as an additional test in a critically ill patient with sputum negative
Evaluating Patients for TB

**FIGURE 16: XPERT MTB RIF ALGORITHM**

1. **All Presumptive TB**

   - Collect 1 spot sample for Xpert MTB/RIF
     - (Sputum, CSF & Aspirates)

2. **MTB detected, RR not detected**
   - Treat with first line regimen
   - Send two specimens for SL LPA and culture/DST
   - Adjust the treatment according to DST result when available

3. **MTB detected, RR detected**
   - Treatment with first line regimen
   - Repeat Xpert MTB/RIF

4. **MTB not detected**
   - Do CXR and broad spectrum antibiotics for at least 7 days
   - If CXR is suggestive, treat for TB
   - If CXR is not suggestive, re-evaluate

5. **No results, error or invalid result**
   - Repeat Xpert MTB/RIF

---

1. For PLHIV who have CD4 counts ≤100 cells/μl or are seriously ill with one or more danger signs, a urine LF-LAM assay may also be used if available.

2. Patients should be initiated on a first-line regimen. A sample may be sent for first-line LPA and culture/phenotypic DST if there is a risk of DR-TB:
   - Previously treated TB patients: loss to follow up, retreatment, failure
   - DR-TB contacts
   - Smear positive at month 2 of first-line treatment
   - Health care worker
   - Miners
   - Prisoners
   - If patient has high risk of DR TB as a contact of a DR TB patient and patient is failing first line treatment, start second-line treatment while waiting DST results

3. Treat the patient according to result of the repeat test. If the second Xpert MTB/RIF is negative, continue the first line TB treatment and send specimen for FL LPA, culture and phenotypic DST
   - Note that FL-LPA is recommended for use with smear-positive sputum samples only.

4. Treat the patient according to result of the repeat test.
**Figure 17** is an interim algorithm in facilities where Xpert MTB/RIF is not yet available for all presumptive TB patients but is only available for priority populations, and smear microscopy is used for other patients.

HCW need to assess carefully the patients and ensure that all the priority patients (i.e. PLHIV, children, EPTB and patient with risk of DR-TB) collect and send samples to a facility where Xpert MTB/RIF is available.

HCW should decide the treatment of the patients without waiting for Xpert MTB/RIF results (as it can be delayed). Consider the possibility of clinically defined TB (i.e., no bacteriological confirmation). Use clinical judgement for treatment decisions. When the Xpert MTB/RIF result is available, treatment can be adjusted accordingly.
**Figure 17: Algorithm of Sputum Smear Plus Priority Patients for Xpert MTB/RIF Testing (for Facilities without Xpert MTB/RIF Acc)**

1. **All Presumptive TB**
   - Evaluate the patient for TB, HIV and DR-TB risk factors

2. **Priority patients for Xpert MTB/RIF testing:**
   - PLHIV
   - Children (0-14 years)
   - EPTB samples
   - Previously treated TB patients (loss to follow up, relapse, failure)
   - DR-TB contacts
   - Smear positive at month 2 of first line treatment
   - Health care worker, miners, prisoners

3. **Collect 3 samples:**
   - Perform 2 smear microscopy on site
   - Refer 1 specimen for Xpert MTB/RIF (don’t wait for the result)

4. **Smear Positive**
   - Treat with First Line Regimen
     - If patient has very High risk of DR TB as Contact of DR-TB patients and patients failing first line treatment start second line treatment while waiting DST Results
   - Review the treatment based on Xpert MTB/RIF result

5. **Smear Negative**
   - Re-evaluate the patient clinically
     - Conduct additional testing (eg. CXR)
     - Use clinical judgment for treatment decisions
   - Review the clinical decisions based on Xpert MTB/RIF result

6. **Other patient categories**
   - Collect 2 sputum samples
     - Perform 2 sputum smears
   - One or both smear positive
     - Treat with first line regimen
   - Both smear negative
     - Re-evaluate the patient clinically
     - Conduct additional testing
     - Send specimen for Xpert MTB/RIF
     - Use clinical judgment to decide treatment
TUBERCULOSIS TREATMENT AND MANAGEMENT

Key Messages

- First Line treatment (previously Category I) remains the same: 2 RHEZ/4 RH
- TB meningitis and Osteoarticular/spine TB are treated for 12 months (2RHEZ/10 RH)
- Category II treatment (2SRHEZ/1RHEZ/5RHE) should no longer be prescribed
- All previously treated patients should have their samples sent for Xpert MTB/RIF, First Line LPA, Culture and phenotypic DST to guide the treatment. Start first line treatment while awaiting the results.
- All DR TB contacts with a diagnosis of TB should start second-line treatment while awaiting the DST Results
- Patients failing first line treatment should start second-line treatment while awaiting the DST results
- Patients diagnosed with TB and are HIV infected should initiate cART within 2-3 weeks once TB treatment is tolerated. In cases of TB Meningitis, TB therapy should be delayed until after 8 weeks on TB therapy

Aims and Principles of TB Treatment

Early case finding and adequate treatment of tuberculosis using DOTS is the cornerstone of TB control.

The aims of treatment are:

- To cure patients and restore their quality of life and productivity
- To prevent further transmission of TB in the community
- To prevent relapse
- To prevent death from active TB or its late effects and complications
- To prevent the development of drug resistance—including MDR-TB and XDR-TB

The Principles of TB Treatment are:

- TB treatment involves use of correct doses of multiple drugs to ensure effectiveness of therapy
- Never add a single drug to a failing regimen
- At no time should monotherapy (use of a single anti-TB drug) be employed as treatment for active TB
- TB drugs should be taken daily for a specified period depending on the severity of the disease

Essential Anti-TB Medicines

The recommended essential first-line anti-TB medicines are Rifampicin (R), Isoniazid (H), Ethambutol (E) and Pyrazinamide (Z). Fixed dose combination (FDC) is preferred over single drug formulation. The fixed dose combination are 4FDC (RHZE) and 2FDC (RH). Drug dosage is based on weight. Monitoring the patient’s weight is essential for proper dosing.

Key Message

- TB medicines are available free of charge
- It is essential that all facilities treating TB patients stock single formulation drugs for use when necessary, especially in an event of side effects
Properties of Anti-Tuberculous Drugs

**TABLE 26: PROPERTIES OF FIRST-LINE TB DRUGS**

<table>
<thead>
<tr>
<th>Drug</th>
<th>Drug Property</th>
<th>Target Bacilli</th>
<th>Site of Action</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rifampicin</td>
<td>Bactericidal within 1 hour. High potency. Most effective sterilizing drug</td>
<td>All populations including dormant bacilli</td>
<td>Intracellular and extracellular</td>
</tr>
<tr>
<td>Isoniazid</td>
<td>Bactericidal after 24 hours. High potency: kills &gt;90% bacilli in the first few days of treatment</td>
<td>Rapid and intermediate growing bacilli</td>
<td>Intracellular and extracellular</td>
</tr>
<tr>
<td>Ethambutol</td>
<td>Bacteriostatic. Low potency. Minimizes the emergence of drug resistance</td>
<td>All bacterial populations</td>
<td>Intracellular and extracellular</td>
</tr>
<tr>
<td>Pyrazinamide</td>
<td>Bactericidal with a low potency. Achieves its sterilizing action within 2-3 months</td>
<td>Slow growing bacilli</td>
<td>Intracellular bacilli in macrophages</td>
</tr>
</tbody>
</table>

Standardized First Line Treatment

A standardized treatment regimen has been adopted comprising the 4FDCs (RHZE) and 2FDC (RH) for a period of 6-12 months depending on the severity and anatomical location of the disease.

**Intensive Phase**
- Designed for the rapid killing of actively growing and semi-dormant bacilli.
- Achieves a shorter duration of infectiousness.
- The duration of the phase is two (2) months in new and retreatment cases.

**Continuation Phase**
- Eliminates bacilli that are still multiplying and reduces the risk of failure and relapse.
- The duration is for at least four (4) months in most cases and ten (10)* months if the patient has meningitis, Osteoarticular or spinal TB.

*It is recommended to extend treatment to 12 months for TB meningitis because of serious risk of disability and mortality and Osteoarticular/spinal TB because of difficulties of assessing response to treatment.

**Recommended Regimens**

**TABLE 27: RECOMMENDED REGIMENS**

<table>
<thead>
<tr>
<th>TB disease category</th>
<th>Recommended Regimen</th>
</tr>
</thead>
<tbody>
<tr>
<td>Treatment Phase</td>
<td>Intensive Phase</td>
</tr>
<tr>
<td>All forms of TB (non-severe)</td>
<td>2RHZE</td>
</tr>
<tr>
<td>TB Meningitis, Osteoarticular and Spinal TB (severe forms)</td>
<td>2RHZE</td>
</tr>
</tbody>
</table>
Weight Bands for Dosing of Anti-Tuberculous Drugs

**TABLE 28: WEIGHT BANDS FOR DOSING OF ANTI-TB DRUGS**

<table>
<thead>
<tr>
<th>Body Weight (Kg)</th>
<th>Intensive Phase (RHZE 150/75/400/275)</th>
<th>Continuation Phase (RH 150/75)</th>
</tr>
</thead>
<tbody>
<tr>
<td>25-37</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>38-54</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>55-70</td>
<td>4</td>
<td>4</td>
</tr>
<tr>
<td>Above 71</td>
<td>5</td>
<td>5</td>
</tr>
</tbody>
</table>

**Key Message**

Dosing for all patients should be according to weight and adjusted according to close weight monitoring.

**TB Treatment of New and Previously Treated Patients**

- Treat all new TB patients (bacteriologically confirmed, clinically diagnosed and extra-pulmonary TB) with first-line TB drugs with the exception of the new patients who are confirmed DR-TB patients.
- For patients with a known DR-TB contact, a second-line regimen based on the DST of the presumed index case should be started while awaiting for DST results.
- In previously treated patients, send samples for Xpert MTB/RIF, first-line LPA, Culture and phenotypic DST. Start first-line treatment while waiting for the results.
- For patients failing first-line regimen, send samples for Xpert MTB/RIF, first-line LPA and culture. Start second-line regimen while waiting for the results. Adjust the therapy once DST results are available.

**Standard Indications of Steroids in the Treatment of Tuberculosis**

- TB meningitis
- Constrictive TB pericarditis with suspected constrictive physiology
- TB IRIS
- Massive Pleural effusion
- Massive lymphadenopathy with pressure effects
- Severe hypersensitivity reactions to anti-TB drugs
- Hypoadrenalism
- Renal tract TB (to prevent ureteric scarring)
- TB laryngitis with life threatening airway obstruction

**Other Possible Indications for Steroids in the Treatment of Tuberculosis:**
**Recommended Doses of Adjuvant Steroid Therapy**

**TABLE 29: RECOMMENDED DOSES OF ADJUVANT STEROID THERAPY (DRUG OF CHOICE IS PREDNISOLONE)**

<table>
<thead>
<tr>
<th>Indication</th>
<th>Prednisolone (Dosage)</th>
</tr>
</thead>
<tbody>
<tr>
<td>TB Meningitis</td>
<td>1-2mg/kg (max 60mg) for 2 weeks then taper off by 10 mg in the daily dose each week over about 6 weeks</td>
</tr>
<tr>
<td>TB Pericarditis</td>
<td>1-2mg (max 60mg for 4 weeks then half for 4 weeks (max 30mg/day) then 15 mg/day x 2 weeks, then 5 mg/kg x 1 week, then off</td>
</tr>
<tr>
<td>TB Pleural effusion (severe)/or IRIS</td>
<td>0.5 to 1mg (max 30mg) for 1-2 weeks then taper off over several weeks</td>
</tr>
</tbody>
</table>

*Note: Steroids doses must not be stopped abruptly, but must be tapered. If prednisolone is unavailable, equivalent doses of dexamethasone may be used as a substitute.*

**Key Message**

Steroids are immunosuppressant and may theoretically increase the risk of developing opportunistic infections in TB/HIV patients. However, used as indicated above, the overall benefit of steroid use outweighs the potential risk.

**TB Patients Monitoring and Follow-Up**

- All TB patients must be seen at least once monthly by a health care provider for clinical review, assessment of side effects and dose adjustment according to weight.
- All patients should have 1 sputum specimen (morning) taken for AFB smear at 2, 5 and 6 months. If sputum smear is positive at 2 months, proceed to continuation phase and send sputum specimens for Xpert MTB/RIF, First line LPA, culture and phenotypic DST.
- Repeat smear microscopy at month 3. If sputum smear is still positive at month 3, send samples for Xpert MTB/RIF, First line LPA, culture and phenotypic DST (continue or adjust the treatment according to the results). Results should be available at these visits and must be recorded on the patient treatment card and registers.

**Key Messages**

1. If a patient is found to have a drug resistant strain of TB at any time during the therapy, treatment is declared as failed and patient referred for DR-TB treatment and re-register as such.

2. For previously treated TB patients, specimens for Xpert MTB/RIF, LPA, culture and phenotypic DST should be sent before starting treatment (DST should be performed for at least Rifampicin and Isoniazid, WHO 2017)
### TABLE 30: SUMMARY OF SPUTUM MONITORING BY SMear IN First-Line Treatment

<table>
<thead>
<tr>
<th>Treatment Phase</th>
<th>Months of Treatment</th>
<th>Sputum Smear Exam</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Intensive Phase</strong></td>
<td>1</td>
<td></td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>If smear positive, send sample for LPA, culture and DST</td>
</tr>
<tr>
<td><strong>Continuation Phase</strong></td>
<td>3</td>
<td>If smear was positive at month 2, repeat smear at month 3. Send samples for culture, LPA and DST if still positive; ensure samples are received at the laboratory.</td>
</tr>
<tr>
<td></td>
<td>4</td>
<td></td>
</tr>
<tr>
<td></td>
<td>5</td>
<td>If smear positive, obtain samples for LPA, Culture and DST. If there is concern for MDR-TB, send sample for Xpert MTB/RIF to assess for rifampin resistance.</td>
</tr>
<tr>
<td></td>
<td>6</td>
<td>If smear negative, assign appropriate treatment outcome. If positive, obtain samples for LPA, Culture and DST.</td>
</tr>
</tbody>
</table>
### Table 31: HIV-TB Co-infection Case Scenarios and Recommended Management for Susceptible TB

<table>
<thead>
<tr>
<th>Scenario</th>
<th>TB management</th>
<th>Recommended cART</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pregnant, on cART and develops TB</td>
<td>Start ATT immediately</td>
<td>Continue EFV-based cART Evaluate for failure and consider switching to 2nd line cART in consultation with next level</td>
</tr>
<tr>
<td>Pregnant, on ATT, and diagnosed with HIV</td>
<td>Continue ATT</td>
<td>Start cART immediately TDF + XTC + EFV-400mg If renal insufficiency, ABC + 3TC + EFV</td>
</tr>
<tr>
<td>Children 3 months to &lt;3 years old with TB-HIV co-infection</td>
<td>Start ATT (RHEZ) immediately</td>
<td>ABC + 3TC + EFV</td>
</tr>
<tr>
<td>Newly diagnosed TB and HIV co-infection: TB retreatment case and HIV co-infection</td>
<td>Start ATT immediately</td>
<td>Start cART as soon as ATT is tolerated (usually within 2-3 weeks) regardless of CD4 count or WHO Clinical Stage TDF + XTC + DTG (DTG 50mg twice daily if single DTG tablet is available). <strong>If not available</strong>, give: TDF + XTC + EFV-400mg* If renal insufficiency, ABC + 3TC + DTG 50mg twice daily</td>
</tr>
<tr>
<td>On cART and develops TB</td>
<td>Start ATT immediately</td>
<td>If NVP-based regimen, switch NVP to DTG 50mg twice daily and continue cART. If on ATV-r, switch to LPV-r and double the dose If on LPV-r, double dose of LPV-r Evaluate for failure and consider switching to 2nd line cART in consultation with next level</td>
</tr>
<tr>
<td>On ATT and diagnosed with HIV</td>
<td>Continue ATT</td>
<td>Start cART as soon as ATT is tolerated (usually within 2-3 weeks*), regardless of CD4 count or WHO clinical stage TDF + XTC + DTG (DTG 50mg twice daily if single DTG tablet is available). <strong>If not available</strong>, give: TDF + XTC + EFV-400mg If renal insufficiency, ABC + 3TC + EFV</td>
</tr>
<tr>
<td>On 2nd line cART with LPV-r and develops TB</td>
<td>Start ATT immediately</td>
<td>Increase LPV-r from 2 tabs BD to 3 tabs BD for 2 weeks and then to 4 tabs BD for the remainder of TB treatment. If Rifabutin available (in place of Rifampicin), start at 150mg Monday/Wednesday/Friday.</td>
</tr>
</tbody>
</table>

- Patients on TB treatment should be initiated on TDF + XTC + DTG. Take note that DTG in this case should be given as 50mg twice daily.
- For treatment experienced patients on DTG who develops TB and DTG single tablet is not available: Switch to TDF+XTC+EFV-400mg if viral load <20 copies/mL, and TDF+XTC+LPV-r if viral load > 20 copies/mL
- **REMEMBER to switch back to DTG 50mg once daily after TB treatment!**
- Patients on cART on TAF who develop TB, should be switched to TDF
- HIV-positive TB patients with profound immunosuppression (e.g., CD4 counts less than 50 cells/µL) should receive cART within the first two weeks of initiating TB treatment.
- TB meningitis patients with a new HIV diagnosis should have ART initiation delayed until after the first 8 weeks of ATT are completed, regardless of CD4 count.
**Drug Resistant TB**

**Drug Resistant TB Patient Detection**

The diagnosis and treatment of persons with drug resistant TB (DR-TB) starts with identification of a presumptive DR-TB patient.

_Sputum samples from all presumptive TB patients should be sent for Xpert MTB/RIF rapid diagnostic testing, and a chest x-ray should be obtained for patients when the diagnosis of TB is uncertain._

Every effort should be undertaken to confirm the diagnosis of RR-TB/MDR-TB with Xpert MTB/RIF, especially for patients in the following risk categories:

- A close contact of a person diagnosed with DR-TB, especially if the person is not on treatment, is failing treatment, or has recently died from DR-TB disease;
- Someone who has a history of TB treatment failure (either DS-TB or DR-TB), lost to follow up from DS-TB or DR-TB treatment, or could be considered to have early relapse from a previously treated case of DS-TB or DR-TB (successfully treated less than two years previously);
- HIV co-infected patients with severe immunosuppression: bacteriologic confirmation may be difficult so a history of contacts and risk factors is important;
- Persons recently from facilities with high rates of DR-TB: the risk of nosocomial infection is high for health care workers, miners, prisoners, and patients admitted for prolonged periods, especially in the absence of appropriate infection control measures;
- DS-TB patients who remain smear positive ≥ 2 months on first line drug treatment, as this may indicate the presence of drug resistance.

**Diagnosis of Drug Resistant Tuberculosis**

a) Clinical Presentation

- The clinical features of DR-TB are not different from those of drug susceptible TB (both pulmonary and extra-pulmonary TB).
- DR-TB is by definition a bacteriological diagnosis. However, in patients where bacteriological confirmation is difficult, such as children, HIV positive patients, or those with extra-pulmonary TB, and who are also close contacts of known DR-TB patients, a clinical diagnosis of DR-TB can be made. Such cases should be discussed with the Clinical Expert Committee (CEC).

b) Bacteriologic Confirmation

Xpert MTB/RIF has been recommended as the primary diagnostic test in all adults and children with signs and symptoms of TB where available

- The diagnosis of DR-TB is done by Xpert MTB/RIF, line probe assay (first and second-line LPA), culture and phenotypic drug susceptibility testing (pDST).
- In facilities where Xpert MTB/RIF is not yet available, samples should be referred to the nearest facility where the test is available, especially for individuals with risk factors of DR-TB.
• Only as a last resort should patients be started on empiric DS-TB treatment based on clinical history and positive smear microscopy results alone (e.g. severely ill patients in whom treatment initiation should not be delayed pending Xpert MTB/RIF, LPA, or culture/DST results

• Patients who require TB re-treatment based on history should NOT get the category II regimen (the standard DS-TB regimen plus streptomycin). Instead, patients should get drug susceptibility testing with rapid molecular testing (Xpert MTB/RIF, FL and SL LPA) to inform the choice of treatment. WHO no longer recommends the use of the category II regimen.

• For all patients with Rifampicin resistance detected on Xpert MTB/RIF, samples should be sent for SL LPA, culture and phenotypic DST; for those eligible, the shorter DR-TB treatment regimen should be started while awaiting results from LPA and/or culture/DST.

• The turnaround time (specimen collection until receipt of results) for LPA and culture/DST results varies on when the test becomes positive and the type of media used (e.g. liquid or solid media for culture):
  o Line probe assay results should take between 3-14 days (turnaround time of LPA within the processing lab should be 48 hours);
  o Liquid culture (MGIT): positive results at 4-14 days, negative result by 42 days;
  o Solid culture (LJ): positive results at 28-56 days, negative result by 60 days;
  o Phenotypic DST results (from the date culture was positive): MGIT 14 days, LJ 30 days;

• Phenotypic DST (pDST) is reliable and reproducible for Rifampicin, Isoniazid, Kanamycin, Amikacin, Ofloxacin, Levofloxacin.
  o Moxifloxacin: there is a need for critical concentrations to be re-evaluated;
  o Ethambutol, Streptomycin, Capreomycin, Ethionamide/Protonamide, Cycloserine, Pyrazinamide, para – Amino Salicylic Acid: pDST is not reliable;
  o New and repurposed drugs Bedaquiline, Delaminid, Clofazimine, Linezolid: pDST needs validation and is not widely available outside of research settings.

Causes of DR-TB

• Transmission from a patient with drug resistant TB
• Poor adherence to treatment by patients
• Use of anti-TB drugs of unproven quality (sale of such medications over the counter and on the black-market).
• Incorrect management of individual cases by clinicians
• Sub-optimal dosage
• Poor drug absorption
• Prolonged shortages of anti-TB drugs

Groups at Risk of DR-TB

• Contacts of DR- TB patients
• Patients previously treated for TB (Treatment failures, relapses, treatment after loss to follow up)
• Patients who are smear positive after 2 months of first line TB treatment
• TB patients who are close contacts of DR-TB cases.
• Health care workers
• Prisoners from facilities with high rates of DR-TB

Management of Presumptive DR-TB Patients
If a patient is presumed to have DR-TB, the following should be done:

• Collect sputum specimens for Xpert MTB RIF, LPA, culture and phenotypic DST
• Do not admit patient to a general ward (especially in high HIV settings as HIV positive individuals can easily get infected).

If hospital admission is necessary, the patient should be admitted to a special ward, which has good ventilation. At home advise patient to sleep in a well-ventilated room that is separate from others (if possible). If DR-TB is confirmed by the laboratory the patient should be referred for treatment at a designated treatment facility under strict supervision.

Detection of DR-TB patients
Case detection for DR-TB is similar to that of TB in general. The basis for identification of DR-TB patient is bacteriological examination, which includes Xpert MTB/RIF, LPA, Culture and Phenotypic Drug Susceptibility Testing (DST) as well as previous history of treatment.

Standardized Shorter Regimen for RR and MDR patients
In order to improve the treatment outcomes, adherence and the quality life for RR/MDR TB patient, the NTLP has adopted the WHO recommended shorter regimen in patients without additional resistance or intolerance to key second-line drugs (SLD), i.e. Fluoroquinolones (FQ) and Second Line Injectable (SLI). For ineligible patients, individualized regimen is recommended that may include the new drugs - Bedaquiline (Bdq) and Delaminid (Dlm).

Eligibility criteria:

All patients with DR -TB are eligible to start DR-TB treatment without delay. The patient should be evaluated to assess the risk of resistance or intolerance to FQ and/or SLI and the eligibility criteria. If there is no risk of intolerance and/or resistance for FQ and/or SLI the patient will start with the shorter regimen. If there is risk of intolerance/resistance to FQ and/or SLI and/or bacterial confirmation of drug resistance or other risk factors for poor treatment outcome (such as severe TB disease), the patient shall start with an individualized treatment regimen.

Before starting treatment, two sputum samples must be sent for Second-line - Line Probe Assay (SL LPA) and for culture, as well as first-line and second-line drug susceptibility tests (phenotypic FL/SL DST). Once the results are available, the initial regimen may then be adjusted if necessary with clear lack of response (clinically, smear grading, culture).

Standard duration of the intensive phase is at least 4 months of Km (Am, Cm), Mfx (Gfx), Cfz, Z, E, HHD, Pto (Eto) given daily. If smear conversion is not achieved at month 4, the intensive phase shall be extended to a maximum of six months until sputum smear conversion. The Km (Am or Cm) will be given three times-weekly from the fourth month onwards; the continuation phase consists of Mfx (Gfx,) Cfz, E, Z for a fixed duration of five months. If the patient remains smear positive and/or is still culture positive at 6 months, the patient will be declared as a failure. Failure declaration and a switch to an individualized treatment will be considered earlier in patients.
Standardized Longer Regimen for RR and MDR-TB patients

Intensive Phase for 8 months:
- Kanamycin (Km), Levofloxacin (Lfx), Ethionamide (Eto), Cycloserine (Cs), Pyrazinamide (Z)

Continuation Phase for 12 months:
- Levofloxacin (Lfx), Ethionamide (Eto), Cycloserine (Cs), Pyrazinamide (Z)

Individualized regimen
For patients with resistance to second-line drugs (pre-XDR/XDR-TB), the treatment is individualized according to contact history, drug history, drug susceptibility results, adherence history, clinical course and adverse reactions to drugs used previously. The design of the individualized regimen will include new and repurposed drugs such as Bedaquiline (Bdq), Delaminid (Dlm), Linezolid (Lnz) and Clofazimine (Clf).

Key Message
It is strongly recommended that individualized regimen should be designed by the DR Clinical Expert Committee
**Figure 18: RR/DR TB Patient Triage Flow Chart**

**RR-TB patient**

SEND SAMPLE FOR SL LPA AND CULTURE/DST

EVALUATE PATIENT USING THE FOLLOWING ELIGIBILITY CRITERIA FOR SHORTER DR-TB TREATMENT REGIMEN

1. No evidence of FQ and/or SLI
2. No contact with patient that has resistance to FQ/SLI
3. No exposure to SLD for ≥ 1 month
4. No known intolerance to drugs in the shorter regimen
5. Not pregnant
6. No EPTB*
7. No other risk of unfavourable outcome**

---

**Initial treatment regimen**

**Eligible**

- Shorter DR-TB Treatment Regimen

**Ineligible**

- Individualized DR-TB Treatment Regimen

**Regimen adjustment based on:**

- SL DST results
- Treatment tolerance

**NO resistance/intolerance to SLI and/or FQ**

- Continue shorter DR-TB Treatment

**Resistance/intolerance to SLI and/or FQ**

- Change to individualized DR-TB Treatment regimen

**Resistance/intolerance to SLI and/or FQ**

- Continue individualized DR-TB Treatment

**NO resistance/intolerance to SLI and/or FQ**

- Continue treatment whilst consulting experts on potential regimen adjustment based on DST

---

# Includes patients with high risk of Rifampicin resistance as contacts of RR-/MDR-TB patients

* Non-severe forms of EPTB that can be eligible for the shorter treatment regimen include TB pleural effusion (adults and children) and TB lymph node (children)

** Risk of unfavorable outcome includes extensive or advanced TB disease (multiple)

Abbreviations: RR-TB = Rifampicin resistant TB; SL DST = Second-line drug susceptibility test; DR-TB = Drug-resistant TB; FQ = Flouroquinolone; SLI = Second-line drugs; EPTB = Extra-pulmonary TB
### Dosage and administration

**Table 32: Weight-based DR-TB drugs in Adults ≥30 kg**

<table>
<thead>
<tr>
<th>Drugs</th>
<th>Daily dose</th>
<th>30–35 kg</th>
<th>36–45 kg</th>
<th>46–55 kg</th>
<th>56–70 kg</th>
<th>&gt;70 kg</th>
</tr>
</thead>
<tbody>
<tr>
<td>Isoniazid- High dose (H&lt;sup&gt;h&lt;/sup&gt;)</td>
<td>10 mg/kg Maximum 600 mg/day</td>
<td>300 mg</td>
<td>400 mg</td>
<td>500 mg</td>
<td>600 mg</td>
<td>600 mg</td>
</tr>
<tr>
<td>Pyrazinamide (Z)</td>
<td>20–30 mg/kg once daily</td>
<td>800 mg</td>
<td>1000 mg</td>
<td>1200 mg</td>
<td>1600 mg</td>
<td>2000 mg</td>
</tr>
<tr>
<td>Ethambutol (E)</td>
<td>15–25 mg/kg once daily</td>
<td>600 mg</td>
<td>800 mg</td>
<td>1000 mg</td>
<td>1200 mg</td>
<td>1200 mg</td>
</tr>
<tr>
<td>Kanamycin/Capreomycin/Amikacin (Km/Cm/Am)</td>
<td>15–20 mg/kg once daily</td>
<td>500 mg</td>
<td>625 mg</td>
<td>750 mg</td>
<td>825 mg</td>
<td>1000 mg</td>
</tr>
<tr>
<td>Levofloxacin (Lfx)</td>
<td>750–1000 mg once daily</td>
<td>750 mg</td>
<td>750 mg</td>
<td>1000 mg</td>
<td>1000 mg</td>
<td>1000 mg</td>
</tr>
<tr>
<td>Moxifloxacin (Mfx)</td>
<td>400 mg once daily</td>
<td>400 mg</td>
<td>600 mg</td>
<td>&lt;50 kg=600 mg &gt;50 kg=800 mg</td>
<td>800 mg</td>
<td>800 mg</td>
</tr>
<tr>
<td>Prothionamide (Pto)/Ethionamide (Eto)</td>
<td>500–750 mg/day in 2 divided doses</td>
<td>500 mg</td>
<td>500 mg</td>
<td>750 mg</td>
<td>750 mg</td>
<td>1000 mg</td>
</tr>
<tr>
<td>Cycloserine (Cs)/Terizidone (Trd)</td>
<td>500–750 mg/day in 2 divided doses</td>
<td>500 mg</td>
<td>500 mg</td>
<td>500 mg</td>
<td>750 mg</td>
<td>750 mg</td>
</tr>
<tr>
<td>p-aminosalicylic acid (PAS)</td>
<td>8 g/day in 2 divided doses</td>
<td>8 g</td>
<td>8 g</td>
<td>8 g</td>
<td>8–12 g</td>
<td></td>
</tr>
<tr>
<td>Bedaquiline (Bdq)</td>
<td>400 mg once daily for 2 weeks then 200 mg 3 times per week</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Delamanid (Dlm)</td>
<td>100 mg twice daily (total daily dose = 200 mg)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Clofazimine (Cfz)</td>
<td>100 mg twice daily for 2 first months, then reduce to 100 mg daily</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Linezolid (Lzd)</td>
<td>600 mg once daily</td>
<td>600 mg</td>
<td>600 mg</td>
<td>600 mg</td>
<td>600 mg</td>
<td>600 mg</td>
</tr>
<tr>
<td>Amoxicillin/clavulanate (Amx-clv) 7/1</td>
<td>80 mg/kg/day in 2 divided doses</td>
<td>2600 mg</td>
<td>2600 mg</td>
<td>2600 mg</td>
<td>2600 mg</td>
<td>2600 mg</td>
</tr>
<tr>
<td>Amoxicillin/clavulanate (Amx-clv) 8/1</td>
<td>80 mg/kg/day in 2 divided doses</td>
<td>3000 mg</td>
<td>3000 mg</td>
<td>3000 mg</td>
<td>3000 mg</td>
<td>3000 mg</td>
</tr>
<tr>
<td>Imipenem/Cilastatin (Imp/cln)</td>
<td>1000 mg Imipenem/1000 mg Cilastatin twice daily</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Meropenem (Mpm)</td>
<td>1000 mg three times daily (alternative dosing is 2000 mg twice daily)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Treatment Monitoring For MDR-TB/RR-TB Patients on Therapy

Adverse effects may occur with MDR-TB drugs and are dose dependent. However adverse effects can occur at normal dose. Patients should be monitored for adverse effects at each contact with a health care provider.

- Patients should be monitored closely for signs of treatment failure and adverse drug reactions (compare baseline and follow up examinations).

- Treatment can be monitored through clinical history; physical examination; psychosocial assessment; chest radiography; audometry, bacteriological test (smear and culture); laboratory monitoring (hematology-FBC, Creatinine, Potassium, LFT, TSH); Pregnancy test, hepatitis B,C and HIV test (if positive CD4 and VL 
every 6 months) should be included when doing the baseline investigations.

- Weight should be monitored monthly and drug dosages should be adjusted accordingly.

- For patient under individualized regimen, additional monitoring is required: ECG (Dlm, Bdq), Serum Albumin (Dlm), and for Linezolid: vision test charts, Serum Amylase/Lipase and monthly hematology-FBC.

For details on adverse effects monitoring and management, refer to the DR-TB manual.
### Table 33: DR-TB Treatment Monitoring Schedule for Conventional DR-TB Regimen

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Month of Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0</td>
</tr>
<tr>
<td>Clinical evaluation</td>
<td>X</td>
</tr>
<tr>
<td>Sputum-smear</td>
<td>X</td>
</tr>
<tr>
<td>Sputum-culture</td>
<td>X</td>
</tr>
<tr>
<td>FBC/DC</td>
<td>X</td>
</tr>
<tr>
<td>LFTs</td>
<td>X</td>
</tr>
<tr>
<td>Na(^{+}), K(^{+}), u, Creatinine</td>
<td>X</td>
</tr>
<tr>
<td>TSH/free T-4</td>
<td>X</td>
</tr>
<tr>
<td>Pregnancy test</td>
<td>X</td>
</tr>
<tr>
<td>HIV test</td>
<td>X</td>
</tr>
<tr>
<td>Audiometry</td>
<td>X</td>
</tr>
<tr>
<td>CXR</td>
<td>X</td>
</tr>
</tbody>
</table>

**KEY:** X = Required, O = Optional, P = If culture is positive, I = If indicated
**Hepatitis B and HIV**

Screening and Management of Hepatitis B Virus (HBV) and HIV Co-Infection

- Patients with HIV-HBV co-infection experience twice the risk of mortality during cART compared to HIV-infected individuals who do not have HBV.
- Both XTC and TDF are active against HBV; however, using XTC as the only HBV-active antiretroviral drug will lead to HBV drug resistance and is not recommended. cART regimens that contain TDF as the only HBV-active antiretroviral are okay because HBV resistance with TDF alone is very very rare.
- Hepatitis B surface antigen (HBsAg) should be done at baseline and in patients with unknown HBV status.
- For children who have been fully vaccinated (i.e., 3 doses), do not screen for HBV unless there is strong clinical suspicion.
- Start TDF-containing cART regardless of CD4 count.
- Patients failing 1st-line TDF + XTC treatment should continue the TDF in their 2nd-line therapy (i.e. TDF+AZT+3TC+LPV-r or ATV-r) to control their HBV infection.
- For HBsAg positive patients with renal insufficiency (CrCl <50mL/min), consult or refer to next level.
- For HBV-HIV co-infection in child <36 months old, consult or refer to next level.

**Hepatitis B Mono-Infection**

Screening and Management of Hepatitis B Virus (HBV)

- Hepatitis B surface antigen (HBsAg) should be used for screening and diagnosis of active HBV infection; a negative HIV test is required to classify a person as having HBV mono-infection.
- The ZAMPHIA study reported that 5.6% of adults were hepatitis B surface antigen positive; of these most were HIV-negative.
- Other hepatitis B tests (like surface antibody or core antibody) cannot be used to know if the person has active infection.
- Many cases of active HBV infection will not require immediate antiviral therapy but instead can be observed and followed up every 6-12 months.
- APRI (AST-to-platelet ratio index) is the preferred non-invasive test (NIT) to assess for the presence of cirrhosis and can be calculated as follows:

\[
\text{APRI} = \frac{\text{AST Level}}{\text{AST (Upper Limit of Normal)}} \times \frac{100}{\text{Platelet Count (10^9/L)}}
\]

**APRI Score Interpretation**

- **AST aminotransferase to Platelet Ratio Index**
  - APRI score >2.0 in adults is highly suggestive of cirrhosis
  - APRI score <1.0 can rule out the presence of cirrhosis
  - APRI score 1.0-2.0 is a gray area
Eligibility Criteria for Antiviral Treatment

- The presence of cirrhosis is a treatment indication in all adults, adolescents, and children with chronic HBV infection regardless of ALT levels, HBeAg status, or HBV DNA levels
- Diagnosis of cirrhosis is based on APRI score >2.0 in adults
- Clinical signs of decompensated cirrhosis may include portal hypertension (ascites, variceal haemorrhage, and hepatic encephalopathy), coagulopathy, or liver insufficiency (jaundice). Other clinical features of advanced liver disease/cirrhosis may include hepatomegaly, splenomegaly, pruritis, fatigue, arthralgia, palmar erythema, and edema.
- Treatment is recommended for adults who do not have clinical evidence of cirrhosis (or based on APRI score >2 in adults) but do have one of the following:
  - Persistently elevated ALT levels and evidence of high-level HBV replication (HBV DNA >20 000 IU/mL), regardless of HBeAg status
  - When HBV DNA testing (and/or HBeAg testing) is not available, treat when ALT is persistently elevated. Persistent means at least two elevated ALT levels over 6-12 months and newer HBV guidelines now define ‘ALT elevation’ as ALT >19 U/L for women and ALT>30 U/L for men.
  - In HBV/HIV co-infected individuals, TDF based cART should be initiated regardless of CD4 count
- Remember in Zambia other common causes of ALT elevation are medications (such as ATT), liver infections (such as TB), and heavy alcohol consumption.
- In treatment-eligible patients, measurement of creatinine is recommended.

Non-Eligible Patients

Antiviral therapy is not recommended or deferred in the following situations:

- No clinical evidence of cirrhosis
- APRI score ≤2.0 in adults
- Persistently normal ALT levels (i.e., ALT ≤20 in women and ≤30 in men)
- Low levels of HBV DNA replication (HBV DNA <2000 IU/mL), regardless of HBeAg status

Continue monitoring in all persons with chronic HBV infection especially those who do not meet the above eligibility and non-eligibility criteria to determine if antiviral therapy may be indicated in the future to prevent progressive liver disease. Monitoring could be done every 3-6 months in those with ALT elevation and every 6-12 months in those with normal ALT.
First-line Regimen
- In all adults, adolescents and children aged 10 years or older the preferred drug is TDF + XTC
- In children aged 2 to <10 years, Entecavir is the preferred drug over Tenofovir
- The dosing should be as follows:
  - Tenofovir 300mg once daily
  - Tenofovir 300mg plus Lamivudine 300mg
  - Entecavir 0.5mg once daily (adult with compensated liver disease and lamivudine naive)
  - Entecavir 1mg once daily (adult with decompensated liver disease)
- Patients with CrCl <50 mL/min should be referred to a higher level for further management
- Counseling patients that HBV treatment is potentially lifelong is important to set their expectations

Monitoring of Therapy in HBV
- There are several goals of HBV antiviral therapy, as follows:
  - Suppression of HBV viral load (i.e., HBV DNA below assay detection)
  - Normalization of the ALT
  - Conversion from HBeAg-positive to negative
  - Conversion from HBsAg-positive to HBsAg-negative
- Repeat ALT every 6 months is recommended during treatment
- Every 1-2 years HBsAg can be repeated; however, conversion to HBsAg-negative occurs at a rate of <5% per year during chronic infection
- Repeat creatinine every 12 months is also recommended as TDF carries a small risk of renal toxicity
- Repeat an HIV antibody test every 12 months; if patient becomes HIV-positive during HBV treatment (i.e., HIV-HBV co-infection), cART should be initiated

When to Discontinue Therapy
- Discontinuation of HBV-active therapy can be associated with a fatal flare-up of hepatitis; therefore, counsel patients that after stopping they should return if they develop fever and jaundice or other signs of liver disease
- When there is evidence of conversion from HBeAg-positive to HBeAg-negative and after completion of at least one additional year of treatment AND the ALT is persistently normal
- When there is conversion to HBsAg loss and completion of at least one additional year of treatment and the ALT is persistently normal
- If HBV DNA testing is available, persistently undetectable HBV DNA in addition to the above criteria should also guide when to discontinue
- IMPORTANT NOTE: Relapse may occur after stopping therapy, especially in patients who were HBeAg-negative at the start of antiviral therapy. Therefore, after discontinuation, ongoing monitoring of ALT (every 6-12 months) is recommended. Restart therapy if there are signs of reactivation such as HBsAg or HBeAg become positive, ALT levels increase significantly, or HBV DNA becomes detectable again
General Measures to Reduce HBV Transmission

• HBsAg-positive persons should adopt correct and consistent condom use during sexual intercourse; not share razors, toothbrushes, or other personal care items; not donate blood, organs, or sperm; and follow standard universal precautions with open cuts or bleeding.

• HBV vaccination of household and sexual contacts to HBsAg-positive individuals. Household members and sexual partners of persons with Chronic Hepatitis B should be vaccinated if they are negative for HBsAg

• Alcohol reduction to reduce disease progression

• Infants should receive all vaccines recommended through the Extended Program on Immunizations.

• Infants born to HBsAg-positive mothers should have an extra “birth dose” of HBV vaccine as soon as possible after birth if possible, which provides protection against mother to baby transmission

Measures to Reduce HBV Transmission in Hospital Settings

• Health care workers should be tested for HBsAg and vaccinated if they are negative for HBsAg

• Hand hygiene: including surgical hand preparation, hand washing, and use of gloves

• Safe handling and disposal of sharps and waste

• Safe cleaning of equipment

• Testing of donated blood

• Improved access to safe blood

• Training of health personnel
CRYPTOCOCCAL DISEASE AND HIV INFECTION

Diagnosis of Cryptococcal Disease

- Prompt lumbar puncture with measurement of Cerebrospinal fluid (CSF) opening pressure and rapid CSF Cryptococcal antigen (CrAg) assay or rapid serum CrAg (either LA or LFA) is the preferred diagnostic approach.

Prevention of Cryptococcal Disease

- The routine use of antifungal primary prophylaxis for Cryptococcal disease in HIV-infected adults, adolescents, and children with a CD4 count less than 100 cells/µL and who are CrAg negative or where CrAg status is unknown is not recommended before cART initiation, unless a prolonged delay in ART initiation is likely.

Treatment Options

- Induction phase of treatment in HIV-infected adults, adolescents, and children with cryptococcal disease (meningeal and disseminated non-meningeal)
  - The following two-week antifungal regimens are recommended in order of preference.
    - Amphotericin B + Fluconazole
    - Amphotericin B + Flucytosine

- For the consolidation phase treatment of HIV-infected adults, adolescents, and children with cryptococcal meningitis or disseminated non-meningeal disease, the following eight-week antifungal regimen is recommended:
  - Fluconazole 400–800mg/day after a two-week induction with Amphotericin B regimen (6–12mg/kg/day up to 400–800mg/day, if below 19 years)
  - Fluconazole 800mg/day after induction treatment with short-course amphotericin B or Fluconazole-based induction regimen (Fluconazole 12mg/kg/day up to 800mg/day, if below 19 years)

- For maintenance treatment of cryptococcal disease in HIV-infected adults, adolescents, and children, oral Fluconazole 200mg daily (6mg/kg/day up to 200mg/day, if below 19 years) is recommended.
MENTAL HEALTH AND HIV INFECTION

All HIV patients should be assessed and managed for neuropsychiatric conditions (e.g., depression, anxiety, mania, alcohol and substance use, HIV-associated neurocognitive disorder, and delirium disorders) may have a substantial impact on HIV disease progression and cART adherence. For individuals with mental illness, refer to a mental health provider. If an individual with mental illness appears to worsen after EFV-400mg initiation, consider switching EFV-400mg to ATV-r or LPV-r.

Non–Communicable Diseases and HIV

Cardiovascular Disease (CVD) assessment and Management of Non-Communicable Diseases (NCDs)

HIV-infected persons are at increased risk of cardiovascular disease and other non-communicable diseases, including cancers. This is in part because of the chronic immune activation that persists even in HIV infection, even if on treatment. Assessment and management of cardiovascular risk should be provided for all individuals living with HIV according to standard protocols recommended for the general population using risk factors:

- Older than 40 years, obesity, diabetes mellitus, known hypertension, waist circumference of >90cm (women) and 110cm (men), family history of premature CVDs

Up to two thirds of premature deaths from the major NCDs are linked to four shared modifiable risk factors:

- Tobacco use, harmful use of alcohol, unhealthy diet, and physical inactivity.

These risk factors result in a series of metabolic and physiological changes that eventually lead to NCDs. Broader social, economic, and environmental determinants of health and inequities associated with globalization and urbanization, alongside population ageing, are the underlying drivers of the behavioural risk factors, and thus the NCD epidemic.
FIGURE 19: CAUSAL LINKS BETWEEN UNDERLYING DRIVERS FOR NCDs, BEHAVIORAL RISK FACTORS, METABOLIC/PHYSIOLOGIC RISK FACTORS AND NCDs

- Raised Blood Pressure,
- Overweight/Obesity,
- Raised Blood Glucose,
- Raised Lipids

- Social Determinants of Health/Globalization, Urbanization, Population Ageing

- Tobacco Use, Unhealthy Diet, Physical Inactivity,
- Harmful Use of Alcohol
### Table 34: Lifestyle Modifications to Prevent and Manage CVDs Among HIV-Infected Individuals

#### Smoking Cessation
- Smoking cessation has multiple short-term and long-term benefits, including:
  - Skin does not age/wrinkle as quickly
  - Improved fitness and quicker recovery from common infections
  - Reduced risk of respiratory infections and chronic lung disease
  - Reduced risk of high blood pressure, diabetes, kidney disease, heart disease, and stroke
  - Improved infant outcomes (for pregnant women who smoke)
  - Evidence of better response to ART (better viral suppression)

#### Dietary Changes and Weight Loss
- Weight loss to maintain a healthy BMI (nutritionists to be engaged in patient care)
- Reduce/abstain from alcohol
- Cut down sugar intake
- Cut down red meat intake
- Cut down consumption of fatty foods, fat for flavouring, and fried foods
- Increase intake of whole grains, vegetables, fruit, and beans (eating at least five servings of fruit and vegetables a day)
- Increase intake of fish
- Cut down salt intake to less than one teaspoon a day

#### Physical Activity
- Active lifestyle with moderate-intensity physical activity

### Table 35: Dyslipidaemia Screening, Diagnosis, and Initial Management for HIV-Infected Individuals

#### Screening
- Fasting lipid profile should be evaluated at baseline for all PLHIV, then annually if baseline screening is normal

#### Diagnosis
- Dyslipidaemia is defined as high fasting total cholesterol (>5.2mmol/L), LDL (>3.4mmol/L) or triglycerides (>2.2mmol/L)

#### Management
- Lifestyle modifications for 3-6 months
- If the patient is on an ARV known to cause or exacerbate dyslipidaemia (primarily LPV-r) then consider a single-drug substitution to a more lipid-friendly drug (such as from LPV-r to ATV-r) as the treatment of choice before adding a lipid-lowering drug.
- If does not meet treatment target with lifestyle modifications, then add drugs:
  - Atorvastatin: starting dose of 10mg OD (maximum dose 20mg if patient is on a PI/r and a maximum dose of 80mg once daily if not on a PI/r)
  - Allow at least 3 months before repeating fasting lipids and titrating dose
- Once targets achieved can monitor lipids every 6-12 months
# TABLE 36: HYPERTENSION SCREENING, DIAGNOSIS, AND INITIAL MANAGEMENT FOR HIV-INFECTED INDIVIDUALS

<table>
<thead>
<tr>
<th>Screening</th>
<th>BP should be measured and recorded at every visit</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diagnosis</td>
<td>Hypertension requiring intervention is defined as BP ≥140/90mmHg on at least two different occasions. It can also be diagnosed at the same visit if the BP is 180/110 or any BP associated with target organ damage.</td>
</tr>
<tr>
<td>Management</td>
<td>If baseline BP is 140-159/90-99:</td>
</tr>
<tr>
<td></td>
<td>• Lifestyle modifications for at least 6 months, along with monthly BP monitoring</td>
</tr>
<tr>
<td></td>
<td>• If does not meet treatment target with lifestyle modifications, then add drugs:</td>
</tr>
<tr>
<td></td>
<td>✓ Introduce 1 drug at a time, and allow 2-3 weeks to achieve maximal effect before titrating up dosage; titrate to maximum dosage before adding an additional drug</td>
</tr>
<tr>
<td></td>
<td>✓ In PLHIV without kidney disease or diabetes, first-line antihypertensive therapy is a thiazide diuretic such as Hydrochlorothiazide starting at 12.5mg OD (maximum dose 25mg OD) OR a calcium channel antagonist such as Amlodipine starting at 2.5mg OD (maximum 10mg OD)</td>
</tr>
<tr>
<td></td>
<td>✓ In PLHIV with kidney disease or diabetes the first antihypertensive should be an ACE-I or ARB such as Enalapril 2.5-10mg OD (maximum dose is 20mg BD); Losartan 50mg OD (maximum dose is 100mg OD)</td>
</tr>
<tr>
<td></td>
<td>✓ If inadequate response once dose has been titrated, an additional agent may be required (e.g., Hydrochlorothiazide starting at 12.5mg OD [maximum dose 25mg OD])</td>
</tr>
<tr>
<td></td>
<td>✓ If inadequate response to two agents, consider consultation with or referral to a clinician experienced in the management of refractory hypertension. Note: Calcium-channel blockers have known drug interactions with PIs and NNRTIs and should be used with caution</td>
</tr>
<tr>
<td></td>
<td>• If baseline BP ≥160/100mmHg: initiate lifestyle modifications and introduce anti-hypertensive medications concurrently</td>
</tr>
</tbody>
</table>

- Target BP measurements:
  - Diabetic patients: <140/90
  - None Diabetic & Chronic Kidney Disease (CKD) patients: 140/90
  - None Diabetics & None CKD patients: <140/90 (<60 years); 150/90 (>60 years old)
# Table 37: Type 2 Diabetes Mellitus Screening, Diagnosis, and Initial Management for HIV-Infected Individuals

<table>
<thead>
<tr>
<th>Screening</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blood glucose (fasting or random) should be evaluated at baseline for all PLHIV, then annually if baseline screening is normal; urine dipstick for protein and glucose can be used if blood glucose testing is not available</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diabetes Mellitus is defined as fasting blood sugar ≥7.0mmol/L, or random blood sugar ≥11.1mmol/L, or HbA1C &gt;6.5%</td>
</tr>
<tr>
<td>Abnormal results should be repeated to confirm the diagnosis</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Management (treatment target is HbA1C ≤7.0% or FBS 4-7mmol/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Monitor HbA1c (or FBS if HbA1c not available) every 3 months for patients with confirmed diagnosis of diabetes mellitus</td>
</tr>
<tr>
<td>Lifestyle modifications (weight loss, nutritional support to manage portion sizes and calculate glycaemic index of various foods to help with control of blood sugar) for 3-6 months</td>
</tr>
<tr>
<td>If does not meet treatment target with lifestyle modifications, then add drugs:</td>
</tr>
<tr>
<td>✓ Metformin</td>
</tr>
<tr>
<td>✓ Obtain baseline Creatinine; do NOT use Metformin if creatinine clearance &lt;45mL/min</td>
</tr>
<tr>
<td>✓ Start with low dose (500mg OD or BD) and titrate up every 1-2 weeks until reaches 1g BD (or maximum tolerated dose if less than 1g BD)</td>
</tr>
<tr>
<td>✓ If does not meet treatment targets with Metformin for 3-6 months at maximum tolerated dose, then consider adding oral drugs from another class (such as glyburide) and/or specialist consultation. Some patients may require Insulin</td>
</tr>
<tr>
<td>At every visit: A thorough history (to elicit features of hypoglycaemia, other cardiovascular disease risk factors, neuropathy, diabetic foot ulcers) and a physical exam (for BP, neuropathy, foot ulcers)</td>
</tr>
<tr>
<td>Additional routine screening for patients with diabetes:</td>
</tr>
<tr>
<td>✓ Annual ophthalmology examination for diabetic retinopathy</td>
</tr>
<tr>
<td>✓ Annual urinalysis: start on an ACE-I/ARB if proteinuria develops (even if BP normal)</td>
</tr>
<tr>
<td><strong>Screening</strong></td>
</tr>
<tr>
<td>---------------------------------------------------</td>
</tr>
<tr>
<td>• Urinalysis (for protein) and serum creatinine should be evaluated at baseline for all PLHIV</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>Diagnosis</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>• Impaired renal function is defined as creatinine clearance &lt; 50mL/min, or dipstick proteinuria ≥ 1</td>
</tr>
<tr>
<td>• Abnormal results should be repeated to confirm diagnosis</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>Management</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>• Management depends on the cause of the renal impairment; additional investigations and/or specialist consultation may be required</td>
</tr>
<tr>
<td>• Treat dehydration promptly and aggressively</td>
</tr>
<tr>
<td>• If on TDF-containing regimen, substitute with another ARV, with the exception of patients with HBV/HIV co-infection who need TDF to be maintained on adjusted doses or switch to Entecavir (see section on Hepatitis B/HIV co-infected)</td>
</tr>
<tr>
<td>• Avoid nephrotoxic drugs</td>
</tr>
<tr>
<td>• Evaluate for and treat hypertension</td>
</tr>
<tr>
<td>• All NRTIs except ABC require dose adjustments for renal impairment, depending on the severity. NNRTIs, PIs, and Integrase Strand Transfer Inhibitors (INSTIs) do not require dose adjustments for impaired renal function</td>
</tr>
</tbody>
</table>
CERVICAL CANCER AND HIV

Cervical cancer is preventable and is curable if diagnosed and treated early. All women regardless of age should be assessed for cervical cancer; women living with HIV have a higher risk of pre-cancer and invasive cancer. Cervical cancer screening leads to early detection with HPV test or visual inspection with acetic acid (VIA).

Terminal Illness/Cancer and HIV

- Palliative care aims to relieve suffering in all stages of disease and is not limited to end-of-life care. The goals of palliative care include:
  - To improve the quality of life
  - To increase comfort
  - To promote open communication for effective decision making
  - To promote dignity
  - To provide a support system to the person who is ill and those close to them

In HIV-infected individuals, palliative care focuses on symptom management and end-of-life care. Throughout all stages of HIV disease, including when on cART, individuals may experience various forms of pain and other discomfort. HCWs should identify and treat the underlying cause when possible, while controlling the pain. Effective management of side effects and possible overlapping cART-associated toxicities is important to support adherence.
The care of the terminally ill child is a particular challenge in Zambia because there are few replicable models of planned terminal care, both institutional and community-based. At the end of life, there are typically more symptoms that must be addressed, and the child may need to take multiple drugs to control and treat a variety of symptoms and conditions.

Terminal care preparation for children and their families is a long-term process and requires continuity of care through providers and services. Families must be involved in decisions about the best place for care and the preferred place of death in the child with end-stage HIV disease.

**Table 39: Recommended Tests for HIV Screening and Monitoring for Co-infections and NCDs**

<table>
<thead>
<tr>
<th>Phase of HIV Management</th>
<th>Recommended</th>
<th>Desirable (<em>if feasible</em>)</th>
</tr>
</thead>
</table>
| HIV Diagnosis           | • HIV testing (serology for adults and children 18 months or older: NAT or children younger than 18 months  
                         • Screen for TB  
                         • CD4 cell count (assess CTX)                                             | • HBV or HCV serology  
                         • Screening for STIs  
                         • Hb or FBC  
                         • Pregnancy test (woman of reproductive age)  
                         • HPV test or visual inspection with acetic acid (VIA) in sexually active adolescent or woman  
                         • Syphilis test (adolescent or adult)  
                         • NCDs risk factors: cholesterol, glucose, and triglycerides |
| cART Initiation         | • Hb  
                         • Pregnancy test (woman of reproductive age)  
                         • BP measurement  
                         • Serum creatinine (for starting TDF)  
                         • Baseline CD4                                                              |                                                        |
| Receiving cART          | • Viral load (at 6 months, 12 months after initiating cART and every 12 months thereafter) | • Pregnancy test, especially for women of childbearing age not receiving family planning or on treatment with TDF+XTC+EFV-400mg  
                         • Serum creatinine for TDF                                                  |                                                        |
| Suspected Treatment Failure | • Serum creatinine for TDF  
                         • Pregnancy test, especially for women of childbearing age not receiving family planning or on treatment with TDF+XTC+EFV-400mg  
                         • And review CTX adherence  
                         • Initiate cART if eligible  
                         • Adherence counseling and positive health dignity and prevention (PHDP) messages | • HBV (HBsAg) serology (for HIV/HBV co-infected already using TDF and develop ART failure, TDF should be maintained regardless of selected second-line regimen) |

*Reference 2016 WHO Guidelines*
**Prophylaxis**

**Tuberculosis Isoniazid Preventive Therapy (TB-IPT)**

These guidelines focus on key interventions branded as the THREE I’s (Intensive case finding, Isoniazid prophylaxis therapy, Infection control for TB) for HIV-TB activities that reduce TB-related morbidity and mortality in HIV-infected individuals. Another key intervention is the provision of cART.

Daily TB-IPT can prevent TB in people who are at a high risk for developing TB, including HIV-infected individuals.

- Screen all patients for TB at any opportunity that presents (see Figure 15)
- Screen all pregnant and breastfeeding women, regardless of HIV status, for TB at every contact as it is part of Focused ANC
- Screen all children for TB at every contact
- Give TB-IPT for 6 months to the following:
  - HIV-infected children <12 months old with TB contact and after ruling out active TB
  - Newly HIV-infected pregnant and breastfeeding women, children ≥12 months old, adolescents, and adults after ruling out active TB
  - After completing a full course of ATT, HIV-infected children should be given an additional IPT x 6 months
- Do not give IPT to a patient who has any signs suggestive of active TB. This patient needs full investigation for TB and combination TB treatment if confirmed to avoid TB drug resistance.

- **Standard TB screening questions include:**
  - Current cough: any duration, productive or non-productive
  - Unexplained weight loss (adults)
  - Failure to thrive and/or malnutrition (children)
  - Fever or night sweats

- **Contraindications and/or when to Stop IPT:**
  - Suspected or confirmed active TB (start ATT)
  - Jaundice and/or icterus (yellow eyes) or active hepatitis
  - Known or suspected hypersensitivity to INH or severe skin rash
  - Confusion/convulsions
  - Dizziness
  - Peripheral neuropathy i.e. Severe numbness/burning pain and muscular weakness of legs and/or arms
  - Concomitant medication: Phenytoin, Carbamazepine, Warfarin, Theophylline, Selective Serotonin Re-uptake Inhibitor antidepressants (e.g. Fluoxetine, Paroxetine) oral Ketoconazole or Itraconazole

- **How to give IPT**
  - Give IPT during pre-cART period and to HIV-infected children <12 months old with TB contact and after ruling out active TB
  - Review and assess for side effects at months 1, 3, and 6 after starting IPT
  - IPT initiation: Give INH and Pyridoxine for 1 month
  - Month 1: Give INH and Pyridoxine for 2 months
  - Month 3: Give INH and Pyridoxine for 3 months
  - Give concomitant Pyridoxine (vitamin B6) 1 tablet 25mg once daily to prevent side effects of Isoniazid in pregnant and breastfeeding women, adolescents, and adults.
### TABLE 40: DOSAGE FOR ISONIAZID PREVENTATIVE THERAPY, CO-TRIMOXAZOLE PROPHYLAXIS, AND COMBINATION INH/CTX/VIT B6 DRUGS

<table>
<thead>
<tr>
<th>Drug</th>
<th>Child tablet or oral suspension</th>
<th>Number of scoops or tablets by weight band</th>
<th>Adult tablet</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>3 to &lt; 6kg</td>
<td>6 to &lt; 10kg</td>
</tr>
<tr>
<td>Isoniazid (INH)</td>
<td>100mg</td>
<td>0.5</td>
<td>1</td>
</tr>
<tr>
<td>Co-trimoxazole (CTX)</td>
<td>Suspension 200/40mg per mL</td>
<td>2.5 mL</td>
<td>5 mL</td>
</tr>
<tr>
<td></td>
<td>Tablet 100/80mg</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>Tablet 400/80mg</td>
<td>NA*</td>
<td>1/2</td>
</tr>
<tr>
<td>Pyridoxine (Vitamin B6)</td>
<td>Tablet 800/160mg</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td></td>
<td>Tablet 25mg</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>INH/CTX/Vit B6</td>
<td>Tablet 300/960/25mg</td>
<td>NA</td>
<td>NA</td>
</tr>
</tbody>
</table>

*NA = Not Applicable

**Co-trimoxazole Preventive Therapy (CPT)**

CPT prevents Pneumocystis Jirovecii Pneumonia (PCP), toxoplasmosis, isosporiasis, malaria, and other HIV- and non-HIV related diseases and prolongs survival. CPT can be safely taken with cART and/or ATT and in pregnancy (Table 17 and Table 18). HIV-infected pregnant women on CPT should not be given Sulfadoxine-Pyrimethamine (SP; malaria prophylaxis in pregnancy).
### TABLE 41: CRITERIA FOR INITIATING, DISCONTINUING, AND MONITORING CO-TRIMOXAZOLE PREVENTIVE THERAPY

<table>
<thead>
<tr>
<th>Specific populations</th>
<th>Whom to Start</th>
<th>When to Start</th>
<th>When to Stop*</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Pregnant &amp; Breastfeeding Women</strong></td>
<td>Pregnant women</td>
<td>Start as early as possible. Do not give SP. If SP taken, start CTX after 14 days.</td>
<td>Continue throughout pregnancy</td>
</tr>
<tr>
<td></td>
<td>Breastfeeding women</td>
<td>Continue if CD4 count &lt;350 cells/µL or WCS 2, 3 or 4</td>
<td>CD4 count ≥350 cells/µL for two consecutive values at least 6 months apart while on cART</td>
</tr>
<tr>
<td><strong>Children (0 to &lt;5 years old)</strong></td>
<td>HIV-exposed (e.g. breastfed) child</td>
<td>At 6 weeks old or first contact</td>
<td>Confirmed HIV-uninfected after full cessation of breastfeeding</td>
</tr>
<tr>
<td></td>
<td>HIV-infected child &lt;24 months old</td>
<td>Start regardless of WCS or CD4%</td>
<td>At 5 years old and CD4 ≥25% and Stage I</td>
</tr>
<tr>
<td></td>
<td>HIV-infected child ≥24 months old to &lt;5 years old</td>
<td>WCS 2, 3 and 4 or CD4 level &lt;25%</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Presumptive HIV diagnosis &lt;18 months old</td>
<td>Start (or continue) regardless of WCS or CD4%</td>
<td>Stop if confirmed HIV negative; if infected, stop at 5 years old and CD4 level ≥25% and Stage I</td>
</tr>
<tr>
<td></td>
<td>Child with a history of PCP</td>
<td>Start regardless of CD4 count or CD4%</td>
<td>At 5 years old and CD4 level ≥25% and Stage I</td>
</tr>
<tr>
<td></td>
<td>HIV-infected children ≥5 years old, adolescents, and adults</td>
<td>CD4 count &lt;350 cells/µL or WCS 2, 3 or 4</td>
<td>CD4 count ≥350 cells/µL for two consecutive values at least 6 months apart while on cART</td>
</tr>
</tbody>
</table>

Stop CTX if the person has Stevens-Johnson syndrome, severe liver disease, severe anaemia, severe pancytopaenia, or HIV negative status.

CPT contraindications: severe allergy to sulfa drugs; severe liver disease, severe renal disease, and glucose-6-phosphate dehydrogenase (G6PD) deficiency and in these conditions DO NOT re-challenge.
Following diagnosis and throughout the spectrum of care, HIV services should be tailored to respond to specific challenges or barriers faced by patients and aim to offer high quality care, client satisfaction and improved health outcomes. In order to ensure timely linkage to care and follow up for all people living with HIV a package of differentiated interventions should be offered to clients.

**Figure 21: HIV Implementation Cascade for the Continuum of Care**

**Recommendations**

- Diversify interventions to ensure timely linkage to HIV Services
- Patient-centeredness to allow for delivery of care based on people’s needs, preferences, clinical characteristics, and context
- Special considerations for Priority and Key Populations
- Task-shifting and investment in staff training and development
- Service delivery should be across the HIV continuum of care
- Establish effective systems for monitoring patients in care
The Ministry of Health (MoH) of the Republic of Zambia is committed to achieving the 90-90-90 targets and is aware that innovative strategies are needed in order to end the HIV epidemic. Critical to this is to ensure the provision of HIV treatment to all. Continuing to provide services in the same way for all clients will not allow for the achievement of reaching 90-90-90 targets. MOH is aware that the conventional human resources and physical infrastructure currently are not adequate to accommodate national scale up of ART. Differentiated service delivery (DSD) is a client-centered approach that simplifies and adapts HIV services across the cascade in order to reflect the preference and expectations of various groups of PLHIV while also reducing unnecessary burdens on the health system.

The MOH supports the promotion and provision of various differentiated service delivery models in order to lessen the burden of care for both patients and providers and to allow the health system to refocus resources on those patients in most need.

**PRINCIPLES OF DIFFERENTIATED CARE**

The principals of DSD are aimed at supporting the achievement of 90-90-90 targets while also improving the quality of care clients receive.

1. **Patient Centeredness**

To allow for delivery of care based on people's needs, preferences and expectations with the aim of empowering clients to manage their disease with support from the health system.

2. **Health System Efficiency**

Ensure the health system is functioning with the highest efficiency. For this to be achieved, investment in human resources for health and infrastructure upgrade is required.
BUILDING BLOCKS OF ART DIFFERENTIATED SERVICE DELIVERY MODELS

The building blocks are key components of a service delivery model and address the ‘when, where, who, and what’ of HIV services and should be used for whichever characteristic(s) (clinical, specific, populations, context) are being considered. At each step in the treatment cascade, DSD models should be designed and implemented as a direct response to specific challenges or barriers identified for clients and health care workers.

Patient Classification for Differentiated Services Delivery

DSD should be provided to all PLHIV across the HIV cascade and extended to other diseases. A growing number of people receiving ART are virally suppressed (stable) and do not require frequent visits to the Health Facility. Offering DSD models of care reduces the burden of frequent visits to the facility for stable clients and allows for resources to be redistributed to patients most in need.

Stable client is defined as follows;

- On cART for at least >6 months
- No adverse drug reactions
- No current illnesses or pregnancy
- Proven record of good adherence and evidence of treatment success
- Viral suppression below 1000 copies /mL within the last 12 months
Unstable client is defined as follows:

- On cART for < 6 months
- On cART for > 6 months but presenting with advanced HIV disease
- CD4 <200
- WHO stage 3 or 4 event
- All children younger than five years old with HIV are considered as having advanced HIV disease
- Not virally suppressed
- Advanced immunosuppression
- Adverse drug reactions
- Active opportunistic infection
- Non-adherent to cART
- Substance use
- Mental illness
- Any other uncontrolled chronic condition/comorbidity like NCDs

Categories of DSD

DSD models can be categorized into four models: ([www.differentiatedcare.org](http://www.differentiatedcare.org))

1. Health care worker managed Group:
   - Clients receive their cART refills in a group and either a professional or a lay health care worker manages this group (e.g., Urban Adherence Groups/Clubs) Health care worker-managed groups meet within and/or outside of health care facilities.

2. Client Managed Groups
   - Clients receive their cART refills in a group but this group is managed and run by clients themselves (e.g. Community Adherence Groups (CAGs). Generally, client- managed groups meet outside of health care facilities.

3. Out of Facility Managed Individuals
   - cART refills and are provided to individuals outside of health care facilities (e.g., of Health Post Dispensation, Home delivery and Community based drug pick-ups)

4. In-Facility Managed Models
   - cART refill visits are separated from clinical consultations. When clients have a cART refill visit, they bypass any clinical staff or adherence support and proceed directly to receive their medication (e.g., appointment spacing and “fast-track”)

DSD for Unstable Clients

There is limited evidence on the building blocks and models for unstable clients however, these clients may also benefit from DSD model access in supporting viral suppression and improving retention. Therefore, DSD building blocks and models should be adapted to accommodate all PLHIV.
Principles of DSD for Specific Populations (children, adolescents, pregnant and breastfeeding women)

- Family based Approach
  Important when considering care for children and their parents. Service provision models for children and their parents/caregivers should be aligned as this can improve the entire family cascade.

- Integration of Services
  Integration of HIV care with other services is a WHO recommendation to strengthen the continuum of treatment care. Integration has been highlighted as key to providing benefits to mothers and their infants, and combining adolescent HIV services with comprehensive services.

- Leveraging and encouraging psychosocial support
  The importance of psychosocial support for all PLHIV, including support from communities and peers, is of particular significance to these special populations

Approach of DSD model to be offered at any given facility should consider:

- Clinical Characteristics of the client (stability, unstable, co-morbid/co infections)
- Client preference
- Model available at the facility
### Table 42: Categorization of Services Offered at Delivery Points

<table>
<thead>
<tr>
<th>HIV/AIDS Management</th>
<th>Facility: Health Centre, Level 1, Level 2, Level 3, and Level 4</th>
</tr>
</thead>
<tbody>
<tr>
<td>- At facility level are “high risk,” i.e., Pregnant and breastfeeding women, HEI, discordant couples, newly diagnosed/initiated patients</td>
<td></td>
</tr>
<tr>
<td>- Community services to focus on “stable” patients</td>
<td></td>
</tr>
<tr>
<td>Community structures such as: Community Adherence Groups (CAGs), Treatment Clubs, Private sector, Faith based groups, Health shops, etc.</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Retention in Care:</th>
<th>Health Centre:</th>
</tr>
</thead>
<tbody>
<tr>
<td>- PMTCT sites should have functional community structure/groups affiliated with timely support and connection between health facility and community</td>
<td>- HIV testing at birth, 6 weeks, 6 months, 9 months, 12 months, 18 months, 24 months and across all populations (see Table 1)</td>
</tr>
<tr>
<td>- Interventions of mother-baby follow up through reminders for appointments, adherence support</td>
<td>- Triple prophylaxis depending on risk assessment</td>
</tr>
<tr>
<td>- Community workers and message on identifying sick infants and sending to facilities</td>
<td>- Co-trimoxazole (CTX)</td>
</tr>
<tr>
<td>- Use of current interventions to follow up patients and infants (e.g., nutritional assessment and</td>
<td>- Growth monitoring</td>
</tr>
<tr>
<td></td>
<td>- Immunization as per EPI schedule</td>
</tr>
<tr>
<td></td>
<td>- Clinical review and follow up</td>
</tr>
<tr>
<td></td>
<td>- Infant feeding counseling</td>
</tr>
<tr>
<td></td>
<td>- Ongoing HIV/AIDS counseling and screening.</td>
</tr>
<tr>
<td></td>
<td>- Uptake of newly diagnosed cases and commence ARVs</td>
</tr>
<tr>
<td></td>
<td>- Treatment of OIs as per Standard Treatment Guidelines</td>
</tr>
<tr>
<td></td>
<td>- Palliative care (pain relief and management of common illnesses)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Task Shifting and Sharing:</th>
<th>Level 1:</th>
</tr>
</thead>
<tbody>
<tr>
<td>- Less frequent clinical visits (3-6 months) being recommended for people stable on cART.</td>
<td>All of the above and:</td>
</tr>
<tr>
<td>- The use of Community cART models for pick-up of cART, while initiation and monitoring at peripheral health facilities with maintenance at community level</td>
<td>- Clinical review/examination</td>
</tr>
<tr>
<td>- Trained and supervised community health workers can dispense cART between regular clinical vests</td>
<td>- FBC, CXR, HIV +/-CD4 count, U+E, Creatinine, urinalysis, treatment, and follow up management of OIs</td>
</tr>
<tr>
<td></td>
<td>- Infant feeding counselling if referred for further management</td>
</tr>
<tr>
<td></td>
<td>- Acceptance of referral back and joint management</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Level 2:</th>
<th>All of the above and:</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>- Management of severe symptoms and investigations</td>
</tr>
<tr>
<td></td>
<td>- Urine protein creatinine ratio</td>
</tr>
<tr>
<td></td>
<td>- LFTs</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Level 3:</th>
<th>All of the above and:</th>
</tr>
</thead>
<tbody>
<tr>
<td>- VL and genotype for treatment failures</td>
<td>- Management of severe symptoms and investigations</td>
</tr>
<tr>
<td>- Metabolic complications management</td>
<td>- Urine protein creatinine ratio</td>
</tr>
<tr>
<td>- Research 3rd line management</td>
<td>- LFTs</td>
</tr>
<tr>
<td>- Triple prophylaxis depending on risk assessment</td>
<td></td>
</tr>
<tr>
<td>- Highly specialized research</td>
<td></td>
</tr>
<tr>
<td>- CTX prophylaxis</td>
<td></td>
</tr>
<tr>
<td>- Complicated cases:</td>
<td></td>
</tr>
<tr>
<td>- HIV plus co-morbidities</td>
<td></td>
</tr>
</tbody>
</table>
MANAGING THE HIV PROGRAM

Tracking and Keeping Patients in Care

Keeping patients in care is essential for achieving good outcomes and preventing resistance. Lost to follow up (LTFU), defaulting and late drug pick-ups may lead to treatment failure, emergence of resistance, and the possibility of transmitting resistant virus. Health facilities should aim to do the following to minimize LTFU:

- Have a structured plan to track patients and prevent LTFU
- Monitor all missed clinic and pharmacy visits
- Create linkages with home-based care workers and volunteers
- Dedicate health facility staff to ensure patients who miss visits are contacted

Attrition

Attrition in an HIV programme can occur as the following: late, LTFU, defaulter, death, transferred out to another facility, or unknown status.

- Late: HIV-infected individual misses a pharmacy refill visit, from 1 to <60 days after the last scheduled pharmacy visit
  - For pregnant and breastfeeding women, late is defined as missing a scheduled pharmacy visit
  - Take immediate action (e.g., CHW follow up, text message or mobile health [mHealth] follow up) and document findings. Every effort must be made to re-engage these women in care
- LTFU: HIV-infected individual is missing for ≥60 days after missed pharmacy refill visit after all active tracking interventions (e.g., documented physical follow up to home, phone calls to client and emergency contacts, text message recall, treatment buddy) have been exhausted and HIV-infected individual cannot be traced
  - For pregnant and breastfeeding women, LTFU is defined as missing for ≥60 days after last scheduled pharmacy refill visit with inability to be traced after all active tracking mechanisms have been exhausted.
- Defaulter: HIV-infected individual has been located while late or LTFU, but chooses not to return to care.
- Unknown status: all active tracking interventions have not been exhaustively done to determine current status of HIV-infected individual (for ≥60 days), see Figure 22.
**FIGURE 22: ALGORITHM FOR ACTIVE INTERVENTIONS WHEN HIV-INFECTED CLIENTS ARE LATE AND DETERMINING THEIR ATTRITION STATUS**

Patient misses a pharmacy refill appointment

**Designate patient as LATE**
Health facility must document the following clearly:
- Method of reconciling late clinic and pharmacy appointments for clients by number of days
- Active tracking interventions employed
- Feedback from tracking interventions documented in chart

**Active tracking interventions**
- Text message to client
- Phone call to client
- Home visit to client
- Contact with community worker or home base care agency
- Text message or phone contact with treatment buddy or emergency contact
- Track patient as soon as he/she has missed a pharmacy refill appointment up to 60 days

**UNKNOWN STATUS**
- No tracking intervention done

**TRANSFERRED OUT or DEAD**
- Tracking intervention done
- Results of tracking intervention: client transferred to another facility or is dead

**DEFAULTER**
- Tracking intervention done
- Results of tracking intervention: client refuses or is unable to come back to health facility

**LOST TO FOLLOW UP**
- Tracking intervention done repeatedly
- Results of tracking intervention: client not found after 60 days
Structured Plan for Tracking Patients

Ideally patients should be tracked as soon as possible after missed pharmacy pickup or clinic appointment. Each day that elapses after missed appointment could be a day without cART, and increasing the likelihood of resistance development and treatment failure. Scheduling patients for appointments and reviewing the list of patients expected on a given day is critical to tracking patients’ missed appointments. If the facility does not schedule patients, then a clear log of pharmacy refills must be reviewed daily to identify patients that have missed pharmacy pickups and are potentially out of cART medications. Once a patient is identified as missing, a plan of action for tracking must be initiated.

Monitoring and Evaluation Tools

There are many government tools to assist sites in providing comprehensive, family-centred HIV care and treatment. The standard data collection and patient care tools include documents for children, adolescents, pregnant and breastfeeding women, and adults.

- Safe Motherhood Card (with SM number)
- cART file/clinical case record with cART number and SmartCard
- Antenatal Care register
- Safe Motherhood register
- L&D register
- Postnatal Care register
- Mother Baby Follow-up register
- Community Follow-up register
- Family Planning register
- Under five cards
- Under five registers
- Early Infant Diagnosis (EID) register/log book/EID lab requisition
- Laboratory register

Wherever feasible, data regarding the continuum of HIV care and treatment should be entered into electronic health record systems (e.g. SmartCare). In addition, all facilities should record birth defects using the forms obtainable from the Zambia Medicines Regulatory Authority (ZAMRA, formerly PRA) to feed into the national Birth Defects Registry.

Use of standard tools is required by all health facilities to ensure a functioning supply chain system to avoid stock outs.

The recommended standard tools include:

- Report and Requisition (R&R) form
- Daily Activity Register
- Interval Monthly Summary Report
- Stock Control Cards
- Laboratory Usage report
- Report for Essential Medicines and Medical Supplies
Quality Improvement

Quality Improvement (QI) is a process that aims to strengthen the quality of services provided at health facilities. The QI Technical Working Group (TWG) at MOH has identified five key QI indicators that will be tracked by all levels in the health sector. Of the five indicators, two are HIV-related:

- Percentage of exposed infants tested for HIV at 9 months old
- Percentage of all HIV positive clients retained on HIV care and treatment the last 12 months
  - Number of HIV testing sites scoring ≥80% in proficiency testing
  - Number of EID testing labs scoring ≥80% in proficiency testing
  - Number of viral load testing labs scoring ≥80% in proficiency testing
  - Number of labs enrolled in the CD4 External Quality Assurance (EQA) program scoring ≥80% in proficiency testing

Lifelong cART in pregnant and breastfeeding women also enhances maternal and child survival. For this reason, the following two QI indicators are also pertinent:

- Number of maternal deaths at the facility recorded in the last 1 month, 3 months (quarter), and 12 months
- Number of under-five children who died in the last 1 month, 3 months (quarter), and 12 months. (If possible, differentiate between early neonatal death, neonatal death, infant death, and under-five death)

Through structures that have been formed at all levels, the QI committees review these indicators regularly to identify performance gaps and root causes using the Performance Improvement Approach (PIA). This should be followed by implementation of appropriate interventions coupled with regular monitoring and evaluation to track progress.

These indicators will be reported through the Health Management Information System (HMIS), as well as tracked through the QI reporting structures from the health facility to the national level QI TWG. QI committees at any level should not be restricted to implement QI projects only related to the key indicators. Other areas of underperformance in health service delivery should be covered at the local level as identified with stakeholders, including clients and the community.

Mentoring and Supervision

Mentorship is a QI strategy that provides motivation to HCWs while building their knowledge and skills base.

In collaboration with cooperating partners, MoH developed national guidelines and a mentorship training package. The multidisciplinary Clinical Care Teams (CCT) at national, provincial, and district level spearhead mentorship and supervision of health facility staff. CCTs comprise clinicians, nurses, nutritionists, pharmacy staff, and laboratory staff and hold regular meetings to review HMIS reports, performance assessment reports, and any other source of information to identify performance gaps in health service delivery, including HIV care and treatment and PMTCT. Appropriate mentors are assigned from the CCT to conduct targeted, needs-based mentorship for QI. Request for specialized mentorship from higher level CCTs is encouraged. The multi-disciplinary approach achieves the following:

- Comprehensive coverage of clinical and support systems, including logistical and health information management
- Coordination, continuity, and availability of a pool of highly experienced mentors in the relevant fields
- Strengthened institutionalized, decentralized system of mentorship
## APPENDIX 1: DOSAGES OF ANTIRETROVIRALS FOR ADULTS AND ADOLESCENTS

### a) DOSAGES OF ANTIRETROVIRALS FOR ADULTS AND ADOLESCENTS

<table>
<thead>
<tr>
<th>Drug</th>
<th>Normal Dose</th>
<th>Renal Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abacavir (ABC)</td>
<td>Adult: 300mg BID PO Paediatrics: 8mg/kg BID PO</td>
<td>No adjustment</td>
</tr>
<tr>
<td>Atazanavir-r</td>
<td>Adult: 300/100mg OD PO Paediatrics: paediatric dosing by weight bands. No data for children &lt;6 years old.</td>
<td>No adjustment</td>
</tr>
<tr>
<td>Darunavir-r</td>
<td>Adult: 600/100mg BID PO Paediatrics: see paediatric dosing by weight bands. Do not use in children &lt;3 years old.</td>
<td>No adjustment</td>
</tr>
<tr>
<td>Dolutegravir (DTG)</td>
<td>Adult: 50mg OD PO No sufficient data for use in adolescents younger than 12 years old</td>
<td>No adjustment</td>
</tr>
<tr>
<td>Efavirenz (EFV)</td>
<td>Pregnant and/or breastfeeding: 400mg OD PO 600mg OD PO</td>
<td>No adjustment</td>
</tr>
<tr>
<td>Emtricitabine (FTC)</td>
<td>Adult: 200mg OD PO Pediatrics: 0-3 months old: 3 mg/kg/day (solution) 3 months-15 years old (&gt;33kg): 6mg/kg/day (solution; max 240mg daily) or capsule: 200mg OD (capsule)</td>
<td>Adul: CrCl 30-49: 200mg every 48 hours CrCl 15-29: 200mg every 72 hours CrCl &lt;15: 200mg every 96 hours (give after hemodialysis if on dialysis) Paediatrics: reduce dose or increase dosing interval following adult recommendations in consultation with experienced clinician in renal dosing</td>
</tr>
<tr>
<td>Etravirine (ETR)</td>
<td>Adult: 200mg BID PO Paediatrics: see paediatric dosing by weight bands. Not approved for children &lt;6 years old (approval under way for 2 months to 6 year old). • 16kg&lt;20kg: 100mg twice daily • 20kg&lt;25kg: 125mg twice daily • 25kg&lt;30kg: 150mg twice daily</td>
<td>No adjustment</td>
</tr>
<tr>
<td>Drug</td>
<td>Adult Dosing</td>
<td>Paediatric Dosing</td>
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<tr>
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<td>------------------------------------------------------------------------------</td>
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<tr>
<td>Lamivudine (3TC)</td>
<td>Adult: 150mg BID or 300mg OD PO</td>
<td>Paediatrics: 2-4mg/kg BID PO</td>
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<tr>
<td>Lopinavir</td>
<td>Adult: 400/100 BID PO</td>
<td>Paediatrics: 10-13mg/kg BID PO for Lopinavir component</td>
</tr>
<tr>
<td>Nevirapine (NVP)</td>
<td>Adult: 200mg OD PO x 14 days then 200mg BID PO</td>
<td>Paediatrics: 4-7mg/kg BID PO</td>
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<tr>
<td>Tenofovir</td>
<td>Adult: 25mg OD PO</td>
<td>Paediatrics: not approved for adolescents less than 12 years old</td>
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<tr>
<td>Alafenamide (TAF)</td>
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<tr>
<td>Tenofovir (TDF)</td>
<td>Adult: 300mg OD PO Paediatrics: 8mg/kg OD PO</td>
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<tr>
<td>Raltegravir (RAL)</td>
<td>Adult: 400mg BID PO (with Rifampicin 800mg BID PO)</td>
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<tr>
<td>Zidovudine (AZT)</td>
<td>Adult: 300mg BID PO</td>
<td>Paediatrics: see paediatric dosing by weight bands.</td>
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</table>
b) SIMPLIFIED DOSING OF CHILD-FRIENDLY FIXED DOSE SOLID FORMULATIONS FOR TWICE DAILY DOSING FOR INFANTS AND CHILDREN 4 WEEKS OF AGE AND OLDER

<table>
<thead>
<tr>
<th>Drug</th>
<th>Strength of tablet</th>
<th>Number of tablets by Weight band morning and evening</th>
<th>Strength of adult tablet (mg)</th>
<th>Number of tablets by Weight band</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>AM PM AM PM AM PM AM PM AM PM AM PM</td>
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<td>AM PM</td>
</tr>
<tr>
<td>Zidovudine/Lamivudine AZT+3TC</td>
<td>Tablet (dispersible) 60mg/30mg</td>
<td>1 1 1.5 5 2 2 2.5 5 3 3</td>
<td>300mg/150mg</td>
<td>1 1</td>
</tr>
<tr>
<td>Zidovudine/Lamivudine/ Nevirapine AZT+3TC+NVP</td>
<td>Tablet (dispersible) 60mg/30mg/50mg</td>
<td>1 1 1.5 5 2 2 2.5 5 3 3</td>
<td>300mg/150mg/200mg</td>
<td>1 1</td>
</tr>
<tr>
<td>Abacavir/Lamivudine ABC+3TC</td>
<td>Tablet (dispersible) 60mg/30mg</td>
<td>1 1 1.5 5 2 2 2.5 5 3 3</td>
<td>600mg/300mg</td>
<td>1 1</td>
</tr>
<tr>
<td>Abacavir/Lamivudine ABC+3TC</td>
<td>Tablet (dispersible) 120mg/60mg</td>
<td>0.5 0.5 1 1 1 1 1.5 1.5 1.5</td>
<td>600mg/300mg</td>
<td>1 1</td>
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</tbody>
</table>
### c) Simplified dosing of child-friendly fixed dose solid and oral liquid formulations for once daily dosing for infants and children 4 weeks of age and older

<table>
<thead>
<tr>
<th>Drug</th>
<th>Strength of tablet (mg)</th>
<th>Number of tablets by Weight band</th>
<th>Strength of adult tablet (mg)</th>
<th>Number of tablets by Weight band</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>3.0-5.9 kg</td>
<td>6.0-9.9 kg</td>
<td>10.0-13.9 kg</td>
<td>14.0-19.9 kg</td>
</tr>
<tr>
<td>Efavirenz (EFV)</td>
<td>Tablet (scored) 200mg</td>
<td>-</td>
<td>PM</td>
<td>PM</td>
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<tr>
<td>Abacavir/Lamivudine ABC+3TC</td>
<td>Tablet (dispersible) 60mg/30mg</td>
<td>2</td>
<td>3</td>
<td>1</td>
</tr>
<tr>
<td>Abacavir/Lamivudine ABC+3TC</td>
<td>Tablet (dispersible) 120mg/60mg</td>
<td>1</td>
<td>1.5</td>
<td>2</td>
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<tr>
<td>Atazanavir (ATV)</td>
<td>Capsules 100mg Oral powder scoops 40mg/scoop</td>
<td>-</td>
<td>-</td>
<td>1</td>
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<tr>
<td></td>
<td>Tablet 150mg or 200mg</td>
<td>-</td>
<td>-</td>
<td>-</td>
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<td></td>
<td></td>
<td>-</td>
<td>-</td>
<td>1(150mg)</td>
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</table>
### Simplified Dosing of Child-Friendly Fixed Dose Solid and Oral Liquid Formulations for Twice Daily Dosing for Infants and Children 4 Weeks of Age and Older

#### Strength of Tablet (mg) or Oral Liquid (mg/mL)

<table>
<thead>
<tr>
<th>Drug</th>
<th>Strength of Tablet (mg) or Oral Liquid (mg/mL)</th>
<th>Number of Tablets or mL by Weight Band</th>
<th>Strength of Adult Tablet (mg)</th>
<th>Number of Tablets by Weight Band</th>
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<tr>
<td></td>
<td></td>
<td>morning and evening</td>
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<tr>
<td></td>
<td></td>
<td>3.0-5.9 kg</td>
<td>6.0-9.9 kg</td>
<td>10.0-13.9 kg</td>
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<tr>
<td>Zidovudine (AZT)</td>
<td>Tablet (dispersible) 60mg</td>
<td>1</td>
<td>1</td>
<td>1.5</td>
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<tr>
<td>Abacavir (ABC)</td>
<td>Tablet (dispersible) 60mg</td>
<td>1</td>
<td>1</td>
<td>1.5</td>
</tr>
<tr>
<td>Nevirapine (NVP)</td>
<td>Tablet (dispersible) 50mg</td>
<td>1</td>
<td>1</td>
<td>1.5</td>
</tr>
<tr>
<td>Lopinavir/ritonavir (LPV-r)</td>
<td>Tablet 100mg/25mg</td>
<td>-</td>
<td>-</td>
<td>-</td>
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<tr>
<td></td>
<td>Pellets 40mg/10mg</td>
<td>2</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>Darunavir (DRV)</td>
<td>Tablet 75mg</td>
<td>-</td>
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</tr>
<tr>
<td>Raltegravir (RAL)</td>
<td>Chewable tablets 25mg</td>
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</tr>
<tr>
<td></td>
<td>Chewable tablets 100mg</td>
<td>-</td>
<td>-</td>
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</tr>
<tr>
<td></td>
<td>Granules (100mg/sachet)</td>
<td>0.25</td>
<td>0.25</td>
<td>0.5</td>
</tr>
<tr>
<td>Zidovudine (AZT)</td>
<td>10mg/mL</td>
<td>6mL</td>
<td>6mL</td>
<td>9mL</td>
</tr>
<tr>
<td>Abacavir (ABC)</td>
<td>20mg/mL</td>
<td>3mL</td>
<td>3mL</td>
<td>4mL</td>
</tr>
<tr>
<td>Lamivudine (3TC)</td>
<td>10mg/mL</td>
<td>3mL</td>
<td>3mL</td>
<td>4mL</td>
</tr>
<tr>
<td>Nevirapine (NVP)</td>
<td>10mg/mL</td>
<td>5mL</td>
<td>5mL</td>
<td>8mL</td>
</tr>
<tr>
<td>Lopinavir/ritonavir (LPV-r)</td>
<td>80/20mg/mL</td>
<td>1mL</td>
<td>1mL</td>
<td>1.5mL</td>
</tr>
<tr>
<td>Darunavir (DRV)</td>
<td>100mg/mL</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>
e) **Drug Dosing of Liquid Formulations for Twice Daily Dosing of Infants Younger than 4 Weeks of Age**

<table>
<thead>
<tr>
<th>Drug</th>
<th>Strength of oral liquid (mg/mL)</th>
<th>2-3 kg</th>
<th>3-4 kg</th>
<th>4-5 kg</th>
</tr>
</thead>
<tbody>
<tr>
<td>Zidovudine (AZT)</td>
<td>10mg/mL</td>
<td>1mL</td>
<td>1.5mL</td>
<td>2mL</td>
</tr>
<tr>
<td>Nevirapine (NVP)</td>
<td>10mg/mL</td>
<td>1.5mL</td>
<td>2mL</td>
<td>3mL</td>
</tr>
<tr>
<td>Lamivudine (3TC)</td>
<td>10mg/mL</td>
<td>0.5mL</td>
<td>0.8mL</td>
<td>1mL</td>
</tr>
<tr>
<td>Lopinavir/ritonavir (LPV-r)</td>
<td>80/20mg/mL</td>
<td>0.6mL</td>
<td>0.8mL</td>
<td>1mL</td>
</tr>
</tbody>
</table>

f) **Simplified Weight Band Dosing Schedule for LPV-R**

<table>
<thead>
<tr>
<th>Weight band (kg)</th>
<th>Number of LPV-r oral pellets 40mg/10mg capsules</th>
<th>LPV-r 80mg/20mg/mL oral liquid</th>
<th>Number of LPV-r 100mg/25mg tablets</th>
</tr>
</thead>
<tbody>
<tr>
<td>AM</td>
<td>PM</td>
<td>AM</td>
<td>PM</td>
</tr>
<tr>
<td>3 – 4.9kg*</td>
<td>2</td>
<td>2</td>
<td>1mL</td>
</tr>
<tr>
<td>5 – 5.9kg</td>
<td>2</td>
<td>2</td>
<td>1mL</td>
</tr>
<tr>
<td>6 – 9.9kg</td>
<td>3</td>
<td>3</td>
<td>1.5mL</td>
</tr>
<tr>
<td>10 – 13.9kg</td>
<td>4</td>
<td>4</td>
<td>2mL</td>
</tr>
<tr>
<td>14 – 19.9kg</td>
<td>5</td>
<td>5</td>
<td>2.5mL</td>
</tr>
<tr>
<td>20 – 24.9kg</td>
<td>6</td>
<td>6</td>
<td>3mL</td>
</tr>
<tr>
<td>25 – 29.9kg</td>
<td>7</td>
<td>7</td>
<td>NR</td>
</tr>
<tr>
<td>30 – 34.9kg</td>
<td>8</td>
<td>8</td>
<td>NR</td>
</tr>
</tbody>
</table>

NR = NOT RECOMMENDED

*Adapted from Cipla package insert approved by USFDA and WHO 2013 dosages of recommended antiretroviral drugs

g) **Dosing of EFV for HIV-infected Children (≥3 Month Old)**

<table>
<thead>
<tr>
<th>Body Weight</th>
<th>Daily Dose</th>
<th>Number of Capsules or Tablets and Strength</th>
</tr>
</thead>
<tbody>
<tr>
<td>3.5 to &lt;5kg</td>
<td>100mg</td>
<td>2 x 50mg capsules</td>
</tr>
<tr>
<td>5 to &lt;7.5kg</td>
<td>150mg</td>
<td>3 x 50mg capsules</td>
</tr>
<tr>
<td>7.5 to &lt;15kg</td>
<td>200mg</td>
<td>1 x 200mg capsule</td>
</tr>
<tr>
<td>15 to &lt;20kg</td>
<td>250mg</td>
<td>1 x 200mg capsule + 1 x 50mg capsule</td>
</tr>
<tr>
<td>20 to &lt;25kg</td>
<td>300mg</td>
<td>1 x 200mg capsule + 2 x 50mg capsules</td>
</tr>
<tr>
<td>25 to &lt;32.5kg</td>
<td>350mg</td>
<td>1 x 200mg capsule + 3 x 50mg capsules</td>
</tr>
<tr>
<td>32.5 to &lt;40kg</td>
<td>400mg</td>
<td>2 x 200mg capsules</td>
</tr>
<tr>
<td>≥40kg</td>
<td>600mg</td>
<td>1 x 600mg capsule OR 3 x 200mg capsules</td>
</tr>
</tbody>
</table>
### APPENDIX 2: Key Drug-Drug Interaction for ARVs

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<tr>
<th></th>
<th>ABC</th>
<th>TDF</th>
<th>AZT</th>
<th>3TC</th>
<th>FTC</th>
<th>d4T</th>
<th>ATV</th>
<th>LPV</th>
<th>RTV</th>
<th>EFV</th>
<th>NVP</th>
<th>DTG</th>
<th>RAL</th>
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<td><strong>Antibiotics (incl. TB drugs)</strong></td>
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Zambia Consolidated Guidelines for Treatment and Prevention of HIV Infection
**COLOUR CODES FOR THE KEY DRUG–DRUG INTERACTIONS FOR ANTIRETROVIRAL DRUGS**

<table>
<thead>
<tr>
<th>Colour Code</th>
<th>Description</th>
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<tbody>
<tr>
<td>Green</td>
<td>No clinically significant interaction or interaction unlikely based on knowledge of drug metabolism.</td>
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<tr>
<td>Yellow</td>
<td>Potential interaction that may require close monitoring, alteration of drug dosage or timing of administration.</td>
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<tr>
<td>Red</td>
<td>Interaction likely: do not use or use with caution.</td>
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<tr>
<td></td>
<td>No clear data, actual or theoretical, indicate whether an interaction will occur.</td>
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## APPENDIX 3: WHO TOXICITY ESTIMATES

<table>
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<tr>
<th>Grade (Severity)</th>
<th>Characteristics</th>
<th>Management</th>
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</table>
| 1 (mild)         | Transient or mild discomfort, no limitation in activity, no medical intervention needed | Does not require change in therapy  
Symptomatic treatment may be given |
| 2 (moderate)     | Limitation in activity, some assistance may be needed, no or minimal medical intervention or therapy required | Consult  
Continue cART if possible  
If no improvement, consider substitution with a drug in the same ARV class, but with a different toxicity profile |
| 3 (severe)       | Marked limitation in activity, some assistance usually required, medical intervention required, possible hospitalization | Refer or consult  
Substitute the offending drug without stopping therapy |
| 4 (life-threatening) | Extreme limitation in activity, significant assistance required, significant medical intervention or therapy required, hospitalization or hospice care | Discontinue all ARV drugs, manage the medical event until patient is stable and toxicity has resolved |
### APPENDIX 4: **Co-Trimoxazole Desensitization Protocol For Adolescents And Adults**

<table>
<thead>
<tr>
<th>Time Point</th>
<th>Dose for desensitization</th>
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<tbody>
<tr>
<td>Day 1</td>
<td>80mg SMX/16mg TMP (2mL of oral suspension)</td>
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<tr>
<td>Day 2</td>
<td>160mg SMX/32mg TMP (4mL of oral suspension)</td>
</tr>
<tr>
<td>Day 3</td>
<td>240mg SMX/48mg TMP (6mL of oral suspension)</td>
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<tr>
<td>Day 4</td>
<td>320mg SMX/64mg TMP (8mL of oral suspension)</td>
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<tr>
<td>Day 5</td>
<td>1 single-strength SMX/TMP tablet (400mg SMX/80mg TMP)</td>
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<tr>
<td>Day 6 onward</td>
<td>2 single-strength SMX/TMP tablets or one double strength tablet (800mg SMX + 160mg TMP)</td>
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</table>

Oral suspension is 40mg TMP/200mg SMX per 5mL of syrup.
APPENDIX 5: POSITIVE HEALTH DIGNITY & PREVENTION (PHDP)

To have a significant effect on slowing the spread of the epidemic, prevention efforts must also be directed towards HIV-infected individuals who can transmit the virus.

Deliver consistent, targeted prevention messages and strategies during routine visits

At every visit, assess for and counsel regarding:

- High risk sexual activity
- Partner’s and children’s HIV status
- Disclosure to partner/guardian/treatment supporter
- Signs and symptoms of STIs and cervical cancer
- Pregnancy status
- Adherence to cART and other medications
- Abuse of alcohol and other substances
- Positive living (nutrition, alcohol and smoking cessation)

Six (6) key steps for PHDP:

- Step 1: Give risk reduction messages to every patient at every visit
- Step 2: Assess adherence to ARVs
- Step 3: TB and STI screening and management
- Step 4: Family planning services and safer pregnancy counselling
- Step 5: Give patient condoms at every visit
- Step 6: Partner HIV testing
APPENDIX 6: Renal insufficiency screening algorithm (in the absence of Creatinine test)

1. Obtain a good history
   - Ask about Kidney Disease, Hypertension, Diabetes, Chronic/acute diarrhoea (recent or on-going)
   - Use of NSAIDS or herbal medications

2. Check BP, weight, height, BMI, urinalysis, RBS or FBS

3. Risk Factors
   - History of hypertension or high or low blood pressure
   - History of diabetes mellitus or high blood sugar
   - BMI ≤ 18.5 or less than 50kg (if > 19 years old)
   - Persistent hematuria/proteinuria (2 weeks apart)
   - Acutely ill patients/recently hospitalized
   - Chronic use of NSAIDs or Herbs

4. Risk factor(s) present → Do not initiate TDF based regimen without eGFR (Creatinine-serum and Clearance)
5. No risk factors → Can initiate TDF based regimen

6. Review for symptoms/signs at 2 and 4 weeks
   - Perform Serum Creatinine as soon as available
APPENDIX 7: Formulae for calculating Creatinine Clearance in different patient populations

IN CHILDREN (10-18 YEARS) GLOMERULAR FILTRATION (SCHWARTZ)

Clinical Use: A simple estimate of Glomerular Filtration Rate in children derived from body length and serum Creatinine.

Formula:
Creatinine Clearance = \( \frac{k \times \text{height}}{\text{Creatinine}} \)

**Units:**
- Creatinine: [mg/dL] mg/dL=88.4µmol/L
- Height: [cm]
- Constant as follows: 0.55 for adolescent girls and 0.7 for adolescent boys
- For pregnant women use serum Creatinine (should be less than 125µmol/L to use TDF)

ADULTS (≥19 YEARS)

- **For Men:**
  \[
  \text{CrCl} = \frac{[140 - \text{age}] \times \text{weight in kg}}{72 \times \text{serum Creatinine (mg/dL)}}
  \]
  OR
  \[
  \text{CrCl} = \frac{[140 - \text{age}] \times \text{weight in kg}}{0.815 \times \text{serum Creatinine (µmol/L)}}
  \]

- **For Women**
  \[
  \text{CrCl} = \frac{[140 - \text{age}] \times \text{weight in kg} \times 0.85}{72 \times \text{serum Creatinine (mg/dL)}}
  \]
  OR
  \[
  \text{CrCl} = \frac{[140 - \text{age}] \times \text{weight in kg} \times 0.85}{0.815 \times \text{serum Creatinine (µmol/L)}}
  \]
GLOSSARY

Combination antiretroviral therapy (cART): Use of antiretroviral regimens consisting of a combination of at least three or more drugs from at least 2 classes

Body Mass Index (BMI): A measure of body fat based on one’s weight in relation to height

Co-trimoxazole Preventive Therapy (CPT): Use of Co-trimoxazole to prevent opportunistic infections in susceptible Persons Living With HIV/AIDS (PLWHA)

Creatinine Clearance (CrCl): An estimation of milliliters of blood filtered by the kidneys per minute

Directly Observed Therapy short course (DOTs): refers to the WHO-recommended strategy for TB control and involves direct observation of patients taking TB medications. This is done to ensure that the patient takes the right medicines, in the right doses, at the right intervals.

Focused Antenatal Care (FANC): A standard package of basic ANC services that all pregnant women should receive. FANC emphasizes the importance of developing a plan of care that meets each woman’s individual needs.

HIV Testing Services (HTS): Refers to the full range of services provided with HIV testing, including counseling; linkage to appropriate HIV prevention, treatment, and care, and other clinical services; and coordination with laboratory services to ensure delivery of accurate results

Isoniazid Preventive Therapy (IPT): Use of Isoniazid for prophylaxis to susceptible patients to offer protection against Mycobacterium TB

Immune Reconstitution Inflammatory Syndrome (IRIS): An exaggerated inflammatory reaction from a re-invigorated immune system

National Unique Patient Number (NUPN): A unique client identification number used in SmartCare patient records system

Nucleic Acid Test (NAT): Virological testing technology used for early infant HIV diagnosis developed and validated for use at the point of care. This test detects both viral RNA and DNA

Polymerase Chain Reaction (PCR): A test done to detect HIV specific genetic material that indicates presence of HIV. In Zambia, through the use of Dry Blood Spot (DBS) specimen, this test diagnoses HIV infection in children below 18 months of age.

Positive Health Dignity and Prevention (PHDP): An HIV prevention strategy among PLWHA that focuses on: risk reduction, ART adherence, correct condom use, family planning, STI screening, and partner HIV testing

Pre-exposure Prophylaxis (PrEP): An HIV prevention strategy where those at high risk of acquiring HIV are covered on prophylactic ARVs before exposure to the HIV virus

Post-exposure Prophylaxis (PEP): Short term antiretroviral treatment to reduce the likelihood of HIV infection after potential exposure to the virus

Severe Liver Disease: Progressive destruction of the liver parenchyma over a period greater than 6 months leading to fibrosis and cirrhosis

Treatment as Prevention (TasP): Refers to use of antiretroviral therapy in PLWHA to decrease the risk of HIV transmission to others

Treat All: WHO recommendation that all clients testing HIV positive should be initiated on cART irrespective of their WHO Clinical staging, CD4 or Viral load levels

Visual Inspection with Acetic acid (VIA): A cervical cancer screening method done using Acetic acid