



**GOVERNMENT OF THE REPUBLIC OF ZAMBIA**

**MINISTRY OF HEALTH**

**ADULT AND ADOLESCENT ANTIRETROVIRAL**

**THERAPY PROTOCOLS 2010**

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## FOREWORD AND ACKNOWLEDGMENT

This document is provided with the aim of standardizing high quality HIV care in all the sectors of health. The document provides health care workers with a knowledge base that will assist in providing appropriate treatment for patients with HIV. The information contained in this document builds upon the foundation established in the Basic Antiretroviral Clinical Training Course. The health care giver is further encouraged to refer to other more extensive literature on the subject. The new protocols presented here are based on evidence from documented long term studies, experiences of a large number of clinicians both local and international, global recommendations from WHO and other international research institutions.

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**Dr Peter Mwaba,**  
**Permanent Secretary**  
**Ministry of Health**



**Editorial Team:**

Katayamoyo P  
Mulenga L  
Mwango A  
Sheneberger R  
Sikazwe I  
Sunkuntu K

**Contributors:**

Dr Bositis C, Dr Bwalya M, Dr Chanda C, Dr Chituwo O, Dr Ishikawa N, Dr Lakhi S, Dr Miyano S, Dr Moyo C, Dr Mshanga G, Dr. Mubiana-Mbewe M, Dr Mwale J, Dr Nalubamba-Phiri M, Dr Nikisi J, Mr Okoth A, Dr Sattin E, Dr Tembo-Zimba S, Dr Trivedi M, Dr Zulu I, Dr Zulu M, Mrs Banda-Ngulube C, Mr Nkhoma Y, Ms Shakwelele H, Dr Shimabale M, Mr Sikasote J and many others whose expertise contribution is greatly appreciated.

## 1.0 OVERVIEW OF HIV

- **Epidemiology, Transmission, and Pathogenesis of HIV**
- **Stages of HIV infection**
- **Diagnosing HIV and AIDS**

### 1.1 EPIDEMIOLOGY AND TRANSMISSION OF HIV

Despite some significant decreases in some populations and in some geographic areas, Zambia's HIV epidemic has stabilized at high levels – it has proven to be tenacious. Overall adult prevalence is 14%, and 1.6% of the adult population becomes newly infected each year – approximately 82,681 people in 2009. More effective prevention is imperative (building on successes already achieved), and essential for achieving and sustaining high rates of access to ARV treatment. Of the next 100 new HIV infections, 71 are estimated to arise through sex with non-regular partners, including being or having one, or having a partner who has one or more other sexual partners. A substantial percentage (21%) of new infections occurs in people who report that they have only one sexual partner. This signals significant HIV risk even for those who are faithful, given large numbers of couples in which one person is HIV-positive. Low levels of male circumcision in most of the country, inadequate condom use, and a range of social norms increase risk and help drive Zambia's varied epidemic.

Zambia is seeing the benefits of rapid scaling-up of PMTCT and access to ART, safe blood supply, and behavior change communication that appears to be showing results in some groups (notably more educated men and women in urban areas, and young women attending antenatal care). But much more effective efforts are needed with regards to multiple and concurrent partners, transactional and intergenerational sex, and discordant couples in order to reduce incidence. Zambia's very rapid scale up of ARV treatment is also an opportunity for concerted prevention with positives. Rapid rolling-out of male circumcision (with careful counseling and information) to act on Zambia's stated commitment is a priority.<sup>1</sup>

Worldwide each day over 7,400 people acquire HIV and over 5,480 people die of AIDS. However there is growing evidence that HIV has now stabilized in much of sub-Saharan Africa. In sub-Saharan Africa, an estimated 22.4 million people are living with HIV, including 1.9 million new infections in 2008. It remains the epicenter of the epidemic, with 66% of adults and 86% of children with HIV and 70% of all AIDS deaths occurring in the region.<sup>2</sup>

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<sup>1</sup>Paragraphs above from the Executive Summary of Zambia HIV Prevention Response and Modes of Transmission Analysis Final Report June 2009

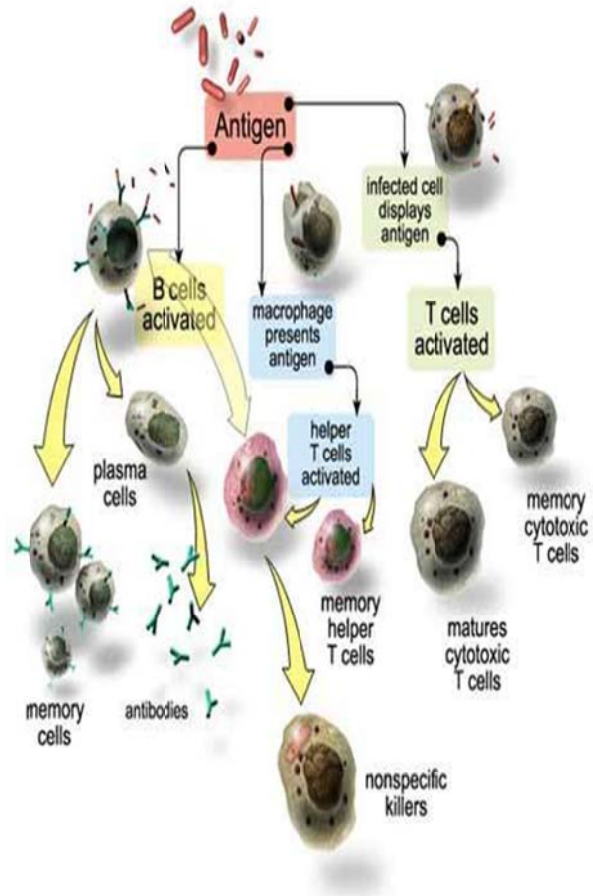
<sup>2</sup> (UNAIDS 2009 Update).

## 1.2 STAGES OF HIV INFECTION

Progression of HIV infection goes through four stages; primary infection, clinically asymptomatic stage, symptomatic HIV infection, and progression to AIDS. The time that it takes for each individual to go through these stages varies. For most people, however, the progression of HIV disease may take several years from infection to the development of severe immune suppression.

HIV infects cells mainly in two important systems: the immune system and the central nervous system. The main type of cell that HIV infects is the **T-helper lymphocyte**. These cells play a crucial role in the immune system, by coordinating the actions of other immunocytes (Figure 1)<sup>3</sup>. When HIV infected T helper cells cannot function properly or die in large numbers, the immune system is weakened.

HIV mainly infects the T helper cell by attaching itself to the protein CD4 on the cell surface. HIV attaches itself to the protein in order to gain entry into the cell. This is why the T helper cell is sometimes referred to as a **CD4+ lymphocyte**. Once it has found its way into a cell, HIV produces new copies of itself, which can then go on to infect other cells. Over time, HIV infection leads to a severe reduction in the number of T helper cells available to help fight disease. This process usually takes several years.



### 1.2.1 Stage 1: Primary HIV Infection

This stage of infection lasts for a few weeks and is often accompanied by a short **flu-like illness**. These symptoms, which usually last no more than several days, might include fevers, chills, night sweats, rashes, enlarged lymph nodes, sore throat, and joint pains. Afterward, the infected person returns to feeling and looking completely well.

<sup>3</sup> Source: <http://www.uta.edu/chagas/images/immunSys.jpg>

Up to 70% of people newly infected with HIV will experience these flu-like symptoms during this stage. In up to about 20% of people the HIV symptoms are serious enough to consult a doctor, but the diagnosis of HIV infection is frequently missed. During this stage there is a large amount of HIV in the peripheral blood and the immune system begins to respond to the virus by producing HIV antibodies and cytotoxic lymphocytes. This process is known as seroconversion. The antibodies can be detected by an antibody HIV test, however if the test is done before seroconversion is complete it may not be positive (that is the result is a false negative). It is important to consider testing for HIV at this point even though the antibody test may be initially negative. The viral load done in such patients is usually very high at greater than 1 million copies/ml of blood. For patients who believe or suspect they have been exposed to HIV it is recommended that they repeat the test after three months. This illness is referred to as the **acute HIV infection**. Patients during acute infection are highly infectious due to their high viral load and it is a critical time for prevention interventions.

### 1.2.2 Window Period

The period of time between when a person is first infected with HIV and when **antibodies** (proteins made by the immune system in response to infection) against the virus are produced by the body (usually 6 to 12 weeks) is known as the "window period".

During the window period, people infected with HIV have no antibodies in their blood that can be detected by an HIV test, even though the person may already have high levels of HIV in their blood, sexual fluids, or breast milk and are highly infectious.

### 1.2.3 Stage 2: Clinically Asymptomatic Stage

This stage may last for an average of ten years, but can be much longer or shorter depending on the individual. In this stage the individual is free from symptoms, although there may be swollen glands. The level of HIV in the peripheral blood drops to much lower levels but people remain infectious and HIV antibodies are detectable in the blood, so antibody tests will show a positive result.

The HIV is not dormant during this stage, but is very active in the lymph nodes, and other vital organs such as the brain, kidney, and heart. The HIV is continually reproducing itself in a process known as replication.

### 1.2.4 Stage 3: Symptomatic HIV Infection

Over time the immune system becomes severely damaged by HIV. This is thought to happen for three main reasons:

- The lymph nodes and tissues are damaged or 'burnt out' because of the years of activity;
- HIV mutates and becomes more pathogenic, in other words stronger and more damaging, leading to more T helper cell destruction;
- The body fails to keep up with replacing the T helper cells that are lost.

As the immune system fails, symptoms develop. Initially many of the symptoms are mild, but as the immune system deteriorates the symptoms worsen.

Symptomatic HIV infection is mainly caused by the emergence of **opportunistic infections** and cancers that the immune system would normally prevent. This stage of HIV infection is often characterised by multi-system disease and infections can occur in almost all body systems.

Treatment for the specific infection or cancer is often carried out, but the underlying cause is the action of HIV as it erodes the immune system. Unless HIV itself can be slowed down the symptoms of immune suppression will continue to worsen.

#### 1.2.5 Stage 4: Progression from symptomatic HIV infection to AIDS

As the immune system becomes more damaged the illnesses that occur become more severe leading eventually to AIDS diagnosis. In this stage, a person is diagnosed as having AIDS. To be diagnosed as having AIDS, a person has a positive HIV test, exhibits certain conditions or opportunistic infections, such as HIV wasting syndrome, pneumocystis pneumonia, or Kaposi sarcoma, or has a CD4 count less than 200 cells/mm<sup>3</sup>.

### 1.3 DIAGNOSING HIV AND AIDS

Research has proven that the earlier HIV is diagnosed and treated, the better the prognosis and the likelihood of a long, healthy life. Diagnosing HIV can be done using blood, saliva, or by using cells from the inside of the cheek. Because HIV carries such stigma and prejudices, great care is taken to protect the identity of those being tested.

#### 1.3.1 Types of HIV Testing

**Mandatory HIV testing:** means that the client/patient has no choice over whether to be tested or not. Essentially it is a compulsory test that cannot be refused. Mandatory testing is generally seen as an unsuitable way of combating HIV and AIDS in Zambia, because it restricts freedom of choice, and can result in stigmatisation and discrimination for anyone who tests positive.

**Voluntary HIV testing:** means on the other hand that the client/patient has to actively and freely choose to take an HIV test, for example visiting a VCT centre.

**Routine HIV testing or provider initiated TC (PITC) or diagnostic CT (DCT):** means an HIV test is offered to everyone within a certain population (for example, pregnant women, or people within a certain age group) on a routine basis. In Zambia where there is a high prevalence of HIV, routine testing should be offered to anyone presenting to any healthcare providers for any reason. It is also referred to as '**opt-out**' screening, which means the test is automatically performed unless the individual concerned raises an objection and 'opts out'.

For screening a certain population for HIV, routine opt-out policies are therefore considered to be more effective from both a public health and an ethical point of view.

### **1.3.2 Testing Without Explicit Consent**

Both voluntary and routine HIV tests require a person's full written or verbal consent.

A list of persons in whom testing can be done without explicit consent includes:

- a. All patients undergoing haemodialysis or organ transplant including the donor
- b. All patients with unknown sero-status, prior to a blood transfusion and/or transfusion of blood products
- c. Patients unable to give consent (unconscious, mentally impaired) in whom HIV testing is deemed essential for management and no next of kin is available
- d. Patients who wish to fully access PEP (with opt out decision resulting in no PEP provision)
- e. Compulsory HIV testing should be undertaken on the person engaged in unlawful sexual intercourse (All children who have been sexually abused should be encouraged to have an HIV test)

**In all the situations pre-test education should be done**

### **1.3.3 Testing Highly Recommended**

Certain situations where HIV testing is highly recommended, but not without explicit consent:

- a. All patients requiring intensive care in an intensive care unit
- b. Patients undergoing surgical procedures
- c. Patients suffering from major opportunistic infections including TB
- d. Pregnant women

### **1.3.4 Different Types of HIV Tests**

There are a number of tests that are used to find out whether a person is infected with HIV. Only antibody and PCR tests are routinely carried out in Zambia.

### **1.3.5 Rapid HIV Antibody Tests**

There is more than one type of HIV test used to determine if a person has been infected with HIV. In Zambia we depend largely on rapid HIV antibody tests. These tests detect HIV antibodies that have been produced by the body after HIV infection has occurred.

- Rapid HIV Testing - This type of HIV testing makes it possible for the patient to get pre-test and post-test counselling, their test results, and any medical referrals they may need all in one visit and in a very short amount of time.

HIV antibody tests are the most appropriate test for routine diagnosis of HIV among adults. Antibody tests are inexpensive and very accurate. When two different types of antibody tests are combined, the chance of getting an inaccurate result is **less than 0.1%**.

Rapid tests can use blood samples, are easy to use and do not require laboratory facilities or highly trained staff. These tests are designed to be used at the point of care, producing a result within 20 minutes, without the need of sending a sample to a laboratory to be analysed. All positive results from a screening rapid test, such as Determine™ HIV-1/2 (Figure 2) must be followed up with a confirmatory test.

**Determine™ HIV-1/2**  
Whole Blood Procedure

(Refer to package inserts for assay procedures) (Refer to the other side for Serum/Plasma procedure)

**1 Remove tests**  
Note: Removal of the test units should start from the right side of the test card to preserve the lot number which appears on the left side of the card.

**2 Remove cover**

**3 Add sample**  
Add sample (50µl) to sample pad (finger stick or venipuncture)  
Wait 1 minute

**4 Add chase buffer**  
Add one drop of chase buffer

**5 Read results**  
Wait 15 minutes

Control: + (blue line), - (no line)  
Patient: + (blue line), - (no line)  
Invalid: (no line in control or patient area)

Lot number: 1011006  
Patient Identification: [blank]  
Name of Test: HIV-1/2  
TestID number: A6  
Read Control Result Here: [blue line]  
Read Patient Result Here: [blue line]  
Add Sample Here: [arrow]

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**Figure 2: Determine Procedure Card**

In Zambia where there are limited resources with relatively high prevalence, a second rapid test is used to confirm a diagnosis. The second test is a different commercial brand and uses a different method of detection from the first.

If the first screening test is negative then the person is determined not to be HIV infected and testing stops there. If the screening test is positive the second step is to confirm the positive result.

1.3.5.1 Confirmation of Result from Rapid Testing

In Zambia, the Uni-Gold Recombigen test is used (Figure 3).

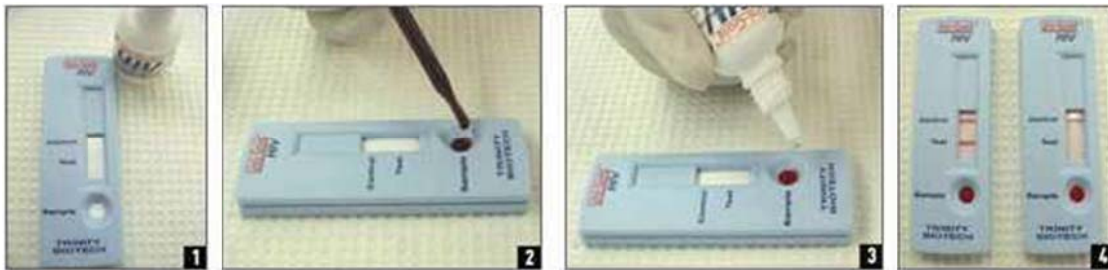


Figure 3: Unigold Procedure Card

Trinity Biotech’s Uni-Gold Recombigen, a CLIA-waived test, is useful for the detection of HIV-1 and 2 antibodies in serum and plasma (Image 1). Add one drop of serum or plasma to well (Image 2). Add four drops of wash solution to well (Image 3). Read results in 10 to 12 minutes (Image 4).

If there is discordance between the screening test and the confirmatory test then a third test is used as the “tie breaker”. In Zambia the Bioline HIV Test is used as the “tie breaker”.

The current screening test, Determine and Uni-gold do not differentiate between HIV-1 and HIV-2 infections. In patients where HIV-2 infection is suspected the Bioline test kits can be used (patients from West Africa or sexual contacts potentially infected from a West African source) to determine if the infection is HIV-1, HIV-2, or a mixed infection.



Figure 4: SD Bioline HIV -1/2 test kit

1.3.5.2 Retesting HIV negative pregnant women

Retesting pregnant women who initially test HIV negative is critical to reduce transmission from mother to child. During pregnancy a woman is at increased risk of acquiring HIV secondary due to anatomic genital changes induced by the pregnancy. Couples testing and family testing should be emphasized during the antenatal period



- The woman initially testing HIV negative during pregnancy should have repeated testing every 3 months during pregnancy and during labour, so that appropriate ARV interventions can be initiated
- HIV retesting should continue if the mother chooses to breastfeed
- Sexual partners of women testing HIV negative during pregnancy should be tested to identify discordant couples and appropriate prevention counselling for the couple should be provided. The HIV positive partner should be evaluated for initiation on ART
- Acute HIV infection during pregnancy or breastfeeding place the exposed infant at high risk for HIV infection due to increased viral load during the period of acute infection
- The best approach to preventing HIV infection during pregnancy or breastfeeding for women testing negative is to identify the sero-status of the woman's sexual partner and take appropriate interventions

### 1.3.6 HIV PCR

The HIV PCR test detects specific Deoxyribonucleic Acid (DNA) and Ribonucleic Acid (RNA) sequences that indicate the presence of HIV in the genetic structure of anyone HIV infected. After HIV infection occurs, RNA and DNA from the HIV virus circulates in the blood. The presence of these DNA and RNA "pieces" indicates the presence of HIV.

During pregnancy and breastfeeding, a mother will pass on many essential antibodies to her baby to enable the child to fight infection. All babies born to mothers with HIV are therefore born with HIV antibodies (though not necessarily HIV itself). If an HIV antibody test is given to a newborn baby then it will always give a positive result if the mother is infected with HIV, regardless of whether the baby actually has the HIV virus. Babies who are not infected lose their antibodies by the time they are around 18 months old. After the baby is 18 months old HIV-antibody tests will give an accurate result.

However, most babies can be diagnosed as either infected or uninfected by the time they are 6 weeks old by using the DNA PCR test. A negative PCR test at 6 weeks should be repeated depending on whether the baby is breastfed, and the age of the baby at the time of repeat testing (see PMTCT/Paediatric guidelines). The PCR test is more sensitive than the HIV antibody test and looks for the presence of HIV itself, not antibodies.

### 1.3.7 Diagnosing AIDS

Acquired Immune Deficiency Syndrome, or AIDS, is diagnosed when a patient with a positive HIV test has an advanced state of HIV infection. With AIDS, the viral infection has progressed, causing significant loss of CD4 cells, weakening the immune system to an extent that the body is at risk for illnesses and infections said to be "AIDS-defining" (WHO Stage 3 and 4 conditions).

An HIV positive person is also diagnosed with AIDS when their CD4 count falls below 200 cells/mm<sup>3</sup> of blood, the level at which the immune system can no longer protect a person from the AIDS-defining illnesses and infections.

## 2.0 PRINCIPLES AND GOALS OF TREATMENT

- **Goals of therapy**
- **General principles of ART**
- **Prerequisites for administration of ART**

Taking Antiretroviral (ARV) therapy requires lifelong commitment from the patient. Correct and consistent use is required for the drugs to be effective. As with all drugs, antiretroviral drugs (ARVs) may have side effects that can limit their tolerability. Thus the decision about when to start therapy is an important one. Treating someone too early may lead to unnecessary toxicity and premature development of drug resistance, while treating too late can increase the risk of morbidity, mortality, and treatment failure.

### 2.1 GOALS OF THERAPY

- Long term viral suppression
- Restoration and/or preservation of immunologic function
- Improvement of quality of life
- Reduction of HIV-related illness and death
- Reduction in transmission to others

### 2.2 GENERAL PRINCIPLES OF ARV THERAPY

- Use of appropriate combinations of three or more antiretroviral drugs
- Maximize adherence to the ARV regimen
- Rational sequencing of ARV regimens
- Avoiding the development of drug resistance
- Provision of comprehensive, integrated family-centred HIV care to families and communities

### 2.3 PREREQUISITES FOR ADMINISTRATION OF ARV THERAPY

- Appropriate drugs are available
- Drug supply can be sustained
- Basic clinical and laboratory measures are available
  - To determine need for treatment
  - To monitor for toxicity
  - To diagnose and treat opportunistic infections
- The patient understands the importance of adherence to lifelong therapy

- Health care providers have been trained in the provision of ARV therapy
- Health facilities are accredited to provide ART services

### 3.0 HAART IN ADULTS AND ADOLESCENTS

- **General points**
- **Who should prescribe HAART?**
- **How to clinically stage HIV disease?**
- **WHO adapted Staging**

Highly Active Antiretroviral Therapy (HAART) consists of a combination of at least three drugs from at least two different classes: namely, any of the following combinations

- 2 Nucleoside Reverse Transcriptase Inhibitors (NRTIs) + 1 Non Nucleoside Reverse Transcriptase Inhibitor (NNRTI)
- 2 NRTIs + Protease Inhibitors (PI)

#### 3.1 GENERAL POINTS

- All patients must have a confirmed HIV serology test and should access counselling services
- HAART is indicated for any patient who meets the Zambian National Guideline Eligibility criteria
- HAART is not an emergency and it has to be initiated after proper treatment preparation
- The goal of HAART is to reduce the viral load to undetectable levels
- HAART needs to be taken for the rest of the patient's life
- Adherence to medication is vital to prevent emergence of resistant strains of HIV
- HAART complements the treatment and prophylaxis of opportunistic infections
- Post exposure prophylaxis (PEP) should be initiated as soon as possible, ideally within two hours of exposure

#### 3.2 WHO SHOULD PRESCRIBE HAART?

Health care providers who fulfil the following requirements

- Legally recognized to prescribe in Zambia (see table 1 below)
- Trained in HIV/AIDS management
- Has access to sustainable drug supply and to facilities to monitor therapy
- Participates in the continuous medical education in the use of ARVs and monitoring of ART

Table 1: ARV Prescribers

Clinician	Supplementary Training	Prescribing of ARVs
Medical doctors	ART trained	1 <sup>st</sup> line & 2 <sup>nd</sup> line regimens
Medical Licentiates	ART trained	1 <sup>st</sup> line & 2 <sup>nd</sup> line regimens
Clinical Officers	ART trained	1 <sup>st</sup> line
Nurses	HIV Nurse Practitioners training	1 <sup>st</sup> line (uncomplicated HIV)
HIV Specialist	MO with Master of Science HIV Medicine or equivalent eg. Registra or Consultant Physician	1 <sup>st</sup> line, 2 <sup>nd</sup> and 3 <sup>rd</sup> line regimens

### 3.3 HOW TO CLINICALLY STAGE HIV DISEASE?

The clinical staging and case definition of HIV for resource-constrained settings were developed by the WHO in 1990 and revised in 2006. Staging is based on clinical findings that guide the diagnosis, evaluation, and management of HIV/AIDS, and does not require a CD4 cell count. This staging system is used in Zambia in conjunction with CD4 Criteria to determine eligibility for antiretroviral therapy. Clinical stages are categorized as 1 through 4, progressing from asymptomatic HIV infection to advanced HIV disease or AIDS. These stages are defined by specific clinical conditions or symptoms. For the purpose of the WHO staging system, adolescents and adults are defined as individuals aged  $\geq 15$  years.

### 3.4 WHO STAGING IN ADULTS AND ADOLESCENTS<sup>4</sup>

Table 2: Adapted WHO Staging

ADAPTED WHO CLINICAL STAGING OF HIV DISEASE IN ADULTS AND ADOLESCENTS
<p><b>CLINICAL STAGE 1</b></p> <ul style="list-style-type: none"> <li>• Asymptomatic</li> <li>• Persistent generalized lymphadenopathy</li> </ul>
<p><b>CLINICAL STAGE 2</b></p> <ul style="list-style-type: none"> <li>• Moderate <i>unexplained</i><sup>1</sup> weight loss (under 10% of presumed or measured body weight)<sup>2</sup></li> <li>• Recurrent respiratory tract infections (sinusitis, tonsillitis, otitis media, pharyngitis)</li> <li>• Herpes zoster</li> <li>• Angular cheilitis</li> <li>• Recurrent oral ulceration</li> <li>• Papular pruritic eruptions</li> <li>• Seborrhoeic dermatitis</li> <li>• Fungal nail infections</li> </ul>
<p><b>CLINICAL STAGE 3</b></p> <ul style="list-style-type: none"> <li>• <i>Unexplained</i><sup>1</sup> severe weight loss (over 10% of presumed or measured body weight)<sup>2</sup></li> <li>• Unexplained chronic diarrhoea for longer than one month</li> <li>• Unexplained persistent fever (intermittent or constant for longer than one month)</li> <li>• Persistent oral Candidiasis</li> <li>• Oral hairy leukoplakia</li> <li>• Pulmonary tuberculosis (current or TB diagnosed 12 months before HIV diagnosis)</li> <li>• Severe bacterial infections (e.g. pneumonia, empyema, pyomyositis, bone or joint infection, meningitis)</li> <li>• Acute necrotizing ulcerative stomatitis, gingivitis or periodontitis</li> <li>• Unexplained anaemia (below 8 g/dl ), neutropenia (below <math>0.5 \times 10^9/l</math>) and/or chronic thrombocytopenia (below <math>50 \times 10^9 /l</math>)</li> </ul>
ADAPTED WHO CLINICAL STAGING OF HIV DISEASE IN ADULTS AND ADOLESCENTS

<sup>4</sup> Source: WHO case definitions of HIV for surveillance and revised clinical staging and immunological classification of HIV-related disease in adults and children. (2006)

**CLINICAL STAGE 4**

- HIV wasting syndrome<sup>3</sup>
- Pneumocystis pneumonia
- Recurrent severe bacterial pneumonia
- Chronic herpes simplex infection (orolabial, genital or anorectal of more than one month's duration or visceral at any site)
- Oesophageal candidiasis (or candidiasis of trachea, bronchi or lungs)
- Extrapulmonary tuberculosis
- Kaposi sarcoma
- Cytomegalovirus infection (retinitis or infection of other organs)
- Central nervous system toxoplasmosis
- HIV encephalopathy
- Extrapulmonary cryptococcosis including meningitis
- Disseminated non-tuberculous mycobacteria infection
- Progressive multifocal leukoencephalopathy
- Chronic cryptosporidiosis
- Chronic isosporiasis
- Disseminated mycosis (extrapulmonary histoplasmosis, coccidiomycosis)
- Recurrent septicaemia (including non-typhoid Salmonella)
- Lymphoma (cerebral or B cell non-Hodgkin)
- Invasive cervical carcinoma
- Atypical disseminated leishmaniasis
- Symptomatic HIV-associated nephropathy or HIV-associated cardiomyopathy

<sup>1</sup> *Unexplained* refers to where the condition is not explained by other conditions.

<sup>2</sup> Assessment of body weight among pregnant woman needs to consider the expected weight gain of pregnancy.

<sup>3</sup> Unexplained weight loss > 10% of baseline body weight associated with either chronic diarrhoea or chronic weakness and documented fever > 1 month

## 4.0 ART ELIGIBILITY CRITERIA

The following tables shows the eligibility criteria

### 4.1 CLINICAL STAGE CRITERIA FOR INITIATION OF ART IN ADULTS AND ADOLESCENTS

Clinical Stage	CD4 count available	CD4 count not available
I	CD4 guided	Do not treat
II	CD4 guided	Total Lymphocyte Count <1200*
III	Treat	Treat
IV	Treat	Treat

\* CD4 count strongly recommended

### 4.2 CD4 COUNT CRITERIA FOR INITIATION OF ART

CD4 count (cell/mm <sup>3</sup> )	Recommendation
<350	Treat all irrespective of clinical stage

Note: Measure CD4 after stabilization of any inter-current illness

### 4.3 CONDITIONS TO INITIATE ART IRRESPECTIVE OF CD4 COUNT

Condition	Recommendation
HIV positive partner in Discordant Couple (see 4.4) Hepatitis B Virus Infection (chronic hepatitis B)* <u>Active Tuberculosis</u>	Treat all irrespective of CD4 count

\*Patients testing HBsAg positive with CD4 counts greater than 350 cells/mm<sup>3</sup> should have ALT or AST checked and if elevated initiate HAART. For patients with normal baseline ALT or AST recheck both ALT or AST and HBsAg in 6-12 months. If ALT or AST are elevated, or persistent HBsAg then start ART regardless of CD4 count or WHO staging. If signs of liver cirrhosis and positive HBsAg start HAART regardless of ALT or AST values.

**4.4 HIV TESTING AND TREATMENT OF DISCORDANT COUPLES**

One of the primary modes of transmission in Zambia is between couples in a relationship where one partner is HIV negative and the other partner is HIV positive (discordant). Fully suppressive HAART will reduce the viral load of the positive partner to such a low level that the risk of HIV transmission becomes significantly lower assuming the patient is 100% adherent with therapy. It is strongly encouraged that clinics make every effort to identify the status of couples through counselling and testing. Those HIV positive clients with HIV negative partners can be initiated on ART to protect their own health and significantly reduce the risk of HIV transmission to their partner regardless of CD4 or clinical criteria. Clients initiating HAART to protect their partner and their own health must be counselled on the importance of 100% adherence and not to stop their ARVs without discussion with a medical provider. Using HAART in a discordant relationship does not lessen the importance of continued use of other prevention methods including male circumcision and consistent condom use.

**5.0 CARE FOR PATIENTS WHO ARE NOT YET ELIGIBLE FOR HAART**

Patients not eligible for initiation of HAART must also be monitored closely:

- To assess disease progression
- To identify eventual eligibility for HAART initiation

Table 3: Follow – up for non ART eligible patients

CD4 count (cell/mm <sup>3</sup> )	Follow Up Actions
>500	Schedule follow up visits for every 6 months <u>with CD4 count every 3 months</u>
350-500	Schedule follow up visits for every 3 months, with CD4 count every <u>36</u> months

**6.0 ART INITIATION**

(ARV Dosing Guideline in 22.0)



## 6.1 CONSIDERATIONS BEFORE STARTING ARV THERAPY

- Patient readiness and likelihood of adequate adherence
- Ability of the patient to return for regular and reliable follow-up
- Potential for serious adverse effects and toxicity
- Side effects and tolerability
- Potential for interactions with other drugs
- Cost and sustainability
- Presence of pregnancy or the risk of becoming pregnant
- Presence of tuberculosis and other illnesses -anaemia, peripheral neuropathy, kidney disease, hepatitis
- Potential for treatment options should the initial drug combination fail
- The provider and patient must endeavour to reduce all risks of treatment failure and early mortality for both treatment naive and treatment experienced patients needing a new regimen

## 7.0 STRATEGIES FOR REDUCING EARLY MORTALITY IN ART

**Prior to initiating ART in all patients ensure that:**

1. Documented treatment preparation is completed
2. Disclosure is documented
3. Co-trimoxazole prophylaxis is initiated
4. Minimum baseline laboratories are completed: CD4, ALT, Creatinine, Hct/Hgb
5. **Absence** of the danger signs of un-resolved Opportunistic Infections (OIs) listed below is documented
  - a. Persistent fever (>14 days)
  - b. Persistent cough (>14 days)
  - c. Severe persistent headache (>14 days)
  - d. Anaemia (Hgb < 8 or Hct < 24)
  - e. Weight loss > 10%

**If ANY of the above five symptoms are PRESENT then investigate and treat as appropriate** (see review of undiagnosed OIs below)

1. Initiate diagnosis with sputum for AFB, CXR, cryptococcal antigen, and oxygen saturation
2. Based on test results initiate appropriate therapy
3. Initiate ART two weeks after documented response to OI treatment
4. If no clear diagnosis obvious from diagnostic test, then consult an HIV Specialist before initiating ART

## **7.1 NOTES ON UNDIAGNOSED OI PRIOR TO INITIATION OF ART**

### **7.1.1 Tuberculosis**

- a. Patients with advanced immunosuppression (very low CD4, <100 cells/mm<sup>3</sup>) often do not present with classic symptoms and often have extra-pulmonary TB
- b. Provider should have a high level of suspicion based on fever, anaemia, and weight loss even without cough
- c. Abdominal symptoms often are suggestive of TB

### **7.1.2 Cryptococcal meningitis**

- a. Patients typically present with fever and headache, but may not necessarily have a stiff neck
- b. If cryptococcal serum antigen test is negative, but symptoms are highly suggestive of cryptococcal disease proceed to do a lumbar puncture (LP)
- c. Initiate therapy upon diagnosis with Amphotericin B followed by fluconazole maintenance
- d. Serial lumbar punctures (LPs) are part of the therapeutic intervention and can be critical to improving patient outcome

### **7.1.3 Pneumocystis Jiroveci Pneumonia (PCP)**

- a. Classic symptoms include extreme dyspnoea; tachypnea; tachycardia; often oxygen saturation less than 90%; and a drop in oxygen saturation on physical exertion
- b. Treatment with high dose co-trimoxazole according to OI guidelines for 21 days with addition of oral steroids for the same period for patients with oxygen saturation < 90% and maintenance co-trimoxazole

### **7.1.4 Bacterial pneumonia**

- a. Diagnosis based primarily on symptoms and CXR
- b. Treatment according to OI guidelines

## 8.0 RECOMMENDED ANTIRETROVIRAL REGIMENS

The following are the recommended regimens for first line and second line therapy.

Table 4: Recommended Regimens

First Line Regimen		Second Line Regimen		
TDF*/FTC or 3TC	EFV or NVP <sup>3</sup>	AZT <sup>1</sup>	3TC <sup>2</sup> or TDF/FTC <sup>5</sup> or 3TC	LPV/r <sup>6</sup>
		d4T <sup>4</sup> /3TC <sup>2</sup>		
* TDF has been associated with renal toxicity: if CrCl <50 ml/min , initiate therapy with ABC/3TC				
<sup>1</sup> AZT/3TC/LPV/r is preferred second line regimen for patients failing Tenofovir based first line. <sup>2</sup> Lamivudine (3TC) or Emtricitabine (FTC) are continued in the second line regimen because their resistance mutations decrease viral replication capacity, increase the HIV susceptibility to Tenofovir (TDF) and AZT <sup>3</sup> For women who have had exposure to sdNVP <b>without</b> tail coverage with 7 days of AZT + 3TC within the last 12 months (for PMTCT), do not use a Nevirapine or Efavirenz containing regimen, use LPV/r. If unsure whether tail coverage for sdNVP was provided then use LPV/r <sup>4</sup> Stavudine (d4T) is associated with long term toxicity and should only be used in the second line if AZT cannot be taken <sup>5</sup> TDF mutations can increase HIV susceptibility to AZT and may increase AZT efficacy, while TDF may maintain some activity <sup>6</sup> If unable to tolerate LPV/r then refer to HIV Specialist				

### 8.1 PRACTICAL HINTS TO AID IN CHOOSING A SPECIFIC REGIMEN

- Initiation of a regimen containing AZT may worsen anaemia because of bone marrow suppression. It is not recommended to start AZT with haemoglobin less than 10 gm/dl. ARV therapy should be delayed until the anaemia has been treated or an alternative NRTI combination should be started in this situation.

- D4T-containing regimens should not be used unless there are no other alternatives as patients may develop toxicities such as peripheral neuropathy (numbness, tingling, or burning sensations in the extremities) and lipoatrophy. Patients also being treated with isoniazid (INH) should not be started on d4T.
- Women with CD4 > 250 cells/mm<sup>3</sup> (men with CD4 > 400 cells/mm<sup>3</sup>) have been associated with a higher incidence (11%) of symptomatic hepatotoxicity when treated with NVP; initiating NVP-containing ART regimens should be done with caution in women between 250-350 cell/mm (monitor ALT/AST during first 12 weeks) and avoided in women who are pregnant or at risk for pregnancy with CD4 > 350 cells/mm<sup>3</sup> (men with CD4 > 400 cells/mm<sup>3</sup>); in cases where NVP cannot be used consider using EFV
- Use of single-dose NVP for perinatal prophylaxis has not been associated with hepatotoxicity
- For women who have had exposure to sdNVP **without** tail coverage with 7 days of AZT + 3TC within the last 12 months (for PMTCT), do not use a Nevirapine or Efavirenz containing regimen, use LPV/r. If unsure if whether tail coverage for sdNVP was provided use LPV/r
- A two-week lead-in NVP dose (200mg once daily) must be initiated before increasing to full dose (200 mg twice daily) to reduce risk of skin rash and/or hepatotoxicity
- EFV has been associated with serious birth defects; avoid EFV use in women of reproductive age who are not using effective and consistent contraception or trying to get pregnant or who are in the 1st trimester of pregnancy
- EFV is associated with CNS side effects (drowsiness, insomnia, abnormal dreams, impaired concentration, etc); these generally occur with the first few doses and usually diminish or disappear after 2-4 weeks, but may persist for months leading to discontinuation. Avoid use of EFV with severe untreated psychiatric illness
- EFV is the recommended NNRTI to be used in HIV/TB co-infection treatment with Rifampicin because of reduced drug interactions
- Consider potential drug-drug interactions or additive toxicity if initiating ART in patients on certain other drugs {e.g. INH and d4T (peripheral neuropathy); co-trimoxazole and NVP or EFV (skin rash); co-trimoxazole and AZT (bone marrow suppression); INH and NVP or EFV (hepatotoxicity)}. In these situations may consider alternate ARV agent or close clinical and/or laboratory monitoring
- Patients with HIV-2 should be treated with PI based regimen (LPV/r) as they are not effectively treated with the NNRTI class of drugs (NVP or EFV (confirm suspicion with Bioline test and refer to HIV Specialist if unclear on best treatment options)

- With decreased Creatinine Clearance there is need for dose adjustment for TDF, 3TC, FTC, and d4T; AZT only with “severe” renal impairment or patient on dialysis (refer to Annex for details)

## 8.2 SPECIAL CONSIDERATIONS FOR PATIENTS ON FIRST LINE AZT AND D4T REGIMENS

- **Switch** patients on d4T or AZT based first line regimens with any signs of toxicity (peripheral neuropathy, lipoatrophy, lactic acidosis, etc), **BUT NOT** clinical failure, to TDF/FTC + NVP or EFV
- **Switch** patients with signs of clinical failure from AZT or d4T based first line regimens to TDF/FTC + LPV/r
- **Do not switch** patients from AZT or D4T if tolerating therapy and definitely no signs of toxicity
- For Paediatric patients who are transitioning to adult care, follow the above recommendations for stable patients, patients with toxicity, and patients with clinical failure
- Patients with discontinued second line regimens will be transitioned as follows:
  - TDF+ddI+LPV/r should be switched to TDF/FTC+LPV/r
  - ABC+ddI with either LPV/r or NFV should be switched to TDF/FTC+LPV/r unless renal insufficiency is present use ABC/3TC+LPV/r; consider consult with HIV Specialist
  - TDF+ddI+NFV should be switched to TDF/FTC+LPV/r
  - d4T/3TC+IDV or AZT/3TC+IDV should be switched to TDF/FTC+LPV/r
  - d4T/3TC+ABC or AZT/3TC/ABC consult with a HIV Specialist Other combinations not covered above consult with a HIV Specialist for transition

## 8.3 FUTURE STOCKS OF ARVs IN THE ZAMBIA PUBLIC SECTOR NATIONAL ARV PROGRAM

Zambia plans to progressively reduce utility of some ARVs and introduce new ones.

- D4T will only be reserved for use in second line (in alternative combinations in situations where there are no viable options for a patient and in salvage regimens). It will no longer be used as a first line regimen for adults and adolescents due to long term toxicity.
- Fixed dose combinations (FDC) will be used more often to enhance adherence such as AZT/3TC/NVP. New FDCs, such as TDF/FTC/EFV, will also be procured.

- Third line drugs will be introduced once the national program has acquired capacity to manage third line patients. This also is contingent on procuring or accessing the newer generation of ARVs necessary to treat treatment-experienced patients.
- The National ARV Program will at all times procure potent cost effective ARVs of both generic or innovator brands.

## 9.0 ADHERENCE TO HAART

Adherence remains the single most important strategy for long term success and sustainability of patients on ART

- Adherence to ART is important to control HIV infection and to prevent resistance to ART
- Treatment failure is generally a failure with adherence and efforts to ensure good adherence from the onset of ART initiation must be mandatory
- Good adherence means
  - Drugs should be taken at the same time of the day to maintain constant drug blood level.
  - Taking all the medications at the right time, in correct doses
  - Not skipping doses
  - Not stopping and restarting therapy without medical advice
  - Adopting health seeking behaviour

**A structured treatment preparation prior to initiating ART should be adopted for all patients for successful treatment and care**

### 9.1 ART PREPARATION VISITS

Listed below are specific topics that must be discussed and understood by the patient prior to starting ART. These sessions can be conducted by any qualified trained personnel (medical officer, medical licentiate, clinical officer, nurse, adherence counsellor, community worker)

#### 9.1.1 Adherence Visit One: Patient has received positive HIV test and has enrolled in care

- First Visit- Enrollment & Assessment
  - HIV Education- difference between HIV and AIDS, basics of HIV infection, prevention, transmission, window period, stages of HIV, CD4 count and viral load, CTX prophylaxis, benefits of early treatment, family disclosure, testing, and partner notification

**1. What is HIV?**

- a. HIV is a virus that attacks the body
- b. It damages your ability to fight germs and disease
- c. The virus makes many copies of itself every day if you are not on treatment
- d. Without treatment people progress from no symptoms to minor illness to severe life threatening illness and death

**2. What is AIDS?**

- a. AIDS occurs when the body is overcome by the HIV virus and becomes weak due to other illnesses
- b. HIV causes AIDS months to years after infection

**3. How is HIV spread?**

- a. Unprotected sex is the most common method
- b. Sharing needles or blood contaminated sharp objects (razors, knives, etc)
- c. Mother to child either before, during or after delivery (in the womb, during delivery, or while breastfeeding)
- d. Infected body fluids in contact with
  - i. Soft moist skin in the mouth, nose, vagina or rectum
  - ii. Cuts in the skin
- e. Traditional beliefs that facilitate HIV transmission (sexual cleansing, wet nursing, dry sex, pre-coital pubic shaving with shared razor, etc)
- f. HIV is NOT spread through sharing food or utensils, touching, kissing, mosquitoes, or curses

**4. How can HIV be prevented?**

- a. Abstaining from sex
- b. Knowledge of sexual partner's HIV status
- c. Being faithful to your one partner/spouse
- d. Using condoms when engaging in sexual contact
- e. Becoming circumcised if an HIV negative male
- f. Taking ARVs perfectly

(Discuss how they can prevent re-infecting themselves or infecting others)

**5. Ask the patient if they have any partners or family members that need to be referred for HIV testing. Review how a person gets tested for HIV.**

- a. A simple blood test
- b. HIV test may not be positive for up to 3-6 months after infection (window period)
- c. Retest every 3-6 months if you are at risk
- d. The standard test looks for a reaction to HIV from your immune system

**6. It is important to disclose your status to someone you trust and notify your sexual partner**

- a. Sharing your test results with someone you trust who can support you is associated with better success in managing HIV
- b. Your family should become a source of support and help in your treatment of HIV
- c. Notifying your sexual partner so they can be tested also can help stop HIV spreading

**7. What is the meaning of CD4 cells?**

- a. The immune system works in your body to fight infections and keep you healthy
- b. CD4 cells are the "soldiers" of your immune system army
- c. CD4 cells recognize germs in your body, and they work with other cells to destroy them
- d. HIV attacks and destroys your CD4 cells
- e. When CD4 cells are destroyed by HIV, the immune system does not know how to fight germs

**8. What is viral load?**

- a. Viral load is the amount of HIV virus in the blood
- b. The lower the amount of HIV virus in the blood the better
- c. When there is more HIV virus in the blood, more CD4 cells are destroyed
- d. When the amount of HIV virus increases, eventually you don't have enough CD4 cells to fight HIV and other germs that enter your body, and you progress to AIDS

**You want to have more CD4 cells in your body and little HIV virus in your body**

**9. Co-trimoxazole can help prevent illnesses before you start HIV treatment**

- a. Taking co-trimoxazole everyday can help your body fight off germs that can cause pneumonia, diarrhoea, toxoplasmosis and malaria
- b. Your provider will tell you if you should be taking co-trimoxazole
- c. Taking co-trimoxazole before HIV treatment is good practice for adhering to HIV treatment

**10. Starting HIV treatment early has many benefits**

- a. Starting HIV treatment before you become sick and have AIDS will make it easier to lower the HIV virus in your blood and increase your CD4 cells faster
- b. It will also make the potential side effects from treatment easier to tolerate
- c. It will prevent you from developing more serious infections, and improve your chance of living a normal life with HIV



**SUMMARY OF VISIT ONE:**

HIV is a disease of the immune system

- HIV is a virus that infects blood
- HIV is passed from one person to another through blood or certain body fluids
- HIV reproduces very fast and attacks and kills CD4 cells
- CD4 cells are needed to fight HIV and other germs
- Viral load measures how much HIV is in your blood and predicts how well you will do
- CD4 cells measure how well your immune system fights germs
- Disclosing your results to someone you trust is very important
- Your examination and laboratory results will help determine whether you need treatment now

### 9.1.2 Adherence Visit Two: Patient has been assessed with examination and laboratory, and qualifies for ART

- Second Visit- ART Eligibility
  - ART Support- treatment supporter, home based care, linkage to support groups, referrals to community for additional services, management of fears, counsel about impact of alcohol use and depression's negative impact on adherence, expectancy of increased CD4 count, more energy, and improved quality of life
  - ART Preparation- general ARV information, understanding that starting ART is not an emergency, understanding the need to treat OI first, benefits of ART, planning for the unexpected (funerals, holidays, travel, etc), 100% rule of adherence, understanding resistance and its consequences

#### 9.1.2.1 What is ARV Therapy?

##### 1. What is ARV?

- a. ARV stands for **Anti-Retro Viral**
- b. ARVs are medicines that help control the HIV virus in the blood
- c. ART is **Anti-Retroviral Therapy**, and refers to the combination of ARVs which are used to fight HIV

##### 2. Who should start ART?

- a. You cannot always tell by looking at someone if they need ART
- b. Even if you look and feel healthy, your immune system may already be weakened (low CD4 cell count), and you may benefit from starting ART to prevent you from getting sick
- c. You should start ART if you are experiencing illnesses or your immune system is weakened (low CD4 cell count)

- d. An HIV+ person does not always need to start ART immediately, and some people may have no illnesses and a healthy immune system (high CD4 cell count) and can delay ART, but should remain in care with regular follow up

### 3. Other considerations before starting ART

- a. Several considerations are associated with success when starting ART
  - i. Disclosing your status to someone that you trust is associated with better success on ART
  - ii. Identifying a treatment supporter or buddy that can help you with ART is very important
  - iii. Identifying linkages to the community through home based care, treatment support groups, and other community services will help you be more successful with your treatment
  - iv. Discuss fears and questions with your health care team members
  - v. Always keeping a supply of medication with you and **NEVER** running out
  - vi. Heavy drinking of alcohol and depression can lower your adherence and reduce your success when taking ART
- b. Medication issues discussed in visit three

#### 9.1.2.2 Starting ART

### 4. Starting ART is never an emergency

- a. Starting ART is an individual decision and one is not forced
- b. Those who are already sick with AIDS will need ART, *however* **STARTING ART IS NEVER AN EMERGENCY**
- c. Opportunistic Infections and other illnesses should be identified and treatment started before starting ART
- d. ARVs may cause side effects, however most people tolerate ART well, and specific potential side effects will be discussed prior to starting ART

### 5. What are the benefits of starting ART?

- a. ART increases the CD4 cell count
- b. ART allows the body to better fight infections by restoring the immune system
- c. A healthy immune system will lead to fewer hospitalizations
- d. ART can allow you to live longer so that you can care for your children and family
- e. ART can help you gain weight, feel more energetic, and improve your sexuality
- f. ART can decrease the risk of transmitting HIV to others

### 6. What are the benefits of delaying ART?

- a. You have more time to prepare yourself to be successful with ART
- b. You don't have to take medication or risk experiencing side effects

**9.1.2.3 Taking ART Correctly**

**7. What is resistance?**

- a. Resistance is when the HIV virus changes itself and the ARVs can no longer work

**8. How does resistance occur?**

- a. Resistance can occur when you miss doses of your medicine or take them incorrectly. HIV virus uses this chance to make more and more different copies of itself that are so different that your medicines stop working
- b. Resistance can also occur if you get infected with an HIV virus that is already resistant to the medications that you are taking, or if you get re-infected with a resistant HIV virus to the medications that you are taking (always practice safe sex to avoid infection or re-infection)

**9. How do you prevent resistance?**

- a. You can prevent resistance through perfect adherence
- b. Perfect adherence requires a patient to take their medicines every day at the right time and in the right way (dose and combination)
- c. It also means always collecting your medicines on time so that you never run out of ART, and making sure that you take them when travelling away from home (funerals, holidays, other emergencies) or while away at work (miners, truck drivers, etc)

**10. Why is perfect adherence necessary?**

- a. The best way to live a long life with HIV is to keep the first ART combination working as long as possible
- b. When ART is not taken properly the virus can change (viral mutation) and then the medicines quit working and resistance has developed
- c. Once resistance occurs, it is NOT reversible and will last forever
- d. When resistance develops you are no longer able to fight the HIV in your body and you risk getting sick and dying
- e. It will then become necessary to find a different combination of ART medicines to treat your HIV virus. The second ART combination may not work as well as the first ART combination and it may have more side effects, and is very expensive
- f. Without perfect adherence eventually you run the risk of having no treatment options for HIV

**SUMMARY OF VISIT TWO:**

ART are medicines that help control the HIV in the blood

- Starting ART is never an emergency
- Not all HIV+ persons need to start ART immediately
- Consider medical and social factors before starting ART
- ART helps the immune system get healthy (higher CD4 cell count)
- Resistance is when the HIV virus changes itself and ART can no longer work
- ART requires perfect adherence for life

### 9.1.3 Adherence Visit Three: Patient is free of Opportunistic Infections or on treatment (for the OI), and has been prescribed ART

- Third Visit- ART Initiation
  - ART Education- ARV drug resistance (avoidable, but not reversible), always maintaining drug supply, keeping in touch with health care facility and provider, plan for successful treatment (good nutrition and physically active) and develop a general adherence plan that includes both the client and family perspective
  - ART Preparation- managing potential side effects and toxicities, discussing specific prescribed regimen (dosing, side effects, toxicity), making a specific treatment plan, assess other social issues
  - Dispense the prescribed ARV medication with clear instructions and verification from pharmacist or dispensers that the patient has understanding of medication dosing schedule, importance of complete adherence, and how to contact health facility if potential side effects occur

#### 9.1.3.1 Resistance Review

1. **Resistant virus can be transmitted from one person to another**
  - a. A resistant virus can be transmitted to another person through sex and other high risk exposures
  - b. Someone who is not taking their ARVs correctly and develops resistant virus can pass the virus to:
    - i. An uninfected person (then they will start their HIV infection with virus that is already resistant to ART)
    - ii. An infected person who is taking their ARVs correctly, and then develops resistance to the new resistant HIV virus that was passed on to them
  - c. Practice safe sex even if you and your partner are both HIV+ to avoid passing on resistant virus
2. **How can resistance be prevented?**
  - a. Resistance can be prevented by perfect adherence
  - b. Partial adherence puts your virus at risk for resistance

- c. Perfect adherence requires a person to take their ART medicines every day at the right time and in the right way, and **NEVER** run out of medication

**3. Can I feel resistance when it happens?**

- a. Resistance is like a silent side effect and you will not feel any different at first when your HIV virus becomes resistant to your ART
- b. Resistance will make your ART become less effective, and eventually the number of HIV viruses in your blood increases then your CD4 cells decrease and eventually you will get sick and feel worse

**9.1.3.2 Keys to success on ART**

**1. Developing a successful treatment plan**

- a. Keep all scheduled appointments and pharmacy refills
- b. Make sure the health facility knows how to contact you and your buddy (up to date phone numbers and address) and contact your health care facility or provider for any problems with medications (side effects, lost medicine, unable to make appointment, etc) or new illnesses
- c. Use a defined schedule for taking your ARVs and use helps such as calendars, pill boxes, checklist to ensure that doses are not missed
- d. Involve family members or a treatment supporter (buddy) in your care and keep them up to date with your progress
- e. Stay active with good nutrition and exercise
- f. Plan for emergencies before they happen (rainy season, floods, funerals, holidays, lost medicine) so that you do not run out of medication
- g. Do not STOP your medicines without discussing with a health care provider
- h. Do not take other herbal or over the counter medicines without discussing with your health care provider

**2. Know your ART medication**

- c. Know the names of the medicines and how they are to be taken
- d. Know the potential side effects and what to do if they occur
- e. Know about potential drug interactions between your medicines

### 9.1.3.3 Patient Readiness Questionnaire

Prior to dispensing ART providers should review the Patient Readiness Questionnaire with the patient and make sure they understand ART by answering the following questions:

1. ART can cure HIV/AIDS?
  - a. True
  - b. False
2. People taking ART should still abstain from sex or use condoms when having sex to be sure not to pass HIV to their sexual partners?
  - a. True
  - b. False
3. ART works well as long as at least half the doses are taken correctly?
  - a. True
  - b. False
4. What would you do if you think you are having a bad side effect from the ART?
  - a. Continue taking your ART and go to the clinic
  - b. Stop the one that you think is making you feel bad, but continue the others
  - c. Stop all the ART medicines and resume taking them when you feel better
5. What is HIV resistance?
  - a. When you don't like your medicines
  - b. When your **body** 'resist' your medicines
  - c. When the **HIV virus changes** in a way that stops your medicines from working to keep your HIV virus under control
  - d. When your **medicine changes** in a way that stops them from keeping your HIV under control
6. What can cause resistance?
  - a. When you forget to take your HIV medicines
  - b. When the amount of medicine in your body is too low from missed doses
  - c. When HIV makes copies of itself that are different from the original
  - d. All of the above
7. If my HIV virus develops resistance it will go away once I become adherent to my medications and I can continue with my current ART?
  - a. True
  - b. False
8. I can be re-infected with HIV that is already resistant to my ART?
  - a. True
  - b. False

9. There is no cure for HIV. If I stop ART after someone says that I am cured (faith healing, herbal medicines, etc) the HIV will come back, and I may develop resistance and the ART will not work?
  - a. True
  - b. False
10. I agree to identify a treatment supporter or buddy, and allow home visits?
  - a. True
  - b. False
11. I understand that herbal medicines can work against ART?
  - a. True
  - b. False
12. I understand that ART, if taken correctly, will help prolong my life?
  - a. True
  - b. False

**SUMMARY OF VISIT THREE:**

Resistance is not reversible and compromises treatment success

- Patients should not start ART if they cannot commit to perfect adherence
- Develop a successful treatment plan
- Review ART medication side effects
- Patients should understand the Patient Readiness Questionnaire and answer correctly

**9.1.4 Patient Preparation Checklist**

O	This patient has completed Adherence Visit One	Date- _____
O	This patient has completed Adherence Visit Two	Date _____
O	This patient has completed Adherence Visit Three	Date _____
O	We have identified a treatment supporter or buddy and contact information is in the patient record	
O	We have gone through the Patient Readiness Questionnaire and believe this patient is ready to start ART	
Adherence Nurse/Counsellor _____ Date _____		
Prescriber Reviewed _____ Date _____		

## 9.2 ASSESSMENT OF ADHERENCE

Adherence assessment is everyone's responsibility. It should be done by all members of the health care team using clinical and laboratory parameters, patient reports, pill counts, pharmacy pickups, and other tools of adherence.

- Assess adherence at every clinic visit and note the following:
  - It is critically important to assess how the patient is taking his or her drugs at each visit
  - An assessment, with open ended and targeted questions and using other tools (e.g. pill counts) must be done at each visit to the clinic
  - **Missing pharmacy refills or clinic appointments is a RED FLAG to poor adherence and should be addressed immediately in any patient on ART**
- Adherence assessment should be done at every contact with an adherence support worker, home-based care giver, or provider
  - Patients with suspected or identified adherence problems must be referred to the ART care team immediately
- Assessing adherence is not a simple question and patients are unlikely to volunteer information about non-adherence
  - Ask how the patient is taking the medications prescribed
  - Probe, verify, ask follow-up questions
  - Find out what the barriers are and help the patient to find ways to overcome these barriers
  - **Pill counts can be helpful**
- Give written dosing instructions to patients and explain in simple language
- Provide one-on-one counselling to each patient
  - This often takes several counselling sessions before a patient is truly "ready" to start ART
  - This should include information about drug-related side effects: how to recognize serious adverse effects, when to seek care and how to prevent or manage mild side effects
- Ensure patients identify treatment supporters (family members, buddies) and encourage buddies to attend counselling sessions and clinic visits
- Find ways to help patients overcome obstacles, such as disclosure and lack of psychosocial support
- Discuss HIV re-infection
- Link patients with adherence support groups, community support systems, and NGOs providing other complimentary services
- Counsel patients to avoid drug abuse and to refrain from excessive alcohol use
- All patients should be given information about how and when to contact their health care provider



### 9.3 ADHERENCE TO ART

The health care provider should bear in mind the following information as they conduct adherence counselling:

- First line regimen- re-enforce the importance of treatment success and preventing resistance, and that failure and switch to second line is associated with more pills, more side effects and toxicity, more drug interactions, and more complicated treatment of TB
- NNRTIs and 3TC or FTC have a low genetic barrier to resistance and near-perfect adherence is essential to prevent development of resistance and ultimately treatment failure
- Second line regimen- stress that limited treatment options remain and increased effort and support is necessary, patient must complete three adherence sessions and develop a treatment plan prior to initiating second line treatment
- DO NOT switch a patient who has failed with poor adherence unless a plan to produce a different outcome is determined by a multidisciplinary team and involves the treatment supporter/buddy of the patient

## 10.0 TRACKING AND KEEPING PATIENTS IN CARE

Keeping patients in care is essential for achieving good outcomes and preventing resistance

- Every facility should have a structured plan to track patients and prevent patients being lost to follow-up
- Monitor **all** missed clinic and pharmacy appointments
- Create linkages with home based care workers and volunteers, and dedicate staff to ensure patients missing appointments are contacted
- **“Lost to follow up leads to treatment failure, emergence of resistance & possibility of transmitting resistant virus”~~is the first step to~~ treatment failure”**

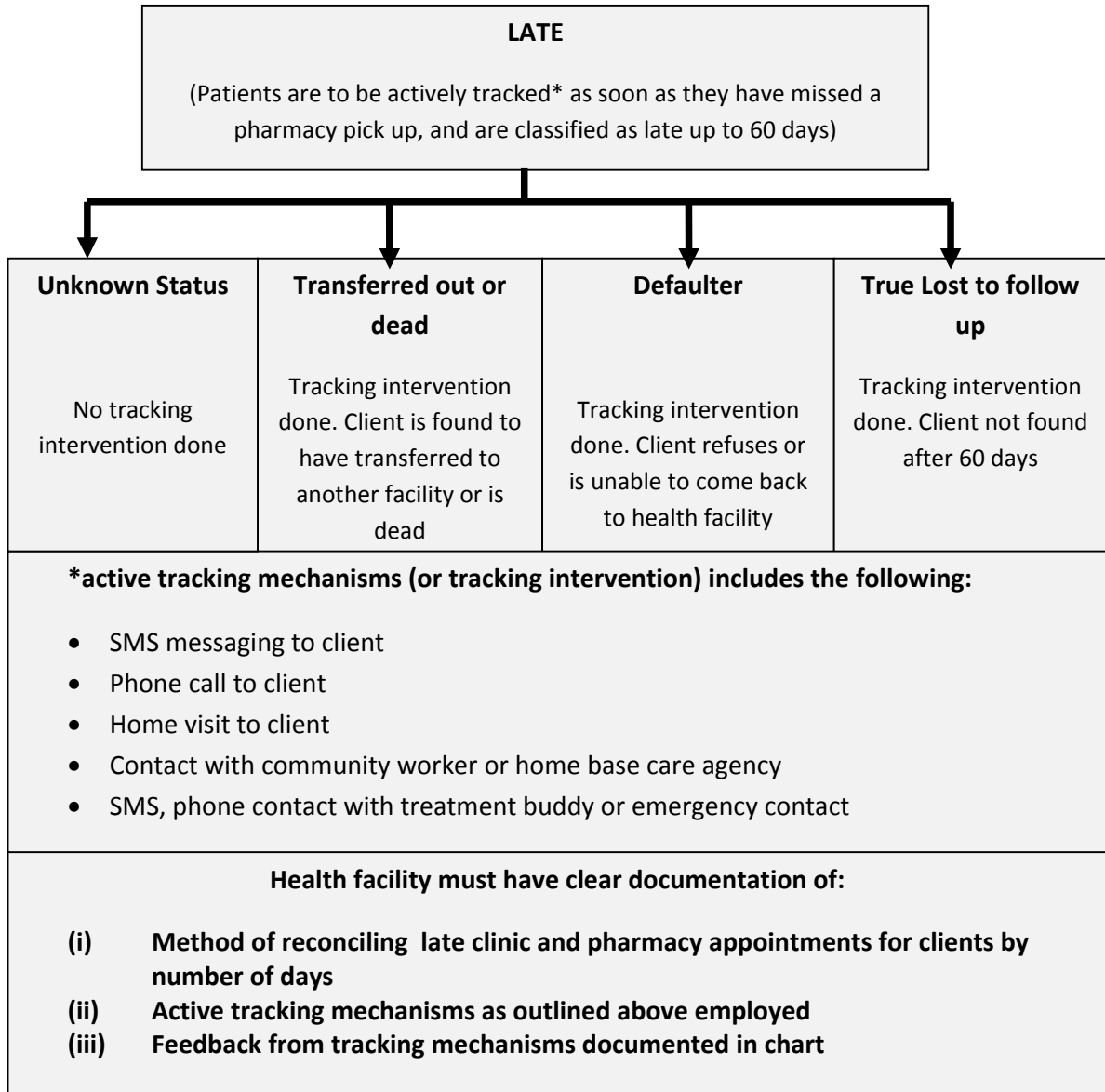
### 10.1 DEFINITION OF LOST TO FOLLOW UP (LTFU) FOR ART

Attrition in an HIV program can occur from death, transferred out to another facility, lost to follow up, late, defaulter, or unknown status. Definitions of some categories are listed below:

- Late- Patients are to be actively tracked as soon as they have missed a pharmacy pick up, and are classified as late up to 60 days
- True 'lost to follow up'- when more than 60 days have elapsed after last scheduled pharmacy pick up (all efforts for patient tracking should have been exhausted such as documented physical follow up to home, phone calls to patient and emergency contacts, SMS recall, treatment buddy) and patient cannot be traced

- Defaulter- when a person who has been located as late or lost to follow up chooses not to return to care
- Unknown status- person who has not had exhaustive tracking measures taken to determine enrolment status

### 10.2 DETERMINING PATIENT ATTRITION STATUS



### 10.3 STRUCTURED PLAN FOR TRACKING PATIENTS

Ideally patients should be tracked as soon as possible after missed pharmacy pick up or clinic appointment. Each day that elapses after missed appointment could be a day without ART, and increasing the likelihood of resistance development and treatment failure.

Scheduling patients for appointments and reviewing the list of patients expected on a given day is critical to tracking patients missed appointments. If the facility does not schedule patients, then a clear log of pharmacy refills must be reviewed daily to identify patients that have missed pharmacy pickups and are potentially out of ART medications.

Once a patient is identified as missing, a plan of action for tracking must be initiated. Depending on levels of communication within the facility and its catchment area these methods of contact may include:

- SMS messaging to client
- Phone call to client
- Home visit to client
- Contact with community worker or home based care agency
- SMS, phone contact with treatment buddy or emergency contact

### 10.4 CONTACT AND CARE TRACKING FORM

Contact and Care Tracking Form					
Patient Name			Smart Care ID		
Patient Contact Information					
Emergency Contact			Phone		
Treatment Buddy			Phone		
Community Health Worker			Phone		
Attempt to Contact	Date	Who attempted Contact?	Mode	Alternative Contacted?	Who contacted? (buddy, CHW, family, etc)
First attempt			<input type="radio"/> Phone <input type="radio"/> SMS <input type="radio"/> Home Visit	<input type="radio"/> Yes <input type="radio"/> No	
Other attempt			<input type="radio"/> Phone <input type="radio"/> SMS <input type="radio"/> Home Visit	<input type="radio"/> Yes <input type="radio"/> No	
Other attempt			<input type="radio"/> Phone <input type="radio"/> SMS <input type="radio"/> Home Visit	<input type="radio"/> Yes <input type="radio"/> No	
Other Attempt			<input type="radio"/> Phone <input type="radio"/> SMS <input type="radio"/> Home Visit	<input type="radio"/> Yes <input type="radio"/> No	
Final Attempt			<input type="radio"/> Phone <input type="radio"/> SMS <input type="radio"/> Home Visit	<input type="radio"/> Yes <input type="radio"/> No	
Patient Care Ended		<input type="radio"/> Lost to Follow up	<input type="radio"/> Defaulter	<input type="radio"/> Transferred out	<input type="radio"/> Died

## 11.0 BASELINE EVALUATION AND MONITORING ARV THERAPY

Before initiation and after starting on ARV therapy, it is critical that the patient receive regular laboratory and clinical monitoring and follow-up. The purpose of monitoring and follow-up is to:

- assist in choice of initial regimen
- assess effectiveness of therapy
- evaluate potential side effects or toxicity from ARV therapy
- assess and re-enforce adherence to therapy
- evaluate for the development of other HIV-related illnesses

Some patients may need to be seen more often than others, because of side effects, difficulty with adherence, or for other reasons. The healthcare provider should be flexible according to the needs of the individual patient. The minimum recommended timing and frequency of follow-ups is outlined in the table below. **Patients suspected of treatment failure (missed pharmacy pickups, weight loss, etc) should have CD4 cell count measured earlier than minimum recommended schedule.**

Table 5 outlines the schedule for visits and appropriate interventions from the baseline enrolment visit through the first year. After the first year the patients should be seen every 3 months, although in special circumstances visits could be extended to a maximum of 6 months (rainy season, patient stable for over 2 years, etc)

### 11.1 MINIMUM RECOMMENDED TIMING AND FREQUENCY OF FOLLOW-UPS

Table 5 : Clinical Timeline and Task for ART Visits

Timeline	Clinical	Laboratory*	Medications
<b>Day 0</b> Baseline Enrolment Visit (Provider)	-Complete History & Physical Examination (including ART history, current medications) -Screen for TB -Risk Reduction -Counselling/Education -Adherence visit one (see Adherence- Basics and HIV ART Preparation)	-Creatinine Clearance** -ALT and/or AST*** -Hgb or FBC -CD4 count -Urinalysis -HBsAg -RPR -Pregnancy test (women of reproductive age) -PAP smear (if unavailable, then visualization with acetic acid screening) or refer to next level of care for PAP smear -If available chemistry panel to include glucose, cholesterol, triglycerides	-Co-trimoxazole if indicated by staging -treatment of identified OI
<b>Week 1-2:</b> First follow up visit (Provider)	-Targeted history and physical examination (fever, cough, weight loss) -Review of laboratory tests (anaemia, renal or liver dysfunction) -Determine eligibility -Adherence visit two (see Adherence- ART Support and Preparation)		-Co-trimoxazole if indicated by CD4 count -treatment of identified OI

Timeline	Clinical	Laboratory*	Medications
<p><b>1-2 weeks later: 3<sup>rd</sup> follow up visit</b></p> <p>ART Initiation visit (Provider)</p>	<ul style="list-style-type: none"> <li>-Targeted history and physical examination (fever, cough, weight loss)</li> <li>-Review CTX adherence</li> <li>-Prescribe ART</li> <li>-Adherence visit three; patient should have a minimum of 3 visits prior to initiation of ART (see Adherence ART Education and Preparation)</li> </ul>		<ul style="list-style-type: none"> <li>-Co-trimoxazole if indicated</li> <li>-ART</li> </ul>
<p><b>Week 2 post-initiation</b></p> <p>(Provider)</p>	<ul style="list-style-type: none"> <li>-Targeted History &amp; Physical Examination</li> <li>-Review adherence, side effects, toxicity</li> <li>-Dose adjustment if on NVP</li> <li>-Risk Reduction</li> <li>-Adherence Support</li> <li>-Counselling/Education</li> <li>-New illness/IRIS</li> </ul>	<ul style="list-style-type: none"> <li>-Request ALT( if not available check AST) if on NVP with rash, CD4 &gt; 250, or pregnancy</li> </ul>	<ul style="list-style-type: none"> <li>-ART,</li> <li>Co-trimoxazole if indicated</li> </ul>
<p><b>Week 4 post-initiation</b></p> <p>(Provider)</p>	<ul style="list-style-type: none"> <li>-Targeted History &amp; Physical</li> <li>-Review adherence, side effects, toxicity</li> <li>-Risk Reduction</li> <li>-Adherence</li> <li>-Counselling/Education</li> <li>-New illness/IRIS</li> </ul>	<ul style="list-style-type: none"> <li>-ALT (if not available check AST) if symptomatic on NVP</li> <li>-Hgb if on AZT</li> </ul>	<ul style="list-style-type: none"> <li>-ART,</li> <li>Co-trimoxazole if indicated</li> </ul>

Timeline	Clinical	Laboratory*	Medications
<b>Week 8 post-initiation</b> (Nurse)	-Review adherence, side effects, toxicity -Risk Reduction -Adherence -Counselling/Education -New illness/IRIS		-ART, Co-trimoxazole if indicated
<b>Week 12 post-initiation</b> (Provider)	-Targeted History & Physical Examination -Review adherence, side effects, toxicity -Risk Reduction -Adherence -Counselling/Education -New illness/IRIS	-Creatinine Clearance** -Hgb if on AZT	-ART, Co-trimoxazole if indicated
<b>Every month: first 6 months</b> (Nurse)	-Review adherence, side effects, toxicity -Risk Reduction -Adherence -Counselling/Education		-ART, Co-trimoxazole if initiated
<b>Six month post-initiation</b> (Provider)	-Targeted History & Physical Examination -Review adherence, side effects, toxicity -Risk Reduction -Adherence -Counselling/Education	-CD4 count -Creatinine Clearance**	-ART, co-trimoxazole if indicated  <b>-NO PATIENT SHOULD BE GIVEN A REFILL OF MORE THAN 3 MONTHS OF ARVs</b>



Timeline	Clinical	Laboratory*	Medications
<b>Every year</b> (Provider)	-Targeted History & Physical Examination -Review adherence, side effects, toxicity -Risk Reduction -Adherence -Counselling/Education	-Creatinine Clearance** -CD4 count -viral load if available -RPR -Repeat PAP or visual screen at 6 months and if normal, every 12 months -If on PI-containing regimen, consider Chemistry profile (including LFT, glucose, cholesterol, and triglycerides)	-ART, Co-trimoxazole until not indicated  <b>-NO PATIENT SHOULD RECEIVE ART FOR MORE THAN SIX MONTHS WITHOUT CLINICAL REVIEW</b>

\* Other laboratory test such as cryptococcal antigen, FBC, ALT or additional chemistries, CD4 cell count and viral load based on clinical presentation

\*\* Calculate Creatinine Clearance (CrCl):

**ALL CREATININE ORDERS TO LABORATORY SHOULD INCLUDE AGE, SEX, HEIGHT, WEIGHT**

(For men)

$$\text{CrCl} = (140 - \text{age}) (\text{ideal body weight in kg}) / 72 \times \text{serum Creatinine (mg/dl)}$$

Or

$$\text{CrCl} = (140 - \text{age}) (\text{ideal body weight in kg}) / 0.815 \times \text{serum Creatinine } (\mu\text{mol/l})$$

(For Women)

$$\text{CrCl} = (140 - \text{age}) (\text{ideal body weight in kg}) (0.85) / 72 \times \text{serum Creatinine (mg/dl)}$$

or

$$\text{CrCl} = (140 - \text{age}) (\text{ideal body weight in kg}) (0.85) / 0.815 \times \text{serum Creatinine } (\mu\text{mol/l})$$

\*\*\* If unable to perform Creatinine, ALT, or other essential laboratories then specimen should be sent to nearest facility where test can be performed.

## 11.2 IDEAL BODY WEIGHT

The ideal body weight is the weight a patient of a given height is expected to weigh. The patient's ideal body weight can be determined from the patients' height.

The ideal body weight is more accurate than actual body weight for calculating Creatinine Clearance and should be used for determining:

- Calculated Creatinine Clearance (using the **Cockcroft-Gault formula**)
- Drug dosing
- Monitoring weight for stable patients both on or not on ARV

### IDEAL BODY WEIGHT TABLE

To find an Ideal Body Weight (IBW), enter the table using the height and read to the right to find the IBW for Males and Females

Table 6: Ideal Body Weights Based on Height and Sex

Height (m)	IBW (kg) for:	
	Male	Female
1.52	50	45.5
1.55	52.3	47.8
1.57	54.6	50.1
1.60	56.9	52.4
1.63	59.2	54.7
1.65	61.5	57
1.68	63.8	59.3
1.70	66.1	61.6
1.73	68.4	63.9
1.75	70.7	66.2
1.78	73	68.5
1.80	75.3	70.8
1.83	77.6	73.1
1.854	79.9	75.4
1.88	82.2	77.7
1.90	84.5	80
1.93	86.8	82.3
1.95	89.1	84.6
1.98	91.4	86.9
2.00	93.7	89.2

The ideal weight calculations used here are based on the Devine Formula for men and the Robinson formula for women.

## 12.0 ADVERSE EFFECTS AND TOXICITY

### 12.1 GOALS OF MANAGING DRUG ADVERSE EFFECTS

- Maintain good adherence
- Reduce the potential adverse impacts of drug side effects
- Identify serious adverse drug reactions and manage or refer appropriately

### 12.2 PRINCIPLES IN MANAGING TOXICITIES

- Determine the seriousness of the toxicity and manage according to severity
- Establish whether the adverse event is due to ART, some other medication or illness (e.g., viral hepatitis, malaria, IRIS)
- An individual drug may be substituted due to toxicity
- Stress adherence despite mild to moderate reactions
- If there is a need to stop ART because of severe life-threatening toxicity, stop all the drugs together until the patient is stabilized
- Adverse events should be recorded and reported regularly to the HIV/AIDS program manager and to the National Pharmacovigilance Unit at the Pharmacy Regulatory Authority
- Early complications are seen most commonly when therapy is started in patients with severe immunodeficiency

### 12.3 GENERAL PREVENTION AND MANAGEMENT OF ADVERSE EFFECTS

- Educate patient about possible adverse effects
- Consider other medical conditions (e.g. hepatitis) and medications when selecting a regimen to decrease risk
- Follow recommendations for laboratory and clinical monitoring while on ART
- Educate about danger signs of life-threatening conditions specifically Nevirapine
- Make sure the patient knows how to reach their provider when they have questions or concerns

## 12.4 WHO TOXICITY ESTIMATES

Table 7: WHO Toxicity Chart

<p>Grade 1 (mild):</p> <ul style="list-style-type: none"> <li>■ Transient or mild discomfort, no limitation in activity no medical intervention needed</li> <li>◆ Does not require change in therapy, symptomatic treatment may be given</li> </ul>
<p>Grade 2 (moderate):</p> <ul style="list-style-type: none"> <li>■ Limitation in activity, some assistance may be needed; no or minimal medical intervention/therapy required</li> <li>◆ Continue ART if possible; if no improvement consider substitution with a drug in the same ARV class but with a different toxicity profile</li> </ul>
<p>Grade 3 (severe):</p> <ul style="list-style-type: none"> <li>■ Marked limitation in activity, some assistance usually required, medical intervention required, possible hospitalization</li> <li>◆ Substitute the offending drug without stopping therapy</li> </ul>
<p>Grade 4 (severe life-threatening):</p> <ul style="list-style-type: none"> <li>■ Extreme limitation in activity, significant assistance required, significant medical intervention/therapy required, hospitalization or hospice care</li> <li>◆ Discontinue all ARV drugs, manage the medical event until patient is stable and toxicity has resolved</li> </ul>

## 13.0 IMMUNE RECONSTITUTION INFLAMMATORY SYNDROME

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

- Onset: usually within 2-12 weeks after starting ART

- Frequency: 10% among all patients on ART, up to 25% when ART initiated with CD4 <50 cells/mm<sup>3</sup>
- Risk factors:
  - Initiating ART close to diagnosis of an opportunistic infection
  - Initiating ART when CD4 is less than 50 cells/mm<sup>3</sup>
  - Rapid initial fall in HIV-1 RNA level in response to ART in patients with low CD4 counts
- Commonly seen with TB, cryptococcal disease, Kaposi's Sarcoma, and Mycobacterium Avium Complex infection

### 13.1 MANAGEMENT OF IRIS

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

## 14.0 CHANGING HAART

### 14.1 INDICATIONS FOR CHANGING TREATMENT

ART may be changed due to:

- Failure- clinical, immunologic, or virologic as outlined below
- Intolerance or unresolved and prolonged side effects
- Toxicity such as anaemia, peripheral neuropathy, lipoatrophy, liver or renal abnormalities
- Poor adherence- change indicated only to simplify dosing schedule and to improve adherence
- Occurrence of active TB: (refer to TB/HIV co infection)
- New therapies: may consider change in regimen as new agents become available with better efficacy and/or lower toxicity
- If unsure if change is indicated for any reason refer to HIV Specialist

Before changing therapy in suspected treatment failure, need to rule out

- Poor adherence: **MUST** be corrected and therapy changed only after adherence issues have been addressed
- Immune Reconstitution Inflammatory Syndrome (IRIS)
- Untreated inter-current OI
- Inadequate dosing
- Drug-drug interactions resulting in reduced ART blood levels (e.g. NVP + Rifampicin, LPV/r + Rifampicin)
- Inter-current infections causing transient decrease in CD4 count (if possible repeat CD4 one month after resolution of illness to confirm immunologic failure)

#### 14.2 GOALS IN CHANGING REGIMENS

- Restore patients clinical, immunologic and virologic response when treatment failure occurs
- Manage serious toxicities and intolerance
- Reduce likelihood of adverse events when certain medical conditions occur such as pregnancy or TB

### 14.3 CHANGING ART DUE TO TOXICITIES

Table 8: ARV Changes Due to Toxicity

ARV Drug	Common Associated Toxicity	Suggested Substitute*
d4T	Lactic acidosis <sup>1</sup>	TDF or ABC <sup>2</sup>
	Lipoatrophy / metabolic syndrome <sup>3</sup>	
AZT	Peripheral neuropathy	TDF or ABC <sup>2</sup>
	Severe anemia <sup>4</sup> or neutropenia <sup>5</sup>	
ABC	Severe gastrointestinal intolerance <sup>6</sup>	TDF (if CrCl normal) or AZT
	Lactic acidosis <sup>1</sup>	
TDF	Hypersensitivity reaction	ABC
EFV	Renal toxicity (renal tubular dysfunction)	NVP or (LPV/r) <sup>9</sup>
	Persistent and severe central nervous system toxicity <sup>7</sup>	
NVP	Potential teratogenicity (first trimester of pregnancy or woman not using adequate contraception)	EFV with caution or if no other options LPV/r <sup>9</sup>
	Hepatitis	
	Severe or life threatening rash (Stevens –Johnsons syndrome) <sup>8</sup>	
		LPV/r Consult HIV Specialist

- <sup>1</sup> Symptomatic lactic acidosis is a potentially life-threatening condition. ARVs should be temporarily discontinued and should not be re-initiated until the patient has fully recovered
- <sup>2</sup> Re-initiation of ART should not include d4T or AZT in this situation. TDF or ABC is preferred
- <sup>3</sup> Substitution of d4T with other ARVs may not reverse lipotrophy
- <sup>4</sup> Exclude malaria in areas of stable malaria; severe anaemia (grade 4) is defined as Hgb <6.5 g/dl
- <sup>5</sup> Defined as neutrophils cell count <500/mm<sup>3</sup> (grade 4)
- <sup>6</sup> Defined as severe, refractory gastrointestinal intolerance that prevents ingestion of ARV drug regimen (e.g. persistent nausea and vomiting)
- <sup>7</sup> e.g. persistent hallucinations or psychosis
- <sup>8</sup> Severe rash is defined as extensive rash with desquamation, angioedema, or a reaction resembling serum sickness; or a rash with constitutional findings such as fever, oral lesions, blistering, facial oedema or conjunctivitis; Stevens-Johnson syndrome can be life-threatening. For life-threatening rash, substitution with EFV is not recommended, although this approach has been reported in a small number of patients in Thailand without recurrence of rash.
- <sup>9</sup> PI Class should preferentially be reserved for second-line therapy as no affordable regimens have been identified for recommendation following initial PI failure

## 14.4 CHANGING ART DUE TO TREATMENT FAILURE

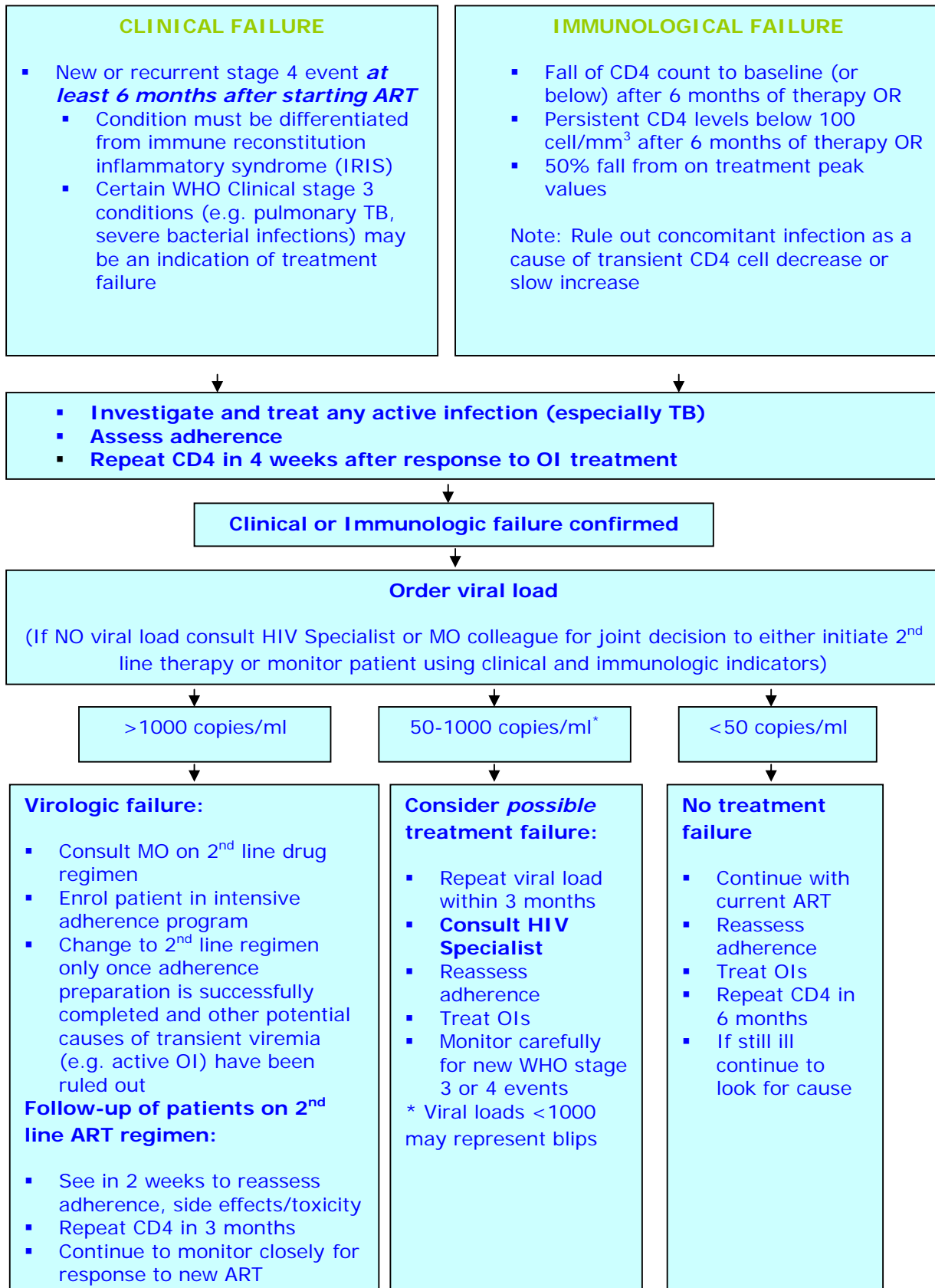
### 14.4.1 Defining Treatment Failure

Recent published data have demonstrated that neither clinical markers (new WHO stage III or IV conditions) nor immunologic markers (fall in CD4, failure to significantly increase CD4) accurately predict virologic failure or are sensitive to identify patients who are virologically suppressed.

*Viral load* is the only marker that accurately identifies patients with virologic failure or suppression. Clinical and immunologic criteria can raise the suspicion of virologic failure and be useful to prompt further investigation. When considering clinical or immunologic failure one must aggressively investigate for either new OI or illnesses, potential IRIS, and **most importantly** issues surrounding patient adherence to therapy. The following algorithm can assist in defining failure and the proper ordering of laboratory test.



14.4.2 Assessment of Patient with Possible Treatment Failure



## 14.5 VIROLOGIC FAILURE

- Where viral load is available, the following may suggest failure
  - Plasma HIV viral load >50 copies/ml after 6 months on therapy
  - NOTE: Blip- defined as a single viral load result of 50-1000 c/ml, is not considered failure, repeat viral load should be performed within three months (if still between 50-1000 copies consult HIV Specialist)
  - In patients who appear to be failing treatment and the viral load is undetectable consider undiagnosed opportunistic infections or other concomitant illnesses

### 14.5.1 Factors Leading to Treatment Failure

- Poor adherence to treatment
- Prior exposure to antiretroviral treatment with development of resistance (sdNVP)
- Primary viral resistance (infected with resistant HIV strain)
- Inadequate drug absorption
- Suboptimal dosing (e.g., sharing drugs, cutting dose because of side effects)
- Inadequate or inconsistent drug supply

### 14.5.2 Changing ART for Virologic Failure

- Durability of the first ART regimen is a major key to long term access, scalability, and sustainability. Treatment failure is a very costly consequence and requires both patient and provider assessment to ensure correction of precipitating factors
- All patients should receive structured treatment preparation prior to starting ART, but patients that have failed first line ART **MUST** be enrolled in intensive adherence counselling sessions until there is agreement between the patient, provider, and adherence counsellor that the patient is ready to commence second line therapy
- HIV resistance mutations vary greatly among different regimens, and the likelihood of second line treatment success is related to the initial first line therapy and the specific resistance mutations acquired
- Specific ART guideline regimens for second line are based on the patient's first line ART regimen and are found in the Recommended Regimen Table
- HIV genotype resistance testing is the only way to know precisely what resistance mutations have developed with the virus. Refer to an HIV Specialist with the patient's complete anti-retroviral drug history and genotype may be ordered for expert interpretation

### 14.6 THIRD LINE THERAPY OPTIONS IN ZAMBIA

- Currently there are **NO** third line therapy options available in the public sector in Zambia, and every effort must be made to support patient success on first and second line ART regimens. With improved adherence patients on second line therapy may re-suppress their virus to non-detectable levels. Current costs for a typical third line ART regimen are over \$2000 per patient per year. If third line therapy is considered refer to an HIV Specialist
- Studies have shown clinical benefit to maintaining second line therapy despite virologic failure; if no therapy options exist then the patient should be left on the failing regimen
- A successful third line regimen requires at least two new active (no or minimal resistance) ARV drugs
- **A detailed ARV treatment history along with a genotype done while on the patient's most recent failing regimen are required to construct a 3<sup>rd</sup> line regimen that is likely to achieve viral suppression**
- As with all patients failing treatment the following principles must be observed prior to the initiation of third line therapy:
  - **The reason for treatment failure must be determined and addressed, e.g. poor adherence, suboptimal dosing, drug-drug interactions, underlying OIs**
  - Patients **MUST** be enrolled in intensive adherence counselling sessions until there is agreement between the patient, provider, and adherence counsellor that the patient is ready to commence third line therapy
    - Use of treatment supporters for such patients is **STRONGLY** recommended
- The most likely ARVs to be successful in patients who have followed National Guidelines are:
  - Raltegravir (Integrase inhibitor)
  - Darunavir boosted with Ritonavir (protease inhibitor)
  - Plus optimal nucleoside background typically either TDF/FTC or AZT/3TC

Other considerations with major constraints:

- Etravirine (only if genotype available at time of first line NNRTI failure)
- Maraviroc (needs special tropism test prior to use, which is currently not available in Zambia)

## 15.0 MANAGING PATIENTS PREVIOUSLY TREATED WITH ART

Patients who have interrupted ART for any reason are at increased risk of resistance and treatment failure. Management in restarting ART is based on several factors and a complete history to establish why the treatment was stopped is critical.

- Patients who have stopped any regimen abruptly after good adherence, with **NO** history of toxicity or treatment failure can be recommenced on their original ART regimen (patients who were on NNRTI and did not cover the NNRTI 'tail' are at increased risk of failure, and should be monitored closely)
  - Viral load testing should be done 4-6 months after re-initiation of the original regimen to document HIV viral suppression
- Patients on first line ART with a history of poor adherence or multiple ART interruptions should be started on appropriate second line ART regimen (patients with poor adherence **MUST** be enrolled in intensive adherence counselling sessions until there is agreement between the patient, provider, and adherence counsellor that the patient is ready to commence second line therapy)
  - Use of treatment supporters for such patients is **STRONGLY** recommended
- Patients with severe toxicity leading to discontinuation of treatment should have appropriate drug substitution
- Patients who have interrupted second line ART should be restarted on their second line regimen unless severe toxicity was present
  - For such cases, referral to an HIV Specialist is recommended

**Patient's ART history, including interruptions/discontinuations/ adverse reactions, should be carefully documented on the HIV Summary Sheet as these strongly influence the future regimen choices.**

### 15.1 STOPPING OR INTERRUPTING ART

#### 15.1.1 Considerations in stopping therapy

- Patient's inability to tolerate all available ARV medications
- Patient's request to stop, after appropriate counselling
- Non-adherence despite counselling: Treatment should be stopped to avoid continued toxicity, continued evolution of drug resistance, and transmitting drug resistant HIV

### 15.1.2 Treatment Failure with No Further Treatment Options

- Continue the failing ART regimen unless toxicities or drug interactions make the clinical situation worse for the patient
- Even with treatment failure the regimen is likely to have some residual antiviral activity
- Stopping therapy in the setting of virologic failure can be associated with rapid falls in CD4 counts and development of opportunistic complications

### 15.1.3 Temporary Discontinuation of ARV Therapy

- May be needed because of serious drug toxicity or interactions, intervening illness or surgery that precludes oral intake, or ARV non-availability
- Stop **ALL** the drugs when discontinuing therapy
  - NNRTI drugs (EFV,NVP) have longer half-lives and may be detected at significant levels up to 3 wks after the last dose; If all components of an NNRTI-based regimen are stopped at the same time, the patient will essentially be on monotherapy for a period of time and at increased risk for resistance
  - Consider discontinuing EFV or NVP and continue the NRTI component for 1-2 additional weeks, if feasible
    - This practice has demonstrated value in the PMTCT settings but its benefits in treatment programs is unclear
- Preventive measures such as condom use and safer sex practices should be strongly emphasized for all patients, especially those requiring temporary discontinuation of their ART

## 15.2 INDICATIONS FOR CONSULTATION WITH OR REFERRAL TO A HIV SPECIALIST

- Before initiating or changing ART in patients with ALT/AST >5-fold the upper limits of normal range
- Second line treatment failure, inability to tolerate second-line therapy, or complications on other PI-based regimen
- Severe or life-threatening adverse reactions
- Before restarting ART after severe or life-threatening adverse reactions
- Inability to tolerate therapy despite change in regimen
- Complex PMTCT or paediatric management issues
- Concerns with drug interactions or toxicity with TB/HIV co-infection treatment
- Complicated OI or TB management

- Patient is asymptomatic with no CD4 count available or with CD4 > 350 and patient wishes to start ART

## 16.0 MANAGEMENT OF CO-MORBIDITIES IN ANTIRETROVIRAL THERAPY

Persons with HIV infection frequently also have other illnesses that are more common in HIV infection than in the general population because of similar modes of acquisition or some other relationship to HIV. With the success of antiretroviral therapy, many HIV treatment centres are seeing co-morbidities as a more common cause of morbidity and mortality than HIV infection itself. Common co-morbidities in HIV infection include tuberculosis, hepatitis B and hepatitis C, human papilloma virus associated diseases, sexually transmitted illness and mental health disorders.

Tuberculosis and Chronic viral hepatitis B or hepatitis C, and mental health disorders **are** particularly important causes of HIV-related morbidity and mortality. Appropriate management of these co-morbidities requires diligence in screening and aggressive management if the co-infected **individuals are** to enjoy the full benefits of antiretroviral therapy.

### 16.1 TUBERCULOSIS AND HIV

Antiretroviral therapy (ART) is the single most important way to reduce the incidence of TB in people living with HIV. However, people with HIV on ART remain highly vulnerable to TB. Co-infection with HIV/TB is a major public health threat for people living with HIV and the community. TB threatens the significant health benefits achieved with scale-up of HIV care and treatment. All people living with or at higher risk of HIV in Zambia should be screened for TB and placed on TB treatment if found with TB.

The emergence of drug resistant TB poses an additional public health threat, not only to people with HIV but also to the broader community. However, people with HIV are at a much greater risk of mortality from multidrug resistant (MDR)-TB and recent case series, reporting on extensively drug resistant (XDR)-TB in people living with HIV in Africa, suggest a greater than 95% mortality rate.

Urgent action is thus required to prevent, diagnose and treat TB in people living with HIV, their families and communities. TB is both curable and preventable — and with the ongoing scale-up of HIV services, it should be possible to address TB/HIV in a manner that is convenient for patients with or at risk of both infections.

### 16.2 INTENSIFIED CASE FINDING (ICF)

Intensified Case Finding for TB means regularly screening all people with or at high risk of HIV or in congregate settings (such as mines, prisons, military barracks) for the symptoms and signs of TB, followed promptly with diagnosis and treatment, and then doing the same for household contacts.

This will be achieved with the application of the following recommendations:

- Simple questionnaires (see below) to screen for TB
- Used on all patients/clients that seeks HIV services (e.g., care, voluntary counselling and testing, etc.)
- By professional health care providers and/or by community based organizations supporting people with HIV.
- TB patients with known positive HIV status and all TB patients living in HIV-prevalent settings should receive daily TB treatment during the intensive phase and the continuation phase
- It is recommended that TB patients who are living with HIV should receive at least the same duration of TB treatment as HIV-negative TB patients

### 16.3 SCENARIOS OF MANAGING HAART AND ATT

**Questionnaire for  
TB case finding in PLWHA**

Patient ID : .....

Date of screening : .....

- |   | Yes                      | No                       |
|---|--------------------------|--------------------------|
| 1. Has the patient been coughing for $\geq$ 2 weeks?            | <input type="checkbox"/> | <input type="checkbox"/> |
| 2. Has the patient been having night sweats for $\geq$ 3 weeks? | <input type="checkbox"/> | <input type="checkbox"/> |
| 3. Has the patient lost $\geq$ 3kg during the last 4 weeks?     | <input type="checkbox"/> | <input type="checkbox"/> |
| 4. Has the patient been having fever for $\geq$ 3 weeks?        | <input type="checkbox"/> | <input type="checkbox"/> |
| 5. Has the patient had contact with someone with TB?            | <input type="checkbox"/> | <input type="checkbox"/> |

- If **"Yes"** to **question 1**: do sputum tests and refer to clinician for further investigation of TB.
- If **"No"** to **question 1** and **"yes"** to **any other question**: Refer to clinic clinician for investigation of TB.
- If **"No"** to **all questions**: repeat screening next visit.

**Sputum examination result:**

Sputum specimen no.	Date	Result (Positive/Negative)
1. On the spot		
2. Day 2 – early morning		
3. Day 2 – on the spot		

**Regardless of sputum results, refer to clinician for further management.**

**Table 9: Categories of TB and recommended Anti-tuberculosis Therapy (ATT)**

<b>Category I (CAT I)</b>	All new cases (smear positive, smear negative, EPTB)
	Intensive phase –EZRH (2 months) Continuation –RH (4 months)
<b>Category II (CAT II)</b>	All re-treatment cases including treatment failure, treatment after default
	Intensive phase –EZRHS (2 months)
	Second intensive- EZRH (1 month) Continuation –ERH (5 months)

**Table 10: TB/HIV Scenarios**

Scenario 1: Newly diagnosed TB (category I) and HIV co-infection		Recommended ART Regimens
Regardless of CD4 count or clinical stage	<ul style="list-style-type: none"> <li>○ Start CAT I TB treatment immediately</li> <li>○ Start ART as soon as TB medications are tolerated (usually within 2-3 weeks)</li> <li>○ Treat all patients for TB regardless of CD4 count.</li> </ul>	<ul style="list-style-type: none"> <li>○ Use TDF/FTC or 3TC + EFV</li> <li>○ If renal insufficiency ABC + 3TC + EFV (alternative)</li> </ul>
Scenario 2: TB Retreatment Cases (category II) and HIV co-infection		Recommended ART Regimens
Regardless of CD4 count or clinical stage	<ul style="list-style-type: none"> <li>○ Commence category II TB treatment</li> <li>○ Start ART as soon as TB medications are tolerated (usually within 2-3 weeks)</li> </ul>	<ul style="list-style-type: none"> <li>○ Use TDF/FTC or 3TC + EFV</li> <li>○ If renal insufficiency ABC + 3TC + EFV (alternative)</li> </ul>
Scenario 3: PLHIV on ART who develops TB		Recommended ART Regimens



Develops TB while on ART	<ul style="list-style-type: none"> <li>○ Start TB treatment immediately and if ART regimen includes Nevirapine, substitute Nevirapine with Efavirenz and continue ART and if on LPV/r start Rifabutin in place of Rifampicin or add Ritonavir 300mg BD or double LPV/r dosing</li> </ul>	<ul style="list-style-type: none"> <li>○ Switch NVP to EFV</li> <li>○ Evaluate for clinical failure and consider for second line ART in consultation with HIV specialist</li> </ul>
Scenario 4: Patient on TB treatment is diagnosed HIV positive		Recommended ART Regimens
Regardless of CD4 count or clinical stage	<ul style="list-style-type: none"> <li>○ Start ART as soon as TB medications are tolerated (usually within 2-3 weeks)</li> <li>○ Treat all patients for TB regardless of CD4 count.</li> </ul>	<ul style="list-style-type: none"> <li>○ Use TDF/FTC or 3TC + EFV</li> <li>○ If renal insufficiency ABC + 3TC + EFV (alternative)</li> </ul>
Scenario 5: HIV and TB treatment in pregnancy		Recommended ART Regimens
HIV pregnant woman on ART develops TB	<ul style="list-style-type: none"> <li>○ Reassess ART regimen in view of potential drug-drug interaction with anti-tuberculosis drugs or clinical failure</li> <li>○ Thereafter commence anti-tuberculosis treatment</li> </ul>	<ul style="list-style-type: none"> <li>○ Change NVP to EFV if after 1st trimester or switch to or ABC/3TC/AZT if during 1<sup>st</sup> trimester</li> <li>○ OR evaluate for clinical failure and consider second line ART in consultation with HIV specialist</li> </ul>
Pregnant woman on TB treatment tested positive for HIV	<ul style="list-style-type: none"> <li>○ Continue TB treatment</li> <li>○ Start ART as soon as baseline laboratories and treatment preparation completed</li> <li>○ Treat all patients for TB regardless of CD4 count. ART is not required for all patients with CD4 &gt;350 and no other Stage III or IV illness*</li> </ul>	<ul style="list-style-type: none"> <li>○ Wait until after 1<sup>st</sup> trimester, and then use TDF/FTC/EFV or</li> <li>○ If renal insufficiency ABC/3TC/EFV (alternative)</li> </ul>
Scenario 6: Patient on second line ART with Lopinavir and develops TB		Recommended ART Regimens
Develops TB while on ART	<ul style="list-style-type: none"> <li>○ Start CAT I or CAT II based on TB treatment guidelines immediately</li> <li>○ Replace Rifampicin with Rifabutin dosed at 150 mg once daily</li> </ul>	<ul style="list-style-type: none"> <li>○ If Rifabutin is unavailable then double dose of LPV/r</li> <li>○ Double dose LPV/r is associated with liver toxicity, and requires close monitoring of liver</li> </ul>

		<p>function</p> <ul style="list-style-type: none"> <li>○ Increase LPV/r from 2 tabs BD to 3 tabs BD for 2 weeks, and then to 4 tabs BD for the remainder of TB treatment</li> <li>○ Alternatively add Ritonavir 300 mg BD to regular dose LPV/r</li> </ul>
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\* Patients with TB that are not on ART with a CD4 > 350, and no other indication for ART (Stage III or IV illness) may be considered for TB treatment only without starting ART. These patients should be seen in clinic as outlined in the section on Care for Patients who are not yet eligible for ART (Table 3, page 23)

#### 16.4 HEPATITIS B AND HIV CO-INFECTION

Markers of HBV exposure are present in a high proportion of HIV-infected individuals. HIV affects HBV viral replication and clearance. HBV co-infection does not appear to influence the rate of HIV progression but may be a surrogate for factors associated with HIV sero-conversion. Treatment of HBV with lamivudine is effective, but drug-resistant mutants occur in a high proportion of patients if provided as mono-therapy. Development of lamivudine-resistant HBV or discontinuation of combination HBV therapy can be associated with a flare of hepatitis. TDF/FTC or 3TC regimens should not be discontinued in patients with HBV. Tenofovir should be used as part of a combination antiretroviral regimen in the treatment of HIV/HBV co-infection. Emtricitabine demonstrates equivalent HBV suppression to lamivudine. Patients with Chronic Hepatitis B should be treated with ART including TDF and FTC or 3TC. Chronic Hepatitis B is diagnosed by a positive HBsAg and a positive HBeAg, or a positive HBsAg that persist longer than 6 months. Elevated ALT or AST are also highly suggestive of chronic hepatitis.

- HBsAg should be done at baseline
- If patient has a positive HBsAg and a CD4 count greater than 350 cell/mm<sup>3</sup>, check ALT or AST and if elevated initiate HAART
- For patients with normal baseline ALT or AST recheck both ALT or AST and HBsAg in 6-12 months. If ALT or AST are elevated, or persistent HBsAg then start ART regardless of CD4 count or WHO staging. If signs of liver cirrhosis and HBsAg positive start HAART regardless of ALT or AST values
- TDF/FTC or 3TC should be prescribed for all patients described above

- Patients failing first line HIV therapy with TDF/FTC or 3TC should continue the TDF in their second line therapy (i.e. TDF/AZT/3TC + LPV/r) to control their HBV infection
- Patients needing ART for their own health should be initiated on the recommended first line regimen.
- If patients have positive HBsAg and renal insufficiency refer to HIV Specialist

### 16.5 HEPATITIS C AND HIV CO-INFECTION

Hepatitis C is rare in Zambia. It is primarily transmitted through injection drug use or blood transfusion, but can be transmitted sexually as well. Any patient suspected or diagnosed with Hepatitis C should be referred to an HIV Specialist.

### 16.6 MENTAL HEALTH AND HIV INFECTION

Mental health conditions in HIV patients are well documented and yet often not addressed in treatment guidelines. Some type of neuropsychiatric disorder has been estimated to be as high as 48% among HIV infected persons. These conditions can be divided into depression, anxiety, mania, substance use, HIV associated neurocognitive disorder, and delirium disorders. Major depression in some studies impact 40% of HIV+ people, and AIDS Dementia Complex (ADC) is a common and clinically important CNS complication of late HIV-1 infection. Substance use disorder, especially alcohol, impacts large numbers of HIV infected persons in resource limited settings. All of these conditions may have a substantial impact on HIV disease progression and poor medication adherence. With people living longer on HAART the need for mental health services will continue to rise.

**Depression** occurs more commonly in HIV infected people compared to the general population, and often is not addressed with appropriate treatment. It is a known risk factor for poor adherence on ART. The most common treatment is typically tri-cyclic anti-depressants (TCA) and selective serotonin reuptake inhibitors (SSRI) drugs. Both have notable drug interactions with ARV drugs and must be evaluated prior to initiation, especially with Lopinavir/r. Typically SSRI drugs have fewer side effects and are better tolerated. Simple screening for major depression refers to the presence of 5 or more of the following symptoms: depressed mood, loss of appetite, hopelessness, suicidal ideation, disturbed sleep, loss of energy, psychomotor retardation, guilty ruminations, or poor concentration occurring for at least 2 weeks.

**Alcohol and substance abuse** can not only impact adherence, but also increase risky sexual behaviour that increase transmission of HIV and other sexually transmitted diseases. The need for treatment of substance use disorders is important for both prevention and limiting treatment failure and resistance.

**HIV associated neurocognitive disorders** including both HIV-associated dementia and AIDS Dementia Complex have important implications in both the asymptomatic period of HIV and late stage AIDS, and warrant evaluation and intervention with HAART.

Mental health disorders significantly impact HIV and must be appropriately screened for during initial evaluation and follow up visits, diagnosed, and provided with appropriate treatment to ensure good outcomes for these patients.

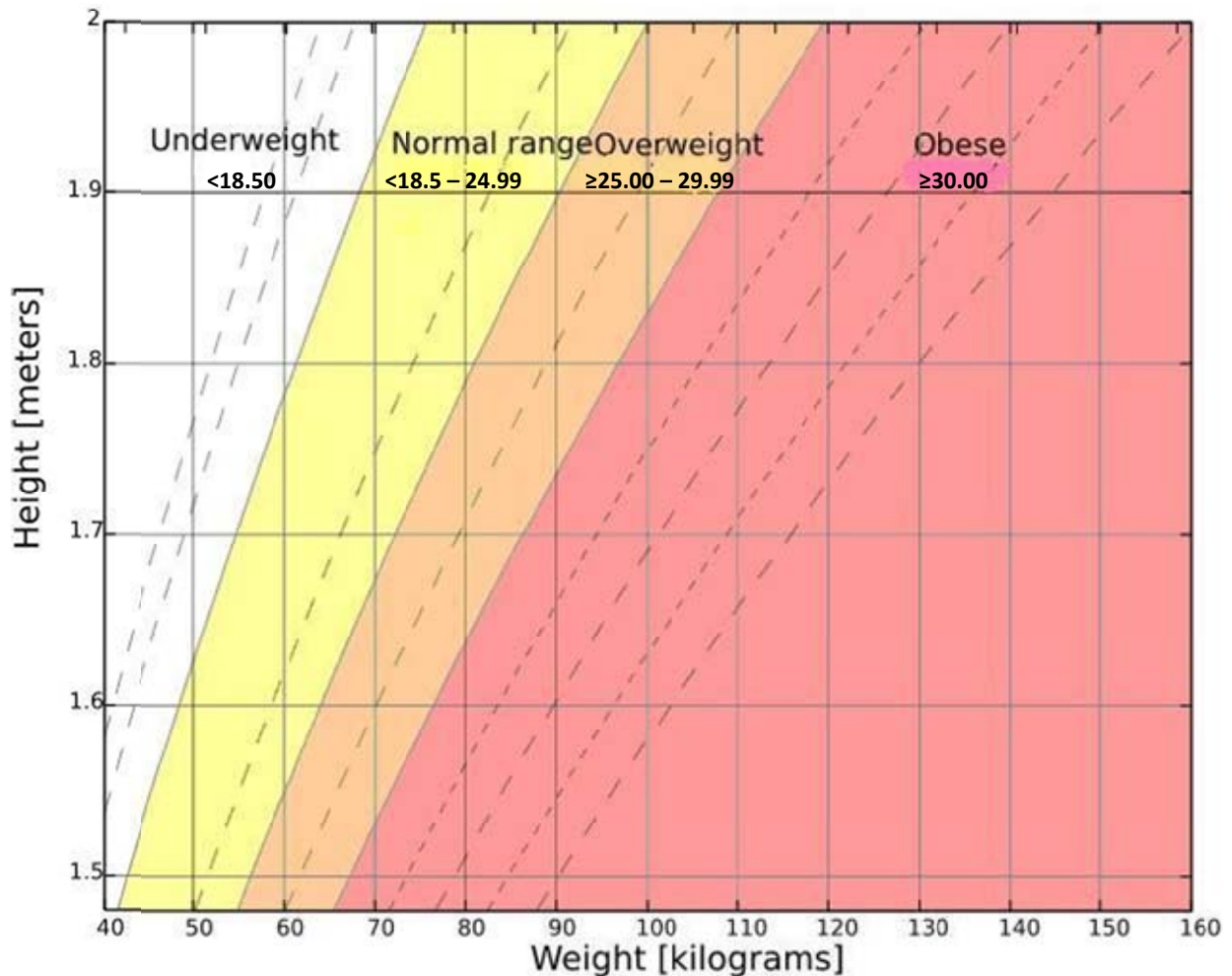
## 17.0 NUTRITION AND HIV

### 17.1 BODY MASS INDEX

The **body mass index (BMI)** is a statistical measure of body weight based on a person's weight and height. Though it does not actually measure the ***percentage of body fat***, it is used to estimate a healthy ***body weight*** based on a person's height. Due to its ease of measurement and calculation, it is to identify weight problems within a population, usually whether individuals are ***underweight, overweight*** or ***obese***.

$$\text{BMI} = \frac{\text{mass (kg)}}{(\text{height (m)})^2}$$

**THE CHART BELOW ALLOWS CALCULATION OF BMI USING THE HEIGHT AND WEIGHT ONLY WITHOUT HAVING TO CALCULATE WITH THE FORMULA ABOVE**



Equally, clients who are found to be obese or overweight should be receive nutritional counselling (including dietary advice and need for physical exercise) accordingly

## 18.0 PREGNANT WOMEN AND HIV

HIV testing should be provided on an opt-out basis for all women presenting to their first antenatal clinic visit. Women who test negative at the first visit should be retested every 3 months at subsequent antenatal visits, when presenting in labour, and during the breastfeeding period (e.g., at the 6 week postnatal visit)

- Diagnosing and treating pregnant women with ARV therapy to prevent transmitting the virus to the foetus is a priority.
- Pregnant, HIV positive women will either be offered
  - HAART to both prevent MTCT of HIV and treat maternal disease or
  - short-term ARV therapy to prevent mother-to-child transmission only

### 18.1 HAART FOR PMTCT OF HIV AND MATERNAL TREATMENT OF HIV

- HAART provides maternal treatment for pregnant women who are eligible
- HAART is also associated with the lowest rates of mother-to-child transmission (1-2%)

### 18.2 WHAT DO YOU DO IF A WOMAN BECOMES PREGNANT WHILE ON HAART

#### I. Woman on first line ART regimen

**Note:** All replacement recommendations assume the patient demonstrates no signs of treatment failure; if treatment failure then changes to appropriate second line regimen. For any situations that are not clear from the guidelines consult an HIV Specialist for advice.

- If she is taking any of the following nucleoside combinations (TDF/FTC or 3TC; ABC/3TC; AZT/3TC; d4T/3TC) with **EFV Continue if gestation age above 14 weeks**
- Replace EFV with NVP if gestation age is before 14 weeks with CD4 less than 350 cell/mm<sup>3</sup> (if CD4 between 250-350 increased risk of hepatotoxicity and patients must be monitored for rash and liver toxicity very closely); may consider switching back to EFV after first trimester
  - If CD4 is greater than 350 cells/mm<sup>3</sup> then use LPV/r until pregnancy beyond 14 weeks and then switch back to EFV
- If she is taking **TDF/FTC or 3TC/NVP**
- **Continue same regimen regardless of gestation age**

- If she is taking **ABC/3TC/NVP**
  - **Continue same regimen regardless of gestation age**
- If she is taking **d4T/3TC/NVP**, and has signs of toxicity
  - **Replace d4T with either TDF or ABC**
- If she is taking **AZT/3TC/NVP**
  - **Replace AZT with either TDF or ABC if signs of AZT toxicity**

## II. Woman on second line ART regimen

In this situation the priority is to treat the mother and help prevent transmission of HIV to the unborn baby. In Zambia there are limited options of which drugs to switch to therefore it is recommended that the woman is maintained on the same 2<sup>nd</sup> line regimen.

- Consultation with an HIV Specialist is strongly recommended for these patients

### 18.3 PROPHYLAXIS FOR EXPOSED INFANTS

- **Prophylaxis for Infants born to mothers on HAART**
  - **For all exposed infants give daily NVP from birth until 6 weeks**
  - **NB:** As with all pregnant women on HAART, it should be ensured that there are no signs of treatment failure with the mother before initiating daily infant NVP
  - In the case of maternal treatment failure, both the mother and the infant must be referred to an HIV Specialist for further management

### 18.4 WHAT DO YOU DO IF AN HIV-INFECTED WOMAN BECOMES PREGNANT AND IS NOT ON HAART?

- In this situation:
  - Patient should be clinically staged, according to WHO staging criteria
  - CD4 should be determined
  - The following are the two options

#### 1. HAART

##### Eligibility Criteria:

- **CD4 is  $<350/\text{mm}^3$  regardless of WHO clinical stage**
- **Stage 3 or 4 regardless of CD4 count**

ARV options:

- Initiate HAART after 14 weeks of gestation age and completed treatment preparation
- ~~AZT+DF/FTG~~ or 3TC + EFV or NVP OR TDF/FTC if anaemic
  - ABC/3TC/EFV if calculated CrCl <50ml/min
- If CD4 <250 Preference to use NVP instead of EFV

Note that:

- HAART should be continued during pregnancy, labour and after delivery (lifelong treatment)
  - **Prophylaxis for Infants born to mothers on HAART**
  - For all exposed infants give daily NVP from birth until 6 weeks
2. Short Course ARV Regimens for PMTCT **should be given if:**
- CD4 is >350 and patient is in WHO stages 1 or 2
  - Refer to the PMTCT guidelines for options of ARVs to be used
  - For short course ARV regimens for PMTCT, there is possible development of resistance with unknown effect on future maternal treatment or on infant treatment, if infected in spite of prophylaxis
  - For all exposed infants born to mothers who received prophylaxis, give daily NVP from birth until 1 week after cessation of breast feeding.



**Table 11: Antiretroviral prophylaxis regimens to prevent mother-to-child transmission of HIV**

Course	Antenatal	Intrapartum	Postnatal	All exposed infants
From 14 weeks of pregnancy	AZT 300 mg twice daily starting at 14 weeks or as soon as possible thereafter	NVP 200 mg single dose at onset of labour  AZT300mg/3TC150mg stat dose at onset of labour and thereafter repeat every 12 hours until delivery	AZT300mg/3TC 150mg twice daily for 7 days	<ul style="list-style-type: none"> <li>• NVP at birth and daily until one week after all exposure to breast milk</li> <li>• Start co-trimoxazole from 6 weeks until a week after all exposure to breast milk has ended and HIV status is confirmed negative</li> <li>• If not breast feeding, using commercial milk formula then NVP at birth and for 6 weeks, and co-trimoxazole from 6 weeks until HIV status confirmed negative</li> </ul>
Women presenting in the 3 <sup>rd</sup> trimester	AZT 300 mg twice daily	NVP 200 mg single dose at onset of labour  AZT300mg/3TC150mg stat dose at onset of labour and thereafter repeat every 12 hours until delivery	AZT300mg/3TC 150mg twice daily for 7 days	Same as above

## 19.0 POST EXPOSURE PROPHYLAXIS

Course	Antenatal	Intrapartum	Postnatal	All exposed infants
Women without prophylaxis antenatally in labour	N/A	NVP 200 mg single dose at onset of labour  AZT300mg/3TC150mg stat dose at onset of labour and thereafter repeat every 12 hours until delivery	AZT300mg/3TC 150mg twice daily for 7 days  Check for ART eligibility	Same as above
Woman who is on ART or is eligible for ART	Continue or start ART	Continue ART	Continue ART	Same as above, but only NVP from birth until 6 weeks of age

### 19.1 RISK OF ACQUIRING HIV AFTER OCCUPATIONAL EXPOSURE

- Risk of acquiring HIV infection following occupational exposure to HIV infected blood is low
- Average risk for HIV transmission after percutaneous exposure to HIV infected blood in healthcare settings is approx 1 per 300
- After mucocutaneous exposure < 1 in 1000
- No risk of transmission where intact skin is exposed to HIV infected blood

### 19.2 FACTORS ASSOCIATED WITH AN INCREASED RISK OF OCCUPATIONALLY ACQUIRED HIV INFECTION

- Deep injury
- Visible blood on the device which caused the injury
- Injury with a large bore needle from artery or vein
- Terminal HIV illness in source patient

### 19.3 BODY FLUIDS AND MATERIALS WHICH POSE A RISK OF HIV TRANSMISSION

- Amniotic fluid
- Cerebrospinal fluid
- Human breast milk
- Pericardial fluid

- Peritoneal fluid
- Pleural fluid
- Saliva in association with dentistry
- Synovial fluid
- Unfixed human tissues and organs
- Vaginal secretions
- Semen
- Any other fluid if visibly bloodstained
- Fluid from burns or skin lesions

Exposure to blood also places health care workers at risk for other blood borne infections, such as hepatitis B and hepatitis C, which are more easily transmitted than HIV. All health care workers should receive hepatitis B vaccination if available.

## 19.4 MANAGEMENT OF OCCUPATIONAL EXPOSURES TO INFECTIOUS SUBSTANCES

### 19.4.1 Immediately after Exposure

#### 1) Clean the Exposure Site

- If a skin wound, wash with soap and running water. If the exposed area is an eye or mucous membrane, flush with copious amounts of clean water
- DO NOT USE BLEACH or other caustic agents/disinfectants to clean the exposure site

#### 2) Contact your On Site In-Charge/ Supervisor

- HIV/ ARV Nurse In-Charge
- Over all Supervisor
- Laboratory Manager

#### 3) Responsibilities of the Clinical Officer or Medical Officer

- Determine the need for post exposure prophylaxis (PEP) based on the nature of the exposure and the risks and benefits of taking (or not taking) anti-retroviral medications. ***PEP should be started preferably within 2 hours of the exposure.*** If not started within 72 hours of the exposure, PEP will not be provided, as it is not likely to be effective after this time period
- Counsel regarding Post Exposure Prophylaxis: risks and benefits
- Determine if the exposure is potentially high risk based on the information in the box below

- If exposure is considered high risk: arrange for **immediate** HIV testing and counselling. If this is likely to take longer than 1 hour, give first dose of PEP before referring
- Explain that all HIV testing is CONFIDENTIAL
- Ensure the exposed employee also has a Creatinine and CrCl done (FBC if starting AZT)
- Arrange post test counseling
- Complete in the Recommended (MOH) PEP Register the details surrounding the exposure and the type of regimen given

#### 19.4.2 Recommended Prophylaxis

NOTE: PEP SHOULD **NOT** BE GIVEN TO EXPOSED EMPLOYEES WHO REFUSE HIV TESTING OR WHO TEST POSITIVE AT THE INTIAL TEST

IF AN EMPLOYEE DOES TEST POSITIVE INITIALLY, REFER TO ART CLINIC FOR ASSESSMENT

No evidence indicates that any specific antiretroviral medication or combination of medications is optimal for use as PEP. However, on the basis of the degree of experience with individual agents in the treatment of HIV-infected persons, certain agents and combinations are preferred.

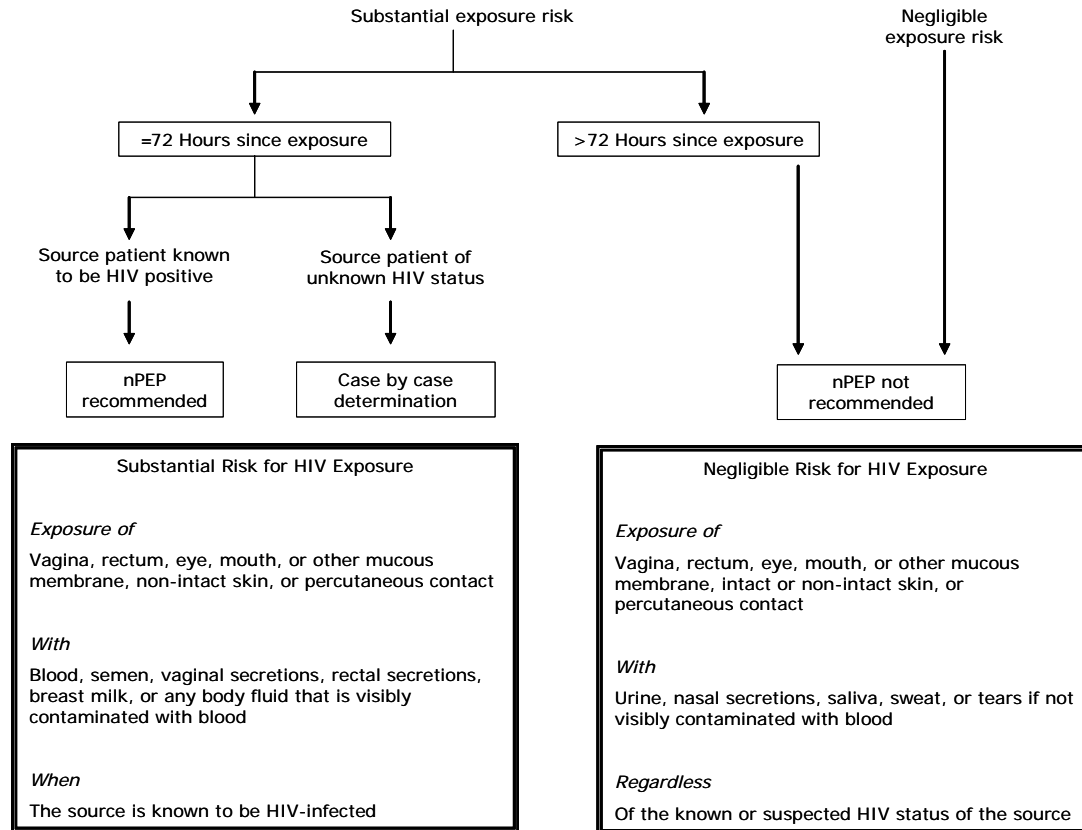
**Table 12 : PEP Recommendations**

Risk Category	ART	Duration
<b>No risk:</b> Intact skin	Not recommended	
<b>Medium risk:</b> Invasive injury, no blood visible on needle  <b>High risk:</b> Large volume of blood/ fluid, known HIV infected patient, large bore needle, deep extensive injury	TDF* plus FTC or 3TC daily plus LPV/r BD  Note: TDF/FTC or 3TC once daily and LPV/r twice daily dosing	28 days
*For patients with CrCl<50ml/min replace TDF with AZT 300mg PO 12hrly FTC can be replaced with 3TC dosed as 150mg 12hrly or 300mg 24hrly		

**19.5 MANAGEMENT OF NON-OCCUPATIONAL EXPOSURE**

**19.5.1 Algorithm for evaluation and treatment of possible non occupational HIV exposures**

(nPEP = non occupational exposure PEP)



Ref MMWR Jan 21, 2005

**19.6 FOLLOW-UP OF EXPOSED PERSONS:**

- If prophylaxis indicated follow the recommended PEP regimens for Zambia
- An HIV blood test on the day of the exposure; if negative this test needs to be repeated at 6 weeks, 3 months and 6 months post exposure
- An HIV blood test if client experiences an acute illness that includes fever, rash, myalgia, fatigue, malaise, and lymphadenopathy

**Arrange evaluation by a Medical Officer or Clinical Officer within 72 hours after starting PEP and monitoring for side effects for at least 2 weeks**

### 19.7 CONSIDERATION FOR A SITE TO PROVIDE POST EXPOSURE PROPHYLAXIS MINIMUM REQUIREMENTS

- Site should provide Counselling and Testing (CT)
- Availability of recommended PEP ARV drugs on site
- Presence of PEP national register
- Presence of focal point person (to facilitate access and confidentiality)
- +/- Presence of national guidelines/protocols and job aids.

It is advised that clients who receive PEP assistance at facilities which do not meet above criterion (e.g. start dose of PEP regimen only), should be counted in the register at the facility where they will have been referred and will ultimately receive comprehensive support (to avoid double counting)

## 20.0 COTRIMOXAZOLE (CTX) PROPHYLAXIS AGAINST OPPORTUNISTIC INFECTIONS

### 20.1 INITIATING CTX PROPHYLAXIS IN INFANTS AND CHILDREN

- Begin CTX prophylaxis at 6 wks in all HIV-exposed infants and continue until HIV infection excluded
- Children with presumptive diagnosis of PCP or other symptomatic HIV disease should be treated and CTX prophylaxis continued until HIV infection has been definitively excluded
- Infants with documented HIV infection
  - Less than 2 yrs: give CTX regardless of symptoms or CD4%
  - More than 2 yrs: give CTX if Stage 2,3, or 4 or if CD4% <25%
- Children with history of treated PCP should be administered secondary CTX prophylaxis with same regimen used for primary prophylaxis
- Desensitization protocols for children are not established. Therefore do not re-initiate CTX prophylaxis in children who have had a treatment limiting reaction

### 20.2 DISCONTINUATION OF CTX PROPHYLAXIS IN INFANTS AND CHILDREN

- CTX prophylaxis can be discontinued when HIV infection has been definitively excluded
- Primary CTX prophylaxis should be continued in HIV-infected children irrespective of immune recovery due to antiretroviral therapy because of their continued increased risk of bacterial infections; in children >5 yrs on ART with good immune recovery clinically and with CD4 count and secure supply of

drugs, discontinuation of CTX prophylaxis can be considered in accordance with adult/adolescent guidelines

- Secondary CTX prophylaxis should be continued in HIV-infected children irrespective of immune recovery due to antiretroviral therapy because of their continued increased risk of bacterial infections; in children >5 yrs on ART with good immune recovery clinically and with CD4 count and secure supply of drugs, discontinuation of CTX prophylaxis can be considered in accordance with adult/adolescent guidelines
- CTX should be restarted if the CD4% falls below the age-specific threshold for initiation or with new or recurrent WHO clinical Stage 2,3,4 condition
- Children with history of severe adverse reactions to CTX or other sulfa drugs should not be prescribed CTX: dapson 2 mg kg is an alternative and the same guidelines apply
- CTX may need to be discontinued if serious adverse events occur that may be due to CTX (extensive exfoliative rash, Stevens-Johnson syndrome, severe anaemia or pancytopenia)



## 20.3 CTX PROPHYLAXIS IN CHILDREN

Table 13: CTX Prophylaxis in Children

RECOMMENDATIONS			
Situation	Age	When to Start	When to Stop
<b>HIV Exposed Infant</b> (Defined as a child born to an HIV infected mother or breastfeeding from an HIV infected mother, until infection can be excluded.)	<12 months	Initiate Cotrimoxazole prophylaxis at 6 weeks of age (or at first postnatal visit or when first recognized) in ALL infants born to an HIV infected mother irrespective of any ARVs received during pregnancy and/or labour.	Discontinue Cotrimoxazole prophylaxis after exclusion of HIV infection at least 6 weeks after complete cessation of breastfeeding (PCR is negative or antibody test is negative,)
<b>HIV Infected child</b> (Including all infants identified as HIV infected during the first year of life by PCR or clinical diagnosis of HIV infection with a positive antibody test.)	<24 months	Cotrimoxazole prophylaxis is indicated regardless of CD4 percentage or clinical status or WHO stage	Children < 5 years:  Maintain on Cotrimoxazole prophylaxis until age 5 years unless guided by CD4 percentage  Children > 5 years:  can be reassessed and consideration to discontinue Cotrimoxazole prophylaxis should be in accordance with the recommendations for adults and adolescents
	≥24 months to 4 years	WHO clinical stages 2, 3 and 4 regardless of CD4 percentage <b>OR</b> any WHO stage & CD4 <25%	
	≥5 years	Follow adult recommendations	
<b>Presumptive Symptomatic HIV Disease</b>	<18 months	Start (or continue) CTX prophylaxis regardless of CD4.	
<b>Any Child with a history of PCP</b>	All ages	Administer secondary prophylaxis.	

## 20.4 COTRIMOXAZOLE DOSING IN INFANTS AND CHILDREN

**Table 14: Dosages of commonly used cotrimoxazole formulations for infants and children living with or exposed to HIV**

Recommended Daily Dosage	Suspension (5ml of syrup 200mg/40mg)	Child Tablet (100mg/20mg)	Single Strength Adult Tablet (400mg/80mg)
<6 mo or < 5 kg 100 mg SMX/20 mg TMP	2.5 ml	One tablet with feed or small amount of milk or water	¼ tablet possibly mixed with small amount of milk or water
6 mo–5 yrs or 5–15 kg 200 mg SMX/40 mg TMP	5 ml	Two tablets	Half tablet
6–14 yrs or 15–30 kg 400 mg SMX/80 mg TMP	10 ml	Four tablets	One tablet
>14 years or >30 kg 800 mg SMX/160 mg TMP	X	x	Two tablets
Frequency- once a day			

Source: World Health Organization. *Guidelines on cotrimoxazole prophylaxis for HIV-related infections among children, adolescents and adults. Recommendations for a public health approach.* Geneva, WHO, 2006:15 (Table 3)

## 20.5 RECOMMENDATIONS FOR CTX PROPHYLAXIS IN ADULTS AND ADOLESCENTS

Adults with history of severe and life-threatening adverse reactions -Grade 3 & 4 (see *WHO toxicity Estimates* table) to CTX or other sulfa drugs should not be prescribed CTX: dapsone 100 mg/day should be given as an alternative

- Dapsone is less effective than CTX in preventing PCP and does not have as broad antibacterial spectrum as CTX, therefore an attempt to desensitize to CTX may be considered, but only if previous non-serious adverse reaction (Grade 1 and 2 only)

Patients are eligible for desensitization if they are at least 6 months removed from their Grade 1 or 2 treatment limiting reaction to CTX. Patients start an antihistamine regimen of choice one day prior to starting the regimen and continue daily until completing the dose escalation.

## 20.6 PROTOCOL FOR COTRIMOXAZOLE DESENSITIZATION AMONG ADULTS AND ADOLESCENTS

Table 15: Cotrimoxazole desensitization protocol for adults and adolescents

STEP	DOSE
<b>Day 1</b>	80 mg sulfamethoxazole + 16 mg trimethoprim (2 ml of oral suspension <sup>1</sup> )
<b>Day 2</b>	160 mg sulfamethoxazole + 32 mg trimethoprim (4 ml of oral suspension <sup>1</sup> )
<b>Day 3</b>	240 mg sulfamethoxazole + 48 mg trimethoprim (6 ml of oral suspension <sup>1</sup> )
<b>Day 4</b>	320 mg sulfamethoxazole + 64 mg trimethoprim (8 ml of oral suspension <sup>1</sup> )
<b>Day 5</b>	One single-strength sulfamethoxazole-trimethoprim tablet (400 mg sulfamethoxazole + 80 mg trimethoprim)
<b>Day 6 - Onwards</b>	Two single-strength sulfamethoxazole-trimethoprim tablets or one double strength tablet (800 mg sulfamethoxazole + 160 mg trimethoprim)

<sup>1</sup> Cotrimoxazole oral suspension is 40 mg trimethoprim + 200 mg sulfamethoxazole per 5 ml

## 20.7 INITIATION OF PRIMARY PROPHYLAXIS IN ADULTS AND ADOLESCENTS

- Initiate for patients with WHO Stage 2, 3 or 4 disease where CD4 count is not available
- If CD4 available, initiate when CD4<350, regardless of clinical stage
- If stage 3 or 4 initiate regardless of CD4 count
  - **Dose: 960 mg daily (800mg sulfamethoxazole + 160mg trimethoprim)**
  - Pregnant women: CTX can be safely continued or initiated during pregnancy regardless of stage of pregnancy.
    - women who are on CTX prophylaxis, no need for additional IPT for malaria (fansidar)
    - CTX can be continued during breastfeeding
  - Secondary prophylaxis: patients with history of treated PCP should be given the same CTX prophylaxis as for primary prophylaxis
  - Timing of CTX prophylaxis in relation to initiation of ART: start CTX first and initiate ART two weeks later if no adverse effects from CTX

- Treatment of bacterial infections, malaria and PCP/Toxoplasmosis in patients on CTX prophylaxis:
  - Use alternative antibiotic for bacterial infections and continue CTX prophylaxis
  - PCP/Toxo: stop CTX prophylaxis and treat infection, then restart prophylaxis after treatment course
  - Malaria: treat with agent that does not include sulfadoxine-pyrimethamine, if possible

### **20.8 DISCONTINUATION OF PRIMARY PROPHYLAXIS IN ADULTS AND ADOLESCENTS**

- Stop CTX if patient develops Adverse Drug Reaction or Drug Toxicity such as: Jaundice, Severe Anaemia or pancytopenia or Rash (extensive exfoliative dermatitis, Stevens-Johnson syndrome)
- Stop CTX if on antiretroviral therapy and CD4 is above 350 for at least six (6) months
- If CTX discontinued, it should be restarted if the CD4 falls below 350 cells/mm<sup>3</sup> or if the patient has a new or recurrent WHO clinical Stage 2,3, or 4 condition
- Discontinuing secondary prophylaxis is as indicated for primary prophylaxis (see table below)

**20.9 COTRIMOXAZOLE PROPHYLAXIS IN ADULT AND ADOLESCENTS**

Table 16: CTX Prophylaxis in Adults and Adolescents

RECOMMENDATIONS		
Situation	When to Start	When to Stop
Regardless of availability of CD4 count or WHO staging		Stop if patient develops Adverse Drug Reaction or Drug Toxicity such as: <i>Jaundice, Severe Anaemia</i> or <i>pancytopaenia</i> or <i>Rash (extensive exfoliative dermatitis, Stevens-Johnson syndrome)</i>
CD4 count is not available	WHO clinical stage 2, 3, 4	Recommend referral for CD4 count, but consider discontinuation of CTX in patients who have been on ART with good adherence for more than 2 years and do not have Stage 2, 3, or 4 events
CD4 count is available	CD4 < 350, in any WHO clinical stage	Stop Cotrimoxazole prophylaxis if there is immune recovery whilst on antiretroviral therapy - CD4 is above 350 for at least six (6) months

## 20.10 COTRIMOXAZOLE TOXICITY GRADING SCALE FOR ADULTS AND ADOLESCENTS

- CTX Adverse effects
  - Monitor potential side effects of CTX clinically every 3 months and manage accordingly (see Table below); no specific lab monitoring required, but lab evaluation may be indicated depending on signs and symptoms. Most common side effects: bone marrow suppression, skin rash, hepatotoxicity

**Table 17: Co-trimoxazole Toxicity Grading Scale for Adults and Adolescents**

TOXICITY	CLINICAL DESCRIPTION	RECOMMENDATION
Grade 1	Erythema	Continue Cotrimoxazole prophylaxis with careful and repeated observation and follow up  Provide symptomatic treatment, such as antihistamines, if available
Grade 2	Diffuse maculopapular rash, dry desquamation	Continue Cotrimoxazole prophylaxis with careful and repeated observation and follow up  Provide symptomatic treatment, such as antihistamines, if available
Grade 3	Vesiculation, mucosal ulceration	Cotrimoxazole should be discontinued until the adverse effect has completely resolved (usually two weeks), and then reintroduction or desensitization can be considered
Grade 4	Exfoliative dermatitis, Stevens-Johnson syndrome or erythema multiforme, moist desquamation	Cotrimoxazole should be permanently discontinued

## 21.0 PREVENTION WITH POSITIVES (PWP)

- Traditional focus of prevention efforts have been on preventing acquisition among HIV negative individuals
- To have a significant impact on slowing the spread of the epidemic, prevention efforts must also be directed toward individuals living with HIV who can transmit the virus
- These HIV+ persons are regularly accessing health care settings and clinics, providing an opportunity to reach a large number of infected persons with prevention messages and interventions
- Health care providers in HIV clinic settings can deliver consistent, targeted prevention messages and strategies during routine visits
- Providers are considered authority figures and trusted sources of health information
- Health care providers can also address biomedical prevention strategies, such as reproductive health and STI management
- Many patients need more in-depth counselling on prevention issues (e.g. disclosure, alcohol use).
- Integrating prevention services into care and treatment can be overwhelming and can require a great deal of effort and resources **but, we can't afford *not* to do it.**

### 21.1 FIVE KEY STEPS FOR PWP

#### STEP 1: GIVE PREVENTION RECOMMENDATIONS TO EVERY PATIENT AT EVERY VISIT

- Clients need to understand that it may feel a little uncomfortable to talk about sex, but protecting their health is very important and hence the importance to talk to all clients about safer sex
- Do clients understand the importance of HIV prevention in PLWHIV? Hints: Re-infection with other HIV strains including resistant strains.
- Is the client currently sexually active or plans to be? If yes, what are they doing to practice safer sex? – provide condoms, counsel on risk reduction
- Providers and counsellors must assess whether each patient's partner has been tested for HIV; if not tested, test or refer to counsellor for HIV testing
- Provider- and/or counsellor-assisted disclosure is encouraged
- Children of HIV+ mothers need to be tested for HIV

- Discordant couples have to be identified and counselled and positive partners linked to care and treatment whereas negative partners have to be counselled on prevention practices to stay negative (condoms!)
- Providers need to deliver brief messages on patient self-protection & partner protection and consequences of unprotected sex

#### **STEP 2: ASSESS ADHERENCE TO ARVs**

- Provide adherence support or refer to counsellor for support

#### **STEP 3: STI MANAGEMENT**

- Assess for signs and symptoms of STIs at *every* visit and treat as indicated
- Remember that STIs
  - can be more severe and more difficult to treat in immunocompromised individuals
  - are a marker of unprotected sex and thus there is need for risk reduction counselling
  - involve partner management to stop the spread of the STI and to reduce re-infection

#### **STEP 4: FAMILY PLANNING SERVICES AND SAFER PREGNANCY COUNSELLING**

- Preventing unintended pregnancy in HIV+ women who do not want children can avert the need for and costs associated with PMTCT, care for HIV+ children and support for orphans
- Other HIV+ women on treatment desire children; they require counselling on safe timing of pregnancy and referrals to PMTCT
- Inquire about pregnancy status/intentions *every* visit
- Refer to Family Planning clinics for contraceptives
- Provide basic counselling on safer conception, pregnancy, and delivery for HIV+ women desiring pregnancy in the HIV care and treatment setting

#### **STEP 5: GIVE PATIENT CONDOMS AT EVERY VISIT!!**

- This is Our Biggest Challenge and yet Our Best Solution. Condomise!



## 22.0 ANTIRETROVIRAL DRUG SUMMARIES

Generic Drug Abbreviation	Dosage & Food Restriction	Renal & Hepatic Insufficiency	Cautions	Frequent side effects	Serious toxicity
<b>Tenofovir TDF</b>	300 mg Q24 hours  Food: none	Renal: adjust If CrCl<50ml/min Hepatic: none	Renal insufficiency; THE COMBINATION OF TDF WITH DDI IS STRONGLY DISCOURAGED. TDF increases levels of DDI leading to DDI toxicity therefore daily dose of DDI should be reduced to 250mg	Nausea Vomiting Diarrhoea Flatulence	Renal dysfunction; Do serum creatinine with calculated CrCl at 3 months and thereafter every 6 months
<b>Emtricitabine FTC</b>	200 mg Q24 hours Food: none	Renal: adjust If CrCl<50ml/ml Hepatic: none		Headache Diarrhoea Nausea Rash Hyper pigmentation of palms	
<b>Lamivudine 3TC</b>	150 mg Q12 hours or 300 mg Q24 hours Food: none	Renal: adjust If CrCl<50ml/min Hepatic: none		Headache Nausea Diarrhoea Abdominal pain Insomnia	Pancreatitis in children
<b>TDF + FTC</b>	1 tablet Q24 hours Food: none	As above for individual drugs	As above for individual drugs	As above for individual drugs	As above for individual drugs

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Generic Drug Abbreviation	Dosage & Food Restriction	Renal & Hepatic Insufficiency	Cautions	Frequent side effects	Serious toxicity
<b>TDF + 3TC</b>	1 tablet Q24 hours Food: none TDF/3TC combination can be used in place of TDF/FTC	As above for individual drugs	As above for individual drugs	As above for individual drugs	As above for individual drugs
<b>Zidovudine ZDV or AZT</b>	300 mg Q12 hours Food: none	Renal: adjust if CrCl < 15ml/min Hepatic: none	Haemoglobin < 10 gm/dl;  Contra-indicated with d4T	Headache Nausea Anorexia Vomiting Insomnia Malaise	Anaemia (monitor Hb first 12 weeks) Neutropenia Myopathy Lactic acidosis Finger nail discolouration
<b>AZT + 3TC</b>	1 tablet Q12 hours Food: none	As above for individual drugs	As above for individual drugs	As above for individual drugs	As above for individual drugs
<b>Stavudine d4T</b>	30 mg Q12 hours	Renal: adjust if CrCl < 50ml/min Hepatic: none	Contra-indicated with AZT/ZDV; Overlapping toxicity with DDI, INH, vincristine	Diarrhoea Nausea Vomiting Headache	Peripheral neuropathy Lipoatrophy Hyperlipidemia Pancreatitis Lactic acidosis

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Generic Drug Abbreviation	Dosage & Food Restriction	Renal & Hepatic Insufficiency	Cautions	Frequent side effects	Serious toxicity
<b>Abacavir ABC</b>	300 mg Q12 hours or 600 mg Q24 hours Food: none	Renal: none Hepatic: none	Caution with alcohol	Nausea Headache Diarrhoea Malaise	Hypersensitivity reaction (peaks within 2 weeks, uncommon after 12 weeks) DO NOT RECHALLENGE
<b>Didanosine DDI</b>	Initiating dose: <60kg: 125 mg Q12 hours >60kg: 200 mg Q12 hours Food: none (if buffered)	Renal: adjust If CrCl<60ml/min Hepatic: none	Reduce dose with TDF; Increased toxicity with D4T, INH, Vincristine, alcohol	Diarrhea Nausea Rash Fever Headache	Pancreatitis Peripheral neuropathy Lipoatrophy Lactic acidosis Hepatic steatosis
<b>Nevirapine NVP</b>	Initiating dose: 200 mg Q24 hours for 14 days; then 200mg Q12 hours Food: none	Renal: none Hepatic: avoid with moderate to severe liver disease	Hepatic failure; caution in women with CD4 count more than 250; Drug interactions: Rifampicin, ketoconazole, Oral contraceptive pills, anti- convulsants, clarithromycin; If stopping cover tail for 7 days*	Rash	Stevens Johnson Syndrome Toxic epidermal necrolysis Hepatotoxicity (monitor ALT/AST first 12 weeks) Liver failure Hypersensitivity

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Generic Drug Abbreviation	Dosage & Food Restriction	Renal & Hepatic Insufficiency	Cautions	Frequent side effects	Serious toxicity
<b>Efavirenz</b> <b>EFV</b>	600 mg Q24 hours Food: without food or low fat meal	Renal: none Hepatic: none	Avoid in potential pregnancy or 1 <sup>st</sup> trimester; Drug interactions: clarithromycin, warfarin, birth control pills; If stopping cover tail for 7 days*	Abnormal dreams Dizziness Insomnia Somnolence Impaired thinking Rash	Teratogenicity
<b>Etravirine</b> <b>ETV</b>	200mg Q12 hours Food: with food	Renal: none Hepatic: none	Drug interactions: Rifampicin, Carbamazepine, Phenorbabitone Contraindication: Do not use with EFV or NVP	Rash	Steven Johnson Syndrome/ Toxic Epidermal Necrosis (both are rare but serious)
<b>Raltegravir</b> <b>RAL</b>	400mg Q12 hours Food: none	Renal: none Hepatic: none	Drug interactions: <b>Rifampicin</b> <b>(reduces plasma levels of RAL</b> <b>and if unavoidable RAL dose</b> <b>should be doubled)</b> Omeprazole or other gastric inhibitors (may increase plasma levels of RAL) NOTE: RAL has a low genetic barrier therefore adherence and proper combination of ARV regimens is required	Very well tolerated. Rarely dizziness, abdominal pains, tiredness	

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Generic Drug Abbreviation	Dosage & Food Restriction	Renal & Hepatic Insufficiency	Cautions	Frequent side effects	Serious toxicity
<b>Lopinavir/r LPV/r</b>	400mg/100mg (2 tablets) Q12 hours (Aluvia) Food: None	Renal: none  Hepatic: none	Multiple drug interactions: Rifampicin, oral contraceptives, statins, anti-convulsants Sildenafil [Viagra] (levels increased leading to hypotension and priapism : Recommendation is to initiate sildenafil 30-45 minutes before sex and not to exceed 25mg in a 48- hour period)	Diarrhoea Nausea Vomiting	Hyperlipidemia Insulin resistance Pancreatitis Transiminitis Fat redistribution
<b>Darunavir DRV</b>	600mg Q12 hours (should always be boosted with ritonavir 100mg Q12 hours) NOTE: In Zambia, Darunavir is reserved for 3 <sup>rd</sup> line. In special settings** where Darunavir has to be used as a 1 <sup>st</sup> line it should be dosed as 800mg Q24 hours Food: with food	Renal: none Hepatic: contraindicated in severe hepatic impairment		Diarrhoea Nausea Rash (within the first two weeks)	Hyperlipidemia

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Generic Drug Abbreviation	Dosage & Food Restriction	Renal & Hepatic Insufficiency	Cautions	Frequent side effects	Serious toxicity
<b>Ritonavir</b> <b>RTV</b>	100mg Q12 hours <b>RITONAVIR SHOULD ONLY BE USED TO BOOST OTHER PIs</b> Food: none	Renal: none Hepatic: none	Drug Interactions : Rifampicin	Nausea Vomiting Diarrhoea (frequent)	Hyperlipidemia Lipodystrophy Transiminitis
<p><b>*Covering the NNRTI tail:</b> NNRTI (NVP and EFV) have prolonged drug concentrations after discontinuing drug. In order to decrease the likelihood of resistance, instruct patient to continue the other 2 ARV drugs after discontinuation of NNRTI for an additional 7 days.</p> <p><b>**Consult HIV Specialist if Darunavir has to be used as part of 1<sup>st</sup> line regimen</b></p>					