CHAPTER 1: Executive Summary

HIV Testing Services

- As a new recommendation; the MOHCC recommends re-testing of all people newly and previously diagnosed with HIV before they initiate ART. Re-testing refers to using the same testing algorithm on a second specimen from the same individual. It should ideally be conducted by a different service provider.
- HIV self-testing (HIVST) is being recommended as an additional approach to HIV testing services.
    - It refers to a process in which a person collects his or her own specimen (oral fluid or blood) and then performs a test and interprets the result, often in private or with someone that he/she trusts.
    - HIVST does not provide a definitive HIV-positive diagnosis and hence people who test positive during self-testing need to confirm the positive test at a health facility and be linked to treatment and care services.

Early Infant Diagnosis

- Birth PCR will be done within 48hrs of birth where available for high MTCT risk infants ONLY.
- Early ART initiation as soon as birth PCR results are available.
- For babies who test HIV positive at birth ALWAYS retest and confirm results with repeat PCR but retesting should not delay ART initiation.
- Babies who test negative at birth (birth PCR) or not tested MUST be tested at 6 weeks.
- Infants at high risk of transmission will receive dual ARVs (AZT and NVP) for 12 weeks as prophylaxis if breastfeeding and 6 weeks if not breastfeeding.
- Cotrimoxazole must be started from 6 weeks of age even in babies on longer duration of prophylaxis and continued through adolescence.

HIV Treatment Services

- The country has adopted the “Treat ALL” recommendation where, all individuals with confirmed HIV diagnosis are eligible for anti-retroviral therapy (ART) irrespective of WHO clinical stage or CD4 count.
- Low-dose 400 mg Efavirenz-based regimens will be phased in and will initially be prioritized to adolescents living with HIV and other HIV infected individuals who cannot tolerate 600 mg Efavirenz or Nevirapine-containing ARV regimens.

Treatment Monitoring

- Viral load should be monitored routinely at 6 months and at 12 months after ART initiation, and then annually thereafter.
- A CD4 test is recommended at baseline to determine degree of immune suppression of a patient to inform ‘differentiated care’ for the patient. However, CD4 count is no longer used to assess eligibility for ART initiation.
- The frequency of clinic visits has been reduced. When clients are clinically stable and on chronic medication, they do not necessarily need to be seen by the clinician at every visit.
- A stable patient on ART should be seen for a clinical assessment every 6 months.
- A stable patient on ART is defined as someone who:
    - Has no current OIs, has a VL<1,000 copies/ml and is at least 6 months on ART
    - Where viral load is not available the client should have no current OIs, a CD4>200 copies/ml and be at least 6 months on ART

PMTCT

- VL should be done on all HIV positive pregnant women who are on ART at first ANC visit and repeated 6 monthly throughout the breast feeding period
- Pregnant women not yet on ART or those newly diagnosed to be HIV positive on the first ANC booking should be initiated on ART on the same day of first booking and should get a VL after 3 month of starting ART
- Viral load testing during pregnancy and breastfeeding period is needed

to stratify HIV exposed infants as either high risk or low risk. A high risk infant is defined as follows;

- An infant whose mother has a high maternal viral load >1000copies/ml during the last 4 weeks before delivery
- An infant born to HIV infected woman who has received less than 8 weeks of ART at the time of delivery
- An infant born to a newly diagnosed HIV infected woman during labor, delivery and postpartum (Incident HIV infection)

- High-risk infants require dual prophylaxis of Daily AZT plus NVP for 12 weeks among the breast-fed infants and Daily AZT plus NVP for 6 weeks among the formula-fed infants

Pre-Exposure Prophylaxis (PreP)

- These guidelines recommend Pre-Exposure Prophylaxis (PrEP) which should be offered as an additional prevention choice for people at substantial risk of HIV infection as part of combination prevention approaches.
- The MOHCC will implement PrEP using a phased approach. An implementation plan and Standard Operating procedures (SOPs) on PrEP will be developed and shared by MOHCC to guide the introduction and scale up of PrEP.

Post Exposure Prophylaxis (PEP)

- The new guidelines recommend the use of TDF/3TC/ATV/r for adults and adolescents for PEP
- There is a more pronounced presence of guidelines pertaining to sexual assault (rape, intimate partner violence, sexual abuse)

Reporting Adverse Drug Events

- A new chapter that provides health workers guidance on reporting adverse drug reactions has been added. Emphasis is made on recording and reporting all suspected adverse drug reactions to MCAZ.

CHAPTER 2: HIV Testing Services (HTS) for Children, Adolescents and Adults and Linkage to Prevention and Treatment

2.1 Introduction

HIV testing services serve as the entry point to prevention, care and treatment programs. HIV Testing Services (HTS) include HIV testing, counselling (pre and post testing services, disclosure, adherence) and linkage to appropriate HIV prevention, treatment and care services. Laboratory services should support quality assurance and delivery of correct results. All HIV Testing Services in Zimbabwe should be conducted in accordance with the best interest of the client (child, adolescent or adult). HIV testing should never be coercive or mandatory, except in unique situations such as court orders.

The goal of the Ministry of Health and Child Care (MOHCC) is to ensure that 90% of all people living with HIV know their HIV status by 2020 as per the 90-90-90 Global Fast Track targets and 95% by 2030. In line with the HTS Strategic framework 2016-2020, the MOHCC has committed to not only increasing testing coverage for the general population, but prioritizing strategies and testing initiatives that are more likely to identify those people living with HIV and those most in need of care and treatment services who currently are unaware of their HIV status. HTS services are guided by 6 core principles (6Cs): consent, confidentiality, counselling, comfort for the woman in labour, correct results and connection-linkage to care and prevention services. These fundamental principles for HTS are described in detail below:

Consent – All clients should receive sufficient information to understand the testing process and possible consequences of being tested. Clients receiving HTS must give informed consent, which can be written or verbal. They should be informed of the process of HTS and their right to defer HIV testing.

Confidentiality – discussions between the service provider and the client should not be disclosed to anyone without the permission of the client. Inform the client of shared confidentiality

Counselling – Pre-test counselling may be given as a group, couple or individual depending on the setting. Post-test counselling may be individual or as a couple.

Comfort: HTS should be offered during the early stage of labour. The health worker should assess the woman's stage of labour, comfort level, and need for analgesics. The content should be short, to the point, and explained based on the comfort level of the woman, between contractions. The health worker should ask the woman to signal for a pause when a contraction is starting.

Correct and accurate HIV test - results should be provided by trained service providers with support for internal and external quality assurance and control from the laboratory personnel as stipulated in the National Rapid HIV testing QA/QC protocols.

Connections to HIV Prevention, Treatment, Care and Support services - must be in place. Clients who test HIV negative should be linked to HIV prevention services, whilst those testing positive are linked to appropriate HIV treatment services.

2.2 Service Delivery Approaches for HTS

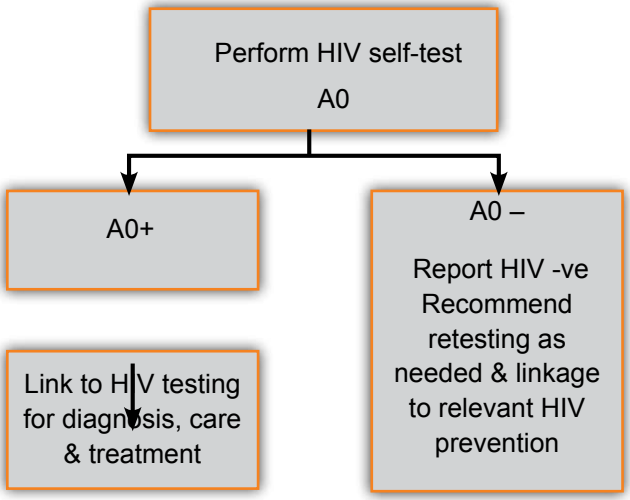
Facility Based HTS: Scale up routine HIV testing to all clients using Provider Initiated Testing and counselling (PITC) for children, adolescents and adults in all clinical settings irrespective of the reason for presenting at a health facility. PITC should be offered routinely within malnutrition and paediatrics clinics, STI, viral hepatitis and TB services, inpatients and outpatients settings, ANC settings and in health services for vulnerable groups that include children, adolescent and also key populations.

Community-based HTS: approaches include door-to-door / home-based testing (including index case testing) and mobile outreach campaigns in workplaces, parks, bars, places of worship and educational establishments.

HIV Self-Testing (HIVST): This refers to a process in which a person collects his or her own specimen (oral fluid or blood) and then performs a test and interprets the result, often in private or with someone he or she trusts. HIV self-testing should be offered as an additional approach to HIV

testing services. HIVST does not provide a definitive HIV-positive diagnosis; meaning a reactive (positive) self-test result always requires further testing from a trained testing provider using the relevant validated national testing algorithm. People who test positive during self-testing need to confirm the positive test at a health facility and if they test positive with confirmatory test they are then linked to treatment and care

Figure 1: HIV Self Testing (HIVST) Strategy



Source: WHO HTS guideline 2015

The proposed distribution models for HIVST are as follows: -

- Community Based Distributors Agents chosen by the Communities (can be village health workers, behaviour change facilitators)
- New Start Network
- VMMC mobilisers and at VMMC sites
- Clinics for key populations
- Public Health Institutions including ANC sites for pregnant women
- Private Sector Pharmacies

Studies are still going on to gather evidence on which cost-effective models

to distribute self-testing kits and the models might change based on evidence gathered. The Ministry is in the process of mobilising funds to procure the kits for scale up of HIVST.

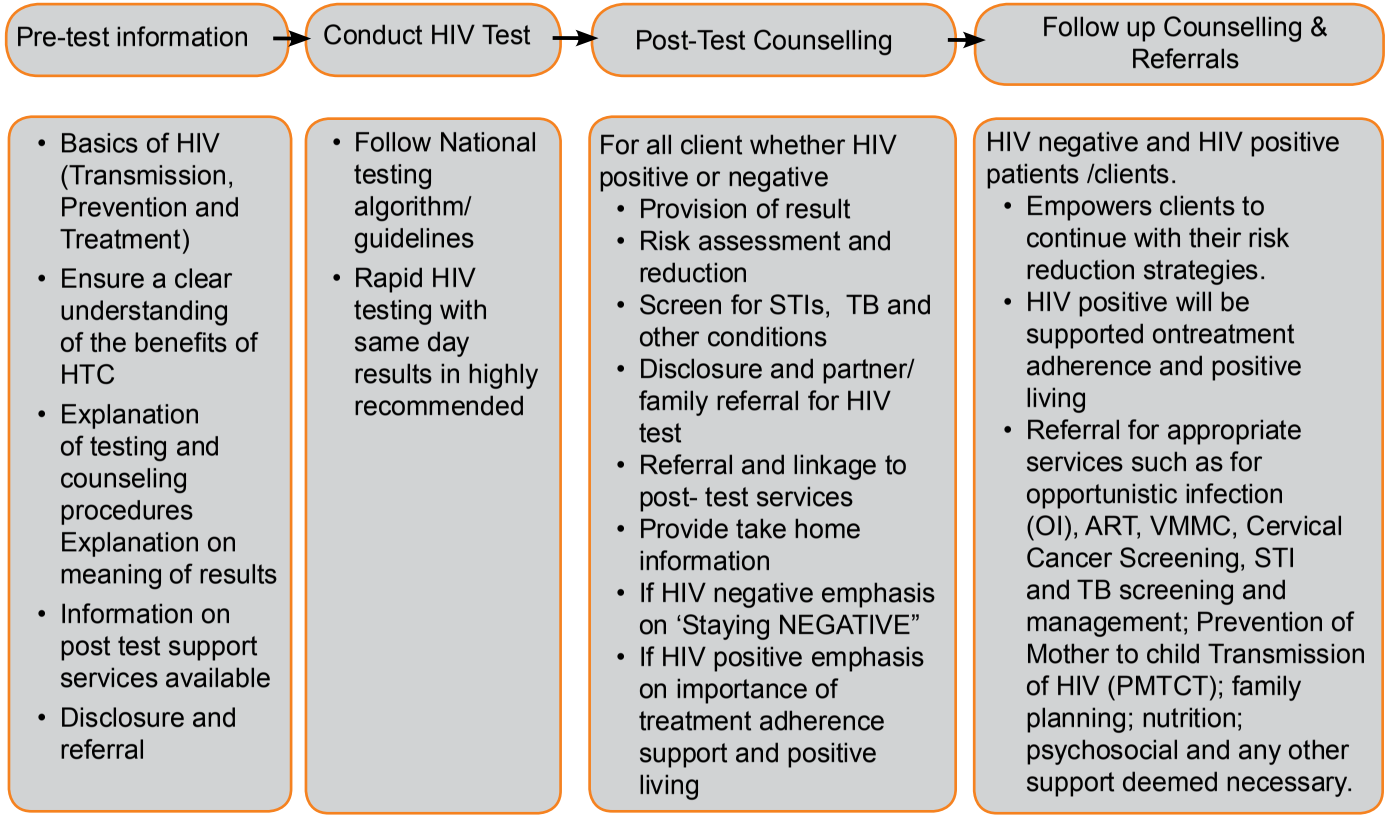
2.3 The HIV Testing Service Package

Figure 2 outlines the components of the HIV testing service package. This includes the pre-test information, conducting the HIV test, Post- test counselling and follow up Counselling and referrals.

With the introduction of treat all three key messages must be given in the post test counselling for those testing positive:

- Treatment is available for all people living with HIV
- Starting treatment as soon as possible will prevent your health from worsening and also prevent transmission to others
- Taking ART properly will allow you to live a long and fulfilling life

Figure 2: Primary Component of HIV Services Package



Source: Adapted from MOHCC PITC Flow Chart

2.2.1 HIV Testing Algorithm for Children Above 18 months, Adolescents and Adults

Figure 3 shows the National HIV Testing Algorithm for children 18 months and above. Serial testing is recommended with Determine or SD bioline followed by Chembio/ First response. If results are discordant then the two tests are repeated in parallel. If still discordant a third test (INSTI) is performed. If negative report as negative. If positive, retesting in 14 days.

Figure 3: HIV testing algorithm for children above 18 months, adolescents and adults

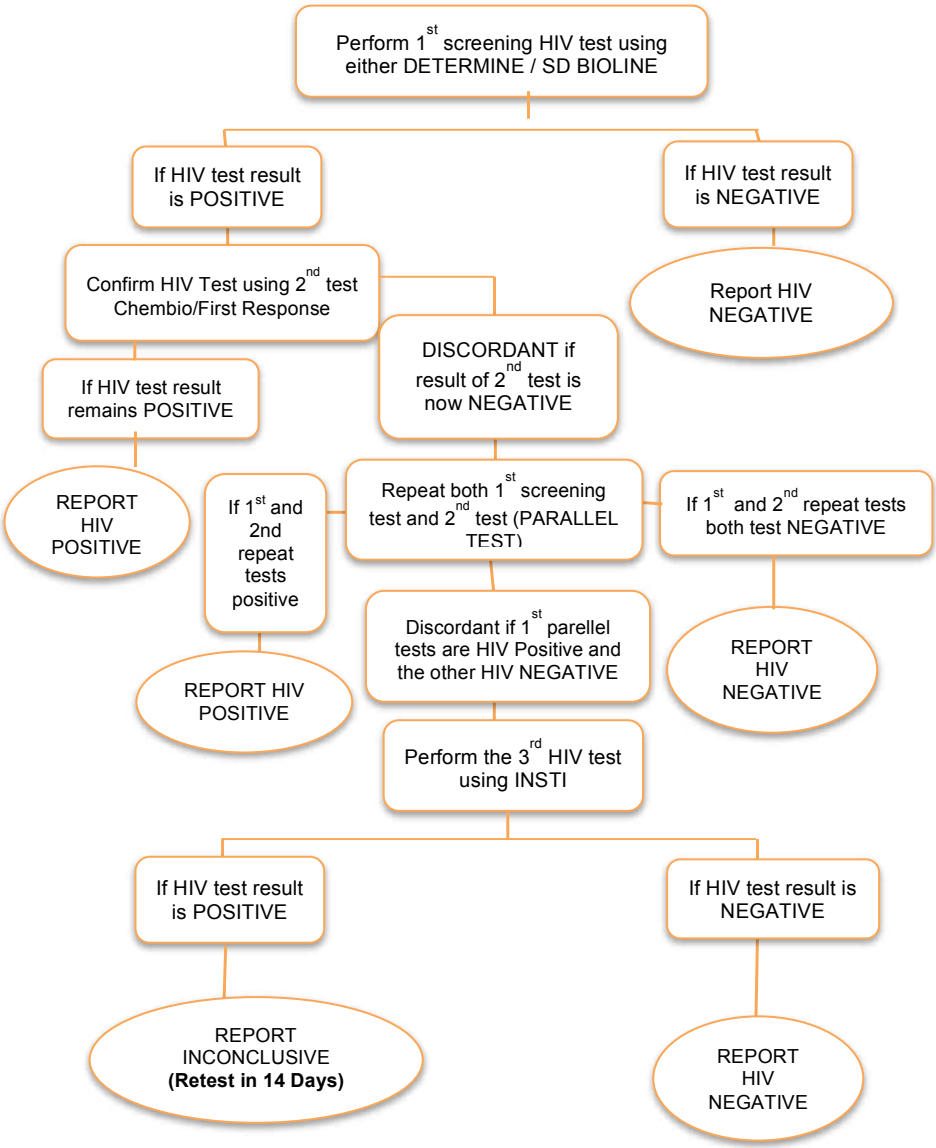


Table 1: Priority Populations to be Considered for HTS

Infants and children	• Infants and children get exposed to HIV mainly from their infected mothers. Therefore exposed infants and children should be tested to determine their HIV status and link them appropriately to care and treatment.
Adolescents and Youth	• Adolescent girls and young women are particularly vulnerable to HIV infection. Early sexual debut, often with older partners, coerced sex and low rates of condom use, combined with their biological vulnerability at that age, increase the risk of HIV infection among adolescent.
Pregnant and breast feeding women	• One of the key steps in preventing mother to child transmission of HIV starts with the pregnant woman knowing her HIV status. HTS should be available and structured to make it easy for the pregnant woman and breast feeding women to access. Breast feeding women to be re tested every 6 months during the period of breast feeding.
Men	• More emphasis should be put in reaching men for HTS services in high HIV prevalent settings in view of fewer men compared to women knowing their HIV status.
Couples	• It is recommended that HTS service providers encourage individual testers to test together with their sexual partners as couples
Key populations	• Key populations are disproportionately affected by HIV and have limited access to HIV prevention, care and treatment services. There is need for friendly or appropriate services for the different key populations.

2.2.2 Retesting for the Window Period

For most people who test HIV-negative, additional retesting to rule out being in the window period is not necessary. This is because most people who receive HIV testing and test HIV-negative will not be at risk from recent infection.

Retesting should only be done for a small minority who identify a specific recent suspected exposure e.g. key populations.

2.2.3 Retesting to Verify HIV Status

Retesting refers to using the same testing algorithm on a second specimen from the same individual.

The majority of individuals do not require retesting to verify an HIV negative status particularly with no on-going HIV risk. However, retesting is required for individuals with on-going risk of contracting HIV where annual retesting is recommended.

Retest all people newly and previously diagnosed with HIV before they initiate ART. Retesting should ideally be conducted by a different service provider with a different specimen.

Retesting people on ART is not recommended as there are potential risks of incorrect diagnosis. The effect of ART in suppressing viral replication may extend to suppression of the immune response and thus of antibody production leading to inaccurate HIV diagnosis.

2.2.4 Linkage to Prevention, Treatment, Care and Support Services

Linkage is defined as a process of actions and activities that support people testing for HIV and people diagnosed with HIV to engage with prevention, treatment and care services as appropriate for their HIV status. For people with HIV, it refers to the period beginning with HIV diagnosis and ending with enrolment in care or treatment.

Therefore, without linkage to prevention, treatment and care, testing and learning one's HIV status has limited value. Those who test HIV-negative, if at continuing high risk, as well as those who test HIV positive, need linkage to prevention services.

Table 2: Linkages to HIV Prevention and Care Services by HIV Test Status

	HIV Positive	HIV Negative
Prevention	Male and female condoms and condom-compatible lubricants	
	Harm reduction for people who use drugs	
	Behavioural interventions to support risk reduction, particularly for people with HIV and key populations	
		PEP following suspected exposure
		VMMC
Treatment	Antiretroviral therapy	PrEP for people at substantial ongoing risk
SRH	Contraception	
	Brief sexuality counselling	
	Cervical cancer screening	
	STI screening	
HTS for partners/ family members	For all partners and family members (includes partner notification and index case testing)	For partners of people from key populations, where appropriate
Retesting for confirmation of HIV test	• Confirmation from community-based testing • Retest for verification before ART initiation	Retesting (as per retesting recommendations pg 8)
Other clinical services	Assessment and provision of vaccinations, tetanus vaccination for adolescent boys and men receiving VMMC where appropriate	
	HBV testing and referral for management	
	Intensified TB case finding and linkage to TB treatment	
Other support services	Mental health services	
	Psychosocial support, Disclosure and Treatment adherence counselling	
	Support for disclosure and partner notification	
	Legal services	

Table 3: Recommendations for HIV retesting

Population	Recommendation
General population not at on-going risk	Offer retesting at least annually
Individuals with Inconclusive HIV test results	Retest after 14 days
Individuals on PEP	Retest at 3 months and 6 months after the initial test
Individuals on PrEP	Retest after every 3 months
Key populations	Retesting according to risk assessments (suggest three months)
HIV-negative pregnant women and lactating women	Retest previously HIV-negative women in the first trimester of pregnancy and at third trimester/ or at delivery; 6 weeks post-natal and 6 monthly during the breastfeeding period. Visits to EPI and 6 weeks(DTP) and at 9 months (measles) should be time points where maternal HIV status is reassessed
HIV positive individuals before initiation of ART	Retest all people newly and previously diagnosed with HIV before they initiate ART. Retesting should ideally be conducted by a different service provider with a different specimen. However if there is only one health worker at the facility they can take another blood sample a few hours apart and retest

2.3 Disclosure of HIV Status

Disclosure in HTS is the process through which a client shares information about their HIV test result with significant others or a third party. The goal of HIV disclosure is to share one's challenges and get support that enhances access to care. However, this support may not always be forthcoming and clients may face situations of stigma and discrimination. Health care providers should encourage and support the client to disclose to significant others.

2.3.1 Disclosure to a Child, Adolescent and Youths of HIV Status

Disclosure is the process of informing the child/adolescent of his or her own HIV status or informing someone else about the child's/ adolescent's HIV status. It may be determined by readiness of the parent/caregiver to talk about it and readiness of the child/adolescent to understand and change their lives as a result of the knowledge of his/her status. A thorough assessment of the child's knowledge and attitude towards HIV and AIDS issues, age and level of maturity is essential for assessing readiness to receive information about HIV status.

- Partial disclosure starts with revelation to a child sometimes as young as 6 years without mentioning "HIV" or "AIDS" and can use age appropriate communication and counselling techniques.
- Progressive disclosure is when more and more information about the child's HIV status is shared with the child/adolescent as he/she develops and matures.
- Full disclosure is when the child is given all the information about his/her HIV status during a counselling session.

Health workers should also be available to provide on-going support and counselling for the family as necessary.

Adolescents below 16 years should be offered their HIV test results in consultation with their parents, guardians, or caretakers. Post-test counselling should be offered to the adolescent together with the parent. Those 16 years and above should receive their HIV test results if they request the HTC services, but where they wish to receive the results in the company of their parents/guardians they can choose to. Adolescents and youth should be counselled about the potential health benefits of disclosing their HIV status to significant others, including their parents/guardians/caregiver and

supported to determine, when, how and to whom to disclose to. Parents / guardian/caregiver, who find it difficult to disclose the HIV status of their children, should be supported by health workers.

2.4 Quality Assurance

Ensuring correct HIV test results is a priority and a crucial component of WHO's 5 Cs for HTS. The cost of misdiagnosis is very high and providers have an ethical obligation to ensure accurate results are given. Quality assurance for HTS will be implemented through quality management systems comprising of Internal and external quality assurance systems. To ensure quality, testing will be conducted only according to the national algorithm and adhering to the Standard Operating Procedures for the program. All sites offering HTS will be accredited to ensure that they meet the minimum standard to provide quality testing. Testing will be conducted only by providers who are trained and are competent. Additionally, care should be taken to ensure that the kits are transported and stored in a way that preserves their quality. Service providers and program managers will continually monitor and evaluate the performance of testing and improve the quality of services including that of counselling.

CHAPTER 3: Principles of Antiretroviral Therapy

3.1 Background

The guiding principles for effective ART include potency of regimens chosen, minimum adverse events, reduced pill burden, and accessibility and affordability of the medicine combinations. The reduced pill burden will be achieved by using FDCs of antiretroviral medicines. Although the potency (efficacy) of the regimen is important, adherence to a simple regimen will ensure that the ongoing viral replication is maximally suppressed, thus allowing the immune status to recover. Plasma viral load (VL) measures viral replication, whereas the effect of ART on the immune system is monitored using the CD4 lymphocyte count in most patients or CD4 percentage in children under five years.

Health-care personnel will need to receive continuing medical education to remain up to date on ART recommendations. Guidelines change as new evidence emerges from clinical trials and lessons are learnt from programme experiences. The need for those involved in managing patients on ART to undergo frequent retraining and evaluation cannot be overemphasised. ART requires in-depth knowledge about antiretroviral agents, their side effects, and issues such as immune reconstitution inflammatory syndrome (IRIS). Being able to detect and manage OIs, knowing when to initiate ART, and knowing when to change medicines as toxicities occur or when to switch to second-line or even third-line therapy, as well as counselling abilities, are all necessary skills. Such skills can be acquired with the relevant training and experiential learning. Clinical attachments and clinical mentoring are tools to improve health-care worker skills in all disciplines, including ART delivery.

Adherence to treatment regimens and schedules is crucial to the success of this therapy. Without high adherence rates, viral resistance to the medicines emerges readily. Hence, there is need to be vigilant and monitor patients during ART for adherence rates, side effects, and treatment failure. Treatment failure should alert the health-care worker on the need to switch to second-line or third-line therapy.

The Ministry of Health and Child Care is progressively increasing access to

viral load testing therefore switching to second or third line treatment should be based on viral load testing. However, switching to second-line therapy can be based on a combination of clinical monitoring plus at a minimum laboratory testing (CD4 count) where access to VL is poor. VL testing is a must before switching a patient to third line ART therapy. Given the maturing ART programme, third-line therapy has become necessary. The use of such third-line regimens will require close consultations with those specialists who have experience treating clients who are "ART experienced."

3.2 Characteristics of Available ARVs

Medicines in use in most of our programmes belong to the following classes:

- Nucleoside reverse transcriptase inhibitors (NRTIs). These medicines block the HIV reverse transcriptase enzyme and prevent the copying of the viral RNA into the DNA of infected host cells by imitating the building blocks of the DNA chain. The resulting DNA chain is incomplete and cannot create new viruses.
- Nucleotide reverse transcriptase inhibitors (NtRTIs). These medicines act at the same stage of the viral life cycle as do NRTIs but have a better resistance profile.
- Non-nucleoside reverse transcriptase inhibitors (NNRTIs). These medicines also block the HIV reverse transcriptase enzyme, but have a different mechanism of action than the NRTIs and the NtRTIs.
- Protease inhibitors (PIs). These medicines block the enzyme protease and prevent the assembly and release of HIV particles from infected cells.
- Integrase inhibitors (IIs). These medicines target HIV's integrase protein, blocking its ability to integrate its genetic code into human cells.

These additional classes of ARVs are not yet in use in Zimbabwe:

- Fusion inhibitors (FIs). These work by preventing HIV from entering healthy CD4 cells by blocking proteins on the surface of CD4 cells.
- CCR5 inhibitors. These block the CCR5 co-receptor that HIV uses to enter and infect the cell. CCR5 works specifically against CCR5-tropic HIV. Before treating a patient with a CCR5 inhibitor, a test to determine the strain of virus is necessary.

Table 4: Antiretroviral Medicines by Mode of Action

Nucleoside Reverse Transcriptase Inhibitors (NRTI)	Non-nucleoside Reverse Transcriptase Inhibitors (NNRTI)	Protease Inhibitors (PI)	Integrase Inhibitors (II)
Tenofovir (TDF) (NtRTI)	Nevirapine (NVP)	Lopinavir/ ritonavir (LPV/r)	Raltegravir (RAL)
Zidovudine (AZT, ZDV)	Efavirenz (EFV)	Atazanavir/ ritonavir (ATV/r)	Dolutegravir (DTG)
Lamivudine (3TC)	Etravirine	Darunavir	
Emtricitabine (FTC)		Ritonavir(RTV)	
Abacavir (ABC)			
Didanosine (ddI)			
Stavudine(d4T)			

3.3 Efficacy and safety

Regimens based on two NRTIs plus one NNRTI are efficacious, are less expensive, have generic formulations, and are available as FDCs. PIs should generally be preserved for second-line or third-line therapy and for children less than 3 years.

The preferred first line regimen of Tenofovir, Lamivudine and Efavirenz has relatively few adverse effects and is taken once daily. Zidovudine (as an alternative to Tenofovir) can cause anaemia but is less likely to cause peripheral neuropathy.

Efavirenz has less adverse effects compared to Nevirapine. Nevirapine can cause a rash and hepatotoxicity and thus should be used with caution when initiating ART at higher levels of CD4 counts (e.g., in women with CD4 counts greater than 250 and in men with CD4 counts greater than 400).

All ARVs have class-specific side effects, and individual medicines may cause specific side effects (see Table 10 in Section 8.4). In addition, significant medicine interactions and toxicities may occur when using some ARVs in combination with each other and with other medicines such as TB medicines.

CHAPTER 4: Initiation of Antiretroviral Therapy in Adults and Adolescents

4.1 Goals of ART

The aims of ART are as follows:

- Maximal and durable suppression of replication of HIV
- Restoration and/or preservation of immune function
- Reduction of HIV-related morbidity and mortality
- Improvement of quality of life
- Prevention of mother-to-child transmission of HIV (vertical transmission)
- Reduction of transmission of HIV from infected to uninfected individuals through use of ARVs by the infected individual now commonly known as 'Treatment as prevention'

Prior to starting ART, patients should be assessed for readiness to take ARVs; the ARV regimen; dosage; and scheduling; the likely potential adverse effects; and the required monitoring. Both medical and psychosocial issues need to be addressed before initiating ART. Patients should be adequately counselled about adopting appropriate lifestyle measures such as safer sex practices (including use of condoms), and any other psychosocial problems that may interfere with adherence (e.g., alcohol, psychiatric disorders) should be addressed. Efforts should be made to reduce the time between HIV diagnosis and ART initiation based on an assessment of a person's readiness.

At each clinic visit, always screen for tuberculosis using a TB symptom checklist, advice patients about adequate nutrition and the importance of medicine adherence and regular follow-up care. People taking ARVs should also be regularly asked about whether they are taking other medications including herbal remedies that may interfere with the efficacy of ARVs. The ART programme should promote treatment literacy for PLHIV including information on the benefits of early treatment, the risks of delaying treatment, the required life-long commitment for adherence to treatment.

Early treatment initiation is associated with clinical and HIV prevention benefits, improving survival and reducing the incidence of HIV infection at the community level. Increasing evidence also indicates that untreated HIV may be associated with the development of severe non-AIDS defining conditions including cardio-vascular disease, kidney disease, liver disease and neurocognitive disorders.

4.2 Medical Criteria for Initiating ART in Adults and Adolescents

All individuals with a confirmed HIV diagnosis are eligible for anti-retroviral therapy (ART) irrespective of WHO clinical stage and CD4 count level i.e. ***TREAT ALL.***

> ***Health workers should retest all people newly and previously diagnosed with HIV before they initiate ART. Retesting should ideally be conducted by a different service provider with a different specimen.***

As a priority, initiate ART in all individuals with severe or advanced HIV clinical disease (WHO clinical stage 3 or 4) or CD4 count less than or equal to 350 cells/ mm3.

It is also recommended to initiate ART, as a priority, in the following categories of patients regardless of CD4 cell count:

- Active TB disease
- Pregnant and breast-feeding women with HIV
- Individuals with HIV in sero-discordant relationships
- HBV co-infection with severe chronic liver disease

Once an individual is confirmed to be HIV positive; health workers should provide adequate counselling and start ART within a week. However, for those patients who are not ready yet to start ART, they should receive on-going counselling and support. EXCEPTIONS: Pregnant and breast-feeding women should be started ART on the same day of HIV diagnosis.

> ***Patients with CD4 cell count <100***
>
> Patients with low CD4 below 100 should be fast-tracked for treatment initiation. They should be screened for symptomatic TB and cryptococcal disease (see section 9.3). They should receive cotrimoxazole and isoniazid (INH) prophylaxis like all other patients and should be closely monitored for 3 months as this is their highest risk period for bacterial infections and TB or cryptococcal IRIS. Health workers should educate them and their families to report immediately to a health facility if they are unwell whilst their CD4 cell count is< 100 copies.

See the WHO clinical staging system (Appendixes I and II).

The revised medical criteria i.e. treating all individuals who are HIV infected, means that many more PLHIV will be eligible for ART and that will include many healthier people. Given our limited resources as a country, there will be need to prioritize as indicated above. The AIDS and TB Directorate of the MOHCC will regularly advise you on availability of funds to procure ARVs, so as to ensure that those started on ARVs are maintained on them to reduce the potential development of HIV medicine resistance.

4.3 Psychosocial Criteria for Initiating ART

Consider the following psychosocial criteria when initiating ART:

- Has the patient been adequately counselled and informed about ARVs?
- Is a treatment partner available and/or has disclosure been made to that treatment partner (strongly encouraged)?
- Is there an easy method of following up on the patient?
- Is the patient ready to take medications indefinitely?

4.4 Reasons for Deferring ART

A patient may be deferred (delayed) from starting therapy if the patient

- has cryptococcal meningitis (defer for at least a month)
- needs further psychosocial counselling (e.g., for alcohol problems),
- has TB (defer starting ART for at least 2 weeks)
- needs further information on HIV and AIDS,
- is terminally ill and unable to swallow oral medication (palliative care is then offered to such a patient).

Such patients should be offered continued monitoring and close follow-up as well as counselling so that ART can be commenced at an appropriate time.

4.5 Adherence to ART

WHO defines treatment adherence as 'the extent to which a person's behaviour- taking medications, following a diet and/or executes lifestyle changes corresponds with agreed recommendations from a health care provider.

It should be noted that motivation to start and adhere to treatment may be more difficult for people who feel well and have higher CD4 counts than for people who are ill. Therefore, health workers should put special emphasis on adherence counselling for this particular group of patients. Efforts to

support adherence should start before ART initiation and should include basic information about HIV, the ARV medicines, expected adverse events, preparations for long-term ART. Many factors affect adherence to treatment. Patients may just forget to take their ARVs, be away from home, be depressed or may abuse alcohol. Medication factors may include adverse events, pill burden, dietary restrictions. Health care factors include medicine stock outs, long distances to health facilities and costs related to care.

Effective adherence support interventions include client-centred behavioural counselling and support, support from peer educators trained as "expert patients," community treatment supporters and mobile text messaging. High quality evidence from randomized trials has shown that text messages contributed to reduced non-adherence and unsuppressed viral load. Other interventions involve encouraging people to disclose their HIV status and providing them with adherence tools such as pill boxes, diaries, and patient reminder aids. During follow-up, patients should be assessed for adherence to whatever treatment plan has been agreed upon (OSDM, 2016).

4.6 ART in Adolescents

4.6.1 Who is an Adolescent?

The WHO defines an adolescent as a child between the ages of 10 and 19 years. This period of life encompasses many physiological and psychological changes that should be taken into account when treating an adolescent.

Adolescence is characterized by rapid physical, neurodevelopmental, emotional and social changes. This age- group appears to be underserved by current HIV services. They have significantly worse access to ART services than adults, high risk of loss to follow-up, sub-optimal adherence, and require comprehensive health care and support services.

Perinatally infected adolescents are likely to experience chronic diseases and neuro-developmental growth and pubertal delays. However, adolescents who acquire HIV behaviourally may not face the same clinical problems, but may potentially have challenges relating to stigma and lack of support to access care.

4.6.2 HIV Testing Services (HTS) for Adolescents

- It is important to increase uptake for HIV testing services by adolescents through: provider-initiated HTS coupled with other entry services such family planning services, VMMC and immunization campaigns
- Ensuring that all health facilities are oriented towards the adolescent-

friendly health services approach

Special attention should be given to:
Post-test counselling; appropriate and successful linkage to prevention, treatment and care services; and consent and confidentiality, which are major concerns for adolescents

Adolescents should be counselled about potential benefits and risks of disclosure of their HIV status and empowered and supported to determine if, when, how and to whom to disclose to.

4.6.3 Principles of ART in Adolescents

The principles of therapy are similar to those in adults and children. However, one should bear in mind specific issues when monitoring and treating HIV positive adolescents, which are discussed in the following sections.

Dosage of ART

Decisions regarding dosage for adolescents should take the following factors into account:

- The age at which to start adult dosing can be difficult to determine.
- Stunting and wasting which are common among HIV-positive adolescents.
- It is recommended that those under the weight of 25 kg should be dosed according to paediatric dosing guidelines. Thus, all adolescents—regardless of age—should be weighed before commencing ART and at each visit.

4.6.4 Staging HIV-Positive Adolescents

HIV-positive adolescents are at risk not only of the HIV-associated infections typically used to stage HIV-positive adults but also of chronic non-infective complications typically used to stage paediatric HIV. These specifically include chronic lung disease, lymphoid interstitial pneumonitis (stage 3) and HIV-associated cardiomyopathy/nephropathy and stunting (stage 4). Such conditions should be taken into account when staging HIV-positive adolescents

4.6.5 Monitoring of HIV Disease

In monitoring adolescents, remember the following:

- Stunting and pubertal delay are common.
- As well as CD4 count and Viral load monitoring, clinical monitoring should include measurement of height and weight at every clinic visit as well as

evaluation of pubertal stage using Tanner staging every six months.

- Girls should specifically be asked about menstruation, including age of menarche and timing of menstrual cycles.

4.6.6 Chronic Complications

As well as looking for and treating OIs, clinicians should monitor patients for chronic complications such as heart failure, lung and skin infections.

4.6.7 Disclosure

Lack of knowledge of HIV status can result in poor adherence to ART. Adolescents should be involved in the discussion about HIV testing, and their HIV status should be disclosed to them. Do not assume that adolescents are aware of their HIV status. Unless exceptional circumstances make it difficult for an adolescent to understand his or her HIV status (severe mental disability), it is strongly recommended that HIV status be disclosed before the patient starts ART. Disclosure is a gradual process and should be carried out with the involvement of the guardian, a counsellor, and the doctor.

4.6.8 Adherence

Adherence is particularly problematic in adolescents. Particular attention should be paid to assessing adherence at every visit and to providing adherence support. Counselling on adherence should include exploring specific reasons that may contribute to poor adherence. Adolescents face many psychosocial issues that can affect their adherence, and those should be assessed:

- In particular, ways of supporting attendance at clinic appointments and taking medicines while at school (especially for those at boarding schools) should be addressed.
- Patients should be encouraged to identify a family member who will help support their treatment.
- Peer support at the clinic level can be very helpful in encouraging adherence e.g. through introduction of Community Adolescents Treatment Support (CATS).
- Counselling should be adolescent-friendly, and counselling patients on their own without the presence of guardians/parents is recommended whenever possible. This ensures that patients can talk about personal issues that affect their ability to take medicines.

4.6.9 Education, Information and Services on Sexual and Reproductive Health

Education about sexual and reproductive health should be part of the counselling and treatment of HIV-positive adolescents. Education and information should be tailored according to the patient's own knowledge and maturity. This clearly varies across the age group and should be assessed during counselling.

Specific information/services that should be given to adolescents include information on;

- Avoiding onward HIV transmission, including delaying sexual relationships and using condoms;
- Specific modes of HIV transmission (it is a common misconception that kissing and non-sexual physical contact can transmit HIV); and
- Where to access family planning services and STI treatment and how to seek help in cases of sexual assault.
- Where available HPV vaccine should be administered to young girls

4.6.10 Transitioning from Adolescence into Adulthood:

Transitioning from adolescence to adulthood can be a difficult period even for those without HIV. Changes in their bodies may affect their emotions and behaviors. HIV is an added burden and adolescents who have previously adhered to therapy from childhood may start to default treatment. Health Care workers should anticipate this and discuss it with adolescents and caregivers as part of the treatment plan. Health workers should prepare adolescents to take control of their own treatment and be less dependent on caregivers. Service providers should encourage mature adolescents (in consultation with caregivers) to attend clinic visits alone where appropriate. As a last step to transitioning to adult care, adolescents should be familiarized with the adult care setting and procedures.

CHAPTER 5: Recommended Treatment Regimens for Adults and Adolescents

5.1 Introduction

The choice of medicine regimen is based on the "essential medicine" concept and the rational use of medicine. To maximise adherence, use of Fixed-Dose Combination (FDCs) medicines is strongly encouraged.

Essential medicines are defined as those medicines that satisfy the healthcare needs of the majority of the population, at a price they and the community can afford; they should therefore be available at all times and in adequate amounts, and in appropriate dosage forms (WHO Expert Committee on Essential Medicines, December 1999). On the other hand; rational use of medicines requires that patients receive medicines appropriate to their clinical needs, in doses that meet their own individual requirements, for an adequate period of time, and at the lowest cost to them and the community. (WHO Conference of Experts, Nairobi, 1985)

The National ART programme uses simplified and user friendly fixed-dose combinations for ARVs. The following FDCs will be used for the first line regimens:

Dual combinations:

- Tenofovir (TDF) 300mg + Lamivudine (3TC)300mg
- Zidovudine (AZT) 300mg + Lamivudine (3TC) 150mg

The above dual FDC should be used in combination with single formulation of:

- Efavirenz (EFV) 400mg (soon to be introduced by the MOHCC)
- Efavirenz (EFV) 600mg
- Nevirapine (NVP) 200mg

Triple combinations:

- Tenofovir (TDF) 300mg + Lamivudine (3TC) 300mg + Efavirenz (EFV) 400mg
- Tenofovir (TDF) 300mg+Lamivudine (3TC) 300mg + Efavirenz (EFV) 600mg

- Zidovudine (AZT) 300mg + Lamivudine (3TC) 150mg + Nevirapine (NVP) 200mg

Tenofovir (TDF) plus Lamivudine (3TC) plus Efavirenz (EFV) is the preferred first-line regimen.

The National ART programme has stocks of Tenofovir 300mg + Lamivudine 300mg + Efavirenz 600mg that will last until early 2018. Wastages and expiration of medicines has to be minimized as much as possible as part of good pharmaceutical management.

To this effect, the National ART programme is going to continue utilizing the Tenofovir 300mg plus Lamivudine 300mg plus Efavirenz 600mg combination until most of the stocks are exhausted.

Exceptions: Only patients with severe adverse events from the Efavirenz 600mg will be given EFV400mg until such a time when the transition phase begins.

When the Efavirenz 400mg becomes available, the Ministry of Health will provide written guidance on when and how to transition from the EFV600mg to the 400mg. Studies have shown comparable efficacy between standard-dose EFV at 600 mg/day and the reduced dose of 400 mg/day in non-pregnant adults. However, the 400 mg Efavirenz formulation has been found to have fewer EFV-related adverse reactions, including fewer CNS symptoms. It is important to note that Efavirenz 400mg CANNOT be used in pregnant women, lactating women and TB patients as currently there is insufficient evidence for its use in these categories of patients.

5.2 First-line Regimen for Adults and Adolescents

Table 5: : First-line Regimen for Adults and Adolescents

	Preferred First line Regimen	**Alternative Regimens**
Adolescents (10-19 years) ≥ 25kg Adults including pregnant & breastfeeding women,	TDF + 3TC + EFV	TDF + 3TC + NVP AZT + 3TC + EFV AZT + 3TC + NVP

A. Preferred First-line Regimen

Tenofovir + Lamivudine and Efavirenz will be taken once a day.

There is no need for a starter pack when using TDF/3TC/EFV.

Initiation and Maintenance
Triple combination of Tenofovir + Lamivudine + Efavirenz

Caution: Tenofovir (TDF)

TDF may be associated with acute kidney injury or chronic kidney disease as well as reduced bone mineral density in pregnant women.

Clinical Considerations when using TDF

- Routine blood pressure monitoring may be used to assess for hypertension.
- Urine dipsticks may be used to detect glycosuria or severe TDF nephrotoxicity in individuals without diabetes using TDF-containing regimens.
- Ideally creatinine test should be performed, use the estimated glomerular filtration rate at baseline before initiating TDF regimens.

Calculation of GFR or Creatinine clearance in ml/min using
Cockcroft Gault Equation
Male: 1.23 X (140 minus Age)x body wt in Kg/ Creatinine (in micromols/L)
Female: 1.04 X (140 minus Age) x body wt in kg/Creatinine (in micromols/L)

- Do not initiate TDF when the estimated glomerular filtration rate is <50ml/min, or in long term diabetes, uncontrolled hypertension and renal failure.

B. Alternative first-line Regimen

When Tenofovir, Lamivudine and Nevirapine is used; there is need for a starter pack and ideally this FDC should be prescribed as follows:

Two-Week Starter Pack	
Morning Dose	**Evening Dose**
Dual combination of Tenofovir (300mg) + Lamivudine (300mg)	Nevirapine (200mg)

After the starter pack has been completed, if there are no adverse events such as rashes, "step up" the dose of the Nevirapine. "Stepping up" means giving Nevirapine twice a day plus FDC Tenofovir + Lamivudine once daily as in the table below:

Step Up After the First Two Weeks	
Morning Dose	**Evening Dose**
Combination of Tenofovir (300mg) + Lamivudine (300mg) + Nevirapine (200mg)	Nevirapine (200mg)

Caution: When Nevirapine is used as 1st line ART; introduce the Nevirapine gradually (i.e., a leading-in dose). Patients are more likely to develop adverse medicine reactions such as Stevens-Johnson syndrome or hepatitis if started on the full regimen including Nevirapine twice a day. If the patient has been using Efavirenz and needs to change to Nevirapine, just start using the Nevirapine at twice-a-day dosing (i.e. no need for the leading-in dose).

A. Starter Pack (2 weeks):

- Dual Zidovudine 300 mg plus Lamivudine 150 mg orally twice a day

  plus
- Nevirapine 200 mg orally once a day

B. Stepping Up, after the First Two Weeks:

Give triple combination of Zidovudine (300mg) + Lamivudine (150g) + Nevirapine (200mg) twice a day.

Substitutions due to Toxicities or Unavailability of Medicines

Some patients may experience adverse events related to ARVs and require appropriate management (Refer to Table 10 on Adverse Events and their management) In the event of unavailability of certain ARV medicines, substitutions should be considered.

The following actions should be taken prior to medicine substitution.

- If patient has been on ART for < 6 months proceed with single drug substitution
- If patient has been on ART for > 6 months do the following:
  - If patient had a VL test within the last 6 months and the VL is <1000 copies/ml proceed with single drug substitution

- If VL within past 6 months is >1000 copies /ml treatment failure is likely, proceed as the national algorithm
- If patient did not have a VL test done in past 6 months, conduct a VL test, if VL results show VL <1000 copies /ml proceed with single drug substitution however if it is over 1000 copies/ml then treatment failure is likely proceed as per national guidelines

If the patient has suspected adverse medicine events, therapy should be altered as follows (change of a single medicine in a multi-medicine regimen is permitted—that is, the offending medicine may be replaced, preferably with an alternative medicine of the same class):

- If a patient cannot tolerate Efavirenz 600mg formulation consider using lower dose efavirenz 400 mg
- In case of severe psychiatric reaction on EFV give NVP.
- Given Zidovudine adverse events such as anaemia or neutropenia, Zidovudine will be replaced by Tenofovir.
- If a patient reacts to Nevirapine, he or she should be changed to Efavirenz 600 mg orally once daily at night.
- In the event of lactic acidosis, the current ARVs should be discontinued and ART restarted after checking for normalization of the lactate levels.
- In case creatinine clearance is known and < 50 ml/min give AZT.

An alternative to Lamivudine (3TC) is emtricitabine (FTC); these medicines are considered pharmacologically equivalent. In the event that you come across a patient on Tenofovir/Emtricitabine/Efavirenz, you may substitute Emtricitabine with Lamivudine.

For patients presenting with renal impairment; consult/ refer for specialist opinion.

5.3 Second-line Treatment Recommendation for Adults and Adolescents

Ideally, patients who fail to respond to first-line treatment should be treated with a different regimen that contains medicines that were not included in the first line regimen. The second-line regimen will still consist of two NRTIs but with the addition of a PI. The second-line regimen should be initiated only after assessing for treatment adherence and failure and in consultation with a specialist in HIV and AIDS treatment or the clinical mentorship team at the OI/ART clinic. Clinical mentors should be consulted where there is

doubt about what to do. More adherence counselling will be required in preparation for the planned new therapy. *(To diagnose treatment failure see Section 8.11.)*

Table 6: Preferred second line regimens for adults and adolescents (10 – 19 years) including pregnant and breastfeeding women

Target Population	Preferred second line regimens	
Adolescents 10 – 19 years Adults, Pregnant and Breastfeeding women	If TDF was used in first line ART	AZT + 3TC + ATV/r or LPV/r
	If AZT was used in first line ART	TDF + 3TC + ATV/r or LPV/r
HIV and TB co-infection	Patients receiving Rifampicin	Same NRTI backbone as recommended for adults and adolescents plus double dose LPV/r (800mg/200mg BD)
HIV and HBV co-infection	AZT + TDF +3TC +ATV/r or LPV/r*	

*Note: * ATV/r is the preferred PI in all cases*

- Those patients with Hepatitis B infection will always need Tenofovir and Lamivudine among their medicines.
- For adults who cannot tolerate both TDF and AZT use ABC/3TC and ATV/r or LPV/r
    - Abacavir /Lamuvudine 600 mg /300mg orally once daily

      plus
    - Atazanavir/ritonavir one daily or Lopinavir/ritonavir twice daily

5.4 Third-line Treatment Recommendations for Adolescents, Adults, Pregnant and Breast-feeding Women

Those failing second-line therapy will need to be referred for Specialist assessment which includes viral load and genotype testing prior to recommending the third-line medicines. Adherence needs to be reinforced all the time.

In adolescents >12 years and adults, the preferred 3rd line ART regimen

should include Dolutegravir (50mg) and Darunavir (600mg)/Ritonavir (100mg) twice daily (for PI-experienced patients) and must be based on genotypic testing results. Raltegravir (400mg) twice a day can be used when DTG is not available. You will need to be advised by the Paediatricians regarding ARV regimens for children. Safety and efficacy data on the use of DTG in adolescents younger than 12 years and pregnant women are not yet available.

5.5 Patients with TB who are not yet on ART

- All people with presumptive and or diagnosed TB should be tested for HIV at first contact with a health care worker and those who test negative should be linked with other HIV preventive services
- All TB patients who test HIV positive should be started on ART within 2 – 8 weeks of commencement of TB treatment regardless of CD4 status, with the ART PREFERABLY GIVEN IN THE TB SETTING and clients should be linked with HIV prevention, treatment and care at the end of the TB treatment.
- All clients co-infected with TB and HIV should be managed for both conditions concurrently with TB treatment taking precedence over ART initiation
- TB/HIV co-infected patients with severe immunosuppression [CD4 count less than 50 cells/mm3] should receive ART within the first 2 weeks of initiating TB treatment. Cotrimoxazole prophylaxis should have been provided with the commencement of the TB therapy if the patient is not on it already.
- All HIV infected persons with intracranial TB who have a severe immunosuppression [CD4 count of equal or less than 50] should be initiated on anti-TB treatment promptly and have their ART initiation delayed until after 8 weeks of commencement of TB treatment to reduce the risk of intracranial TB – Immune Reconstitution Inflammatory Syndrome (IRIS) which could end fatally.
- RECOMMENDATIONS FOR ART IN HIV INFECTED CHILDREN BEING TREATED FOR TB REMAIN THE SAME AS THOSE IN ADULTS.

5.5.1 Key Considerations for ART in TB/HIV Co-infected Populations

Drug – drug interactions can complicate TB and HIV treatment. The rifamycins used in TB treatment (Rifampicin, Rifabutin and Rifapentine) are hepatic enzyme inducers and will lower the serum concentration of many medicines used to treat HIV. This effect is most pronounced with Protease Inhibitors (PIs) and rifampicin. For these reasons the following is recommended in management TB/HIV co-infected clients:

- There is limited information on use of EFV 400mg among TB patients on ART and as such an EFV 600mg based triple ART regimen once daily remains the recommended treatment regimen and dose of choice.
- In patients receiving PIs for the treatment of HIV, Rifabutin given at a dose of 150 mg once daily, should be substituted for Rifampicin. If Rifabutin is not available the doses of Ritonavir boosted Lopinavir (LPV/r) should be doubled or the doses of ritonavir increased to 400 mg twice daily (super boosting). Clinicians should be aware that both double dosing and super boosting are associated with increased risk of adverse drug reactions.
- In children being treated for TB with a Rif based regimen, using a triple NRTI regimen (such as AZT+3TC+ABC) may be considered. This regimen may however be inferior in children with high plasma viral loads.
- Bedaquiline is primarily metabolised by CYP3A4 therefore its concomitant use with EFV and PIs for patients with XDR/MDR TB can interfere with drug concentrations and should be undertaken with extreme caution and close clinical, bacteriological and virological monitoring. Therapeutic drug monitoring should be considered in these patients
- Rifampicin is known to significantly lower plasma concentrations of Dolutegravir (DTG) and therefore in patients receiving TB treatment with a Rif based regimen, the dose of DTG should be increased from 50 mg once daily to 50 mg twice daily.

5.5.2 Patients who Develop TB when already on ART

Treat TB as per national TB guidelines.

CHAPTER 6: Prevention of Mother to Child Transmission

6.1 Introduction

Mother to child transmission of HIV is an important contributor of HIV transmission. The MOHCC is committed to the elimination of MTCT of both HIV and Syphilis and as such efforts should be intensified to reach this goal. The aim of 'elimination' is to have an eMTCT rate of HIV of less than 5% in breast-feeding communities.

The national PMTCT programme therefore aims to achieve the following targets:

- ANC coverage of ≥ 95%
- Coverage of HIV and Syphilis testing of pregnant women ≥ 95%
- ART coverage of HIV positive pregnant women of >90%
- Treatment of Syphilis sero-positive pregnant women of ≥95%

The Zimbabwe PMTCT programme has four main strategies:

- Primary prevention of HIV infection among women of reproductive age
- Prevention of unintended pregnancies in HIV infected women.
- Prevention of HIV transmission from HIV infected women to their infants during pregnancy, labour, child birth and beast-feeding through HIV counselling and testing, ARV prophylaxis, ART for life for all pregnant and breast-feeding women and safer infant feeding practices
- Provision of comprehensive care to mothers living with HIV, their children and families.

In view of the increasing evidence around the benefits of life-long ART for all adults and the successful uptake of Option B+ by many programmes; WHO 2015 ARV guidelines now recommend moving away from 'options' for PMTCT to providing lifelong ART for all HIV positive pregnant and breast-feeding women regardless of their immune status or clinical stage of the woman.

Figure 4: below summarizes the synergistic purposes of providing ART to all pregnant and breast-feeding women

6.2 HIV Testing Services for Pregnant and Lactating Women

PITC for women should be considered a routine component of the package of care in all antenatal, childbirth, postpartum and paediatric care settings. In our settings, where breastfeeding is the norm, lactating mothers who are HIV negative should be retested periodically throughout the period of breastfeeding.

Health workers should retest previously HIV-negative women as follows:

- first trimester of pregnancy
- third trimester/ or at delivery
- 6 weeks post-natal and
- 6 monthly during the breastfeeding period.

In antenatal care settings, couples and partners should be offered voluntary HIV testing services with support for mutual disclosure.

Service package for pregnant women whose test result is HIV positive (including those already on ART) should include the following:

- HIV prevention during pregnancy and breastfeeding period, including dual protection, condoms and PrEP
- Discussion of childbirth plans and encouragement to deliver in a health

facility for health reasons and to ensure access to services for PMTCT

- Use of ARV drugs both for the mother's health and to prevent transmission to the infant
- Importance of partner testing and information on the availability of couples testing services
- Screening for TB and testing for other infections, such as syphilis and hepatitis B
- Counselling on maternal nutrition, including iron and folic acid supplementation
- Advice on infant-feeding and support to carry out the mother's infant-feeding choice
- HIV testing for the infant and necessary follow up for HIV-exposed infants
- Counsel on sexual and reproductive health including family planning and the need for dual contraception (reliable hormonal contraceptives plus barrier methods i.e. male and female condoms)

Acquisition of HIV infection in pregnancy or during the breastfeeding period is associated with peak viremia and increased risk of HIV transmission to the baby. As such women at risk of new infections (sero-discordant couples), should be provided with PrEP during pregnancy and breast feeding (Refer to PrEP chapter).

6.3 When to start Lifelong ART in HIV Positive Pregnant and Lactating Women

All HIV positive pregnant and breastfeeding women should initiate lifelong ART as soon possible after their HIV positive status is confirmed irrespective of their CD4 count or WHO clinical stage; and continue ART throughout the breastfeeding period and beyond. Health workers should conduct rapid assessment of a person's readiness for ART (refer to OSDM, 2016). In the context of pregnancy and breastfeeding and to minimize risk of MTCT, same day initiation is recommended. Women who are not yet ready for lifelong ART should be initiated on triple ARVs (ART), which should be continued at least for the duration of breastfeeding.

In Zimbabwe, due to the high HIV prevalence in ANC and the need to scale up towards eliminating mother to child transmission of HIV, ART should be initiated urgently in all pregnant and breastfeeding women, even if they are identified late in pregnancy or postpartum, because the most effective way to prevent mother-to-child HIV transmission is to reduce maternal viral load.

ART should be initiated and maintained in eligible pregnant and postpartum women and in infants at maternal and child health-care settings, with linkage and referral to on-going HIV care and ART at the end of 5 years or earlier at 2 years as appropriate.

Table 7: First and second-line ARVs for Pregnant and breast-feeding women

Pregnant and Lactating women	**1st line therapy**	**2nd line therapy**
Preferred Option	TDF + 3TC+ EFV600	If TDF was used as first line, use AZT plus 3TC plus ATV/r or LPV/r If AZT was used as first line, use TDF plus 3TC plus ATV/r or LPV/r
Alternative Options	AZT + 3TC + EFV600 AZT + 3TC + NVP TDF + 3TC + NVP	

There is INSUFFICIENT DATA for using low dose EFV in pregnant women, and therefore TDF +3TC+ EFV600 will continue to be used for HIV positive pregnant women till more information on dosing becomes available.

6.4 Use of Viral Load Testing in Pregnancy

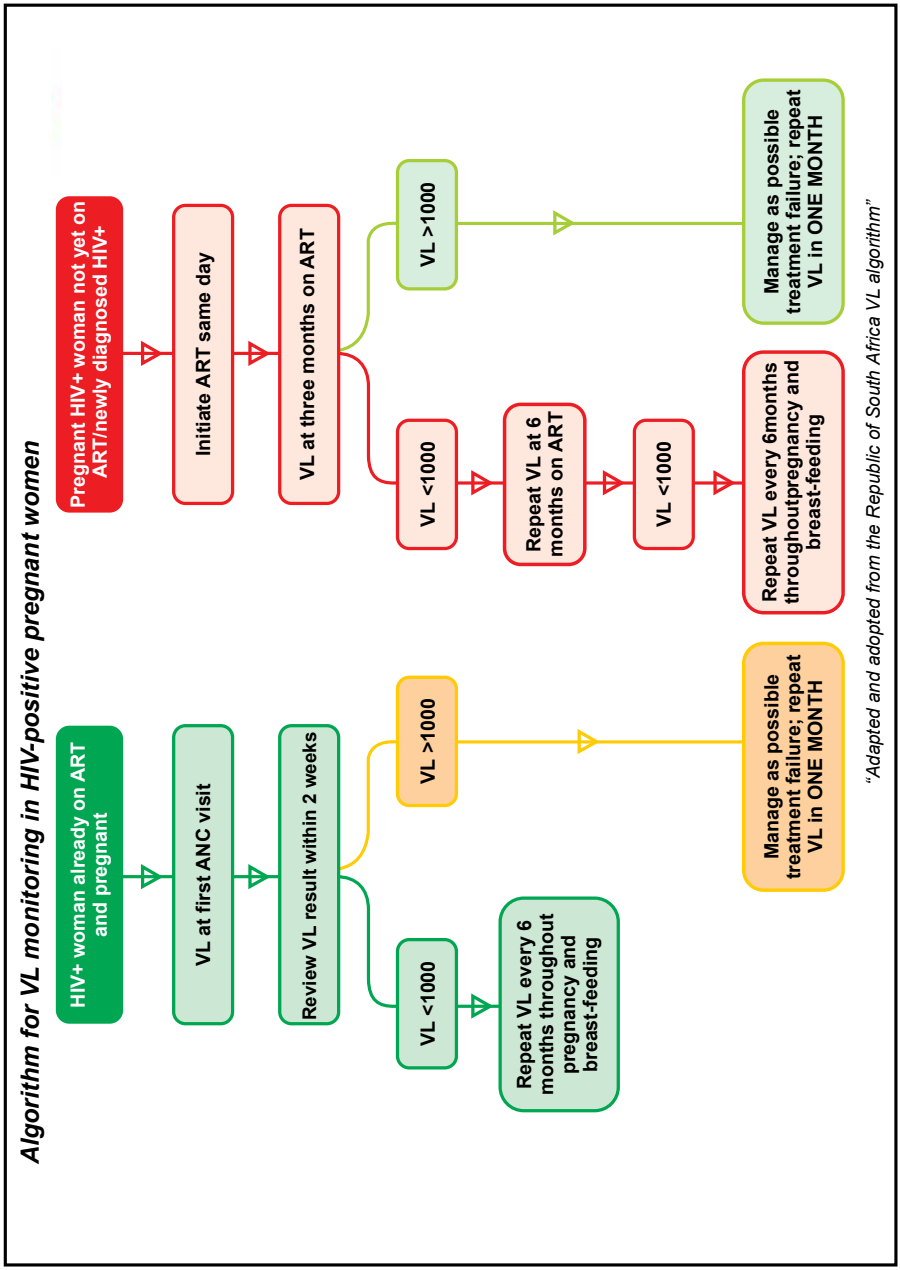
Viral load testing has additional value for assessing the risk of transmission of HIV from mother to child. For HIV infected pregnant and lactating women on ART, Health workers should

- Perform a Viral load at first ANC visit and provide adherence counselling
- If VL is > 1000 copies/ml explore possible reasons for their high viral load, commence enhanced adherence counselling immediately and VL should be repeated after 1 months and patient managed according to the national VL algorithm
- For women with a VL< 1000 copies/ml repeat VL every 6 months throughout pregnancy and breast feeding

For newly identified HIV pregnant women and those who initiate ART on their current pregnancy health workers should

- Perform a VL Test after 3 months from date of commencing ART recommendations of what to do for VL > 1000 copies/ml and < 1000 copies/ml are the same as above

Below is the VL algorithm to be used during pregnancy



6.5 HIV Exposed Infant Prophylaxis

VL testing during pregnancy and breastfeeding period is needed to stratify HIV exposed infants as either high risk or low risk. It is important not to use a "one size fits all" for infant prophylaxis as infants are not all at the same risk for HIV transmission.

A high risk infant is defined as follows:

- An infant whose mother has a high viral load >1000copies/ml during the last 4 weeks before delivery
- An infant born to HIV infected woman who has received less than 4 weeks of ART at the time of delivery
- An infant born to a newly diagnosed HIV infected woman during labor, delivery and postpartum (Incident HIV infection)

All infants who do not meet the criteria for 'high-risk' infants are classified as 'low-risk' infants.

The figure below shows infant prophylactic ARV regimen.

Figure 5: Prophylaxis for the high and low risk infants

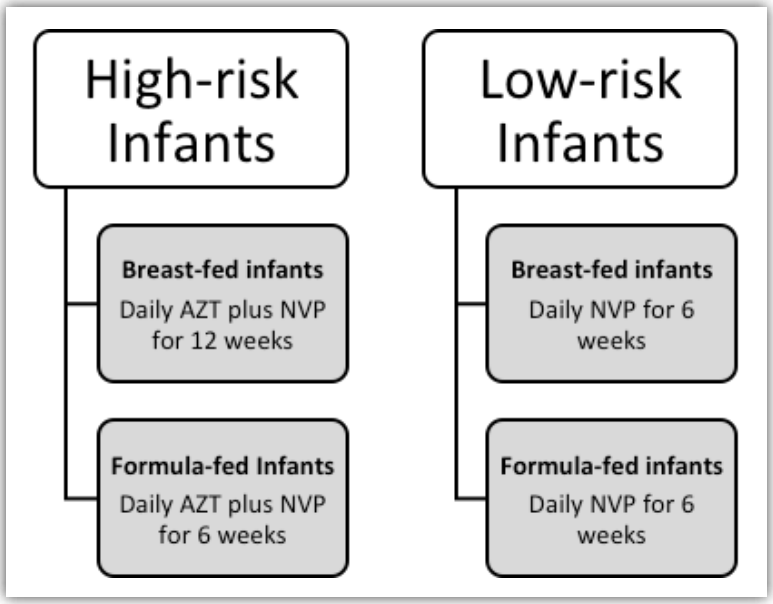


Table 8: Infant dosing table for Nevirapine and Zidovudine

Infant age	Dosing NVP	Dosing AZT
Birth to 6 weeks		
Birth weight 2000−2499 g	10 mg once daily (1 ml of syrup once daily)	10 mg twice daily (1 ml of syrup twice daily)
Birth weight ≥2500 g	15 mg once daily (1.5 ml of syrup once daily)	15 mg twice daily (1.5 ml of syrup twice daily)
>6 weeks to 12 weeks		
	20 mg once daily (2 ml of syrup once daily or half a 50 mg tablet once daily)	No dose established for prophylaxis; use treatment dose 60 mg twice daily 6 ml of syrup twice daily or a 60 mg tablet twice daily)

For infants weighing <2000 g and older than 35 weeks of gestational age, the suggested doses are: NVP 2 mg/kg per dose once daily and AZT 4 mg/kg per dose twice daily. Premature infants younger than 35 weeks of gestational age should be dosed using expert guidance.

6.7 Infant Feeding in the Context of HIV

The Ministry of Health and Child Care (MOHCC) promotes, supports and protects breastfeeding because it is the first and best investment for a child's nutrition and health.

Appropriate feeding methods including their advantages and disadvantages should be explained to all mothers to allow them to make an informed decision.

Mothers who chose to breastfeed are advised to

- Exclusively breastfeed their infants for the first 6 months of life, introducing appropriate complementary foods at 6 months, and continue breastfeeding up to 24 months and beyond.
- Avoid mixed feeding (feeding infants with breast milk and other fluids, and semi-solid or solid foods).

- Exclusive breastfeeding is recommended however mixed feeding is not a reason to stop breastfeeding in the presence of ARV drugs.

- HIV-infected mothers may consider expressing and heat-treating breast milk as an interim feeding strategy:
  - In special circumstances such as when the infant is born with low birth weight or is otherwise ill in the neonatal period and unable to breastfeed; or
  - When the mother is unwell and temporarily unable to breastfeed or has a temporary breast health problem such as mastitis;
  - If ARV drugs are temporarily unavailable

- Expressing breastmilk should also be taught to mothers to assist mothers to stop breastfeeding;
  - Breastfeeding mothers who decide to stop breastfeeding at any time should stop gradually within one month. Abrupt cessation of breastfeeding is not advised
  - Breastfeeding mothers should be counseled on how to solve common difficulties, such as sore nipples, perceptions of "insufficient milk," engorgement, manual expression, and storage of breast milk
  - Breastfeeding mothers are advised to immediately seek treatment for mastitis, cracked nipples, infant mouth lesions, and thrush to decrease the risk of MTCT
  - Breastfeeding mothers should be counseled on appropriate complementary foods that must be introduce to the infants' diet beginning at 6 months as per the Zimbabwe Infant and Young Child Feeding Guidelines.

For HIV infected mothers who choose not to breastfeed, they can adopt exclusive Formula Feeding* for the first six months, introducing appropriate complementary foods at 6 months, and continue formula feeding up to 12 months and beyond if they chose. It is important to support the mother in the feeding option they may choose. The following conditions must be met in their entirety for safe Exclusive Replacement Feeding. (AFASS)

- Safe water and sanitation are assured at the household level and in the community, and
- The mother, or other caregiver can reliably provide sufficient infant

formula* milk to support normal growth and development of the infant, and

- The mother or caregiver can prepare it cleanly and frequently enough so that it is safe and carries a low risk of diarrhoea and malnutrition, and
- The mother or caregiver can, in the first six months, exclusively give infant formula milk, and
- The family is supportive of this practice, and
- The mother or caregiver can access health care that offers comprehensive child health services.

6.8 Early Infant Diagnosis of HIV Infection (EID)

All infants with unknown or uncertain HIV exposure being seen in health-care facilities at or around birth or at the first postnatal visit (usually 4–6 weeks) or other child health visit should have their HIV exposure status ascertained. This can be done in by:

- Asking if the mother knows she is HIV positive or is on ART
- Checking the hand held child health card for information on maternal HIV status
- Performing a rapid HIV test on the mother
- Performing a rapid HIV test on the baby- N.B. this can be used to assess HIV exposure only in infants less than 4 months of age. HIV-exposure status in infants and children 4–18 months of age should be ascertained by undertaking HIV serological testing in the mother

6.9 Testing of HIV Exposed Infants

All babies of HIV-infected mothers are born with maternal anti-HIV antibodies that are passed on to them transplacentally. These antibodies start to wane from about 4months, and by 18 months have cleared off completely.

Due to the presence of these maternal antibodies, HIV antibody tests in infants under the age of 18 months cannot be used to definitively diagnose HIV infection. Diagnosis of HIV infection in children less than 18 months requires testing for the virus itself (called virologic testing, or PCR testing). Infants with an initial positive virological test result should be commenced on ART without any delay and, at the same time, a second specimen should be collected to confirm the initial positive virological test result. Immediate initiation of ART saves lives and should not be delayed while waiting for the results of the confirmatory test.

Infants testing HIV PCR negative and those HIV-exposed infants who are well should undergo HIV serological testing at around 9 months of age (or at the time of the last immunization visit). Infants who test positive by HIV rapid test at 9 months should have a virological test to definitively diagnose HIV infection and the need for ART.

Nucleic Acid Testing (NAT) at birth (birth PCR) for high Risk Infants is recommended to improve the identification of infants at highest risk for early disease progression. Nucleic acid testing (NAT) technologies that are developed and validated for use at or near to the point of care (POC) can be used for early infant HIV testing. If the birth PCR is negative, the baby should have DBS collected at 6 weeks for re-testing with PCR.

It is strongly recommended that test results from virological testing in infants be returned to the clinic and child/mother/caregiver as soon as possible, but at the very latest within four weeks of specimen collection. Positive test results should be fast-tracked to the mother–baby pair as soon as possible to enable prompt initiation of ART

Rapid diagnostic tests for HIV serology can be used to diagnose HIV infection in children older than 18 months following the national HIV testing strategy

CHAPTER 7: Paediatric Antiretroviral Treatment

Infants and young children have an exceptionally high risk of poor outcomes from HIV Infection. Upto 52% of children die before the age of 2 years in the absence of any intervention. By 5 years of age, as many as 75% of HIV positive children will be dead if they are not initiated on ART.

The goal of ART for children is to increase survival and decrease HIV related morbidity and mortality.

- Always offer PITC every time a child is in contact with healthcare services.
- ART should be initiated in ALL children living with HIV
- Children are a priority for HIV treatment and should be started on ART the same day
- Counselling to prepare caregivers and children for ART is very important but should not delay ART
- Health workers should retest ALL children newly and previously diagnosed with HIV before they initiate ART
- Investigate and manage opportunistic infections including TB before ART initiation.

  N.B. ART should be started in any child with active TB disease as soon as possible and within 8 weeks following the initiation of anti-tuberculosis treatment, regardless of the CD4 cell count and clinical stage.
- ALWAYS initiate Co-trimoxazole prophylaxis at first contact with an exposed infant or infected child.
- A baseline CD4 test is recommended at baseline to determine degree of immune suppression of a child. However, CD4 count is no longer used to assess eligibility of ART initiation.
- Health workers should develop a plan for age appropriate disclosure to children and disclosure assistance to care givers

7.1 When to Start ART in Children Younger than 10 Years of Age

Test earlier, test closer and treat earlier. ART should be initiated in ALL children living with HIV, regardless of WHO clinical stage and at any CD4 count. Children less than 5 years or with WHO clinical stage III/IV or CD4 < 25% (< 5 years) or ≤ 350 (>5 years) should be a priority.

What regimens to use in children

LPVr-based regimens are preferred for children less than 3 years. This is due to documented high levels of NNRTI resistance as a result of exposure to maternal ART and infant postnatal prophylaxis.

First line for children less than 3 years

For infants and children younger than 3 years

Preferred first line

- ABC+3TC+LPV/r

Alternate:

- AZT+3TC+LPV/r
- ABC +3TC + NVP

N.B. If LPV/r is not feasible, treatment should be initiated with an NVP-based regimen instead of holding off treatment. If HIV positive children less than 3 years develop TB, a ''triple nuc regimen'' of ABC + 3TC + AZT is recommended as an option due to the interactions of LPV/r or NVP with rifampicin. Once TB therapy has been completed, this regimen should be stopped and the initial regimen should be restarted

First line for children 3 years to less than 10 years

Preferred first line

- ABC+3TC+ EFV

Alternative first line:

- AZT+3TC+ EFV
- AZT+3TC+ NVP
- TDF+3TC+EFV (or NVP)

The recommended second line ART regimen will depend on the regimen the child was taking when the diagnosis of treatment failure was made.

7.2 Third Line ART Regimen in Children

Third line ART regimen should be based on genotypic test results.

Children 0-10yrs
RAL + 2 NRTIs
DRV/r + 2 NRTIs
DRV/r + RAL +/- 1–2

Table 9: Recommended ART regimens in children

Age	First line	Second line	Third line
0-2 weeks	AZT +3TC+NVP		RAL + 2 NRTIs DRV/r + 2 NR-TIs DRV/r + RAL **+/-** 1–2
2 weeks to Less than 3 yrs	Preferred: ABC + 3TC + LPV/r	Preferred : AZT+3TC +RAL	
	Alternative: AZT+ 3TC + LPV/r ABC+ 3TC+ NVP	Alternative: ABC+3TC+RAL	
3years to less than 10yrs	Preferred: ABC + 3TC + EFV	AZT+3TC+LPV/r or RAL	
	Alternative: AZT + 3TC + EFV AZT + 3TC + NVP TDF + 3TC+ EFV (or NVP)	ABC +3TC + LPV/r ABC+3TC+ATV/r	

- LPV/r can be substituted for EFV at 3 years of age if viral suppression has been proven to be sustained
- LPV/r pellets should be avoided in children less than 3 months old
- For children younger than 2 weeks initiated on AZT+3TC+NVP , NVP should be substituted with LPV/r at 2 weeks of age
- Regimens and dosage should be adjusted appropriately based on age and weight at each visit
- When the Child gets to 10 years of age or > 25kgs they are ready for the adult regimen and should be followed up in the adolescent clinic.

7.3 Scheduled Visits

Post initiation visits are monthly then change to 3 monthly when patient stable.

1. Services should be delivered across a continuum of care. This requires integrated and linked service provision at all levels of the health system, from primary to secondary to tertiary (specialist) care, embracing all elements of the health system.

2. During these visits the following actions should be taken:
    - Growth should be monitored and development assessed (see Appendixes VI, VII, and VIII on growth monitoring).
    - Infant-feeding practice should be reviewed regularly and appropriate supportive counselling provided.
    - Breast feeding is recommended for all babies - Exclusive breastfeeding for 6 months with addition of complementary feeding thereafter.
    - The baby should continue breastfeeding for up to 2 years.
    - Immunisations should be given according to the national guidelines. The BCG vaccination should still be given at birth, but BCG should not be given to children with symptomatic HIV infection.
    - Always look for and treat opportunistic infections at each and every visit at the clinic.
    - Be aware of and watch for potential drug interactions. The management of TB in HIV-infected children and the treatment of severe HIV infection with ARVs is complicated by the potential for multiple drug interactions.
    - Monitoring schedule for children for viral load…

7.4 Psychosocial Factors

It is important to identify and counsel at least one dedicated caregiver who can supervise and/or give drugs. Disclosure to another adult in the same household (secondary caregiver) is encouraged to assist with medication.

The process of disclosure to the child should be initiated as early as possible, usually after seven years of age. Please note that adherence is good in children who know their status and are supported to adhere to medicines. Health workers, in consultation with the care givers, should develop a plan for disclosure that age appropriate for the child. Care givers may require assistance and health workers should provide the necessary guidance.

Recommendations for children need to take into consideration the age and weight of the child, the availability of paediatric formulations of the medications, the palatability of the medications, and the effect of food on the absorption of the drugs. Always ask about the PMTCT regimens used. Infants who have been exposed to nevirapine and have confirmed HIV infection should be treated with a PI-based regimen.

7.5 Administering Medicines

- Medicine doses must be adjusted as the child grows.
- Dosing is by weight. So weighing the child at ALL visits is essential
- Tablets may be crushed and mixed with a small amount food or water and administered immediately.
- Give explanation to the caregiver.
- Use pill boxes if available.
- Standardization is important to safely dispense correct doses.

7.6 Adverse Effects of Medicines

Always check for possible adverse effects of the medicines

AZT: Anaemia, Neutropenia

NVP: Stevens Johnson, Hepatitis

EFV: Neuropsychiatric symptoms, gynaecomastia.

ABC: Hypersensitivity reaction is very rare in our population and occurs in patients with the human leukocyte antigen HLA–B 5701 allele

CHAPTER 8: Monitoring Patients on Antiretroviral Therapy

Patients on ART need close monitoring to assess adherence to the treatment regimen, tolerance, the side effects of the medications, and the efficacy of the treatment. Health workers should document patient visit's record in the patient-held booklet (OPD card). Clinical assessments and laboratory tests are important in assessing individuals following a positive HIV diagnosis to assess for co-infections, NCDs and other co-morbidities that may impact on treatment response.

8.1 Initial Evaluation

Before commencing ART, all patients should have a detailed history taken, a physical examination carried out, and basic laboratory tests performed. Prior to commencing ART, the patient should be re-tested to verify HIV positive status, plus it is essential to screen and test for TB in all patients. Document the patient's WHO clinical staging in his or her facility-held booklet 'Green book' and in the patient-held booklet.

It is preferable in most instances to perform the following baseline tests/ measurements:

- Full blood count (especially if Zidovudine will be used)
- Serum creatinine test (if Tenofovir will be used)
- Baseline CD4 lymphocyte count (or CD4 percentage for children under 5 years)
- Pregnancy test
- Alanine transaminase test (ALT)
- Mantoux test (useful in children)
- GeneXpert test or Chest X-ray (to exclude TB)
- Blood pressure measurement

NB. A baseline CD4 test is recommended at baseline to determine degree of immune suppression of a patient to inform 'differentiated care' for the patient (refer to the OSDM manual).

If possible, perform the following tests also prior to commencing ART:

- Syphilis serology test
- Hepatitis B and C virus screening

8.2 Monitoring Adherence to Treatment

Strict adherence (which is at least 95% adherence) to recommended treatment regimens is important for treatment to be effective. Counselling and the provision of accurate information to all patients (treatment literacy) is an important determinant of treatment adherence. Information on side effects should be provided, and patients should be told what to expect from the treatment. Patients should be encouraged to seek help between visits as needed. Patients should be instructed to bring all medications and containers at each visit. Providers should carry out an adherence assessment to determine whether the medications have been taken as per schedules agreed upon.

8.3 Frequency of Clinic Visits

Initially the patient should be seen every two weeks for the first month after initiating treatment, and thereafter monthly for another three months, then every two months thereafter.

After the first six months, the patient can be seen at reduced frequency depending on whether they are stable or not.

When clients are clinically stable and on chronic medication, they do not necessarily need to be seen by the clinician at every visit. (Refer to the Operational and Service Delivery Manual/OSDM).

A stable patient on ART is defined as someone who:

- Has no current OIs, has a VL<1,000 copies/ml and is at least 6 months on ART
- Where viral load is not available the client should have no current OIs, a CD4>200 copies/ml and be at least 6 months on ART

There are three main types of clinic visits:

- A clinical visit is a scheduled appointment where the clinician makes a thorough assessment and reviews monitoring blood tests. A stable patient on ART should be seen for a clinical assessment every 6 months.
- A refill visit is a scheduled appointment where a patient has a pre-filled prescription and attends pharmacy directly to collect their medicine. Clients coming from a re-fill do not need to see a nurse for a consultation.
- An unscheduled visit is when a patient attends in-between refills or clinical visits when they develop any problems.

8.4 Monitoring Adverse Medicine Events or Medicine Side Effects

A patient on ART may develop new symptoms whilst on treatment. Such symptoms may be indicative of inter-current illnesses, adverse medicine events, or immune reconstitution inflammatory syndrome. All patients should be examined carefully at each visit. Any inter-current illness should be treated appropriately. If in doubt, refer the patient to your clinical mentor or higher level OI/ART clinic.

The patient should be provided with written and verbal information on potential side effects and should be requested to report immediately for examination should side effects occur. See Appendix III for the grading of side effects. There is a need to watch out for common side effects such as anaemia, renal impairment, CNS symptoms and peripheral neuropathy.

Central Nervous System Toxicities

Hallucinations, abnormal dreams, depression, mental confusion and convulsions can occur especially with Efavirenz. These events tend to occur within the first month. In some cases, they can persist for months and not resolve at all. Patients should be warned about them but if the symptoms do not settle down, consider using Nevirapine. However, if both NNRTIs cannot be tolerated use boosted PIs.

Metabolic Abnormalities

Hyperglycaemia i.e. development of diabetes and hyperlipidaemia should be anticipated with the long-term use of ARVs. Check blood sugar and lipid levels at least with every CD4-level check or when clinically indicated.

Anaemia

Check haemoglobin after the first month of Zidovudine use.

Lactic Acidosis

Lactic acidosis is characterized by non-specific symptoms and signs such as shortness of breath, hyperventilation, fatigue, weight loss, abdominal pain, vomiting, and tachycardia. Lactate levels are currently not routinely available, but one needs to have a high index of suspicion. Use a full urea and electrolytes screen with bicarbonate levels as a surrogate marker. The treatment for this is to stop all ARVs and keep the patient well hydrated. When the patient's symptoms have settled down, restart an ARV regimen that contains Tenofovir. Referral to a higher level of care or a specialist is encouraged.

Lipodystrophy / Fat Redistribution

With longer duration of use of ART, cosmetic problems such as loss of fat in the face or limbs and buttocks or increasing breast size and abdominal fat accumulation will be encountered more frequently. If the patient is on a Zidovudine -containing regimen, consider changing to Tenofovir, but counsel the patient appropriately.

Other Side Effects

Mild side effects such as headache, fatigue, gastrointestinal upsets, and diarrhoea occur fairly frequently, but serious side effects occur rarely. Mild side effects usually occur early in treatment and often wear off and should be treated symptomatically. Side effects of medicines are summarized to follow.

Table 10: Some Important Side Effects of Antiretroviral Agents

Medicine	Side Effects	Risk Factors	Action to be taken
Nucleotide/Nucleoside Reverse Transcriptase Inhibitors (NRTIs)			
Tenofovir (TDF)	Renal complications	Underlying renal disease; Age > 50 years; untreated diabetes and hypertension; concomitant use of nephrotoxic medicines or PI	Monitor creatinine. Substitute with Zidovudine
	Decreases in bone mineral density	Vitamin D deficiency; risk factors for oesteoporosis or bone mineral density loss	
	Other SE: Gastrointestinal (GI) symptoms, rash		
Zidovudine (AZT)	Anaemia, neutropenia, Lipoatrophy, lipodystrophy, myopathy, headache, lactic acidosis	CD4 < 200 cells/ mm3 Anaemia at baseline	Monitor full blood count; if severe anaemia change to Tenofovir (TDF) or Abacavir (ABC)
Lamivudine (3TC)	Usually nil		

Medicine	Side Effects	Risk Factors	Action to be taken
Nucleotide/Nucleoside Reverse Transcriptase Inhibitors (NRTIs)			
Efavirenz (EFV)	Central nervous system symptoms (dizziness, confusion, convulsions headache, sleep disturbance, abnormal dreams) or mental sysmptoms (anxiety, depression, mental confusion) usually during the first three weeks and then resolve	Pre-existing psychiatric disorder e.g. depression History of seizures	For CNS symptoms: consider dosing at night or use low dose EFV (400mg/day); if this fails then withdraw EFV and substitute with Nevirapine (NVP)
	Hepatotoxicity	Underlying hepatic disease or concomitant use of hepatotoxic medicines	Withdraw EFV and substitute with boosted PIs
	Gynaecomastia	Risk factors unknown	substitute Efavirenz (EFV) with Nevirapine (NVP)

Nevirapine (NVP)	Liver toxicity, abnormal liver function tests (LFTs); Mild or severe skin rashes (e.g. Stevens- Johnson syndrome [rare]), Fever, fatigue, nausea,	Underlying hepatic disease or concomitant use of hepatotoxic medicines High baseline CD4 cell count (>250 cells/mm3 in women and >400 cells/mm3 in men)	If LFTs are suggestive of hepatitis or if jaundice is present, discontinue; if rash is severe, discontinue and replace with Efavirenz
Protease Inhibitors (PIs)			
Atazanavir (ATV/r)	Jaundice, nausea, diarrhoea, headache, hyperbilirubinaemia		Monitor; withdraw medicine if symptoms are severe
Lopinavir/ ritonavir (LPV/r)	Hepatotoxicity Pancreatitis Hyperlipidaemia, GI intolerance, diarrhoea, hyperglycaemia, Lipodystrophy,	Underlying hepatitic disease Advanced HIV disease and alcohol misuse Obesity, diabetes	Give loperamide for the diarrhoea
Darunavir (DRV/r)	Hepatotoxicity Severe skin and hypersensitivity reactions	Underlying hepatic disease or concomitant use of hepatotoxic medicines Sulfonamide allergy	Monitor; withdraw medicine if symptoms are severe.

Integrase inhibitor			
Raltegravir (RAL)	Mood changes, depression, myopathy. skin reactions e.g., Stevens- Johnson syndrome,		Monitor; withdraw medicine if symptoms are severe
Dolutegravir (DTG)	Hepatotoxicity and hypersensitive reactions	Underlying liver disease	Monitor; withdraw medicine if symptoms are severe

8.5 Key Antiretroviral Medicine Interactions

Drug-drug interactions can reduce or increase the efficacy of ARV-related toxicities. Care providers should be aware of all medicines used by the patient, including alternative medicines products such as herbal remedies, vitamins and dietary supplements that may interact with ARV medicines (Refer to Table 8 to follow)

Table 11: Key ARV drug interactions and management

ARV Medicine	Key interactions	Suggested management
Efavirenz (EFV)	EFV may lower the efficacy of some long-acting hormonal contraceptives	Use alternative or additional contraceptive methods e.g. condoms
	Amodiaquine (Anti-malarial)	Use alternative anti-malaria drug
Nevirapine (NVP)	Rifampicin	Substitute nevirapine (NVP) with Efavirenz (EFV)
	Ketoconazole and Itraconazole	Use alternative antifungal drug
Boosted PIs (ATV/r, LPV/r and DRV/r)	Hormonal contraceptives	Use alternative or additional contraceptive methods
	Rifampicin	Substitute rifampicin with rifabutin if available For children adjust dose of LPV/r or substitute with three NRTIs
	Tenofovir (TDF)	Monitor renal function
Dalutegravir (DTG)	Carbamazepine, phenobarbital and phenytoin	Use alternative anti-consultants

8.6 Immune Reconstitution Inflammatory Syndrome

Immune reconstitution inflammatory syndrome (IRIS) is characterized by a clinical deterioration after starting ART. It is the immune system interacting with latent infections. This syndrome should be considered if the following occur within 2 to 12 weeks of commencing ART:

- Patients with advanced HIV disease, particularly those with a CD4 count of less than 50, may become ill with IRIS. Typical symptoms are fever, sweats, loss of weight, and occasionally skin rash and lymphadenopathy.
- Immune reconstitution illnesses occur when improving immune function unmasks a previously occult OI (an infection that was present in the patient's body but was not clinically evident).
- Common immune reconstitution illnesses in Zimbabwe are TB, cryptococcal meningitis and recurrent herpes simplex virus.

An immune reconstitution illness is not indicative of treatment failure or medicine side effects. It is not a reason to stop ART or to change the ARV regimen, but the emerging OI must be treated.

8.7 Monitoring Effectiveness of ART

The effectiveness of ART may be monitored by assessing clinical improvement, immunologic function (CD4 count/CD4%), and HIV viral load (VL). It is necessary to make an assessment of response to treatment through regular careful clinical examinations backed where possible by simple laboratory tests.

WHO is recommending VL testing as the gold standard for monitoring response to ARV medicines as it is more sensitive and can detect adherence problems and treatment failure much earlier than CD4 count testing.

The Ministry of Health has in its plans to scale up routine viral load testing, however if VL testing is not yet available, CD4 testing should be conducted regularly at six-monthly intervals.

8.8 Clinical Monitoring

Monitoring ART in adults and adolescents

The following clinical indices suggest that the patient is responding to ART:

- The patient feels better and has more energy to perform daily tasks.
- The patient is gaining weight (record the patient's weight at each visit).

- There is an improvement in symptoms and signs of the original presenting illness.
- Infections such as oral thrush, hairy leukoplakia, genital herpes, skin rash, and molluscum contagiosum have improved.
- There has been an improvement in chronic diarrhoea.
- There has been an improvement in Kaposi's sarcoma.
- The patient is free of new moderate or severe infections.

Monitoring ART in Children

In children, growth and development are important clinical monitoring indicators and are assessed using growth charts. Laboratory indices of CD4 lymphocyte counts and HIV VL levels may also be used in assessing response to therapy, noting that sometimes the VL will come down but may still not be undetectable.

Clinical assessment involves the following:

- Always check the child's and caregiver's understanding of ART as well as anticipated support and adherence to ART.
- Always check for symptoms of potential medicine toxicities.
- Always assess for treatment failure (i.e. reassessment of clinical stage).

Important signs of infants' and children's response to ART include the following:

- Improvement in growth—in children who have been failing to grow
- Improvement in neurological symptoms and development—in children with encephalopathy or who have been demonstrating delay in the achievement of developmental milestones
- Decreased frequency of infections (bacterial infections, oral thrush, and/or other OIs)

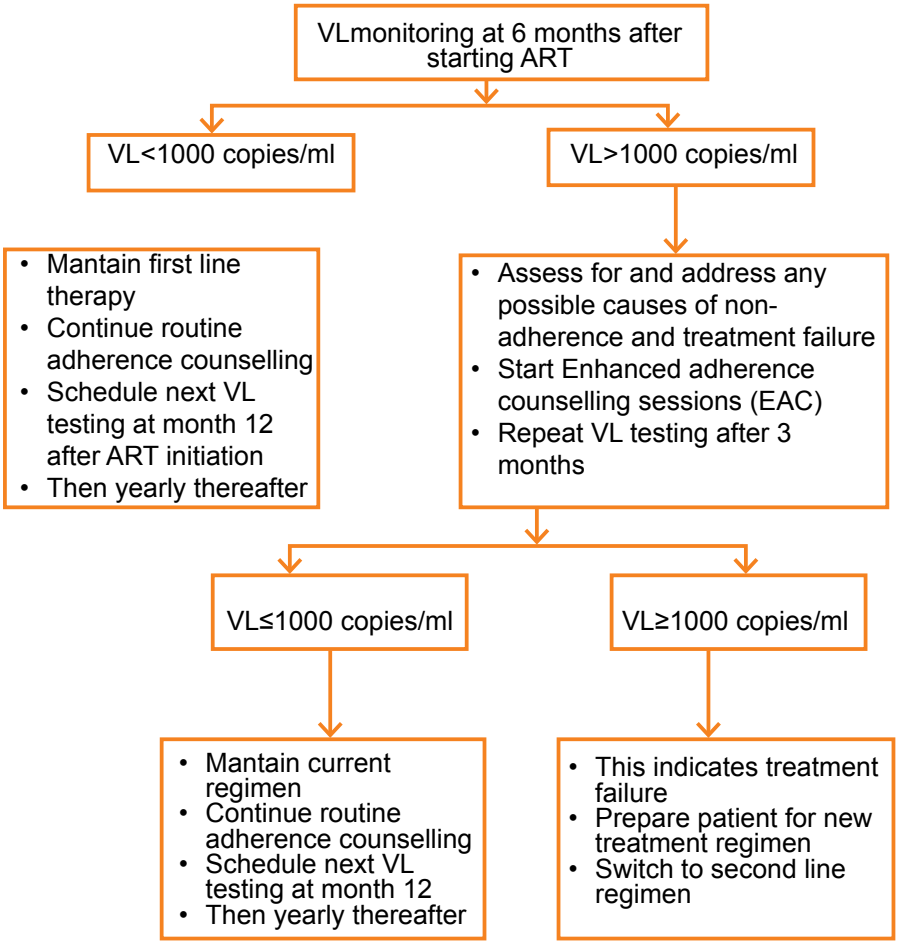
8.9 Virological (HIV Viral Load) Monitoring

WHO is recommending VL testing as the gold standard for monitoring response to ARV medicines. Compared to clinical or immunological monitoring, viral load provides an early and a more accurate indication of treatment failure and the need to switch to second or third-line drugs. The VL usually decreases to undetectable levels within six months with greater than 95% adherence to ART. Dried blood spot specimens using venous or capillary copies/ml can be used to determine viral failure when using DBS samples as defined for testing using plasma.

Viral load should be monitored routinely at 6 months and at 12 months after ART initiation, and then annually thereafter.

Figure 12 below is an algorithm for routine VL testing. It is important to note that studies have shown that around 70% of patients on first-line ART who have a first high viral load will suppress following an adherence intervention. Enhanced adherence counselling is therefore, crucial to reduce unnecessary switches of patients. (Refer to OSDM for Job Aid on Enhanced Adherence Counselling).

Figure 12: Viral Load testing strategies to detect or confirm treatment failure and switch in adults, adolescents and children



8.10 Immunological Monitoring (CD4 count)

With successful ART, the CD4 lymphocyte count increases. The rate of increase depends on the initial CD4 count. Persistently declining CD4 counts (as measured on two occasions, at least three to six months apart) and clinical deterioration as described above are suggestive of treatment failure. CD4 count testing should be performed six-monthly, particularly after the first two years of initiation of ART. More frequent testing should be performed if immunological failure is suspected. CD4 testing will continue to be used for some time while viral load testing is being scaled up.

8.11 Treatment Failure

Clinical criteria that suggest treatment failure

Before diagnosing treatment failure, one must assess adherence to treatment. The decision to switch from first-line to second-line or even third line therapy should not be taken lightly. Treatment failure can be determined clinically (this tends to result in delayed switching to second-line therapy), immunologically using CD4 trends over time, or virologically (e.g., VL greater than 1000 copies/ml based 2 consecutive VL measurements 3 months apart with enhanced adherence (EAC) support).

Table 13: Treatment Failure (WHO. 2015)

Clinical failure Children:	**Children:** New or recurrent clinical event indicating advanced or severe immunodeficiency (WHO stage 3 and 4 clinical conditions with exception of TB) after 6 months of effective treatment **Adults and Adolescents** New or recurrent clinical event indicating severe immunodeficiency (WHO stage 4 clinical condition) after 6 months of effective treatment
Immunological failure (CD4 failure)	**Children** Decrease to pre-therapy CD4 count/percentage Younger than 5years – Persistent CD4 level below 200 cells/ mm3 or CD4% < 10% Older than 5 years – Persistent CD4 levels below 100 cells/mm3

	Adults and adolescents CD4 counts falls to the baseline (or below) or persistent CD4 levels below 100 cells/mm
Virological failure	Viral load greater than 1,000 copies/ml based on two consecutive VL measurements after 3 months with enhanced adherence counselling

Note: A second-line regimen should be started only after consultation with an appropriate specialist in HIV and AIDS care/treatment or your mentor.

Treatment Failure in Children

Consider the following before switching ART regimens:

- The child should have received the regimen for at least 24 weeks (six months).
- Adherence to therapy should be assessed and considered to be optimal.
- Any inter-current OIs should have been treated and resolved.
- Before considering changing treatment due to growth failure, ensure that the child is receiving adequate nutrition.

In children on ART, the main clinical indications to switch therapy are the development of new or recurrent stage 3 or 4 events at least 24 weeks (six months) after starting therapy with a first-line regimen. Of note are

- a lack of or decline in growth rate in children who showed an initial response to treatment (moderate or severe unexplained malnutrition not adequately responding to standard therapy despite adequate nutritional support and without other explanation); loss of neurodevelopmental milestones (see Appendix VI) or development of encephalopathy; OR
- occurrence of new OIs or malignancies or recurrence of infections, such as oral candidiasis that is refractory to treatment or oesophageal candidiasis.

Note: A second-line regimen should be started only after consultation with a specialist in HIV and AIDS care/treatment or your mentor.

CHAPTER 9: Opportunistic Infections and Co-morbidities

Various opportunistic infections (TB, cryptococcosis) co-infections (hepatitis B or C), co-morbidities and other health conditions are common among people living with HIV and have implications for the treatment and care, including the timing and choice of antiretroviral medicines HIV is also associated with cancers such as Kaposi Sarcoma, Non-Hodgkins' Lymphoma, invasive cervical cancer as well as non-communicable diseases such as diabetes, cardiomyopathies and chronic kidney disease. This section provides a brief overview of the most common and important conditions.

9.1 Cotrimoxazole Preventive Therapy

Immunosuppressed people are prone to develop OIs such as Pneumocystis jirovecii pneumonia, toxoplasmosis, and lower respiratory tract bacterial infections and bacterial skin infections.

Cotrimoxazole prophylaxis can potentially prevent the following OIs:

- Streptococcus pneumoniae pneumonia
- Nontyphoid salmonelloses
- Pneumocystis jirovecii pneumonia (PCP)
- Cerebral toxoplasmosis
- Nocardiosis
- Isosporiasis

Cotrimoxazole prophylaxis for adults including pregnant and breast-feeding women should be given to the following:

- All patients with WHO clinical stages II, III, and IV disease
- All patients with CD4 counts of less than 350 cells/mm3
- Pregnant women with CD4 counts of less than 350 cells/mm3

Cotrimoxazole prophylaxis for HIV infants, children and adolescents should be given to the following:

- All HIV positive infants, children and adolescents irrespective of clinical and immunological condition
- Priority should be given to all children younger than 5 years regardless of CD4 count or clinical stage and children with severe or advanced HIV

clinical disease (WHO clinical stage 3 and 4) and all those with CD4 count ≤350.

- All children born to HIV-positive mothers at six weeks of age until they are tested and confirmed to be HIV free

In settings where malaria/or severe bacterial infections are highly prevalent; provide CTX to all HIV infected infant, children, adolescents and adults including pregnant and breast-feeding women regardless of CD4 cell count and WHO clinical stage.

Cotrimoxazole prophylaxis should be started as soon as any of the above conditions are suspected; this should be done at every entry point and not just be left to the OI clinics.

Cotrimoxazole Prophylaxis in Aults

Cotrimoxazole (sulphamethoxazole 800 mg and trimethoprim 160 mg) should be given once daily orally.

Cotrimoxazole Prophylaxis in Children

Give once daily orally according to the following table.

Table 13: Cotrimoxazole Dosing Chart for Children

Age	**Dose (ml)**		
	Suspension (240 mg / 5 ml)	**Adult tablets (480 mg)**	**Paediatric tablets (120 mg)**
0 to 6 months	2.5	¼	1
6 months through 3 years	5	½	2
Over 3 years	10	1	3

Health-care providers should keep the following recommendations in mind when offering cotrimoxazole prophylaxis:

- Cotrimoxazole prophylaxis should be commenced at least one to two weeks before the commencement of ART. This allows time to identify those who might be allergic to cotrimoxazole.

- For patients who are allergic to cotrimoxazole, consider desensitization (see Appendix IV).

When to discontinue Cotrimoxazole:

In settings with low prevalence for both malaria and bacterial infections;

CTX may be discontinued for children 5 years of age and older who are clinically stable /or virally suppressed on ART for at least 6 months and with a CD4 count more than 350 cell count.

For adults, pregnant and breast-feeding women, discontinue when clinically stable on ART, with evidence of immune recovery and viral suppression.

In malaria endemic settings/or areas with high prevalence of severe bacterial infections; once CTX has been initiated, it should be continued (do not stop).

9.2 TB/HIV Collaborative Activities

The association between TB and HIV is now well documented with an estimated 72% of TB patients in Zimbabwe co-infected with HIV. Management of TB and HIV requires close collaboration between the NTP and AIDS programmes. This will help reduce the burden of TB in HIV and the burden of HIV in TB patients.

HIV care settings should implement the three I's strategy:

- Intensified TB case- finding
- Isoniazid Preventive Therapy (IPT) – as part of TB Preventive Therapy (TBPT)
- Infection Control at all clinical encounters

9.2.1 Intensified TB case- finding

- All HIV positive clients should be routinely screened for TB at every encounter with a health care worker, using a four symptom checklist (current cough, night sweats, loss of weight and fever) and/or a CXR (where available) in order to timely assess their eligibility to be commenced on TB Preventive Therapy or TB treatment
- All HIV positive clients with a positive enquiry to any one of the symptoms on the checklist and or having an ABNORMAL CXR should be classified as presumptive TB cases and MUST have one sputum sample collected and submitted for TB investigation using the Xpert MTB/Rif assay as preferred diagnostic platform of choice.

- All HIV positive clients who are seriously ill and or have a CD4 T cell count of equal or less than 100 should have the Urine Lateral flow -Lipoarabinomannan Assay (LF-LAM) to assist in TB diagnosis.
- Where resources are available ALL NEWLY DIAGNOSED HIV POSITIVE PATIENTS should submit one spot sputum sample for Xpert MTB/Rif to rule out active TB disease even if when they have a negative symptom screen

9.2.2 TB Preventive Therapy [TBPT]

Both ART and Isoniazid Preventive Therapy are effective in preventing HIV associated TB individually and with additive effects when combined.

In adults, adolescents and pregnant women eligible for IPT, OI/ART clinics should aim to initiate IPT immediately or within 3 months and according to current practices and visit frequency in the facility. Health workers should provide sufficient information to patients on the benefits of IPT.

The following are the target groups for IPT in Zimbabwe:

- Adults and adolescents including pregnant women living with HIV (Pre-ART & on ART)
- Children living with HIV (Pre-ART & on ART)
- HIV infected adults, adolescents and children contacts of active TB cases
- HIV infected health care workers

Adults and adolescents living with HIV should be screened with a clinical algorithm; those who do not report any one of the symptoms of current cough, fever, weight loss or night sweats are unlikely to have active TB and should be offered IPT. The following patients should be excluded

- Symptoms and signs suggestive of active TB
- Patient on treatment for TB
- Completion of IPT within the past 3 years
- Patients who have been on ART for 3 months or less
- PATIENTS ON ART FOR MORE THAN 3 YEARS WHO ARE DOING WELL [CD4 > 450]*
- Signs of active liver disease or history of INH induced hepatitis
- In the subgroup of patients eligible and in the process of being 'worked up' for ART, there is a high prevalence of undiagnosed TB even among those that do not have TB symptoms. It is reasonable in this subgroup therefore to wait 3 months before considering initiation of IPT during

which TB symptom screening should be repeated at each clinic visit.

- Adults and adolescents including pregnant women living with HIV and unlikely to have active TB will receive IPT for 6 months at a daily dose of 5mg/kg with maximum dose not supposed to exceed 300mg/day.
- Adults and adolescents (including pregnant women) will be given 6 months of IPT immediately following the successful completion of TB treatment (i.e. as secondary prevention).

9.2.3 IPT and Unknown or Positive TST Status

Adults and adolescents living with HIV who have an unknown or positive tuberculin skin test (TST) status and are unlikely to have active TB should receive at least six months of IPT as part of a comprehensive package of HIV care. IPT should be offered to such individuals regardless of the degree of immunosuppression, and also to those on ART, those who have previously been treated for TB and pregnant women

Figure 13: TB Screening Algorithm for Children More Than One Year of Age and Living with HIV

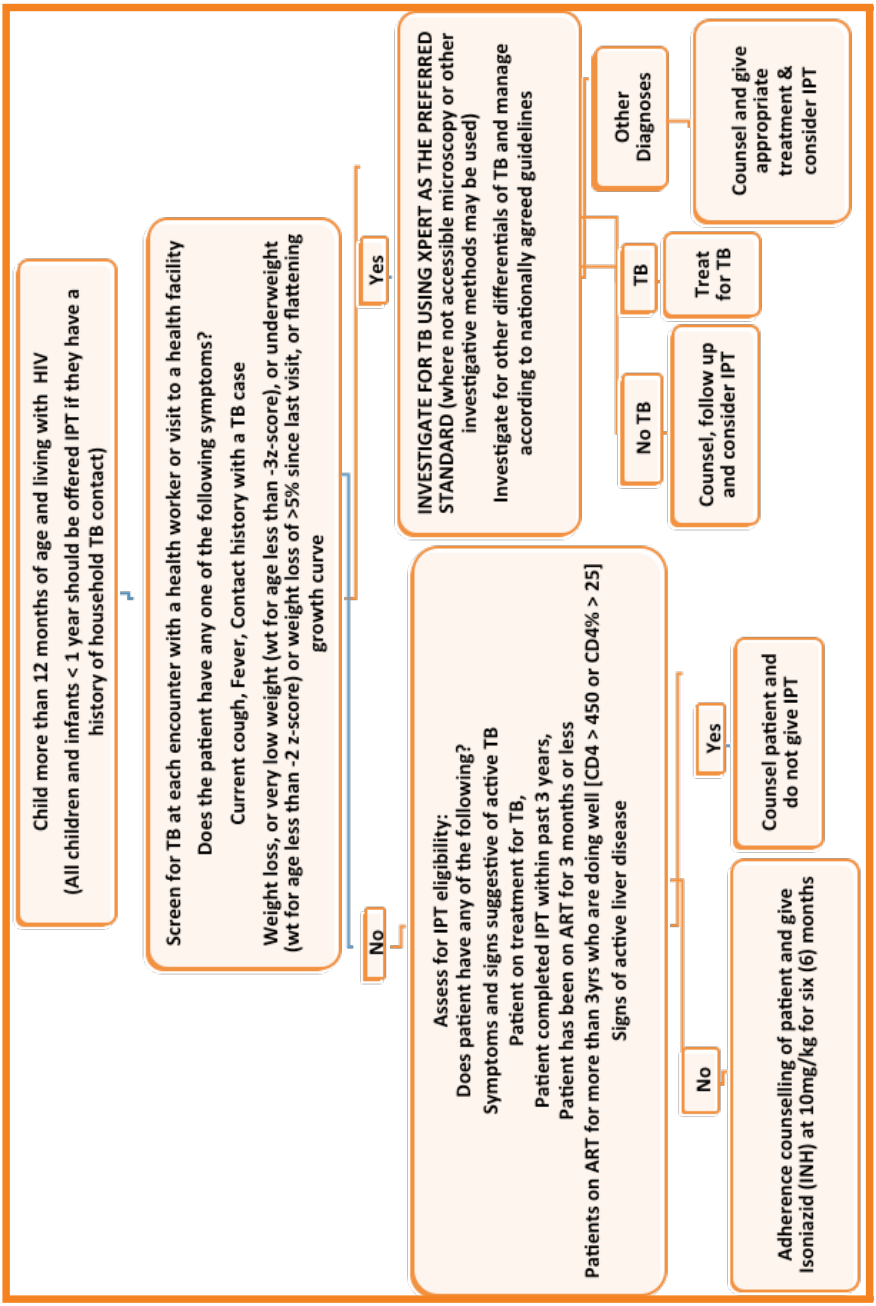
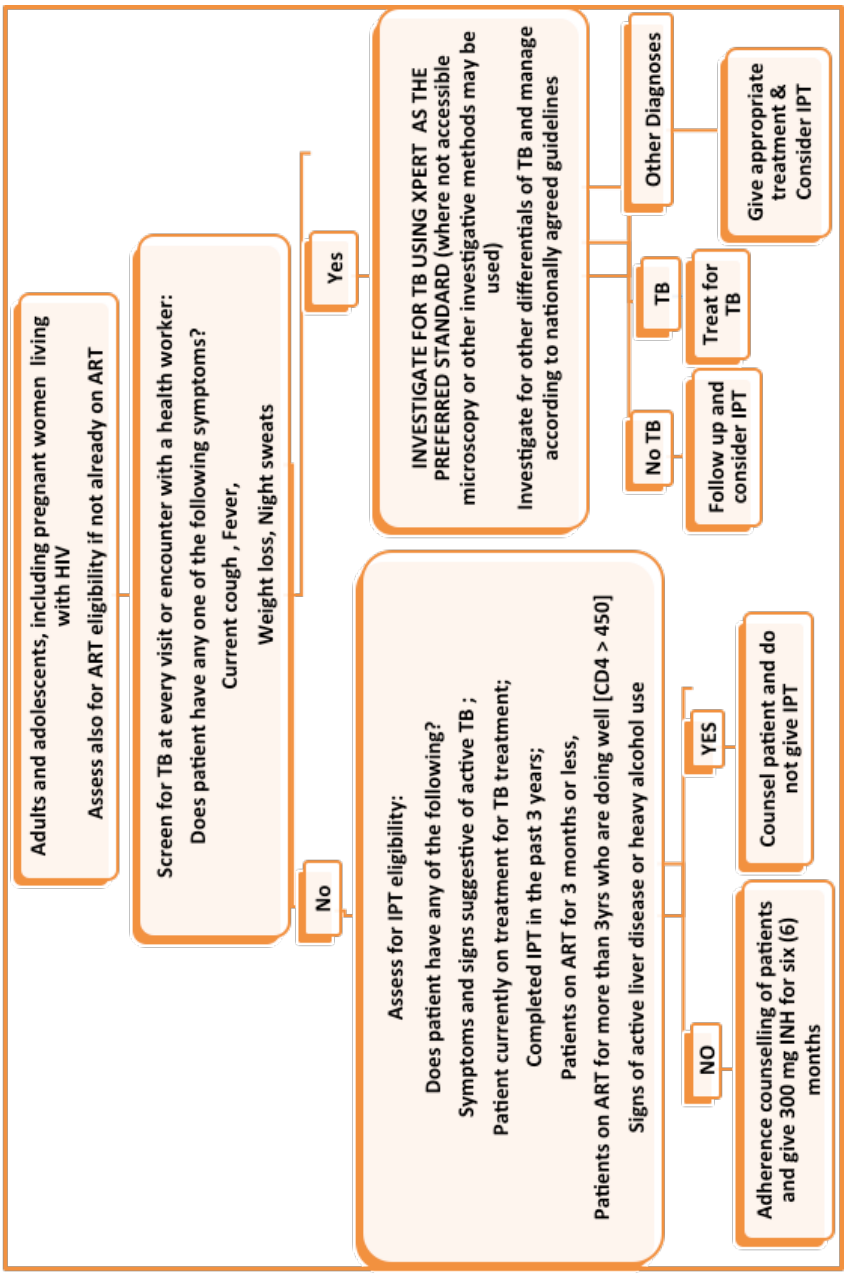


Figure 14: TB Screening Algorithm for Adults and Adolescents Including Pregnant Women Living with HIV



9.2.4 Infection Control at all Clinical Encounters

People who work or receive care in health care settings are at higher risk for becoming infected with TB; therefore, it is necessary to have a TB infection control plan as part of a general infection control program designed to ensure the following:

- prompt detection of infectious patients,
- airborne precautions, and
- treatment of people who have suspected or confirmed TB

The following measures should be in place;

- Administrative
- Environmental controls
- Use of respiratory protective equipment

Figure 15: Infection Control Recommendations

Administrative	• A triage system should be in place to identify people suspected of having TB and minimize diagnostic delays with rapid diagnostics, e.g. Xpert MTB/RIF • Separate people with suspected or confirmed TB • Ensure cough etiquette and respiratory hygiene • Minimize the time spent in health-care facilitie
Health workers and care-givers	• Inform and encourage health workers with TB symptoms to undergo TB diagnostic investigation as well as HIV testing and counselling • HIV testing and counselling • Provide a package of care for HIV-positive workers (ART and IPT) living with HIV to a lower-risk area
Use of particulate respirators	• Protective equipment (such as N95 respirators) should be provided for health-care workers caring for patients with infectious TB (suspected or confirmed)
Environmental	• Ventilation (natural or mechanical)

Source: WHO policy on TB infection controls in health-care facilities, congregate settings and households. Geneva: World Health Organization; 2009 (http://www.who.int/tb/publications/2009/9789241598323/en).

9.2.5 Laboratory Diagnostic Tools

Use of Xpert MTB/RIF

Xpert MTB/RIF should be used rather than conventional microscopy, culture and drug susceptibility testing (DST) as the initial diagnostic test in all patients suspected to have TB.

Xpert MTB/RIF should be used in preference to conventional microscopy and culture as the initial diagnostic test for cerebrospinal fluid specimens from patients suspected of having TB meningitis.

Use of LF-LAM

Urine lateral flow (LF-LAM) may be used to assist in the diagnosis of active TB in adult inpatients living with HIV, with signs and symptoms of TB (pulmonary and/or extra-pulmonary), who have a CD4 count less than or equal to 100 cells/mm3, or people living with HIV who are seriously ill, a regardless of CD4 cell count or with unknown CD4 cell. LF-FAM use is limited to admission/inpatient institutions. LF-LAM should not be used as a screening test for active TB

9.2.5 Summary of Management of TB/HIV co-infection:

The activities to be undertaken in the management of TB/HIV co-infected persons are summarised below;

- HIV testing and counselling should be routinely offered to all persons suspected or known to have TB
- HIV-related prevention, care and support services should be routinely offered to all persons suspected or known to have TB
- Case definitions and anti-TB treatment regimens are the same for HIV-positive and HIV-negative TB patients, and drug dosages in mg/kg are also the same.
- In TB / HIV co-infection the first priority is to initiate anti -TB treatment followed by cotrimoxazole, and then ART
- All TB patients co-infected with HIV should be given co-trimoxazole preventive therapy (CPT) for the whole duration of TB treatment.
- All people living with HIV with active TB disease, irrespective of CD4 cell count and the site of TB disease, should be initiated on ART as soon as practicable (Refer to Section 4.4)

- All PLHIV should be screened for TB at every contact with health services. Patients should be screened for current cough, fever, night sweats and loss of weight.
- PLHIV who develop TB should be started on anti-TB treatment immediately.
- TB/HIV patients benefit from the use of steroids for the same indications as found in HIV-negative TB patients (refer to TB Guidelines)

9.3 Treatment of Cryptococcal Disease

9.3.1 Prevention of Cryptococcal Disease

Patients initiating ART with undiagnosed cryptococcal disease are at higher risk of early mortality than patients who are pre-emptively diagnosed and treated for cryptococcal disease. All patients initiating ART should be clinically screened for evidence of symptomatic cryptococcal disease – headache, neck stiffness, fever, focal neurologic signs, confusion, altered mental status. All those who screen positive should be referred for further diagnostic work up for meningitis. Screening of asymptomatic ART naïve individuals with CD4 count <100cells/mm3 is recommended and should be done with a Cryptococcal neoformans antigen test (CrAg)using latex agglutination tests (LA) or lateral flow assays (LFA) on serum, plasma or CSF. A lumbar puncture should be offered to individuals who screen positive for cryptococcal antigen, as a positive cryptococcal antigen may precede the onset of clinical cryptococcal meningitis by many weeks.

Individuals who are screened for cryptococcal disease should be managed as indicated in Table 9.

Table 14: Treatment decisions for asymptomatic cryptococcal disease

Serum CrAg negative	No LP necessary. No fluconazole required. Initiate ART.
Serum CrAg positive	If available recommend LP:
	If CSF CrAg positive, manage for cryptococcal meningitis
	If CSF CrAg negative treat with Fluconazole 800mg orally once daily for 2 weeks, then Fluconazole 400mg orally daily for 8 weeks, followed by maintenance therapy with Fluconazole 200mg orally daily until CD4>200 cells/mm3 for 6 months

Timing of ART for individuals with asymptomatic cryptococcal antigenemia is unknown. We recommend initiation of ART 2-4 weeks after initiation of antifungal therapy in individuals who screen positive for serum CrAg without any evidence of disseminated cryptococcal meningitis.

9.3.2 Treatment of Cryptococcal Meningitis

Cryptococcal meningitis remains a major cause of death in HIV infected patients. Early diagnosis and prompt treatment of cryptococcal meningitis is critical to improve clinical outcomes. The mainstay of treatment is rapid diagnosis, prompt initiation of appropriate antifungal therapy and management of raised intracranial pressure. Patients at greatest risk of cryptococcal meningitis are those with low CD4 counts and clinical suspicion must be high for all patients presenting with headaches, confusion, altered mental status.

Diagnosis of cryptococcal meningitis must be made by lumbar puncture. Opening pressure must be measured. If a manometer is not available, intravenous tubing may be used and a tape measure used to measure the column of CSF fluid. CSF samples must be tested for cryptococcus by India ink staining and/or CSF cryptococcal antigen test. Sensitivity and specificity for India ink staining are not as high as cryptococcal antigen testing, and a negative test does not exclude cryptococcal meningitis in the right clinical setting.

Treatment of cryptococcal disease must be with amphotericin B based regimens. Ideally amphotericin B must be combined with flucytosine.

However, flucytosine is typically not available in resource limited settings, including Zimbabwe. Combination therapy with amphotericin B and fluconazole is strongly recommended. In the absence of amphotercin B, high dose fluconazole can be used as alternative therapy (See Table 15).

Therapy is characterized by a 2 week induction phase, followed by an 8 week consolidation phase, and maintenance therapy which is continued until adequate immune reconstitution is achieved.

Table 15: Recommended Therapy for Cryptococcal Meningitis

	Treatment Phase	***Regimen***	***Duration of therapy***
Preferred	Induction phase	Amphotericin B 0.7-1mg/kg/day IV + Fluconazole 800mg orally once daily	2 weeks
	Consolidation Phase	Fluconazole 800mg orally once daily	8 weeks
	Maintenance/ Secondary Prophylaxis	Fluconazole 200mg orally once daily	Until CD4 count >200 cells/mm3 for 6 months
Alternate	Induction Phase	Fluconazole 1200mg orally daily	2 weeks
	Consolidation Phase	Fluconazole 800mg orally daily	8 weeks
	Maintenance/ Secondary prophylaxis	Fluconazole 200mg orally once daily	Until CD4 count >200 cells/mm3 for 6 months

9.3.3 Management of Raised Intracranial Pressure

Mortality and morbidity from cryptococcal meningitis is high with a significant proportion attributable to raised intracranial pressure. Management of raised ICP is critical to ensure good clinical outcomes. If the intracranial pressures is >25cm of water, remove 10-30ml of CSF and continue with daily lumbar punctures until CSF pressures have normalized (<25cm of water).

Failure to adequately manage intracranial pressures can result in persistent headache, cranial nerve abnormalities which include hearing loss, vision loss, and death.

A repeat lumbar puncture at 2 weeks after initiation of appropriate induction antifungal therapy is not necessary except in the setting of persistently elevated intracranial pressure and evidence of poor clinical response. Cryptococcal latex agglutination titres are not indicated for monitoring response to therapy.

9.3.4 Management of Amphotericin B Associated Toxicities

Amphotericin B, particularly amphotericin deoxycholate is associated with renal tubular toxicities and can lead to electrolyte abnormalities such as hypokalemia and hypomagnesemia. It can also result in anaemia and administration related febrile reactions.

- Amphotericin B is often provided as a powder and should be mixed with 5% dextrose water. It should never be mixed with normal saline or half normal saline as this will result in precipitation of the amphotericin B. To minimize renal toxicities, amphotericin B must be administered slowly over 4 hours. Initial therapeutic doses should be given as Amphotericin B 1mg/kg/day.
- Prehydration with 500ml-1L of normal saline with 20mEq of potassium chloride is recommended based on the volume status of the patient.
- Patients must receive oral potassium supplementation – e.g. 1200mg twice a day. The potassium supplementation minimizes the extent of hypokalemia that can develop. Where available supplementation with magnesium trisilicate 500mg orally twice daily is also recommended.
- Renal function must be monitored at baseline. U & Es should be measured twice weekly.

If the creatinine doubles a dose of amphotericin B can be omitted, and

prehydration increased to 1L of normal saline every 8 hours and creatinine rechecked. If creatinine normalizes, prehydrate with IL normal saline with 20mEq KCL and restart at amphotericin B (0.7mg/kg/day) given over 4 hours. Monitor renal function twice weekly.

If repeat creatinine remains elevated or continues to increase, amphotericin B should be discontinued and high dose fluconazole 1200mg orally once daily initiated (Table 15).

Monitoring of haemoglobin at baseline and weekly is also recommended. Timing of ART in cryptococcal meningitis

The timing of the initiation of ART in patients with cryptococcal meningitis is still uncertain. Early initiation of ART is recommended for all OIs except for intracranial OIs such as TB meningitis and cryptococcal meningitis. In cryptococcal meningitis ART can be initiated 2- 4 weeks after initiation of

antifungal therapy with amphotericin B based regimens. In patients who are predominately treated with fluconazole monotherapy, ART should be initiated at least 4 weeks after initiation of antifungal therapy.

ART should not be commenced at the same time that amphotericin B and/or fluconazole therapy is commenced for cryptococcal meningitis.

9.4 Hepatitis (B and C)

Viral Hepatitis is an increasing cause of mortality and morbidity among PLHIV. A comprehensive approach including preventation (screening, vaccination) testing treatment and care of people who are coinfected is advised.

Use of ARVs in HIV and Hepatitis B Coinfected Patients

- ART should be prioritised for people coinfected with HIV and HBV with evidence of severe chronic liver disease.
- Treatment should be provided regardless of ALT levels if client has chronic HBV with clinical evidence of liver cirhosis.
- Treatment regimens of choice should include a TDF/3TC backbone (refer to Table 6).

Ministry of Health is currently in the process of developing guidelines strategies and SOPs for use in the management of Hepatitis.

9.5 Mental Health

Assessment and management of mental health issues among people living with HIV

People living with HIV are at high risk of mental, neurological and substance-use disorders. All individuals living with HIV should be assessed and managed for mental health problems, including depression. People living with HIV who have depression are less likely to achieve optimal treatment adherence. Treatment or lack of it for mental health disorders can affect general health, adherence to ARV drugs and retention in care and may lead to potential side-effects and drug interactions being overlooked. Management of depression improves mental health and general well-being in people with HIV.

Standard tools are available for the routine screening of depression among PLHV

9.6 HIV and Non Communicable Diseases (NCDs)

People with HIV have an increased risk of NCDs compared to HIV-negative people in the same age ranges and NCDs account for an increasing proportion of mortality observed in this population. This includes cardiovascular disease (CVD), hypertension, diabetes, chronic obstructive pulmonary disease (COPD), kidney disease and cancers. Both HIV and NCDs require health systems that can deliver effective acute and chronic care and support adherence to treatment. Chronic HIV care provides the opportunity for assessment, monitoring and managing NCDs, especially through primary care.

Assessment and management of cardiovascular risk should be provided for all individuals living with HIV according to standard protocols recommended for the general population

Strategies for the prevention and risk reduction of cardiovascular diseases by addressing modifiable factors such as high blood pressure, smoking, obesity, unhealthy diet and lack of physical activity should be applied to all people living with HIV.

Table 16 A core set of interventions for reducing morbidity and mortality from major NCDs that are feasible for implementation in primary care in low resource settings

Essential Interventions for primary care
Primary prevention of heart attacks and strokes: • Tobacco cessation, Regular physical activity 30 minutes a day, Reduced intake of salt <5 g per day, Fruits and vegetables at least 400g per day • Aspirin, statins and antihypertensives for people with 10 year cardiovascular risk >30% • Antihypertensives for people with blood pressure ≥160/100 • Anthypertensives for people with persistent blood pressure ≥140/90 and 10 year cardiovascular risk >20% unable to lower blood pressure through life style measures
Acute myocardial infarction: • Aspirin
Secondary prevention (post myocardial infarction): • Tobacco cessation, healthy diet and regular physical activity • Aspirin, angiotensin-converting enzyme inhibitor, beta-blocker, statin
Secondary prevention (post stroke): • Tobacco cessation, healthy diet and regular physical activity • Aspirin, antihypertensive (low dose thiazide, angiotensin-converting enzyme inhibitor), and statin
Secondary prevention (Rheumatic heart disease): • Regular administration of antibiotics to prevent streptococcal pharyngitis and recurrent acute rheumatic fever
Type 1 diabetes: • Daily insulin injections

Type 2 diabetes:

- Oral hypoglycemic agents for type 2 diabetes, if glycemic targets are not achieved with modification of diet, maintenance of a healthy body weight and regular physical activity
- Metformin as initial drug in overweight patients and non overweight
- Other classes of antihyperglycemic agents, added to metformin if glycemic targets are not met
- Reduction of cardiovascular risk for those with diabetes and 10 year cardiovascular risk >20% with aspirin, angiotensin converting enzyme inhibitor and statins

Prevention of foot complications through examination and monitoring

- Regular (3-6 months) visual inspection and examination of patients' feet by trained personnel for the detection of risk factors for ulceration (assessment of foot sensation, palpation of foot pulses inspection for any foot deformity, inspection of footwear) and referral as appropriate

Prevention of onset and delay in progression of chronic kidney disease:

- Optimal glycemic control in people with type 1 or type 2 diabetes
- Angiotensin converting enzyme inhibitor for persistent albuminuria

Prevention of onset and delay of progression of diabetic retinopathy:

- Referral for screening and evaluation for laser treatment for diabetic retinopathy
- Optimal glycemic control and blood pressure control

Prevention of onset and progression of neuropathy:

- Optimal glycemic control

Bronchial asthma:

- Relief of symptoms: Oral or inhaled short-acting ß2 agonists
- Inhaled steroids for moderate /severe asthma to improve lung function, reduce asthma mortality and frequency and severity of exacerbations

Prevent exacerbation of COPD and disease progression:

- Smoking cessation in COPD patients

Relief of breathlessness and improvement in exercise tolerance

- Short-acting bronchodilators

Improvement of lung function

- Inhaled corticosteroids when FEV1 < 50% predicted
- Long-acting bronchodilators** for patients who remain symptomatic despite treatment with short-acting bronchodilators

Cancer:

- Identify presenting features of cancer and refer to next level for confirmation of diagnosis

Adapted from Package of Essential Non communicable Disease Interventions for Primary Health Care in Low-Resource Settings, WHO, 2010

9.7 Cervical Cancer

Cervical cancer is a preventable disease and is curable if diagnosed and treated early. Women living with HIV have a higher risk of pre-cancer and invasive cervical cancer. Women living with HIV should be followed closely for evidence of precancerous changes in the cervix, regardless of whether they are taking ART or their CD4 count or viral load. Cervical cancer screening leads to early detection of precancerous and cancerous cervical lesions that will prevent serious morbidity and mortality. All women with HIV should therefore be screened for cervical cancer regardless of age. Immediate management for precancerous and cancerous lesions should be provided according to the standard national guidelines.

CHAPTER 10: Oral Pre-Exposure Prophylaxis (PrEP)

10.1 Introduction

PrEP is defined by WHO as the use of antiretroviral drugs before HIV exposure by people w ho are not infected with HIV in order to prevent the acquisition of HIV.

WHO recommends that a PrEP regimen, containing Tenofovir Disoproxil Fumarate (TDF), should be offered as an additional prevention choice for people at substantial risk of HIV infection as part of a combination of prevention approaches that include: HIV Testing Services (HTS), male and female condoms, lubricants, ART for HIV-positive partners among sero-discordant couples, voluntary medical male circumcision (VMMC) and STI prevention and management.

Zimbabwe has had experience with PrEP in demonstration projects involving sex workers. As such the country needs to gain more experience with implementing PrEP and put in place functional surveillance, support and monitoring systems. The Ministry of Health and Child Care (MOHCC) will implement PrEP using a phased approach. An implementation plan and Standard Operating procedures (SOPs) on PrEP will be developed and shared by MOHCC to guide the introduction and scale up of PrEP. Regular updates will be provided by the MOHCC on progress in implementation of PrEP in the country.

10.2 Indications for PrEP

Oral PrEP will be made available to all individuals who are HIV uninfected and are at substantial risk of HIV infection after individual risk assessment. The following are indications for PrEP by history over the past 6 months:

- HIV negative and sexual partner with HIV who has not been on effective therapy for the preceding 6 months OR
- HIV negative and sexually active in a high HIV prevalence population AND any of the following:
- Vaginal or anal intercourse without condoms with more than one partner, OR
- A sexual partner with one or more HIV risk factors, OR

- A history of an STI by lab testing or self-report or syndromic STI treatment, OR
- Any use of post-exposure prophylaxis (PEP), OR
- Requesting PrEP

However, individuals belonging to certain population groups may be at higher risk of HIV infection than others and should be offered PrEP. These may include:

- Female and male sex workers;
- Sero-discordant couples (the HIV sero-negative partner)
- Adolescent girls and young women;
- Pregnant women in relationships with men of unknown status
- High-risk men (MSMs, prisoners, long distance truck drivers) and
- Transgender people.

Individual risk assessment will be made based on various behavioural factors and other factors to assess vulnerability.

10.3 Contraindications for PrEP

- HIV positive status
- Unknown HIV status
- Allergy to any medicine in the PrEP regimen
- Unwilling/unable to adhere to daily PrEP
- Known renal impairment
- Estimated creatinine clearance <60 cc/min (if known)

10.4 Ruling out Current HIV Infection when Starting PrEP

Before starting PrEP:

- Conduct a rapid HIV test to rule out existing HIV infection preferably on the same day that PrEP is being started.
- Take a complete history and full physical examination to rule out any signs or symptoms of an acute viral syndrome, including a flu-like illness, then consider the possibility that acute HIV infection could be the cause. In such circumstances testing for HIV RNA or antigen is helpful, if such tests are available. Alternatively, PrEP can be deferred for 4 weeks and the person tested again. This allows time

for possible seroconversion to be detected

- Blood creatinine should be measured before starting PrEP and at every 6 months after PrEP where available. Blood creatinine is mandatory in people with comorbid conditions that can affect renal function, such as diabetes mellitus and uncontrolled hypertension.

Who Should Administer PrEP

- PrEP should be administered by medical doctors and nurses trained in ARV management.

Table 16: Medicines Recommended for Oral PrEP

	Drug	***Dosage***	***Duration***
Preferred Regimen	Tenofovir (TDF (300mg) plus Emtricitabine (FTC) (200mg)	Fixed dose combination one tablet once a day	Period of substantial risk
Alternative Regimens	TDF (300mg) plus 3TC (300mg)	Fixed dose combination one tablet once a day	Period of substantive risk

Figure 17: Medicines Recommended for Oral PrEP

Screening Form for PrEP

Start Up or Follow-Up Visits

Date of Birth (DD/MM/YYYY)
_____/_____/_____

What is your sex? (Tick what is applicable) Male [ ] Female [ ]

* Consider offering PrEP

1.In the past 6 months: How many people did you have vaginal or anal sex with?

0 [ ] 1 [ ] 2+* [ ]

(If response is zero (0) skip to question 6)

2.In the past 6 months: Did you use a condom every time you had sex?

Yes [ ] No* [ ] Don't Know* [ ]

3.In the past 6 months: Did you have a sexually transmitted infection?

Yes* [ ] No [ ] Don't Know* [ ]

4.Do you have a sexual partner who has HIV?

Yes* [ ] No [ ] Don't Know* [ ]

	Yes	No*	Don't Know*
a. If, "Yes, has he or she been on therapy for 6 or more months?			
b. If "Yes," has the therapy suppressed viral load?			

**Consider offering PEP
1. In the past 3 days: Have you had sex without a condom with someone with HIV who is not on treatment? Yes** [ ] No [ ] Don't Know** [ ]

*** Consider acute HIV
1. Have you had a "cold" or "flu" like symptoms such as sore throat fevers, sweats, swollen glands, mouth ulcers, headache, or rash? Yes*** [ ] No [ ] Don't Know*** [ ]

PrEP is safe, with no side-effects for 90% of users. However, about 10% of people who start PrEP will have some short-term mild side-effects. These may include gastrointestinal symptoms (diarrhoea, nausea, decreased appetite, abdominal cramping, or flatulence). Dizziness or headaches have also been experienced. Such side-effects are usually mild and resolve without stopping PrEP. Typically, these symptoms start in the first few days or weeks of PrEP use and last a few days and almost always less than 1 month.

Providers may dispense a one-month supply at the first visit and then a 3 to 4 month supply at subsequent visits. Providers trained to provide ART can also provide PrEP.

Table 18: Procedures when PrEP is Started (first visit)

Investigation/ intervention	Rationale
Mandatory	
HIV test	Assessment of HIV infection status
	Symptom checklist for possible acute HIV infection
Brief counselling	To assess whether the client is at substantial risk for HIV
	To discuss prevention needs and provide condoms and lubricants
	To discuss desire for PrEP and willingness to take PrEP
	To develop a plan for effective PrEP use, sexual and reproductive health
	Assess fertility intentions and offer contraception or safer conception counselling.
	Assess intimate partner violence and gender based violence
	Assess substance use and mental health issues
Other STI screening	To diagnose and treat STI
Where available	
Pregnancy testing	To guide antenatal care, contraceptive and safer conception counselling, and to assess risk of maternal to child transmission. Pregnancy is not a contraindication for PrEP use.
Serum creatinine Hepatitis B surface antigen (HBsAg)	To identify pre-existing estimated creatinine clearance less than 60 ml/min. To identify undiagnosed current hepatitis B (HBV) infection.
Hepatitis B surface antibody	If negative, consider vaccination against hepatitis B.
Hepatitis C antibody	If positive, consider HCV treatment.
Rapid Syphilis Test	To diagnose and treat syphilis infection

10.5 PrEP Follow Up and Monitoring

After initiating PrEP the client should be reviewed after 1 month to monitor adherence and side effects as well as for resupply of medicines and thereafter 3 monthly.

Table 19: PrEP follow-up procedures

Intervention	Schedule following PrEP initiation
Mandatory	
Confirmation of HIV-negative status	Every 3 months
Address side-effects	Every visit
Provide STI screening, condoms, contraception or safer conception services	As needed
Counselling regarding effective PrEP use (adherence), prevention of sexually transmitted infections, recognition of symptoms of sexually transmitted infections, and issues related to mental health, intimate partner violence, and substance use and HIV risk assessment	Every visit
Where available	
Estimated creatinine clearance	Every 6 months. Consider more frequently if there is a history of conditions affecting the kidney, such as diabetes or hypertension; consider less frequently if age less than 45, baseline estimated creatinine clearance more than 90ml/min, and weight more than 55 kg.
Hepatitis C antibody	Consider testing MSM every 12 months. Incident HCV infections have been reported among PrEP users who deny injection drug use

10.6 When to Discontinue PrEP

- The duration of PrEP use may vary and individuals are likely to start and stop PrEP depending on their risk assessment at different periods in their lives. PrEP can be stopped 28 days after the last possible exposure to HIV if the client is no longer at substantial risk for HIV infection. It can also be stopped if client:
    - Has a positive HIV test
    - Develops renal disease (Creatinine Clearance <60ml/Min)*
    - Has an adverse medicine reaction and
    - In sero-discordant couples, when HIV infected partner on ART has achieved viral suppression

**Refer to Chapter 5, section 5.2 for calculation of Creatinine Clearance*

10.7 Practical Screening Questions

These questions are provided to make the screening of potential PrEP users easy and should be not used to ration or exclude people from accessing PrEP. People who ask for

PrEP are likely to have made this choice based on a careful assessment of their own personal circumstances, risk and desire for additional HIV prevention and should not be excluded on the basis of these questions. Screening questions can also be used to introduce the consideration and offer of PrEP to people who are attending services but had not presented specifically to access PrEP.

Any "yes" answer should prompt a discussion of the risks and benefits of PrEP.

General Screening Questions

In the past 6 months,

- Have you had sex with more than one person?
- Have you had sex without a condom?
- Have you had sex with anyone whose HIV status you do not know?
- Are any of your partners at risk of HIV?
- Do you have sex with a person who has HIV?
- Have you received a new diagnosis of a sexually transmitted infection?
- Do you desire pregnancy?

• Have you used or wanted to use PEP or PrEP for sexual exposure to HIV?

Additional Factors to Ask About:

Are there aspects of your situation that may indicate higher risk for HIV? Have you…

- Started having sex with a new partner?
- Ended a long-term relationship and are looking for a new partner?
- Received money, housing, food or gifts in exchange for sex?
- Been forced to have sex against your will?
- Been physically assaulted, including assault by a sexual partner?
- Injected drugs or hormones using shared equipment?
- Used recreational or psychoactive drugs?
- Been forced to leave your home (especially if due to sexual orientation or violence)?
- Moved to a new place (possibly having a higher prevalence of HIV exposure)?
- Lost a source of income (such that you may need to exchange sex for shelter, food, or income)?
- Left school earlier than you planned?

Any "yes" answer may indicate situations that confer increased vulnerability to HIV and help to identify someone who may benefit from PrEP.

The sexual partner of someone with HIV who is not on suppressive ART

PrEP can protect the uninfected partner in a sero-discordant relationship when the HIV-infected partner is either not on antiretroviral therapy (ART) or has not yet achieved viral

Antiretroviral therapy (ART) that suppresses viral load is highly effective for preventing transmission to others. Still, PrEP may provide additional protection to sero-discordant couples in a number of situations:

- The partner with HIV has been taking ART for less than 6 months. ART may take up to 6 months to suppress viral load; in studies of sero-discordant couples, PrEP has provided a useful bridge to full viral suppression during this time.
- The uninfected partner has doubt about the effectiveness of the partner's treatment or has other partners besides the HIV-positive partner on treatment.

- There have been gaps in the partner's treatment adherence or the couple is not communicating openly about treatment adherence and viral load test results.
- In addition, any sign of intimate partner violence, controlling behaviour, or anger or fear in response to questions about HIV treatment should prompt discussion about PrEP as a way to control risk for HIV.

For people who have a sex partner with HIV, the following questions will help to ascertain whether that person might benefit from PrEP:

- Is your partner taking antiretroviral therapy (ART) for HIV?
- Has your partner been on ART for more than 6 months?
- At least once a month, do you discuss whether your partner is taking therapy daily?
- If you know, when was your partner's last HIV viral load test? What was the result?
- Do you use condoms every time you have sex?

Any "no" answer to any of the above questions including a desire for pregnancy with HIV positive partner may indicate increased risk for HIV infection.

CHAPTER 11: Post-Exposure Prophylaxis

In people who have been exposed to HIV through needle-stick inoculation or through contamination of mucous membranes by secretions, it has been shown that administration of ARVs within 72 hours of exposure reduces the likelihood of HIV infection being transmitted. There are also similar benefits of reduction of HIV transmission by the use of PEP within 72 hours for those who have been sexually assaulted (rape, intimate partner violence or sexual abuse) or had a high risk unprotected sexual encounter. In these situations, ART needs to be continued for one month. The following guidelines should be followed in the event of accidental occupational exposure to material (i.e., blood, secretions, excretions) that may contain HIV, and also after sexual assault or high risk sexual encounter. Occupational exposure to potentially infectious material may occur through an injury with a sharp object that has been used on a patient or through the contamination of mucous surfaces with patients' blood or secretions.

The following types of exposures should be considered for post-exposure prophylaxis:

- Needle-stick injury or injury with a sharp object used on a patient
- Mucosal exposure of the mouth or eyes by splashing fluids
- Broken skin exposed to a small volume of blood or secretions such as may occur with sexual assault (rape, intimate partner violence or sexual abuse)

Occupational exposure can be classified as high risk or low risk for HIV infection, as follows:

Low risk:

- Small volume (e.g., drops of blood) on mucous membranes or non-intact skin
- Source patient asymptomatic or with VL less than 1,500 copies/ml

High risk:

- Large-bore needle, deep injury
- Large-volume splash on mucous membranes or non-intact skin
- Source patient symptomatic or with high VL levels

11.1 Prevention of Occupational Exposure in Health Facilities

All health facilities in the private and public sector should adopt a policy for the prevention of occupational accidental exposure to blood-borne pathogens. Universal precautions (i.e., the use of disposable latex gloves when handling bodily fluids, single-use equipment, and proper management of sharp and contaminated materials) should be observed by all levels of health-care workers. Universal precautions are designed to prevent transmission of HIV, hepatitis B virus (HBV), hepatitis C virus (HCV) and other blood-borne pathogens when providing health care. Under universal precautions, the blood and certain body fluids of all patients are considered potentially infectious for HIV, HBV, HCV and other blood-borne pathogens.

Universal precautions involve the use of protective barriers such as gloves, gowns, aprons, masks, or protective eyewear, which can reduce the risk of exposure of the health-care worker's skin or mucous membranes to potentially infective materials.

Health facilities should implement universal precautions for the prevention of exposure to potentially infectious material. The programme should include the training of all employees in the handling and disposal of infectious material. All personnel should be made aware of the risks involved in improper handling of such material, and the steps necessary for preventing exposure should be clearly displayed in posters.

The greatest risk of accidental exposure is in the handling of sharp objects that have been used on patients. All personnel should be taught how to safely handle and dispose of sharp objects. Messages should promote the avoidance of recapping needles, using "sharps bins" for disposing of sharps, and taking care in performing procedures.

Health personnel should also be conscious that blood and secretions from patients may be infectious and that simple contamination of unbroken skin does not comprise a significant risk, but contamination of intact mucous surfaces of the mouth and eyes does. The health facility should ensure the continuous supply of personal protective equipment, educational materials, disposable syringes and needles, and sharps bins. Health facilities should ensure the availability and accessibility of medicines for post-exposure prophylaxis.

11.2 Procedure to be Followed in the Event of Injury with a Sharp Object

In the event of an injury with a sharp object, such as a needle or scalpel, that has been used on a patient or in the event of a mucous surface being contaminated with blood or secretions from a patient, the following steps should be followed:

1. Wash the exposed area thoroughly with soap and water (do not pinch or press would to try to express blood).
2. Rinse the eye or mouth with plenty of water if contaminated.
3. Report the injury to a senior member of staff or the supervisor.
4. Start the ARVs recommended for post-exposure prophylaxis immediately—these should be started within 1 hour if possible and at the latest within 72 hours of the exposure.
5. Ascertain the HIV status of the source patient and the injured health worker after providing appropriate counselling—the standard rapid HIV antibody tests should be used and the results of tests obtained as quickly as possible. Offer viral DNA or RNA testing if source is suspected to be in the window period.
6. Depending on the results of the HIV tests, the following actions should be taken:
    - If the source patient is HIV-negative, no further post-exposure prophylaxis is necessary for the exposed health worker. There will be need to consider exposure to other infections such as hepatitis B.
    - If the exposed health worker is HIV-positive, no further post-exposure prophylaxis is necessary for the health worker. The health worker should be referred for further counselling and the long-term management of his or her HIV infection, which would have occurred prior to the exposure.
    - If the health worker is HIV-negative and the source patient is HIV positive, continue ARVs for a period of one month; repeat the health worker's HIV tests at three months and at six months after the initial test. If the health worker should seroconvert during this time, provide appropriate care and counselling and refer for expert opinion and long-term treatment.
    - If the health worker refuses to be tested, he or she may have no claim for possible future compensation.

7. If it is not possible to determine the HIV status of the source patient, then assume that the source is positive and proceed according to the guidelines in the previous bullets.
8. In the event of HIV infection exposure to the HCW, the greatest risk of transmission to other individuals is in the first six weeks. The exposed Health Care Worker should be instructed to use measures to reduce the potential risk of HIV transmission to others, e.g. condom use, abstinence and refraining from blood transfusion until the 6 month serologic test is negative.
9. Healthcare workers who are breastfeeding should consider discontinuing breastfeeding following exposure to HIV. This avoids infant exposure to ARVs and HIV in breast milk should the mother be infected.
10. Post-exposure prophylaxis with hepatitis B immune globulin (HBIG) and/or hepatitis B vaccination series should be considered for occupational exposure (within 24 hours) after evaluating the hepatitis B status of the source patient and the vaccination status of the exposed person. Hepatitis B vaccine and HBIG can be given at the same time but using different injection sites. Routine pre-exposure hepatitis B vaccination should be offered to all health-care workers. Ideally the Hepatitis C status of the source patient should be ascertained.

11.3 Post Exposure Prophylaxis after Sexual Assault (Rape or Sexual Abuse) or High Risk Sexual Encounter.

It is recommended that a victim of rape or sexual abuse or who has had an unprotected high risk sexual encounter, presenting within 72 hours of exposure be counselled and provided with the medicines recommended for post–occupational exposure prophylaxis. It is important to try to determine the HIV status of the perpetrator. If that is not possible, it may be assumed that the perpetrator is HIV-positive, and the victim is provided with the treatment as listed in the preceding section. Refer the client to the nearest support centre for sexual assault survivors.

11.4 ARVs to be used in Post Exposure Prophylaxis

Immediately after exposure, all exposed adult adolescent individuals should take the following:

- Tenofovir 300 mg orally once daily

plus

- Lamivudine 300 mg orally once daily

Plus

- Atazanavir (300mg)/ ritonavir 100mg orally once daily

The above regimen is given for one month.

The Dosage for Children is as follows:

AZT + 3TC is recommended as the preferred backbone regimen for HIV post-exposure prophylaxis for children 10 years and younger.

ABC + 3TC or TDF + 3TC (or FTC) can be considered as alternative regimens.

LPV/r is recommended as the preferred third drug for HIV post-exposure prophylaxis for children younger than 10 years.

An age-appropriate alternative regimen can be identified among ATV/r, RAL, DRV, EFV and NVP.

The exposed individuals should be counselled regarding side effects prior to receiving the medicines. If the source is HIV-negative, medicine administration should be discontinued.

11.5 Toxicity Monitoring

All people on Atazanavir/Ritonavir based PEP should have a baseline liver function test and a repeat at two weeks. If there is any derangement in transaminases urgent advice must be sought. Please note that atazanavir causes hyperbilirubinaemia which is a normal part of treatment. Patients on atazanavir may develop a rash. If this happens urgent advice must be sought.

If there is intolerance to Atazanavir due to rash or liver toxicity then Atazanavir/Ritonavir can be replaced with Lopinavir/ritonavir or Raltegravir or Dolutegravir.

All people on Zidovudine based PEP should have a baseline full blood count. It should be repeated at two weeks looking for anaemia, neutropenia, or thrombocytopaenia.

All people on Tenofovir based PEP should have a baseline U&E. It should be repeated at two weeks, looking for elevations in creatinine from baseline. If there is elevation in creatinine from baseline, then Tenofovir/Lamivudine should be replaced with Zidovudine/Lamivudine.

HBV Testing

There is concern about the potential risk of hepatic flares among people with chronic HBV once TDF-, 3TC- or FTC-based PEP is stopped. Assessment of HBV infection status should not be a precondition for offering TDF-, 3TC- or FTC-based PEP, but people with established chronic HBV infection should be monitored for hepatic flare

after PEP discontinuation. Among people with unknown HBV status and where HBV testing is readily available, people started on TDF-, 3TC- or FTC-based PEP should be tested for HBV to detect active HBV infection and the need for on-going HBV therapy after discontinuing PEP.

Sexually transmitted infections after Sexual Assault (rape, intimate partner violence, or sexual abuse) or after high risk sexual encounter

Exposure to sexually transmitted infections will often co-exist with HIV exposure through sexual routes. Screening, diagnosis and presumptive treatment of sexually transmitted infections should follow established guidelines.

11.6 Access to PEP

All health facilities should have known easy access points for PEP such as the casualty or emergency room of hospitals, OI clinics, or city health or rural health clinics. In addition operating theatres and labour wards should have easy access points for PEP. A hospital ward also may be designated as an access point for PEP.

Health staff or those potentially exposed to HIV through sexual assault (rape, intimate partner violence, or sexual abuse) or through a high risk unprotected sexual encounter should be able to access PEP easily 24 hours a day 365 days a year. The key to success in PEP is avoiding delay in starting PEP-ideally PEP should be started straight away within 1 hour of exposure. Health-care workers should not wait to ascertain the HIV status of the source patient, but they should start PEP straight away.

Every staff member of a health care institution (whether they be a doctor, dentist, nurse, nurse aid, laboratory technician, researcher, healthcare student, domestic cleaner, security guard et al) should be trained to know what to do in the event of an occupational injury. Please note students be they medical or nursing, and also staff members under contract to hospitals such as cleaners and security guards are all entitled by right to access PEP-there should be no discrimination.

Each health care facility should have a specific PEP policy and procedure in line with National Guidelines.

For occupational injuries a 24 hour started pack should be issued (or a 72 hour starter pack for a weekend) until the health care worker can be seen at a staff health clinic or its equivalent and also the HIV status of the source patient and health care worker is ascertained. The health care worker should be able to access a starter pack straight away within 1 hour of injury without delay. If the source patient is found to be HIV positive (and the health worker negative) then the healthcare worker should continue the PEP for a full 28 day course accessed through the OI clinic or Pharmacy. Thus starter packs must be kept at known 24 hour accessible sites as documented above.

For those who have been sexually assaulted (rape, intimate partner violence or sexual abuse) a full 28 day course of PEP should be given at the onset (a starter pack may be started again to avoid delay of obtaining the 28 Day PEP course).

11.7 Psychosocial Support

Exposure to HIV through occupational injury or through sexual exposure is a potentially stressful event and the person will need counselling support at baseline and regularly over the 4 weeks of PEP and at the 3 month and 6 month HIV tests. Enhanced adherence counselling is recommended for individuals initiating HIV post-exposure prophylaxis as there is a high defaulter rate owing to side-effects of medication and other factors. There should be a designated Staff Heath Nurse-Counsellor or equivalent who is focus person to trace and follow-up occupational injured staff or students in an intentional way to make sure they do not default follow-up visits and to check how they are doing.

CHAPTER 12: Reporting of Adverse Drug Reactions (ADRs) By Health Workers

12.1 Reporting of Suspected ADRs

Adverse Drug Reaction (ADR): A response to a medicine which is noxious and unintended, which occurs at doses normally used in man for the prophylaxis, diagnosis, or therapy of disease, or for the modification of physiological function.

Adverse Event: Any untoward medical occurrence that may present during treatment with a pharmaceutical product, but which does not necessarily have a causal relationship with this treatment. Treatment failure is also considered as an adverse event.

All health care workers, including doctors, pharmacists, nurses, other health professionals and the patients are requested to report all suspected adverse reactions to drugs (including vaccines, X-ray contrast media, complementary medicines), especially when the reaction is unusual, potentially serious or clinically significant. It is vital to report an adverse drug reaction and adverse events to the Medicines Control Authority of Zimbabwe pharmacovigilance programme even when all the facts are not available or there is uncertainty that the medicine definitely caused the reaction.

12.1.2 Who Should Report

- All health professionals (in the public or private sector). They include physicians, pharmacists, and nurses, including public health professionals, staff in medical laboratories and pathology departments, and pharmaceutical companies.
- Health and community workers (who are literate) should be encouraged to report, preferably to the clinician who prescribed the treatment, or directly to the MCAZ.
- Patients or patient's family members
- General public

12.1.3 When to Report Suspected ADRs and ADR Reporting Tools

An ADR report should be submitted to the MCAZ, as soon as possible

after the reaction. To report an ADR, the MCAZ e-ADR reporting platform http://www.mcaz.co.zw/index.php/2016-01-08-06-40-00/e-reporting can be used. Once submission is made on-line, the e-ADR form is received by the MCAZ. A standard ADR reporting form can also be completed (Annex 2), and submitted to the MCAZ. It is better not to wait until final results and information such as hospital letters are received, because the report may be forgotten. These additional details can be sent to the MCAZ later. All ADR reports once submitted, are treated in an anonymous format

12.1.4 ADRs to be Reported to the MCAZ

- All ADRs to marketed medicines or medicines added to the Essential Medicines List
- All serious reactions and interactions
- All known and unknown ADRs
- Unusual or interesting adverse medicine reactions
- All adverse reactions or poisonings to traditional or herbal remedies

Product Quality Problems to be reported to MCAZ

- Suspected contamination
- Questionable stability
- Defective components
- Poor packaging or labeling
- Therapeutic failures

12.1.5 Reporting a Suspected ADR

The following steps should be followed when reporting ADRs:

Step 1: Obtain Patient History and Do a Proper Examination

- Take a full medicine and medical history
- Conduct physical examination as some medicines produce distinctive physical signs.
- Establish time relationships i.e. the time from the start of therapy to the time of onset of the suspected reaction.
- Determine if there are other possible causes for the new symptoms (e.g. patient's underlying disease, other medicine/s, over-the-counter medicines or complementary medicines; toxins or foods) and conduct further investigations e.g. FBC, ALT, U & E. Laboratory tests are especially

important if the medicine is considered essential in improving patient care or of the lab test results will improve management of the patient

- Describe the reaction as clearly as possible and, where possible provide, an accurate diagnosis

Step 2: Check the Known Pharmacology of the Medicine.

- Is the reaction known to occur with the particular medicine as stated in the package insert or other reference?
- If the reaction is not documented in the package insert, it does not mean that the reaction cannot occur with that particular medicine.

Step 3: Management of the ADRs

Manage the patient based on the findings and the guidance in table 10

In addition, consider Dechallenge and Rechallenge.

- Re-challenge refers to starting the same medicine after having stopped usually for an adverse event.
- A positive rechallenge refers to the adverse events recurring after restating the medicine. Stop the medicine
- A negative rechallenge is when the adverse event does not recur after restarting the medicine. Continue the medicine
- Rechallenge is only justifiable when the benefit of re-introducing the medicine to the patient outweighs the risk of recurrence of the reaction
- Dechallenge refers to the stopping of a drug usually after an adverse event
- Positive dechallenge refers to the adverse events disappearing after the stopping of the drug. In this event consider substituting with another drug OR rechallenging with the same drug
- Negative dechallenge refers to the adverse event not disappearing after the stopping of the drug. In this event, refer for further investigations and consider other potential drugs that can cause similar adverse events.

Example see Cotrimoxazole desensitization Appendix 4

12.1.6 Components of a Complete Case Report

Complete case reports include the following elements:

- Description of the adverse events or disease experience, including time to onset of signs or symptoms;

- Suspected and concomitant product therapy details (i.e., dose, lot number, schedule, dates, duration), including over-the-counter medications, dietary supplements, and recently discontinued medications;
- Patient characteristics, including demographic information (e.g., age, race, sex), baseline medical condition prior to product therapy, co-morbid conditions, use of concomitant medications, relevant family history of disease, and presence of other risk factors;
- Documentation of the diagnosis of the events, including methods used to make the diagnosis
- Clinical course of the event and patient outcomes (e.g., hospitalization or death)
- Relevant therapeutic measures and laboratory data at baseline, during therapy, and subsequent to therapy, including blood levels, as appropriate;
- Information about response to dechallenge and rechallenge; and
- Any other relevant information (e.g., other details relating to the event or information on benefits received by the patient, if important to the assessment of the event).

12.1.7 How to Minimize Occurrence of ADRs

Some ADRs are unavoidable and cannot be prevented. However, most ADRs can be prevented by following the basic principles of rational use of medicines that are described as follows:

- Use few medicines, whenever possible
- Use medicines that you know well
- Do not change therapy from known medicines to unfamiliar one without good reasons.
- Use text books and other reference material providing information on medicine reactions and interactions.
- Take extra care when you prescribe medicines known to exhibit a large variety of interactions and adverse reactions (anticoagulants, hypoglycemic, and drug affecting the CNS) with careful monitoring of patients with such reactions.
- Beware of the interaction of medicines with certain food stuffs, alcohol and even with house hold chemicals.
- Review all the medicines being used by your patients regularly, taking special notice with those bought without prescription (over the counter, complementary).

- Be particularly careful when prescribing to children, the elderly, pregnant and nursing women, the seriously ill and patients with hepatic and renal diseases. Careful ongoing monitoring is also essential in these patients.

If the patient shows signs and/or symptoms not clearly explained by the course of their illness, think of adverse drug reaction. If you suspect an adverse reaction, consider stopping the medicine or reduce the dosage as soon possible and please report the adverse drug reaction to the Medicines Control Authority of Zimbabwe.

12.1.8 Follow-Up

All reports of serious events should be followed up if details are incomplete. This may require the involvement of health professionals in a clinical setting who have been trained and appointed for this type of work. Occasionally follow-up information is required to fully assess reports of non-serious events. Follow-up requests should be kept to a minimum as they can discourage further reporting. Examples of follow-up information might be: essential missing details, information on the final outcome, the result of re-challenge, the results of laboratory tests, and post-mortem results from health facilities where autopsy is undertaken.

12.1.9 Feedback to Reporters

The pharmacovigilance centre (MCAZ) will provide feedback to anyone who reports an ADR. Further feedback information will be provided to the reporter after causality assessment by the MCAZ PVCT Committee.

Benefits of reporting to the health worker and the patient;

- Improved patient confidence in professional practice
- Improved quality of care offered to patients
- Reduced medicine related problems leading to better treatment outcomes
- Satisfaction in fulfilling moral and professional obligation on the part of the health worker
- Improvement in the knowledge of the health worker

Protection of Health worker who reports an ADR

Adverse drug reaction reports do not constitute an admission that a health professional contributed to the event in any way. The outcome of the report, together with any important or relevant information relating to the reaction that has been reported, will be sent back to the reporter as appropriate.

The details of the report will be stored in a confidential database. The name

of the reporter or any other health professionals named on a report and the patient will be removed before any details about a specific adverse drug reaction are used or communicated to others. The information obtained from the report will not be used for commercial purposes. The information is only meant to improve understanding of the medicines used in Zimbabwe.

APPENDIX 1: Clinical Staging for Adults and Adolescents

(Adapted from WHO, WHO Case Definitions of HIV for Surveillance and Revised Clinical Staging and Immunological Classification of HIV-Related Disease in Adults and Children, 2007. Available at: http://www.who.int/hiv/pub/guidelines/hivstaging/en/index.html)

Clinical Stage 1
• Asymptomatic • Persistent generalized lymphadenopathy
Clinical Stage 2
• Weight loss,<10% of body weight • Recurrent RTI • Herpes Zoster • Angular Cheilitis • Recurrent ulcerations occurring twice or more then in six months. • Papular pruritic eruptions • Seborrheic dermatitis • Fungal nail infections of the fingers
Clinical Stage 3
• Weight loss; >10 % of body weight • Unexplained chronic diarrhoea >1 month. • Unexplained prolonged fever >1 month • Pulmonary Tuberculosis ,current or within the past 2 months or TB adenitis • Severe infection including pneumonia, meningitis, bone or joint infection. • Oral Candidiasis • Oral hairy leukoplakia • Acute necrotising ulcerative gingivitis or necrotizing ulcerative periodontitis • Unexplained anaemia >1 month.

Clinical Stage 4
• HIV wasting syndrome • Pneumocystis Pneumonia • Recurrent severe or radiological bacterial pneumonia (two or more episodes within a year). • Cryptococcal meningitis or other extra pulmonary. • Cryptococcus infections • Extra Pulmonary Tuberculosis except TB adenitis • Kaposi Sarcoma • HIV Encephalopathy • Candidiasis of the oesophagus, trachea, bronchi or lungs • Chronic Herpes simplex virus (HSV)infection (orolabial, genital or anorectal >1 month, or visceral any duration) • Cytomegalovirus (CMV) disease of an organ other than liver, spleen or lymph nodes. • Progressive Multifocal Leukoencephalopathy (PML) • Any disseminated mycosis (e.g. histoplasmosis, coccidioidomycosis, or penicilliosis) • Lymphoma (cerebral or B cell non-Hodgkin) • Recurrent non typhoidal salmonella septicaemia (2 or more episodes in last year). • Invasive cervical cancer • Visceral leishmaniosis • Cryptosporidiosis with diarrhoea lasting more than 1 month. • Psoriasis • Disseminated non-tuberculous mycobacterial infection. • CNS toxoplasmosis

APPENDIX 2: Revised WHO Clinical Staging of HIV/AIDS for Infants and Children with Established HIV Infection

(Adapted from WHO, WHO Case Definitions of HIV for Surveillance and Revised Clinical Staging and Immunological Classification of HIV-Related Disease in Adults and Children, 2007. Available at: http://www.who.int/hiv/ pub/guidelines/hivstaging/en/index.html.)

Primary HIV Infection
• Asymptomatic • Acute retroviral syndrome
Clinical Stage 1
• Asymptomatic • Persistent generalized lymphadenopathy
Clinical Stage 2
• Unexplained persistent hepatosplenomegaly • Papular pruritic eruptions • Extensive wart virus infection • Extensive molluscum contagiosum • Recurrent oral ulcerations • Unexplained persistent parotid enlargement • Lineal gingival erythema • Herpes zoster • Recurrent or chronic upper respiratory tract infections (otitis media, otorrhoea, sinusitis, tonsillitis) • Fungal nail infections
Clinical Stage 3
• Moderate unexplained malnutrition not adequately responding to standard therapy • Unexplained persistent diarrhoea (14 days or more) • Unexplained persistent fever (above 37.5° C intermittent or constant, for longer than 1 month) • Persistent oral candida (outside first 6 to 8 weeks of life) • Oral hairy leukoplakia • Acute necrotizing ulcerative gingivitis/periodontitis • Lymph node TB • Pulmonary TB • Severe recurrent presumed bacterial pneumonia

Clinical Stage 3
• Symptomatic lymphoid interstitial pneumonitis • Chronic HIV-associated lung disease, including bronchiectasis • Unexplained anaemia (< 8 g/dL), neutropenia (< 500/mm3), or chronic thrombocytopenia (< 50,000/mm3) • HIV-associated cardiomyopathy or HIV-associated nephropathy
Clinical Stage 4
• HIV wasting syndrome • Pneumocystis pneumonia • Recurrent severe bacterial pneumonia • Chronic herpes simplex infection (orolabial, genital, or anorectal of more than 1 month's duration) or visceral at any site • Oesophageal candidiasis (or candidiasis of trachea, bronchi, or lungs) • Extrapulmonary TB • Kaposi's sarcoma • Central nervous system toxoplasmosis • HIV encephalopathy • Extrapulmonary cryptococcosis, including meningitis • Disseminated nontuberculous mycobacteria infection • Progressive multifocal leukoencephalopathy • Chronic cryptosporidiosis • Chronic isosporiasis • Cytomegalovirus (CMV) infection (retinitis, or CMV infection of other organs) • Disseminated mycosis (e.g., extrapulmonary histoplasmosis, coccidiomycosis) • Recurrent septicaemia (including nontyphoidal salmonella) • Lymphoma (cerebral or B-cell non-Hodgkin's) • Invasive cervical carcinoma • Atypical disseminated leishmaniasis • Symptomatic HIV-associated nephropathy or HIV-associated cardiomyopathy

APPENDIX 3: Grades of Adverse Events

Grade 1 (Mild)	Transient or mild discomfort; no limitation in activity; no medical intervention/therapy required
Grade 2 (Moderate)	Mild to moderate limitation in activity; some assistance may be needed; no or minimal medical intervention/therapy required
Grade 3 (Severe)	Marked limitation in activity; some assistance usually required; medical intervention/therapy required; hospitalization possible
Grade 4(Life-threatening)	Extreme limitation in activity; significant assistance required; significant medical intervention/therapy required; hospitalization or hospice care probable

APPENDIX iv: Rapid Cotrimoxazole Desensitization Protocol

(Adapted from Zimbabwe Ministry of Health and Child Welfare, HIV/AIDS Standard Treatment Guidelines, 2004)

Suitable for prophylactic-dose cotrimoxazole or high-dose cotrimoxazole for treatment of Pneumocystis jirovecii pneumonia

Desensitization can be offered rapidly or over a longer period of time. Do not desensitize anyone who has had an anaphylactic reaction to cotrimoxazole or a severe skin rash such as Stevens-Johnson syndrome. Desensitization is usually about 60% effective. Rapid desensitization ideally should be performed during the day in a setting where emergency resuscitation can be provided and adrenaline can be given. Observations during rapid desensitization should take place every 30 minutes, before each dose is given, and should include temperature, pulse, and blood pressure.

If only mild rash or pruritus occurs, administer antihistamine (e.g., chlorpheniramine or promethazine) and continue. If more serious side effects occur, such as severe wheeze, severe or symptomatic hypotension, severe rash, and so on, discontinue desensitization, manage appropriately, and do not try to restart desensitization.

Once cotrimoxazole has been started, it can be continued indefinitely as long as no reactions are noted, but if the medicine is stopped at any time, there may be a risk of reaction when it is restarted.

Using a 1 ml syringe, put 0.5 ml of paediatric cotrimoxazole 240 mg / 5 ml syrup in 1,000 ml of 5% dextrose and mix well.

Minutes	Quantity of Above Mixture Given Orally
0	1 ml (use 10 ml syringe)
30	10 ml (use 10 ml syringe)
60	100 ml (use 10 ml syringe)
90	0.5 ml
120	5 ml
150	480 mg tablet
180	Start full prophylactic or therapeutic dose.

APPENDIX 5: Some Important Medicine Interactions

Avoid giving the following medicines together:

Medicines Involved	Effects of the Interaction
Avoid giving Nevirapine and ketoconazole together.	Both medicines are toxic to the liver. The level of Nevirapine is increased while that of ketoconazole is reduced.
Use alternative contraception with Nevirapine.	ARVs can make oral contraceptives less effective. Encourage dual methods of contraception (including using condoms).
Avoid giving Efavirenz and diazepam together except in an emergency that requires diazepam.	Efavirenz increases the levels of diazepam in the blood.
Avoid giving Stavudine and Zidovudine together.	Both medicines work to prevent the virus from entering the CD4 lymphocyte. They antagonize each other when given together.

APPENDIX 6: Developmental Milestones

Age	Psychosocial	Gross Motor	Fine Motor / Visual	Communication/ Hearing
1 month	Follows faces to the midline	Moves all extremities equally; lifts head when lying on stomach	Opens hands spontaneously	Startled by loud sounds; cries; quiets when fed and comforted
2 months	Follows faces past midline; Smiles responsively	Lifts head up 45 degrees when on stomach	Looks at own hand	Makes baby sounds (cooing, squealing, gurgling)
3 months	Recognizes mother; smiles responsively	Supports head for a few seconds when held Upright	Opens hands frequently	Responds to voices; laughs
4 months	Follows an object with eyes for 180 degrees; regards own hand; anticipates food on sight	Bears weight on legs; good neck control when pulled to sitting; lifts chest and supports self on elbows when pulled to sit	Brings hands together in midline (clasps hands); grabs an object (such as a rattle); reaches for objects	Turns head to sound
6 months	Reaches for familiar people	Rolls from stomach to back or back to stomach; sits with anterior support	Plays with hands by touching them together; sees small objects such as crumbs	Responds to name; babbles
9 months	Indicates wants; waves bye-bye; has stranger anxiety	Can sit without support; creeps or crawls on hands and knees	Looks for a toy when it falls from his or her hand; takes a toy in each hand; transfers a toy from one hand to the	Responds to soft sounds such as whispers

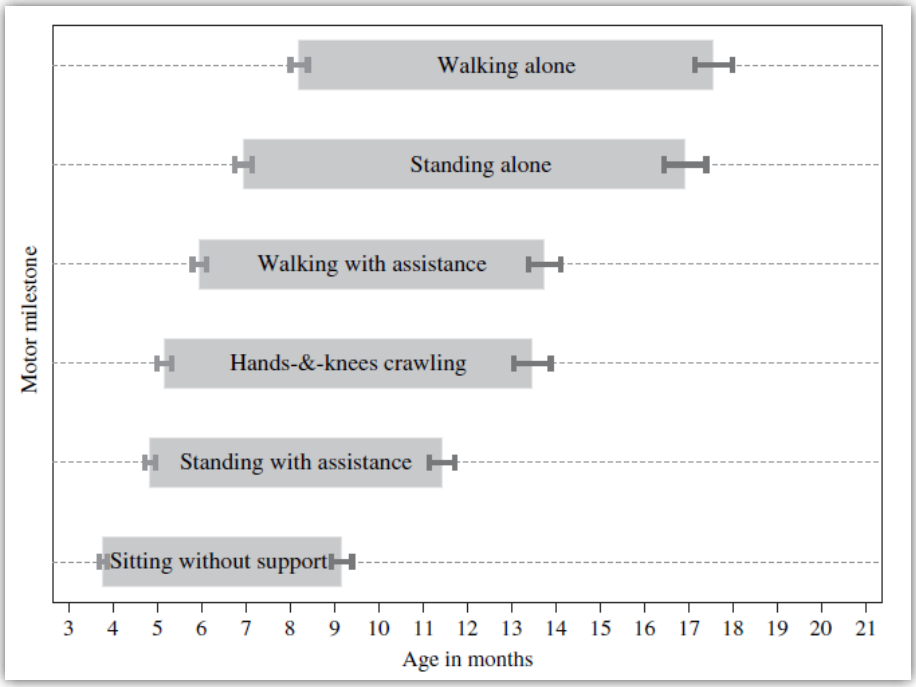
			Other	
12 months	Has separation anxiety; social interactions intentional and goal directed	Pulls self up to standing position; walks with support	Points at objects with index finger	Says at least one word; makes “ma-ma” or “da-da” sounds; locates sounds by turning head
15 Months	Imitates activities; finds a nearby hidden object	Can take steps by himself or herself; can get to a sitting position from a lying position	Can stack one cube on top of another	Able to say mama and dada to respective parents
18 Months	Initiates interactions by calling to adult	Walks without help	Takes off own shoes; feeds self	Says at least 3 words
2 years	Does things to please others; engages in parallel (imitative) Play	Runs without falling	Looks at pictures in a book; imitates drawing a vertical line	Combines 2 different words

APPENDIX 7: Developmental Red Flags

Birth to 3 months	• Failure to alert to environmental stimuli • Rolling over before 2 months (hypertonia) • Persistent fisting at 3 months
4 to 6 months	• Poor head control • Failure to smile • Failure to reach for objects by 5 months
6 to 12 months	• No baby sounds or babbling • Inability to localise sounds by 10 months
12 to 24 months	• Lack of consonant production • Hand dominance prior to 18 months (contralateral weakness) • No imitation of speech and activities by 16 months
Any age	• Loss of previously attained milestones

APPENDIX 8: Six Gross Motor Milestones

Windows of achievement for six gross motor milestones



Reference: WHO Multicentre Growth Reference Study Group. WHO Motor Development Study: Windows of achievement for six gross motor development milestones. Acta Paediatrica Supplement 2006:450:86-95.

APPENDIX ix: ARVs Paediatric Dosing Chart

Medicine	Strength of paediatric tablet (mg) or liquid (mg/ml	Number of tablets or ml by weight band (AM + PM)					Strength of adult tab (mg)	Number of tablets by weight band (AM + PM)	
		Children 6 weeks of age and over							
		3–5.9 kg AM + PM	6–9.9 kg AM + PM	10–13.9 kg AM + PM	14–19.9 kg AM + PM	20–24.9 Kg AM + PM		25–29.9 kg AM + PM	30–34.9 kg AM + PM
	6/30	1 + 1	2 + 1	2 + 2	3 + 2	3 + 3	30/150	1 + 1	1 + 1
	12/60	0.5 + 0.5	1 + 0.5	1 + 1	1.5 + 1	2 + 1			
		1 + 1	2 + 1	2 + 2	3 + 2	3 + 3	30/150 /200	1 + 1	1 + 1
		0.5 + 0.5	1 + 0.5	1 + 1	1.5 + 1	2 + 1			
NVP	200; 10 mg/ml	5 ml + 5 ml	8 ml + 8 ml	10 ml + 10 ml	1 + 0.5	1 + 0.5	200	1 + 1	1 + 1
AZT	60	1 + 1	2 + 1	2 + 2	3 + 2	3 + 3	300	1 + 1	1 + 1
AZT	300; 10 mg/ml	6 ml + 6 ml	9 ml + 9 ml	12 ml + 12 ml	0.5 + 0.5	1 + 0.5	300	1 + 1	1 + 1
AZT/3TC	60/30	1 + 1	2 + 1	2 + 2	3 + 2	3 + 3	300/150	1 + 1	1 + 1
AZT/3TC /NVP	60/30 /50	1 + 1	2 + 1	2 + 2	3 + 2	3 + 3	300/150 /200	1 + 1	1 + 1
ABC	60	1 + 1	2 + 1	2 + 2	3 + 2	3 + 3	300	1 + 1	1 + 1
ABC	300; 20 mg/ml	3 ml +3 ml	4 ml + 4 ml	6 ml + 6 ml	0.5 + 0.5	1 + 0.5	300	1 + 1	1 + 1
ABC/3TC	60/30	1 + 1	2 + 1	2 + 2	3 + 2	3 + 3	600/300	1 + 0	1 + 0
Lop/r	100/25	n/r	n/r	2 + 1	2 + 2	3 + 2	100/25 (paed)	3 + 3	3 + 3
Lop/r	80/20 mg/ ml	2 ml + 1 ml	2 ml + 1 ml	2 ml + 2 ml	3 ml + 2 ml	3 mL+ 3 ml	200/50 (adult)	2 + 1	2 + 1

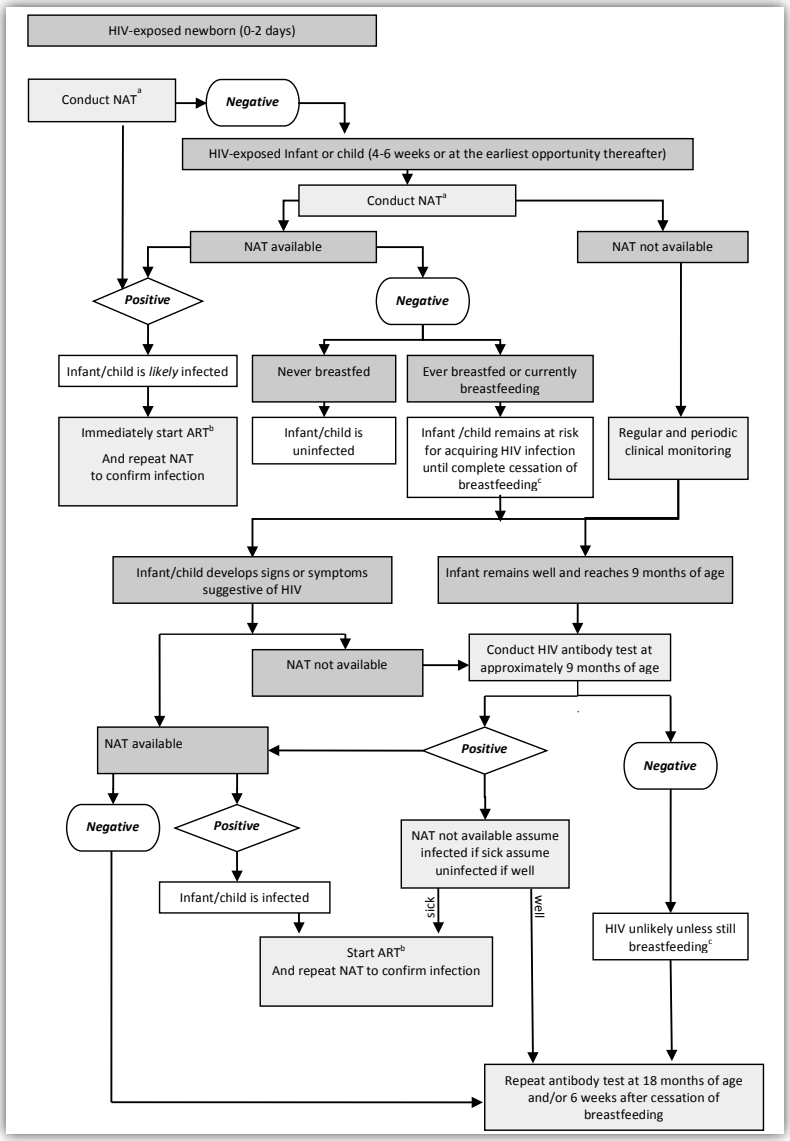
Note: Higher doses of Lop/r may be required when co-administered with enzyme-inducing medicines such as NVP, EFV; n/r = not recommended.

Medicine	Strength of paediatric tablet (mg)	Number of tablets by weight band once daily Children 3 years and over					Strength Of paediatric tablet (mg)	Number of tablets by weight band once daily (PM dosing preferred)	
EFV	200, 50	n/r	n/r	1x200 mg	1x200 mg +	1x200 mg +	200, 50	1.5x200 mg +	2x200 mg
					1x50 mg	2x50 Mg		1x50 mg	
EFV	200, 50	n/r	n/r	0 + 1	0 + 2	0 + 3		0 + 2.5	0 + 2

(Note: Pediatric Dosing Chart on preceding page was adapted from: International Center for AIDS Care and Treatment Programs, Global AIDS Program, Baylor International Pediatric AIDS Initiative, Pediatric Antiretroviral Dosing in Resource-Limited Settings, Updated November 2006. Available at: http://www.cdc.gov/globalAIDS/pa_pmtct_ pediatric.htm.)

APPENDIX x: Early Infant Diagnosis Algorithm

Establishing the presence of HIV infection in HIV-exposed infants and children less than 18 months of age in resource-limited settings.



a POC NAT to provide testing closer to the point of care can be used
bStart ART, without delay. At the same time, retest to confirm infection.
cThe risk of HIV transmission remains as long as breastfeeding continues.

APPENDIX xi: Spontaneous Adverse Drug Reaction Report Form

Medicines Control Authority of Zimbabwe

PVF 01

Spontaneous Adverse Drug Reaction Report (ADR) Form						
Identities of Reporter, Patient and Institute will remain confidential						
MCAZ Reference Number (MCAZ use only)						
Patient Details (to allow linkage with other reports)						
Clinic/hospital Name:		**Clinic/Hospital Number**				
Patient Initials:		**VCT/OI/TB Number**				
Date of Birth:		Weight (Kg)		Sex:		
Age:		Height (meters)				
Adverse Reaction						
Date of Onset:						
Duration:	Less than one hour	Hours	Days	Weeks	Months	
Description of ADR and/or therapeutic failure or lack of effectiveness						
Serious: Yes ☐ No ☐	Reason for Seriousness	☐ Death	☐ Life-threatening			
		☐ Hospitalization/prolonged	☐ Disabling			
		☐ Congenital-anomaly	☐ Other medically important condition			
Relevant Medical History						
Relevant Past Drug Therapy						
Outcome of ADR	Recovered	Not yet recovered	Fatal	Unknown		
Current Medication						
Generic Name	Brand Name	Batch Number	Dose	Indication	Date Started	Date Stopped
Concomitant (Other) drugs taken & Dates/period taken:	Name of drug:				Dated started	Date stopped
Suspected drug (s), if known:						
Laboratory tests results:						
Reported by						
Forename (s) & Surname:						
Designation:						
Address:						
Signature:		Date:				
Send to: The Director-General, Medicines Control Authority of Zimbabwe 106 Baines Avenue, P O Box 10559, Harare **Tel**: +263-4-708255 or 792165, **E-mail**: mcaz@mcaz.co.zw, **website**: www.mcaz.co.zw						

NB. This form may be completed for any ADR related to medicines or medical devices

Rev 5_ March 2015

Page 1 of 1

APPENDIX xii: Medicinal/Pharmaceutical Product Defect Form

Medicines Control Authority of Zimbabwe

PVF 05

PHARMACOVIGILANCE AND CLINICAL TRIALS DIVISION

REPORT ON MEDICINAL (PHARMACEUTICAL) PRODUCT DEFECT OR PROBLEM

To be completed by Pharmacists, Pharmacy Technicians, Medical Practitioners, Nurses, Veterinary Surgeons and other Distributors of Medicines.

1. Product Name (Brand and Generic)			
2. Description of the Device/Medicine	3. Intended Use	4. Size/Type of Container	5. Registration No.
6. Batch Number		7. Expiry Date	
8. Name and Address of Manufacturer			
9. Name and Title of Reporter			
10. Your Practice Location and Address of Hospital, Clinic, Retail Surgery etc.			
11. Phone Number		12. Date Problem Occurred or Observed	
13. If requested will the actual product involved be available for examination by MCAZ. **YES** **NO**			
14. Signature of Reporter		15. Date	
16. Defects/Problem Noted or Suspected (see a-j below)			

NATURE OF DEFECT OR PROBLEM

a) Presence of foreign material
b) Unusual odour
c) Colour changes
d) Fungal growth
e) Suspected contamination
f) Parenteral solution – leaks, particulate matter, discoloration etc.
g) Wrong label, wrong packaging, wrong strength
h) Lack of therapeutic response
i) Leakages
j) Other (specify)

Return To: The Director-General
Medicines Control Authority of Zimbabwe
106 Baines Avenue
P O Box 10559
Harare
Tel: +263-4-736981/2/3/4/5, 708255 or 792165
Email: mcaz@mcaz.co.zw

For Office Use Only
Report Number:
Date Received:

Rev 2_March 2015

Page **1** of **1**

APPENDIX xiii: Medication Error Form

MCAZ Medicines Control Authority of Zimbabwe

PVF 45

PHARMACOVIGILANCE AND CLINICAL TRIALS DIVISION

MEDICATION ERROR FORM

Date of event: **Time of event:**	**Type of Facility:** **Govt / Private** **Hospital** **Clinic** **Pharmacy** **Others**	**Location of event:** **Ward** **Casualty** **Clinic** **Pharmacy** **Theatre** **Others**
Please describe the error: description/sequence of events and medical/nursing care or management done: Immediate action or intervention done: Corrective action taken on the error:		**In which process did the error occur?** Prescribing Dispensing Administration Others (specify):
Did the error reach the patient? **Yes** **No** Was the incorrect medication, dose or dosage form administered to or taken by the patient? **Yes** **No**	**PLEASE TICK THE APPROPRIATE **ERROR OUTCOME CATEGORY (SELECT ONE)** **NO ERROR** **A** Potential error, circumstances/events have potential to cause incident	**ERROR, HARM** **D** Treatment intervention required – caused temporary harm
Describe the direct result on the patient (eg death, type of harm, additional patient monitoring)	**ERROR, NO HARM** **B** Actual error **C** Additional monitoring required – caused no harm	**E** Treatment intervention required – caused temporary harm **ERROR, DEATH** **I** Death
INDICATE THE POSSIBLE ERROR CAUSES(S) AND CONTRIBUTING FACTORS		
Inexperienced personnel Wrong dose administered Medication administration record not accurately documented Failure to adhere to work procedure	Peak hour Illegible prescription Patient information/record unavailable/inaccurate Error due to use of product with similar packaging	Wrong medication given Medication not given Family error
Which category made the error? Doctor Pharmacy Nurse Pharmacist Assist. Clinical Officer Others (specify):	**Other category involved in the error?** Doctor Pharmacy Nurse Pharmacist Assist. Clinical Officer Others (specify):	**Which category detected the error or recognized the potential error?** Doctor Pharmacy Nurse Pharmacist Assist. Clinical Officer Others (specify):
IF AVAILABLE, PLEASE PROVIDE PATIENT'S PARTICULARS – NO PATIENT IDENTIFIERS ARE NEEDED **Age** years/months **Gender** Male Female **Indication for therapy:**		
PRODUCT DESCRIPTION	**Intended product**	**Product administered in error**
Medication brand		
Generic name		
Dose, frequency, duration, route		
Manufacturer		
Dosage form		
Strength		
Type and size of container		

Reported by		
Name:	Address:	
Designation:	Email address:	
Contact number:	Signature:	Date:

Rev 0_July 2016 Page 1 of 1