Guidelines for

Antiretroviral Therapy for the Prevention and Treatment of HIV in Zimbabwe

National Medicines and Therapeutics Policy Advisory Committee (NMTPAC)

and

The AIDS and TB Directorate, Ministry of Health and Child Care, Zimbabwe

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The information presented in these guidelines conforms to current medical, nursing, and pharmaceutical practice. It is provided in good faith, and hence, whilst every effort has been made to ensure that the medicine doses are correct, no responsibility can be taken for errors or omissions.

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HIV and AIDS remains a major public threat in the country with a prevalence of 13% among the adult population. The introduction of antiretroviral therapy (ARTs) has revolutionized the care and management of HIV and AIDS and has transformed the disease from being life-threatening into a chronic and manageable condition. Whilst ARVs do not cure HIV and AIDS, they dramatically reduce mortality and morbidity if used appropriately. It must still be emphasised that treatment with ARVs is for life. Evidence supports HIV treatment as a prevention intervention for HIV transmission and hence underscores the importance of ART.

The national antiretroviral therapy (ART) roll-out programme continues to register successes in terms of wide national coverage for treatment to those in need despite a difficult marco-environment. Through continued decentralization of ART services more people are now able to access such services closest to their homes. The government continues committed to offer ARVs free of charge to PLHIV at public institutions as a policy in order to overcome potential economic related access challenges. The rational use of these medicines is imperative if we are to reach more of those in need of this life-saving therapy. There is also continued need to use the public-health approach for the management of HIV and AIDS. Health-care workers need to have simplified treatment regimens as exemplified by our current national ART guidelines as well as the widely used Essential Medicines List of Zimbabwe. Using guidelines simplifies clinical decision making, which allows the use of other cadres and not just doctors in the delivery of ART as well as the associated monitoring.

We should all pursue and promote a standardised approach to treatment to minimise the development of HIV drug resistance and ensure the sustainability of our programme. The guidelines are meant for use in the public and private sectors. These guidelines will be regularly updated as new information and evidence becomes available.

I encourage you to make use of the latest edition of the guidelines. You will find this easy given that we use a different colour for the cover each time we produce a new version. Again, note that some recommendations might change in the future as evidence and resources dictate.

We hope you will use these guidelines consistently.

Dr David P Parirenyatwa
Minister of Health and Child Care, Zimbabwe 2016
Acknowledgements

We are grateful to those people currently involved in the national antiretroviral therapy (ART) programme and research programmes for sharing their experiences as well as best practices and thus contributing to the revision of these guidelines. Special thanks are still extended to those who developed the original guidelines, whose basis remains the backbone of this current edition, as well as to the World Health Organization (WHO) for continually updating its ART guidelines (latest revision 2016) and allowing them to be adapted freely by national programmes.

The following people and organisations were actively involved in the current guideline revision group and hence deserve special mention:

• Dr. C. Chakanyuka, National Professional Officer, HIV and Tuberculosis, WHO Country Office, Zimbabwe
• Dr. H. Mujuru, Paediatrician, UZCHS
• Professor. M. Borok, Physician, UZCHS
• Dr A. Mushavi, PMTCT and Paediatric HIV, Care and Treatment Coordinator, MOHCC
• Dr. T. Mutasa-Apollo, Deputy Director, HIV & AIDS and STIs, MOHCC
• National Medicine and Therapeutics Policy Advisory Committee (NMTPAC) members

Thank you.

Dr. C.E. Ndhlovu
MMedSc (Clin Epi), FRCP
Chairperson, NMTPAC

Dr. O. Mugurungi
MBChB, MSc
Director, AIDS and TB Unit
### Acronyms/Abbreviations

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<tr>
<th>Acronym</th>
<th>Description</th>
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<tr>
<td>3TC</td>
<td>Lamivudine</td>
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<tr>
<td>ABC</td>
<td>Abacavir</td>
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<tr>
<td>AIDS</td>
<td>Acquired immunodeficiency syndrome</td>
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<td>ART</td>
<td>Antiretroviral therapy</td>
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<tr>
<td>ARVs</td>
<td>Medicines for treating HIV</td>
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<tr>
<td>ATV</td>
<td>Atazanavir</td>
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<tr>
<td>AZT</td>
<td>Zidovudine</td>
</tr>
<tr>
<td>BCG</td>
<td>Bacille Calmette-Guérin</td>
</tr>
<tr>
<td>BHIVA</td>
<td>British HIV Association</td>
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<tr>
<td>CHAI</td>
<td>Christian Health Access Initiative</td>
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<tr>
<td>CHBC</td>
<td>Community- and home-based care</td>
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<tr>
<td>CD4</td>
<td>Cluster of differentiation 4</td>
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<tr>
<td>CMV</td>
<td>Cytomegalovirus</td>
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<tr>
<td>CSF</td>
<td>Cerebrospinal fluid</td>
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<tr>
<td>D4T</td>
<td>Stavudine</td>
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<tr>
<td>ddI</td>
<td>Didanosine</td>
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<tr>
<td>DNA</td>
<td>Deoxyribonucleic acid</td>
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<tr>
<td>EFV</td>
<td>Efavirenz</td>
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<tr>
<td>EID</td>
<td>Early infant diagnosis</td>
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<tr>
<td>FCH</td>
<td>Family and child health</td>
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<td>FDC</td>
<td>Fixed-dose combination</td>
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<tr>
<td>FP</td>
<td>Family planning</td>
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<tr>
<td>GI</td>
<td>Gastrointestinal</td>
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<tr>
<td>HBIG</td>
<td>Hepatitis B immune globulin</td>
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<tr>
<td>HBV</td>
<td>Hepatitis B virus</td>
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<tr>
<td>HCW</td>
<td>Health Care Worker</td>
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<tr>
<td>HIV</td>
<td>Human immunodeficiency virus</td>
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<td>HL</td>
<td>Hodgkin's Lymphoma</td>
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<tr>
<td>HPV</td>
<td>Human papilloma virus</td>
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<tr>
<td>ICP</td>
<td>Intracranial pressure</td>
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<tr>
<td>IDV</td>
<td>Indinavir</td>
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<tr>
<td>II</td>
<td>Intergrase Inhibitor</td>
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<tr>
<td>IRIS</td>
<td>Immune reconstitution inflammatory syndrome</td>
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<tr>
<td>LA</td>
<td>Latex agglutination</td>
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<tr>
<td>LFA</td>
<td>Lateral flow assay</td>
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<td>LFT</td>
<td>Liver function test</td>
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<tr>
<td>LPV</td>
<td>Lopinavir</td>
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<td>MCAZ</td>
<td>Medicines Control Authority of Zimbabwe</td>
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<td>MOHCC</td>
<td>Ministry of Health and Child Care</td>
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NADCs  Non-AIDS defining cancers
NMTPAC National Medicine and Therapeutics Policy Advisory Committee
NGO Nongovernmental organisation
NHL Non-Hodgkin's Lymphoma
NNRTI Non-nucleoside reverse transcriptase inhibitor
NRTI Nucleoside reverse transcriptase inhibitor
NtRTI Nucleotide reverse transcriptase inhibitor
NVP Nevirapine
OI Opportunistic infection
PCP Pneumocystis jirovecii pneumonia
PCR Polymerase chain reaction
PI Protease inhibitor
PITC Provider-initiated testing and counselling
PLHIV People living with HIV
PMTCT Prevention of mother-to-child transmission of HIV
RNA Ribonucleic acid
RTV Ritonavir
SEQAAAR Safe, efficacious, quality, affordable, accessible, available, rationally used
SQV Saquinavir
STI Sexually transmitted infection
TB Tuberculosis
TDF Tenofovir
USA United States of America
UZCHS University of Zimbabwe College of Health Sciences
VCT Voluntary counselling and testing
VEN Vital, essential, necessary
VL Viral load
WHO World Health Organization
ZDV Zidovudine
ZNMP Zimbabwe National Medicine Policy
Chapters were allocated to members of the National Medicines and Therapeutics Policy Advisory Committee (NMTPAC) according to their areas of expertise or interest. Furthermore, other experts e.g. working with the World Health Organization (WHO) and the national programmes for the HIV & AIDS and TB programmes were consulted. Use was made of the latest WHO recommendations as well as the comments from the report of a Consensus meeting held on 21-23 June 2016 in Harare which was convened by the AIDS and TB Directorate to enable a discourse on the 2015 WHO ART for Prevention and HIV treatment recommendations. This meeting was attended by various stakeholders including the Steering Committee that had been set up by the AIDS and TB Directorate to adapt the newly released WHO guidance as well as people living with HIV.

The principles of applying the “essential medicines” concept were maintained, and the need to maintain evidence-informed recommendations as well as the rational use of medicine was paramount. The recommendations had to be deemed cost-effective and feasible in our health-care delivery. Essential medicines are those medicines that satisfy the needs of the majority of the population and therefore should be available at all times. Relevant ART guidelines and in particular the latest WHO guidance informed the revision process. The aim was to have an evidence-informed consensus view of the acceptability, affordability, and feasibility of implementing the recommendations within the Zimbabwean healthcare delivery system.

The Zimbabwean health delivery system can be divided into four levels: primary care, first referral level (district hospital), second referral level (provincial hospital), and third referral level (central hospital). Selection of medicines is based on SEQAAAR (i.e., safety, efficacy, quality, affordability, accessibility, availability, and rational use). Medicine availability is also classified by the level of prescribing—that is, S (specialist), A, B, or C. S level medicines require special expertise and/or diagnostic tests before being prescribed. A level medicines should be prescribed only at the central or provincial levels.

B level medicines are prescribed from the district level upward, and C level medicines should be the only medicines freely available at the rural primary care level. B-level medicines can be made available at the C level with the consent of the district medical officer. ARV medicines are classified as C level and therefore can be available at primary care level. The VEN (vital, essential, necessary) classification allows for priority setting for medicine selection, procurement, and availability: V medicines are vital, given first priority, and supposed to be available 100% of the time; E medicines are essential and given second priority; and N medicines are necessary or nonessential and last on the list of priority needs. The Essential Medicine List of Zimbabwe categorizes the medicines selected for Zimbabwe by level as well as by VEN classification. These classifications are reviewed from time to time to correspond to the country’s current needs.

NMTPAC’s overall objective is to oversee the implementation of the specific objectives of the Zimbabwe National Medicine Policy (NMP). The overall goal of the NMP is to provide quality health care for most of the population.
through the provision of safe, effective, good-quality, and affordable medicines.

Rational use of medicines is enhanced by the development, distribution, and use of treatment protocols and hence the need to keep revising our guidelines while taking into cognisance the feasibility of implementing the desired recommendations within our health care delivery system.

NMTPAC is responsible for reviewing the Essential Medicines List and treatment guidelines as well as monitoring the rational use of medicines in Zimbabwe. NMTPAC is a multidisciplinary team of health-care workers who provide voluntary service for the committee. Including its secretariat i.e. the Directorate of Pharmacy Services, the current NMTPAC membership has HIV experts, physicians, paediatricians, public-health specialists, pharmacists, and regulatory officers and is as follows:

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<thead>
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<td>Chief Pharmacist, Parirenyatwa Central Hospital</td>
</tr>
<tr>
<td>Wellington M, Dr</td>
<td>Public Health Specialist, Newlands Clinic</td>
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HIV Testing and Counselling Services

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

Early Infant Diagnosis

- Birth PCR will be done within 48hrs of birth where available.
- Early ART initiation as soon as birth PCR results are available.
- ALWAYS retest and confirm results with repeat PCR but retesting should not delay ART initiation.
- Babies who test negative at birth (birth PCR) or not tested MUST be tested at 6 weeks.
- Infants at high risk of transmission will receive dual ARVs (AZT and NVP) for 12 weeks as prophylaxis.
- Cotrimoxazole must be started from 6 weeks of age even in babies on longer duration of prophylaxis and continued through adolescence irrespective of CD4 count.

HIV Treatment Services

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

Treatment Monitoring

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

**PMTCT**

- Viral load should be done on all pregnant women at the first ANC visit and repeated 6 monthly through breastfeeding.
- Identifying the pregnant women at high risk of transmitting HIV to the baby where there is no access.
- Viral load testing during pregnancy and breastfeeding period is needed to stratify HIV exposed infants as either high risk or low risk. A high risk infant is defined as follows:
  - High maternal viral load >1000 copies/ml during the last 4 weeks before delivery
  - An infant born to HIV infected woman who has received less than 4 weeks of ART at the time of delivery
  - An infant born to a newly diagnosed HIV infected woman during labor, delivery and postpartum (Incident HIV infection)
- High-risk infants require dual prophylaxis of Daily AZT plus NVP for 12 weeks among the breast-fed infants and Daily AZT plus NVP for 6 weeks among the formula-fed infants

**Post Exposure Prophylaxis**

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

**Reporting Adverse Drug Events**

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

**Pre-Exposure Prophylaxis**

- These guidelines recommend Pre-Exposure Prophylaxis (PrEP) regimen, containing Tenofovir Disoproxil Fumarate (TDF) plus Emtricitabine (FTC) or TDF plus 3TC (alternate regimen) and should be offered as an additional prevention choice for people at substantial risk of HIV infection as part of combination prevention approaches. The MOHCC will implement PrEP using a phased approach. An implementation plan and Standard Operating procedures (SOPs) on PrEP will be developed and shared by MOHCC to guide the introduction and scale up of PrEP.
2.1 Introduction

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

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

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

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

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

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

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

Connections to HIV Prevention, Treatment, Care and Support services - must be in place. Clients who test HIV negative should be linked to HIV prevention services such as VMMC, whilst those testing positive are linked to appropriate HIV treatment services.
2.2 Service Delivery Approaches for HTS

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

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

HIV Self-Testing (HIVST): This refers to a process in which a person collects his or her own specimen (oral fluid or blood) and then performs a test and interprets the result, often in private or with someone he or she trusts. HIV self-testing should be offered as an additional approach to HIV testing services. HIVST does not provide a definitive HIV-positive diagnosis; meaning a reactive (positive) self-test result always requires further testing from a trained testing provider using the relevant validated national testing algorithm. People who test positive during self-testing need to confirm the positive test at a health facility and if they test positive with confirmatory test they are then linked to treatment and care.

The proposed distribution models for HIVST are as follows:

- Community Based Distributors Agents chosen by the Communities (can be village health workers, behaviour change facilitators)
- New Start Network
- VMMC mobilisers and at VMMC sites

HIVST Testing Strategy

![HIVST Testing Strategy Diagram]

- Clinics for key populations
- Public Health Institutions including ANC sites for pregnant women
- Private Sector Pharmacies

Studies are still going on to gather evidence on which cost-effective models to distribute self-testing kits and the models might change based on evidence gathered. The Ministry is in the process of mobilising funds to buy the kits for scale up of HIVST.

2.2 The HIV Testing service package

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

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

- Treatment is available for all people living with HIV
• Starting treatment as soon as possible will prevent your health from worsening and also prevent transmission to others

• Taking ART properly will allow you to live a long and fulfilling life

**Figure 1: Primary component of HIV Services Package**

![Diagram of the primary component of HIV Services Package]

- **Pre-test information**
  - Basics of HIV (Transmission, Prevention and Treatment)
  - Ensure a clear understanding of the benefits of HTC
  - Explanation of testing and counseling procedures
  - Explanation on meaning of results
  - Information on post test support services available
  - Disclosure and referral

- **Conduct HIV Test**
  - Follow National testing algorithm/guidelines
  - Rapid HIV testing with same day results in highly recommended

- **Post-Test Counselling**
  - For all client whether HIV positive or negative
    - Provision of result
    - Risk assessment and reduction
    - Screen for STIs, TB and other conditions
    - Disclosure and partner referral for HIV test
    - Referral and linkage to post-test services
    - Provide take home information
    - If HIV negative emphasis on ‘Staying NEGATIVE’
    - If HIV positive emphasis on ‘Support and positive living’

- **Follow up Counselling & Referrals**
  - HIV negative and HIV positive patients /clients.
    - Empowers clients to continue with their risk reduction strategies.
    - HIV positive will be supported on positive living
    - Referral for appropriate services such as for opportunistic infection (OI), ART, VMMC, Cervical Cancer Screening, STI and TB screening and management; Prevention of Mother to child Transmission of HIV (PMTCT); family planning; nutrition; psychosocial and any other support deemed necessary.

2.2.1 HIV Testing Algorithm for children above 18 months, adolescents and adults

Figure X shows the National HIV Testing Algorithm for children 18 months and above. Serial testing is recommended with Determine or SD bioline followed by Chembio/ First response. If results are discordant then the two tests are repeated in parallel. If still discordant a third test (INSTI) is performed. If negative report as negative. If positive, repeat testing in 14 days.
Figure 2: HIV testing algorithm for children above 18 months, adolescents and adults
### 2.2.2 Priority Populations to be considered for HTS

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

### 2.2.3 Retesting to verify HIV status

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

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

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

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

<table>
<thead>
<tr>
<th>Population</th>
<th>Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>General population at on-going risk behaviours including people with a known HIV positive partner, individuals seen for diagnosis or treatment of STIs, people with known recent HIV exposure, TB patients who are at high risk of HIV exposure, OPD patients with OIs, individuals taking PEP and PrEP</td>
<td>Offer retesting at least annually</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Key populations</th>
<th>Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>HIV-negative pregnant women and lactating women</td>
<td>Retest previously HIV-negative women in the first trimester of pregnancy and at third trimester/ or at delivery; 6 weeks post-natal and 6 monthly during the breastfeeding period. Visits to EPI and 6 weeks(DTP) and at 9 months (measles) should be time points where maternal HIV status is reassessed</td>
</tr>
</tbody>
</table>

| HIV positive individuals before initiation of ART | Retest all people newly and previously diagnosed with HIV before they initiate ART. Retesting should ideally be conducted by a different service provider with a different specimen. However if there is only one health worker at the facility they can take another blood sample a few hours apart and retest |

### 2.3 Disclosure of HIV status

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

#### 2.3.1 Disclosure to a Child, Adolescent and Youths of HIV status

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

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

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

Adolescents below 16 years should be offered their HIV test results in consultation with their parents, guardians, or caretakers. Post-test counselling should be offered to the adolescent together with the parent. Those 16 years and above should receive their HIV test results if they request the HTC services, but where they wish to receive the results in the company of their parents/guardians they can choose to. Adolescents and youth should be counselled about the potential health benefits of disclosing their HIV status to significant others, including their parents/guardians/caregiver and supported to determine, when, how and to whom to disclose to. Parents / guardian/caregiver, who find it difficult to disclose the HIV status of their children, should be supported by health workers.

2.4 QUALITY ASSURANCE

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

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

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

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

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

3.2 Characteristics of available ARVs

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

- Nucleoside reverse transcriptase inhibitors (NRTIs). These medicines block the HIV reverse transcriptase enzyme and prevent the copying of the viral RNA into the DNA of infected host cells by imitating the building blocks of the DNA chain. The resulting DNA chain is incomplete and cannot create new viruses.

- Nucleotide reverse transcriptase inhibitors (NtRTIs). These medicines act at the same stage of the viral life cycle as do NRTIs but have a better resistance profile.

- Non-nucleoside reverse transcriptase inhibitors (NNRTIs). These medicines also block the HIV reverse transcriptase enzyme, but have a
different mechanism of action than the NRTIs and the NtRTIs.

- **Protease inhibitors (PIs).** These medicines block the enzyme protease and prevent the assembly and release of HIV particles from infected cells.
- **Integrase inhibitors (IIs).** These medicines target HIV’s integrase protein, blocking its ability to integrate its genetic code into human cells.

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

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

Table 2 on the following page shows the different categories of ARVs.

**Table 1: Antiretroviral medicines by mode of action**

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

**3.3 Efficacy and safety**

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

The preferred first line regimen of Tenofovir, Lamivudine and Efavirenz has relatively few adverse effects and is taken once daily. Zidovudine (as an alternative to Tenofovir) can cause anaemia but is less likely to cause peripheral neuropathy. Efavirenz has less adverse effects compared to Nevirapine. Nevirapine can cause a rash and hepatotoxicity and thus should be used with caution when initiating ART at higher levels of CD4 counts (e.g., in women with CD4 counts greater than 250 and in men with CD4 counts greater than 400).

All ARVs have class-specific side effects, and individual medicines may cause specific side effects (see Table 14 in Section 7.3). In addition, significant medicine interactions and toxicities may occur when using some ARVs in combination with each other and with other medicines such as TB medicines.
CHAPTER: Initiation of Antiretroviral Therapy in Adults and Adolescents

4.1 Goals of ART

The aims of ART are as follows:

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

Prior to starting ART, patients should be assessed for readiness to take ARVs; the ARV regimen; dosage; and scheduling; the likely potential adverse effects; and the required monitoring. Both medical and psychosocial issues need to be addressed before initiating ART. Patients should be adequately counselled about adopting appropriate lifestyle measures such as safer sex practices (including use of condoms), and any other psychosocial problems that may interfere with adherence (e.g., alcohol, psychiatric disorders) should be addressed. Efforts should be made to reduce the time between HIV diagnosis and ART initiation based on an assessment of a person’s readiness. At each clinic visit, always screen for tuberculosis using a TB symptom checklist, advice patients about adequate nutrition and the importance of medicine adherence and regular follow-up care. People taking ARVs should also be regularly asked about whether they are taking other medications including herbal remedies that may interfere with the efficacy of ARVs. The ART programme should promote treatment literacy for PLHIV including information on the benefits of early treatment, the risks of delaying treatment, the required lifelong commitment for adherence to treatment.

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

4.2 Medical criteria for initiating ART in adults and adolescents

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

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

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

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

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

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

Patients with CD4 cell count <100

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

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

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

4.3 Psychosocial criteria for initiating ART

Consider the following psychosocial criteria when initiating ART:

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

4.4 Reasons for deferring ART

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

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

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

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

It should be noted that motivation to start and adhere to treatment may be more difficult for people who feel well and have higher CD4 counts than for people who are ill. Therefore, health workers should put special emphasis on adherence counselling for this particular group of patients. Efforts to support adherence should start before ART initiation and should include basic information about HIV, the ARV medicines, expected adverse events, preparations for long-term ART. Many factors affect adherence to treatment. Patients may just forget to take their ARVs, be away from home, be depressed or may abuse alcohol. Medication factors may include adverse events, pill burden, dietary restrictions. Health care factors include medicine stock outs, long distances to health facilities and costs related to care.

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

4.6 ART in adolescents

4.6.1 Who is an adolescent?

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

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

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

4.6.2 HIV Testing Services (HTS) for Adolescents

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

Special attention should be given to: Post-test counselling; appropriate and successful linkage to prevention, treatment and care services; and consent and confidentiality, which are major concerns for adolescents
Adolescents should be counselled about potential benefits and risks of disclosure of their HIV status and empowered and supported to determine if, when, how and to whom to disclose to.

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

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

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

4.6.5 Monitoring of HIV disease
In monitoring adolescents, remember the following:
• Stunting and pubertal delay are common.
• As well as CD4 count and Viral load monitoring, clinical monitoring should include measurement of height and weight at every clinic visit as well as evaluation of pubertal stage using Tanner staging every six months.
• Girls should specifically be asked about menstruation, including age of menarche and timing of menstrual cycles.

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

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

4.6.8 Adherence
Adherence is particularly problematic in adolescents. Particular attention should be paid to assessing adherence at every visit and to providing adherence support. Counselling on adherence should include exploring specific reasons that may contribute to poor adherence. Adolescents face many psychosocial issues that can affect their adherence, and those should be assessed:
• In particular, ways of supporting attendance at clinic appointments and taking medicines
while at school (especially for those at boarding schools) should be addressed.

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

4.6.9 Education, information and services on sexual and reproductive health

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

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

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

4.6.9 Transitioning from adolescents into adulthood:

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

5.1 Introduction

The choice of medicine regimen is based on the "essential medicine" concept and the rational use of medicine. To maximise adherence, use of Fixed-Dose Combination (FDCs) medicines is strongly encouraged. Essential medicines are defined as those medicines that satisfy the healthcare needs of the majority of the population, at a price they and the community can afford; they should therefore be available at all times and in adequate amounts, and in appropriate dosage forms (WHO Expert Committee on Essential Medicines, December 1999). On the other hand; rational use of medicines requires that patients receive medicines appropriate to their clinical needs, in doses that meet their own individual requirements, for an adequate period of time, and at the lowest cost to them and the community. (WHO Conference of Experts, Nairobi, 1985)

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

Dual combinations:
• Tenofovir (TDF) 300mg + Lamivudine (3TC) 300mg
• Zidovudine (AZT) 300mg + Lamivudine (3TC) 150mg

The above dual FDC should be used in combination with single formulation of:
• Efavirenz (EFV) 400mg (soon to be introduced by the MOHCC)
• Efavirenz (EFV) 600mg
• Nevirapine (NVP) 200mg

Triple combinations:
• Tenofovir (TDF) 300mg + Lamivudine (3TC) 300mg + Efavirenz (EFV) 400mg
• Tenofovir (TDF) 300mg + Lamivudine (3TC) 300mg + Efavirenz (EFV) 600mg
• Zidovudine (AZT) 300mg + Lamivudine (3TC) 150mg + Nevirapine (NVP) 200mg

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

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

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

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

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

5.2 First-line regimen for adults and adolescents

Table 2: First-line regimen for adults and adolescents

<table>
<thead>
<tr>
<th>Preferred First line Regimen</th>
<th>Alternative Regimens</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adolescents (10-19 years) ≥ 35kg</td>
<td>TDF + 3TC + EFV</td>
</tr>
<tr>
<td>Adults including pregnant &amp; breastfeeding women,</td>
<td>TDF + 3TC + NVP</td>
</tr>
<tr>
<td>TB/HIV, HBV/HIV</td>
<td>AZT + 3TC + EFV</td>
</tr>
<tr>
<td></td>
<td>AZT + 3TC + NVP</td>
</tr>
</tbody>
</table>

A. Preferred First-line regimen

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

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

<table>
<thead>
<tr>
<th>Initiation and Maintenance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Triple combination of Tenofovir + Lamivudine + Efavirenz</td>
</tr>
</tbody>
</table>

Caution: Tenofovir (TDF)

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

Clinical considerations when using TDF

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

Calculation of GFR or Creatinine clearance in ml/min using Cockcroft Gault Equation

**Male:** 1.23 X (140 minus Age)x body wt in Kg/ Creatinine (in micromols/L)

**Female:** 1.04 X (140 minus Age) x body wt in kg/ Creatinine (in micromols/L)

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

B. Alternative first-line regimen

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

<table>
<thead>
<tr>
<th>Two-Week Starter Pack</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Morning Dose</strong></td>
</tr>
<tr>
<td>Dual combination of Tenofovir (300mg) + Lamivudine (300mg)</td>
</tr>
</tbody>
</table>

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

<table>
<thead>
<tr>
<th>Morning Dose</th>
<th>Evening Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Combination of Tenofovir (300mg) + Lamivudine(300mg) + Nevirapine (200mg)</td>
<td>Nevirapine (200mg)</td>
</tr>
</tbody>
</table>

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

A. Starter pack (2 weeks):

- Dual Zidovudine 300 mg plus Lamivudine 150 mg orally twice a day plus
- Nevirapine 200 mg orally once a day

B. Stepping up, after the first two weeks:

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

Substitutions due to toxicities or unavailability of medicines

Some patients may experience adverse events related to ARVs and require appropriate management (Refer to Table XX on Adverse Events and their management) In the event of unavailability of certain ARV medicines, substitutions should be considered. The following actions should be taken prior to medicine substitution.

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

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

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

(See Section 7.3 on monitoring medicine side effects.)
An alternative to Lamivudine (3TC) is emtricitabine (FTC); these medicines are considered pharmacologically equivalent. In the event that you come across a patient on Tenofovir/Emtricitabine/Efavirenz, you may substitute Emtricitabine with Lamivudine.

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

5.3 Second-line treatment recommendation for adults and adolescents

Ideally, patients who fail to respond to first-line treatment should be treated with a different regimen that contains medicines that were not included in the first line regimen. The second-line regimen will still consist of two NRTIs but with the addition of a PI. The second-line regimen should be initiated only after assessing for treatment adherence and failure and in consultation with a specialist in HIV and AIDS treatment or the clinical mentorship team at the OI/ART clinic. Clinical mentors should be consulted where there is doubt about what to do. More adherence counselling will be required in preparation for the planned new therapy. (To diagnose treatment failure see Section 7.9.)

Table 3: Preferred second line regimens for adults and adolescents (10 – 19 years) including pregnant and breastfeeding women

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

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

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

5.4 Third-line treatment recommendations for adolescents, adults, pregnant and breast-feeding women

Those failing second-line therapy will need to be referred for Specialist assessment which includes viral load and may be genotype testing prior to recommending the third-line medicines. Adherence needs to be reinforced all the
time. In adolescents >12 years and adults, the preferred 3rd line ART regimen is Dolutegravir (50mg) and Darunavir (600mg)/Ritonavir (100mg) twice daily (for PI-experienced patients). Raltegravir (400mg) twice a day can be used when DTG is not available. You will need to be advised by the Paediatricians regarding ARV regimens for children. Safety and efficacy data on the use of DTG in adolescents younger than 12 years and pregnant women are not yet available.

### 5.5 Use of ARVs in patients with TB

TB is the most common OI encountered among people with HIV infection in Zimbabwe. Since the advent of the pandemic of HIV, TB has remained a serious public-health problem. In Zimbabwe, among TB patients with known HIV status; 70% are HIV positive while 72% are receiving ART. In addition, TB accounts for a third of HIV related deaths. There is a need to integrate the HIV and TB services, as TB and HIV co-infection is common. Rifampicin interacts adversely with some antiretroviral agents such as PIs and Nevirapine. The preferred regimen for HIV positive TB patients is Tenofovir 300mg plus Lamivudine 300mg and Efavirenz 600mg.

#### 5.5.1 Patients with TB who are not yet on ART

In patients who have HIV-related TB but are not yet on ART, treatment of TB takes priority. ART should be started at least two weeks after the start of TB therapy i.e. during the intensive phase when the patient has stabilized on TB treatment regardless of their CD4 count status. TB/HIV co-infected patients with severe immunosuppression such as CD4 count less than 50 cells/mm3, should receive ART early i.e. within the first 2 weeks of initiating TB treatment. Cotrimoxazole prophylaxis should have been provided with the commencement of the TB therapy if the patient is not on it already.

#### 5.5.2 Patients who develop TB when already on ART

Treat TB as per national TB guidelines.

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CHAPTER: Prevention of Mother to Child Transmission

6.1 Introduction

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

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

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

The Zimbabwe PMTCT programme has four main strategies:

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

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

*Figure 3 below summarizes the synergistic purposes of providing ART to all pregnant and breast-feeding women*

6.2 HIV Testing Services for pregnant and lactating women

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

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

- first trimester of pregnancy
- third trimester/ or at delivery
6 weeks post-natal and
6 monthly during the breastfeeding period.
In antenatal care settings, couples and partners should be offered voluntary HIV testing services with support for mutual disclosure.

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

- HIV prevention during pregnancy and breastfeeding period, including dual protection, condoms and PrEP
- Discussion of childbirth plans and encouragement to deliver in a health facility for health reasons and to ensure access to services for PMTCT
- Use of ARV drugs both for the mother’s health and to prevent transmission to the infant
- Importance of partner testing and information on the availability of couples testing services
- Screening for TB and testing for other infections, such as syphilis and hepatitis B
- Counselling on maternal nutrition, including iron and folic acid supplementation
- Advice on infant-feeding and support to carry out the mother’s infant-feeding choice
- HIV testing for the infant and necessary follow up for HIV-exposed infants
- Counsel on sexual and reproductive health including family planning and the need for dual contraception (reliable hormonal contraceptives plus barrier methods i.e. male and female condoms)

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

6.3 When to start lifelong ART in HIV positive pregnant and lactating women

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

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

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

Table 4: First and second-line ARVs for Pregnant and breast-feeding women
### Pregnant and Lactating women

<table>
<thead>
<tr>
<th></th>
<th>1st line therapy</th>
<th>2nd line therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Preferred Option</td>
<td>TDF + 3TC + EFV600</td>
<td>If TDF was used as first line, use AZT plus 3TC plus ATV/r or LPV/r</td>
</tr>
<tr>
<td></td>
<td></td>
<td>If AZT was used as first line, use TDF plus 3TC plus ATV/r or LPV/r</td>
</tr>
<tr>
<td>Alternative Options</td>
<td>AZT + 3TC + EFV600</td>
<td></td>
</tr>
<tr>
<td></td>
<td>AZT + 3TC + NVP</td>
<td></td>
</tr>
<tr>
<td></td>
<td>TDF + 3TC + NVP</td>
<td></td>
</tr>
</tbody>
</table>

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

#### 6.5 Use of viral load testing in pregnancy

Viral load testing may have additional value for assessing the risk of transmission of HIV from mother to child. For an HIV infected pregnant woman who is not on ART, her viral load is proportionate to her risk of mother to child transmission².

For HIV infected pregnant women already on ART during current pregnancy, health workers should:

- Check the most recent routine VL to ascertain if the VL is suppressed
- If a VL was not done within the last 6 months, it should be repeated at the first visit and adherence counselling should be done.
- If the VL was/is > 1000 copies/ml (within last 6 months), intensive adherence counseling should immediately be done and the VL should be repeated in 3 months and patient managed according to the national VL algorithm (chapter XX)

- Repeat VL testing between 32 and 36 weeks of pregnancy

For newly identified HIV positive pregnant women who initiate ART, health workers should:

- Should perform a VL at base-line (first ANC visit) and a repeat viral load test between week 32 and 36 weeks of pregnancy

#### 6.6 HIV exposed Infant prophylaxis

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

A high risk infant is defined as follows:

---

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

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

The table below shows infant prophylactic ARV regimen.

**Table 5: Infant dosing table for Nevirapine and Zidovudine**

<table>
<thead>
<tr>
<th>Infant age</th>
<th>Dosing NVP</th>
<th>Dosing AZT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Birth to 6 weeks</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Birth weight 2000–2499 ga</td>
<td>10 mg once daily (1 ml of syrup once daily)</td>
<td>10 mg twice daily (1 ml of syrup twice daily)</td>
</tr>
<tr>
<td>Birth weight ≥2500 g</td>
<td>15 mg once daily (1.5 ml of syrup once daily)</td>
<td>15 mg twice daily (1.5 ml of syrup twice daily)</td>
</tr>
<tr>
<td>&gt;6 weeks to 12 weeks</td>
<td>20 mg once daily (2 ml of syrup once daily or half a 50 mg tablet once daily)</td>
<td>No dose established for prophylaxis; use treatment dose 60 mg twice daily 6 ml of syrup twice daily or a 60 mg tablet twice daily</td>
</tr>
</tbody>
</table>

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

**6.7 Infant feeding in the context of HIV**

Mothers known to be infected with HIV should exclusively breastfeed their infants for the first 6 months of life, introducing appropriate complementary foods thereafter, and continue breastfeeding up to 24 months and beyond.

**6.8 Early Infant diagnosis of HIV infection (EID)**

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

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

**6.9 Testing of HIV exposed infants**

All babies of HIV-infected mothers are born with maternal anti-HIV antibodies that are passed on to them transplacentally. These antibodies start to wane from about 9 months, and by 18 months have cleared off completely.

Due to the presence of these maternal antibodies, HIV antibody tests in infants under the age of 18 months cannot be used to definitively diagnose HIV infection. Diagnosis of HIV infection in children less than 18 months requires testing for the virus itself (called virologic testing, or PCR testing). Infants with an initial positive virological test result should be commenced on ART without any delay and, at the same time, a second specimen should be collected to confirm the initial positive virological test result. Immediate initiation of ART saves lives and should not be delayed while waiting for the results of the confirmatory test. Infants testing HIV PCR negative and those HIV-exposed infants who are well should undergo HIV serological testing at around 9 months of age (or at the time of the last immunization visit). Infants who test positive by HIV rapid test at 9 months should have a virological test to definitively diagnose HIV infection and the need for ART.

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

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

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

*Need the EID Algorithm here or as an appendix*
CHAPTER: Pediatric Antiretroviral Treatment

1. Always offer PITC every time a patient is in contact with healthcare services.
2. Counselling is important but should not delay ART initiation.
3. Investigate and manage opportunistic infections including TB before initiation.
   N.B. ART should be started in any child with active TB disease as soon as possible and within 8 weeks following the initiation of anti-tuberculosis treatment, regardless of the CD4 cell count and clinical stage.
4. ALWAYS initiate Cotrimoxazole prophylaxis at first contact with an exposed infant or infected child.

7.2 Scheduled visits

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

1. Services should be delivered across a continuum of care. This requires integrated and linked service provision at all levels of the health system, from primary to secondary to tertiary (specialist) care, embracing all elements of the health system.
2. During these visits the following actions should be taken:
   a) Growth should be monitored and development assessed (see Appendixes VI, VII, and VIII on growth monitoring).
   b) Infant-feeding practice should be reviewed regularly and appropriate supportive counselling provided.
   a. Breast feeding is recommended for all babies - Exclusive breastfeeding for 6 months with addition of complementary feeding thereafter.
   c) The baby should continue breastfeeding for up to 2 years.
   d) Immunisations should be given according to the national guidelines. The BCG vaccination should still be given at birth, but BCG should not be given to children with symptomatic HIV infection.
   e) Always look for and treat opportunistic infections.
   f) Be aware of and watch for potential drug interactions. The management of TB in HIV-infected children and the treatment of severe HIV infection with ARVs is complicated by the potential for multiple drug interactions.
   g) Counselling on safer sex behaviour; including the use of condoms during the breastfeeding period is recommended.
   h) Counsel on family planning.

7.3 WHEN TO START ART IN CHILDREN YOUNGER THAN 10 YEARS OF AGE

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

What regimens to use in children

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

First line for children less than 3 years
For infants and children younger than 3 years

**Preferred first line**
- ABC+3TC+LPV/r

**Alternate:**
- AZT+3TC+LPV/r
- ABC +3TC + NVP

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

First line for children 3 years to less than 10 years

**Preferred first line**
- ABC+3TC+ EFV

**Alternative first line:**
- AZT+3TC+ EFV
- AZT+3TC+ NVP
- TDF+3TC+EFV (or NVP)

### Table 6: Recommended ART regimens in children

<table>
<thead>
<tr>
<th>Age</th>
<th>First line</th>
<th>Second line</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-2 weeks</td>
<td>AZT +3TC+NVP</td>
<td></td>
</tr>
<tr>
<td>2 weeks to Less than 3 yrs</td>
<td>Preferred: ABC + 3TC + LPV/r</td>
<td>Preferred : AZT+3TC +RAL</td>
</tr>
<tr>
<td></td>
<td>Alternative: AZT+ 3TC + LPV/r</td>
<td>Alternative: ABC+3TC+RAL</td>
</tr>
<tr>
<td></td>
<td>ABC+ 3TC+ NVP</td>
<td></td>
</tr>
<tr>
<td>3years to less than 10 yrs</td>
<td>Preferred: ABC + 3TC + EFV</td>
<td>AZT+3TC+LPV/r or RAL</td>
</tr>
<tr>
<td></td>
<td>Alternative: AZT + 3TC + EFV</td>
<td>ABC +3TC + LPV/r</td>
</tr>
<tr>
<td></td>
<td>AZT + 3TC + NVP</td>
<td>ABC+3TC+ATV/r</td>
</tr>
<tr>
<td></td>
<td>TDF + 3TC+ EFV (or NVP)</td>
<td></td>
</tr>
</tbody>
</table>

Children 3 – 10 years, stable on NVP or EFV or AZT based regimens should continue until stocks are exhausted OR until they are ready for the adult regimen at 10 years or >35kgs.

**7.4 Psychosocial factors.**

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

The process of disclosure to the child should be initiated as early as possible, usually after seven years of age. Please note that adherence is good in children who know their status and are supported to adhere to medicines.

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

### 7.5 Administering Medicines

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

### 7.6 Adverse effects of medicines:
Always check for possible adverse effects of the medicines o
AZT: Anaemia, Neutropenia
NVP: Stevens Johnson, Hepatitis
EFV: Neuropsychiatric symptoms, gynaecomastia.
ABC: Hypersensitivity reaction is very rare in our population and occurs in patients with the human leukocyte antigen HLA–B 5701 allele

### 7.7 THIRD LINE ART REGIMEN in Children

Children 0-10yrs
RAL + 2 NRTIs
DRV/r + 2 NRTIs
DRV/r + RAL +/- 1–2
 Patients on ART need close monitoring to assess adherence to the treatment regimen, tolerance, the side effects of the medications, and the efficacy of the treatment. Health workers should document patient visit’s record in the patient-held booklet (OPD card). Clinical assessments and laboratory tests are important in assessing individuals following a positive HIV diagnosis to assess for co-infections, NCDs and other co-morbidities that may impact on treatment response.

8.1 Initial evaluation

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

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

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

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

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

• Syphilis serology test
• Hepatitis B and C virus screening

8.2 Monitoring adherence to treatment

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

8.3 Frequency of Clinic Visits

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

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

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

A stable patient on ART is defined as someone who:

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

There are three main types of clinic visits:

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

8.4 Monitoring adverse medicine events or medicine side effects

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

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

Central nervous system toxicities

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

Metabolic abnormalities

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

Anaemia

Check haemoglobin after the first month of Zidovudine use.

Lactic acidosis

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

**Lipodystrophy / fat redistribution**

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

**Other side effects**

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

*Table 7: Some Important Side Effects of Antiretroviral Agents*

<table>
<thead>
<tr>
<th>Medicine</th>
<th>Side Effects</th>
<th>Risk Factors</th>
<th>Action to be taken</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Nucleotide/Nucleoside Reverse Transcriptase Inhibitors (NRTIs)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tenofovir (TDF)</td>
<td>Renal complications</td>
<td>Underlying renal disease; Age &gt; 50 years; untreated diabetes and hypertension; concomitant use of nephrotoxic medicines or PI</td>
<td>Monitor creatinine. Substitute with Zidovudine</td>
</tr>
<tr>
<td></td>
<td>Decreases in bone mineral density</td>
<td>Vitamin D deficiency; risk factors for osteoporosis or bone mineral density loss</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Other SE: Gastrointestinal (GI) symptoms, rash</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Zidovudine (AZT)</td>
<td>Anaemia, neutropenia, lipoatrophy, lipodystrophy, myopathy, headache, lactic acidosis</td>
<td>CD4 &lt; 200 cells/mm3 Anaemia at baseline</td>
<td>Monitor full blood count; if severe anaemia change to Tenofovir (TDF) or Abacavir (ABC)</td>
</tr>
<tr>
<td>Lamivudine (3TC)</td>
<td>Usually nil</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Abacavir</td>
<td>Severe hypersensitivity reactions</td>
<td>Withdraw medicine immediately; give alternative like Tenofovir (TDF) or Zidovudine (AZT). Do not restart medicine, as this can be fatal</td>
<td></td>
</tr>
<tr>
<td>----------</td>
<td>-----------------------------------</td>
<td>----------------------------------------------------------------------------------------------------------------------------------</td>
<td></td>
</tr>
</tbody>
</table>

**Non-nucleoside reverse transcriptase inhibitors**

<table>
<thead>
<tr>
<th>Efavirenz (EFV)</th>
<th>Central nervous system symptoms (dizziness, confusion, convulsions headache, sleep disturbance, abnormal dreams) or mental symptoms (anxiety, depression, mental confusion) usually during the first three weeks and then resolve</th>
<th>For CNS symptoms: consider dosing at night or use low dose EFV (400mg/day); if this fails then withdraw EFV and substitute with Nevirapine (NVP)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hepatotoxicity</td>
<td>Underlying hepatic disease or concomitant use of hepatotoxic medicines</td>
<td>Withdraw EFV and substitute with boosted PIs</td>
</tr>
<tr>
<td>Gynaecomastia</td>
<td>Risk factors unknown</td>
<td>substitute Efavirenz (EFV) with Nevirapine (NVP)</td>
</tr>
<tr>
<td>Nevirapine (NVP)</td>
<td>Liver toxicity, abnormal liver function tests (LFTs); Mild or severe skin rashes (e.g. Stevens-Johnson syndrome [rare]), Fever; fatigue, nausea,</td>
<td>Underlying hepatic disease or concomitant use of hepatotoxic medicines High baseline CD4 cell count (&gt;250 cells/mm³ in women and &gt;400 cells/mm³ in men)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>If LFTs are suggestive of hepatitis or if jaundice is present, discontinue; if rash is severe, discontinue and replace with Efavirenz</td>
</tr>
</tbody>
</table>
### Protease Inhibitors (PIs)

<table>
<thead>
<tr>
<th>Drug</th>
<th>Side Effects</th>
<th>Precautions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Atazanavir (ATV/r)</td>
<td>Jaundice, nausea, diarrhoea, headache, hyperbilirubinaemia</td>
<td>Monitor; withdraw medicine if symptoms are severe</td>
</tr>
<tr>
<td>Lopinavir/ritonavir (LPV/r)</td>
<td>Hepatotoxicity, Pancreatitis, Hyperlipidaemia, GI intolerance, diarrhoea, hyperglycaemia, Lipodystrophy, Underlying hepatitic disease Advanced HIV disease and alcohol misuse Obesity, diabetes</td>
<td>Give loperamide for the diarrhoea</td>
</tr>
<tr>
<td>Darunavir (DRV/r)</td>
<td>Hepatotoxicity, Severe skin and hypersensitivity reactions</td>
<td>Monitor; withdraw medicine if symptoms are severe.</td>
</tr>
</tbody>
</table>

### Integrase inhibitor

<table>
<thead>
<tr>
<th>Drug</th>
<th>Side Effects</th>
<th>Precautions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Raltegravir (RAL)</td>
<td>Mood changes, depression, myopathy, skin reactions e.g., Stevens- Johnson syndrome,</td>
<td>Monitor; withdraw medicine if symptoms are severe</td>
</tr>
<tr>
<td>Dolutegravir (DTG)</td>
<td>Hepatotoxicity and hypersensitive reactions</td>
<td>Monitor; withdraw medicine if symptoms are severe</td>
</tr>
</tbody>
</table>

### 8.5 Key Antiretroviral Medicine interactions

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

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

8.6 Immune reconstitution inflammatory syndrome

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

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

- Common immune reconstitution illnesses in Zimbabwe are TB, cryptococcal meningitis and recurrent herpes simplex virus.

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

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

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

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

8.8 Clinical monitoring

Monitoring ART in adults and adolescents

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

• The patient feels better and has more energy to perform daily tasks.
• The patient is gaining weight (record the patient’s weight at each visit).
• There is an improvement in symptoms and signs of the original presenting illness.
• Infections such as oral thrush, hairy leukoplakia, genital herpes, skin rash, and molluscum contagiosum have improved.
• There has been an improvement in chronic diarrhoea.
• There has been an improvement in Kaposi’s sarcoma.
• The patient is free of new moderate or severe infections.

Monitoring ART in children

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

Clinical assessment involves the following:

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

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

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

8.9 Virological (HIV viral load) monitoring

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

Viral load should be monitored routinely at 6 months and at 12 months after ART initiation, and then annually thereafter.
Figure XX below is an algorithm for routine VL testing. It is important to note that studies have shown that around 70% of patients on first-line ART who have a first high viral load will suppress following an adherence intervention. Enhanced adherence counselling is therefore, crucial to reduce unnecessary switches of patients. (Refer to OSDM for Job Aid on Enhanced Adherence Counselling).

**Figure 5: Viral Load testing strategies to detect or confirm treatment failure and switch in adults, adolescents and children**

8.10 **Immunological monitoring (CD4 count)**

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

8.11 **Treatment failure**

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

**Figure 6: Treatment Failure (WHO, 2015)**

<table>
<thead>
<tr>
<th>Clinical failure Children:</th>
<th>Children: New or recurrent clinical event indicating advanced or severe immunodeficiency (WHO stage 3 and 4 clinical conditions with exception of TB) after 6 months of effective treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td><strong>Adults and Adolescents</strong> New or recurrent clinical event indicating severe immunodeficiency (WHO stage 4 clinical condition) after 6 months of effective treatment</td>
</tr>
<tr>
<td>Immunological failure (CD4 failure)</td>
<td><em>Children</em> Decrease to pre-therapy CD4 count/percentage Younger than 5 years – Persistent CD4 level below 200 cells/mm³ or CD4% &lt; 10% Older than 5 years – Persistent CD4 levels below 100 cells/mm³</td>
</tr>
<tr>
<td></td>
<td><strong>Adults and adolescents</strong> CD4 counts falls to the baseline (or below) or persistent CD4 levels below 100 cells/mm³</td>
</tr>
<tr>
<td>Virological failure</td>
<td>Viral load greater than 1,000 copies/ml based on two consecutive VL measurements after 3 months with enhanced adherence counselling</td>
</tr>
</tbody>
</table>

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

**Treatment failure in children**

Consider the following before switching ART regimens:

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

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

- a lack of or decline in growth rate in children who showed an initial response to treatment (moderate or severe unexplained malnutrition not adequately responding to
standard therapy despite adequate nutritional support and without other explanation); loss of neurodevelopmental milestones (see Appendix VI) or development of encephalopathy; OR

- occurrence of new OIs or malignancies or recurrence of infections, such as oral candidiasis that is refractory to treatment or oesophageal candidiasis.

Note: A second-line regimen should be started only after consultation with a specialist in HIV and AIDS care/treatment or your mentor.
Various opportunistic infections (TB, cryptococcosis) co-infections (hepatitis B or C), co-morbidities and other health conditions are common among people living with HIV and have implications for the treatment and care, including the timing and choice of antiretroviral medicines. HIV is also associated with cancers such as Kaposi Sarcoma, Non-Hodgkins Lymphoma, invasive cervical cancer as well as non-communicable diseases such as diabetes, cardiomyopathies, and chronic kidney disease. This section provides a brief overview of the most common and important conditions.

9.1 COTRIMOXAZOLE PREVENTIVE THERAPY

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

Cotrimoxazole prophylaxis can potentially prevent the following OIs:

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

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

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

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

- All HIV positive infants, children and adolescents irrespective of clinical and immunological condition
- Priority should be given to all children younger than 5 years regardless of CD4 count or clinical stage and children with severe or advanced HIV clinical disease (WHO clinical stage 3 and 4) and all those with CD4 count ≤ 350.
- All children born to HIV-positive mothers at six weeks of age until they are tested and confirmed to be negative
- In settings where malaria/or severe bacterial infections are highly prevalent; provide CTX to all HIV infected infant, children, adolescents and adults including pregnant and breast-feeding women regardless of CD4 cell count and WHO clinical stage.

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

Cotrimoxazole prophylaxis in adults

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

Cotrimoxazole prophylaxis in children

Give once daily orally according to the following table.
Notes on the provision of cotrimoxazole to adults and children

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

• Cotrimoxazole prophylaxis should be commenced at least one to two weeks before the commencement of ART. This allows time to identify those who might be allergic to cotrimoxazole.
• For patients who are allergic to cotrimoxazole, consider desensitization (see Appendix IV).

When to discontinue Cotrimoxazole:

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

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

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

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

9.2 TB/HIV Collaborative Activities

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

HIV care settings should implement the three I’s strategy:
1. Intensified TB case- finding
2. Isoniazid Preventive Therapy(IPT)
3. Infection control at all clinical encounters

9.2.1 Intensified TB case- finding

All HIV positive clients should be routinely screened for TB in order to timely assess their eligibility to be commenced on IPT or TB treatment

9.2.2 Isoniazid Preventive Therapy (IPT)

Adults and adolescents including pregnant women living with HIV should be screened for TB at every clinic visit with a TB screening tool and an algorithm (refer to algorithms on TB screening in annexe 1.0); and those who report any one of the following symptoms history

<table>
<thead>
<tr>
<th>Age</th>
<th>Dose (ml)</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Suspension (240 mg / 5 ml)</td>
<td>Adult tablets (480 mg)</td>
<td>Paediatric tablets (120 mg)</td>
</tr>
<tr>
<td>0 to 6 months</td>
<td>2.5</td>
<td>¼</td>
<td>1</td>
</tr>
<tr>
<td>6 months through 3 years</td>
<td>5</td>
<td>½</td>
<td>2</td>
</tr>
<tr>
<td>Over 3 years</td>
<td>10</td>
<td>1</td>
<td>3</td>
</tr>
</tbody>
</table>
of current cough, fever, weight loss or night sweats are likely to have active TB and should be evaluated for TB and other disease. Xpert MTB/RIF (GeneXpert) should be used as the initial diagnostic test in adults and children suspected of having HIV-associated TB.

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

The following are the target groups for IPT in Zimbabwe:

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

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

- Symptoms and signs suggestive of active TB
- Patient on treatment for TB
- Completion of IPT in the past 3 years
- Patients who have been on ART for 3 months or less
- Signs of active liver disease or history of INH induced hepatitis
- In the subgroup of patients eligible and in the process of being ‘worked up’ for ART, there is a high prevalence of undiagnosed TB, including a considerable proportion that do not have TB symptoms. In this subgroup, it is reasonable to wait 3 months before considering initiation of IPT, during which time TB symptom screening should be repeated at each clinic visit.

- Adults and adolescents including pregnant women living with HIV and unlikely to have active TB will receive IPT for 6 months.
- Adults and adolescents (including pregnant women) will be given 6 months of IPT immediately following the successful completion of TB treatment (i.e. as secondary prevention).
- The recommended dose of INH in adults and adolescents is 5 mg/kg/day to a maximum of 300 mg/day

### IPT and unknown or positive TST status

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

### 9.2.3 Infection control at all clinical encounters

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

- prompt detection of infectious patients,
- airborne precautions, and
- treatment of people who have suspected or confirmed TB
The following measures should be in place;

- Administrative controls
- Environmental controls
- Use of respiratory protective equipment

Figure 7: Infection Control Recommendations

9.2.4 Laboratory Diagnostic Tools

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

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

Use of LF-LAM

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

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

1. HIV testing and counselling should be routinely offered to all persons suspected or known to have TB
2. HIV-related prevention, care and support services should be routinely offered to all persons suspected or known to have TB
3. Case definitions and anti-TB treatment regimens are the same for HIV-positive and HIV-negative TB patients, and drug dosages in mg/kg are also the same.
4. In TB/HIV co-infection the first priority is to initiate anti-TB treatment followed by cotrimoxazole, and then ART
5. All TB patients co-infected with HIV should be given co-trimoxazole preventive therapy (CPT) for the whole duration of TB treatment.
6. All people living with HIV with active TB disease, irrespective of CD4 cell count and the site of TB disease, should be initiated on ART as soon as practicable (Refer to Section 4.4)
7. All PLHIV should be screened for TB at every contact with health services. Patients should be screened for current cough, fever, night sweats and loss of weight.
8. PLHIV who develop TB should be started on anti-TB treatment immediately.

9. TB/HIV patients benefit from the use of steroids for the same indications as found in HIV-negative TB patients (refer to TB Guidelines)

9.3 Treatment of Cryptococcal disease

8.3.1 Prevention of Cryptococcal Disease

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

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

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

Table 9: Treatment decisions for asymptomatic cryptococcal disease
Timing of ART for individuals with asymptomatic cryptococcal antigenemia is unknown. We recommend initiation of ART 2-4 weeks after initiation of antifungal therapy in individuals who screen positive for serum CrAg without any evidence of disseminated cryptococcal meningitis.

9.3.2 Treatment of Cryptococcal Meningitis

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

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

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

However, flucytosine is typically not available in resource limited settings, including Zimbabwe. Combination therapy with amphotericin B and fluconazole is strongly recommended. In the absence of amphotericin B, high dose fluconazole can be used as alternative therapy (See Table XX 7).

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

<table>
<thead>
<tr>
<th>Table 10: Recommended therapy for cryptococcal meningitis</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Treatment Phase</strong></td>
</tr>
<tr>
<td>Preferred</td>
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<td></td>
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<tr>
<td></td>
</tr>
<tr>
<td>Alternate</td>
</tr>
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</tr>
</tbody>
</table>
9.3.3 Management of Raised Intracranial pressure

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

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

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

9.3.4 Management of Amphotericin B associated toxicities

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

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

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

If repeat creatinine remains elevated or continues to increase, amphotericin B should be discontinued and high dose fluconazole 1200mg orally once daily initiated (Table XX 7). Monitoring of haemoglobin at baseline and weekly is also recommended. Timing of ART in cryptococcal meningitis

The timing of the initiation of ART in patients with cryptococcal meningitis is still uncertain. Early initiation of ART is recommended for all OIs except for intracranial OIs such as TB meningitis and cryptococcal meningitis. In cryptococcal meningitis ART can be initiated 2-4 weeks after initiation of antifungal therapy with amphotericin B based regimens. In patients who are predominately treated with fluconazole monotherapy, ART should be initiated at least 4 weeks after initiation of antifungal therapy.

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


10.1 Introduction

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

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

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

10.2 Indications for PrEP

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

- HIV negative and sexual partner with HIV who has not been on effective therapy for the preceding 6 months OR
- HIV negative and sexually active in a high HIV prevalence population AND any of the following:
  - Vaginal or anal intercourse without condoms with more than one partner; OR
  - A sexual partner with one or more HIV risk factors; OR
  - A history of an STI by lab testing or self-report or syndromic STI treatment; OR
  - Any use of post-exposure prophylaxis (PEP); OR
  - Requesting PrEP

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

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

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


10.3 Contraindications for PrEP

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

10.4 Ruling out current HIV infection when starting PrEP

Before starting PrEP:
- Conduct a rapid HIV test to rule out existing HIV infection preferably on the same day that PrEP is being started.
- Take a complete history and full physical examination to rule out any signs or symptoms of an acute viral syndrome, including a flu-like illness, then consider the possibility that acute HIV infection could be the cause. In such circumstances testing for HIV RNA or antigen is helpful, if such tests are available. Alternatively, PrEP can be deferred for 4 weeks and the person tested again. This allows time for possible seroconversion to be detected.
- Blood creatinine should be measured before starting PrEP and at every 6 months after PrEP where available. Blood creatinine is mandatory in people with comorbid conditions that can affect renal function, such as diabetes mellitus and uncontrolled hypertension.

Who should administer PrEP

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

10.5 Medicines Recommended for Oral PrEP

<table>
<thead>
<tr>
<th>Preferred Regimen</th>
<th>Drug</th>
<th>Dosage</th>
<th>Duration</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Tenofovir (TDF (300mg) plus Emtricitabine (FTC) (200mg))</td>
<td>Fixed dose combination one tablet once a day</td>
<td>Period of substantial risk</td>
</tr>
</tbody>
</table>

| Alternative Regimens | TDF (300mg) plus 3TC (300mg) | Fixed dose combination one tablet once a day | Period of substantive risk |
PrEP is safe, with no side-effects for 90% of users. However, about 10% of people who start PrEP will have some short-term mild side-effects. These may include gastrointestinal symptoms (diarrhoea, nausea, decreased appetite, abdominal cramping, or flatulence). Dizziness or headaches have also been experienced. Such side-effects are usually mild and resolve without stopping PrEP. Typically, these symptoms start in the first few days or weeks of PrEP use and last a few days and almost always less than 1 month.

Providers may dispense a one-month supply at the first visit and then a 3 to 4 month supply at subsequent visits. Providers trained to provide ART can also provide PrEP.
## 10.6 Procedures when PrEP is started (first visit)

<table>
<thead>
<tr>
<th>Investigation/intervention</th>
<th>Rationale</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Mandatory</strong></td>
<td></td>
</tr>
<tr>
<td>HIV test</td>
<td>Assessment of HIV infection status</td>
</tr>
<tr>
<td></td>
<td>Symptom checklist for possible acute HIV infection</td>
</tr>
<tr>
<td>Brief counselling</td>
<td>To assess whether the client is at substantial risk for HIV</td>
</tr>
<tr>
<td></td>
<td>To discuss prevention needs and provide condoms and lubricants</td>
</tr>
<tr>
<td></td>
<td>To discuss desire for PrEP and willingness to take PrEP</td>
</tr>
<tr>
<td></td>
<td>To develop a plan for effective PrEP use, sexual and reproductive health</td>
</tr>
<tr>
<td></td>
<td>Assess fertility intentions and offer contraception or safer conception counselling.</td>
</tr>
<tr>
<td></td>
<td>Assess intimate partner violence and gender based violence</td>
</tr>
<tr>
<td></td>
<td>Assess substance use and mental health issues</td>
</tr>
<tr>
<td>Other STI screening</td>
<td>To diagnose and treat STI</td>
</tr>
</tbody>
</table>

### Where available

<table>
<thead>
<tr>
<th>Investigation</th>
<th>Rationale</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pregnancy testing</td>
<td>To guide antenatal care, contraceptive and safer conception counselling, and to assess risk of maternal to child transmission.</td>
</tr>
<tr>
<td></td>
<td>Pregnancy is not a contraindication for PrEP use.</td>
</tr>
<tr>
<td>Serum creatinine</td>
<td>To identify pre-existing estimated creatinine clearance less than 60 ml/min.</td>
</tr>
<tr>
<td>Hepatitis B surface antigen (HBsAg)</td>
<td>To identify undiagnosed current hepatitis B (HBV) infection.</td>
</tr>
<tr>
<td>Hepatitis B surface antibody</td>
<td>If negative, consider vaccination against hepatitis B.</td>
</tr>
<tr>
<td>Hepatitis C antibody</td>
<td>If positive, consider HCV treatment.</td>
</tr>
<tr>
<td>Rapid Syphilis Test</td>
<td>To diagnose and treat syphilis infection</td>
</tr>
</tbody>
</table>

## 10.7 PrEP Follow Up and Monitoring

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

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

#### 10.8 When to discontinue PrEP

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

\[
\text{Estimated Cr Clearance} = \text{Sex} \times (((140 - \text{Age}) / (\text{SerumCreat})) \times (\text{Weight} / 72))
\]

**Notes:**
- Sex : use 1 if male, 0.85 if female
- Age in years
- Serum creatinine in mg/dL
- Weight in kilograms (should be lean body weight)
10.9 Practical screening questions

These questions are provided to make the screening of potential PrEP users easy and should be not used to ration or exclude people from accessing PrEP. People who ask for PrEP are likely to have made this choice based on a careful assessment of their own personal circumstances, risk and desire for additional HIV prevention and should not be excluded on the basis of these questions. Screening questions can also be used to introduce the consideration and offer of PrEP to people who are attending services but had not presented specifically to access PrEP.

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

General screening questions

In the past 6 months,
• Have you had sex with more than one person?
• Have you had sex without a condom?
• Have you had sex with anyone whose HIV status you do not know?
• Are any of your partners at risk of HIV?
• Do you have sex with a person who has HIV?
• Have you received a new diagnosis of a sexually transmitted infection?
• Do you desire pregnancy?
• Have you used or wanted to use PEP or PrEP for sexual exposure to HIV?

Additional factors to ask about:

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

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

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

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

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

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

• The partner with HIV has been taking ART for less than 6 months. ART may take up to 6 months to suppress viral load; in studies of sero-discordant couples, PrEP has provided a useful bridge to full viral suppression during this time.
• The uninfected partner has doubt about the effectiveness of the partner’s treatment or has other partners besides the HIV-positive partner on treatment.
• There have been gaps in the partner’s treatment adherence or the couple is not communicating openly about treatment
adherence and viral load test results.

- In addition, any sign of intimate partner violence, controlling behaviour, or anger or fear in response to questions about HIV treatment should prompt discussion about PrEP as a way to control risk for HIV.

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

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

Any “no” answer to any of the above questions including a desire for pregnancy with HIV positive partner may indicate increased risk for HIV infection.
In people who have been exposed to HIV through needle-stick inoculation or through contamination of mucous membranes by secretions, it has been shown that administration of ARVs within 72 hours of exposure reduces the likelihood of HIV infection being transmitted. There are also similar benefits of reduction of HIV transmission by the use of PEP within 72 hours for those who have been sexually assaulted (rape, intimate partner violence or sexual abuse) or had a high risk unprotected sexual encounter. In these situations, ART needs to be continued for one month. The following guidelines should be followed in the event of accidental occupational exposure to material (i.e., blood, secretions, excretions) that may contain HIV, and also after sexual assault or high risk sexual encounter. Occupational exposure to potentially infectious material may occur through an injury with a sharp object that has been used on a patient or through the contamination of mucous surfaces with patients’ blood or secretions.

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

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

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

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

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

### 11.1 Prevention of occupational exposure in health facilities

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

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

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

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

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

11.2 Procedure to be followed in the event of injury with a sharp object

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

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

8. In the event of HIV infection exposure to the HCW, the greatest risk of transmission to other individuals is in the first six weeks. The exposed Health Care Worker should be instructed to use measures to reduce the potential risk of HIV transmission to others, e.g. condom use, abstinence and refraining from blood transfusion until the 6 month serologic test is negative.

9. Healthcare workers who are breastfeeding should consider discontinuing breastfeeding following exposure to HIV. This avoids infant exposure to ARVs and HIV in breast milk should the mother be infected.

10. Post-exposure prophylaxis with hepatitis B immune globulin (HBIG) and/or hepatitis B vaccination series should be considered for occupational exposure (within 24 hours) after evaluating the hepatitis B status of the source patient and the vaccination status of the exposed person. Hepatitis B vaccine and HBIG can be given at the same time but using different injection sites. Routine pre-exposure hepatitis B vaccination should be offered to all health-care workers. Ideally the Hepatitis C status of the source patient should be ascertained.

11.3 Post-exposure prophylaxis after sexual assault (rape or sexual abuse) or high risk sexual encounter.

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

11.4 ARVs to be used in post-exposure prophylaxis

Immediately after exposure, all exposed adult adolescent individuals should take the following:
- Tenofovir 300 mg orally once daily plus
- Lamivudine 300 mg orally once daily
- Atazanavir (300mg)/ ritonavir 100mg orally once daily

The above regimen is given for one month.

The dosage for children is as follows:

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

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

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

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

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

11.5 Toxicity Monitoring

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

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

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

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

**HBV Testing**

There is concern about the potential risk of hepatic flares among people with chronic HBV once TDF-, 3TC- or FTC-based PEP is stopped. Assessment of HBV infection status should not be a precondition for offering TDF-, 3TC- or FTC-based PEP, but people with established chronic HBV infection should be monitored for hepatic flare after PEP discontinuation. Among people with unknown HBV status and where HBV testing is readily available, people started on TDF-, 3TC- or FTC-based PEP should be tested for HBV to detect active HBV infection and the need for on-going HBV therapy after discontinuing PEP.

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

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

### 11.6 Access to PEP

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

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

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

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

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

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

### 11.7 Psycho-social support

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

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

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

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

12.1.2 Who Should Report

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

12.1.3 When to Report Suspected ADRs and ADR reporting tools

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

ADRs to be reported to the MCAZ

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

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

The following steps should be followed when reporting ADRs:

**Step 1: Obtain Patient History and Do a Proper Examination**

- Take a full medicine and medical history
- Conduct physical examination as some medicines produce distinctive physical signs.
- Establish time relationships i.e. the time from the start of therapy to the time of onset of the suspected reaction.
- Determine if there are other possible causes for the new symptoms (e.g. patient’s underlying disease, other medicine/s, over-the-counter medicines or complementary medicines; toxins or foods) and conduct further investigations e.g. FBC, ALT, U & E. Laboratory tests are especially important if the medicine is considered essential in improving patient care or if the lab test results will improve management of the patient.
- Describe the reaction as clearly as possible and, where possible provide, an accurate diagnosis

**Step 2: Check the Known Pharmacology of the Medicine.**

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

**Step 3: Management of the ADRs**

Manage the patient based on the findings and the guidance in table XXX (Table on adverse chapter XXX)

In addition, consider Dechallenge and Rechallenge.

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

Example see Cotrimoxazole desensitization Appendix XXX

### 12.1.4 Components of a Complete Case Report

Complete case reports include the following elements:

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

12.1.5 How to minimize occurrence of ADRs

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

• Use few medicines, whenever possible
• Use medicines that you know well
• Do not change therapy from known medicines to unfamiliar one without good reasons.
• Use text books and other reference material providing information on medicine reactions and interactions.
• Take extra care when you prescribe medicines known to exhibit a large variety of interactions and adverse reactions (anticoagulants, hypoglycemic, and drug affecting the CNS) with careful monitoring of patients with such reactions.
• Beware of the interaction of medicines with certain food stuffs, alcohol and even with house hold chemicals.
• Review all the medicines being used by your patients regularly, taking special notice with those bought without prescription (over the counter, complementary).
• Be particularly careful when prescribing to children, the elderly, pregnant and nursing women, the seriously ill and patients with hepatic and renal diseases. Careful ongoing monitoring is also essential in these patients. If the patient shows signs and/or symptoms not clearly explained by the course of their illness, think of adverse drug reaction. If you suspect an adverse reaction, consider stopping the medicine or reduce the dosage as soon possible and please report the adverse drug reaction to the Medicines Control Authority of Zimbabwe.

12.1.6 Follow-Up

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

12.1.7 Feedback to Reporters

The pharmacovigilance centre (MCAZ) will provide feedback to anyone who reports an ADR. Further feedback information will be provided to the reporter after causality assessment by the MCAZ PVCT Committee.
Benefits of reporting to the health worker and the patient;

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

Protection of Health worker who reports an ADR

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

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

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


<table>
<thead>
<tr>
<th>Primary HIV Infection</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Asymptomatic</td>
</tr>
<tr>
<td>• Acute retroviral syndrome</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Clinical Stage 1</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Asymptomatic</td>
</tr>
<tr>
<td>• Persistent generalized lymphadenopathy</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Clinical Stage 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Unexplained persistent hepatosplenomegaly</td>
</tr>
<tr>
<td>• Papular pruritic eruptions</td>
</tr>
<tr>
<td>• Extensive wart virus infection</td>
</tr>
<tr>
<td>• Extensive molluscum contagiosum</td>
</tr>
<tr>
<td>• Recurrent oral ulcerations</td>
</tr>
<tr>
<td>• Unexplained persistent parotid enlargement</td>
</tr>
<tr>
<td>• Lineal gingival erythema</td>
</tr>
<tr>
<td>• Herpes zoster</td>
</tr>
<tr>
<td>• Recurrent or chronic upper respiratory tract infections (otitis media, otorrhoea, sinusitis, tonsillitis)</td>
</tr>
<tr>
<td>• Fungal nail infections</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Clinical Stage 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Moderate unexplained malnutrition not adequately responding to standard therapy</td>
</tr>
<tr>
<td>• Unexplained persistent diarrhoea (14 days or more)</td>
</tr>
<tr>
<td>• Unexplained persistent fever (above 37.5°C intermittent or constant, for longer than 1 month)</td>
</tr>
<tr>
<td>• Persistent oral candida (outside first 6 to 8 weeks of life)</td>
</tr>
<tr>
<td>• Oral hairy leukoplakia</td>
</tr>
<tr>
<td>• Acute necrotizing ulcerative gingivitis/periodontitis</td>
</tr>
<tr>
<td>• Lymph node TB</td>
</tr>
<tr>
<td>• Pulmonary TB</td>
</tr>
<tr>
<td>• Severe recurrent presumed bacterial pneumonia</td>
</tr>
</tbody>
</table>

| • Symptomatic lymphoid interstitial pneumonitis |
| • Chronic HIV-associated lung disease, including bronchiectasis |
| • Unexplained anaemia (< 8 g/dL), neutropenia (< 500/mm3), or chronic thrombocytopenia (< 50,000/mm3) |
| • HIV-associated cardiomyopathy or HIV-associated nephropathy |
### Clinical Stage 4

- HIV wasting syndrome
- Pneumocystis pneumonia
- Recurrent severe bacterial pneumonia
- Chronic herpes simplex infection (orolabial, genital, or anorectal of more than 1 month’s duration) or visceral at any site
- Oesophageal candidiasis (or candidiasis of trachea, bronchi, or lungs)
- Extrapulmonary TB
- Kaposi’s sarcoma
- Central nervous system toxoplasmosis
- HIV encephalopathy
- Extrapulmonary cryptococcosis, including meningitis
- Disseminated nontuberculous mycobacteria infection
- Progressive multifocal leukoencephalopathy
- Chronic cryptosporidiosis
- Chronic isosporiasis
- Cytomegalovirus (CMV) infection (retinitis, or CMV infection of other organs)
- Disseminated mycosis (e.g., extrapulmonary histoplasmosis, coccidiomycosis)
- Recurrent septicaemia (including nontyphoidal salmonella)
- Lymphoma (cerebral or B-cell non-Hodgkin’s)
- Invasive cervical carcinoma
- Atypical disseminated leishmaniasis
- Symptomatic HIV-associated nephropathy or HIV-associated cardiomyopathy
### APPENDIX: Grades of Adverse Events

<table>
<thead>
<tr>
<th>Grade Level</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Grade 1 (Mild)</td>
<td>Transient or mild discomfort; no limitation in activity; no medical intervention/therapy required</td>
</tr>
<tr>
<td>Grade 2 (Moderate)</td>
<td>Mild to moderate limitation in activity; some assistance may be needed; no or minimal medical intervention/therapy required</td>
</tr>
<tr>
<td>Grade 3 (Severe)</td>
<td>Marked limitation in activity; some assistance usually required; medical intervention/therapy required; hospitalization possible</td>
</tr>
<tr>
<td>Grade 4 (Life-threatening)</td>
<td>Extreme limitation in activity; significant assistance required; significant medical intervention/therapy required; hospitalization or hospice care probable</td>
</tr>
</tbody>
</table>
APPENDIX: Rapid Cotrimoxazole Desensitization Protocol


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

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

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

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

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

<table>
<thead>
<tr>
<th>Minutes</th>
<th>Quantity of Above Mixture Given Orally</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>1 ml (use 10 ml syringe)</td>
</tr>
<tr>
<td>30</td>
<td>10 ml (use 10 ml syringe)</td>
</tr>
<tr>
<td>60</td>
<td>100 ml (use 10 ml syringe)</td>
</tr>
<tr>
<td>90</td>
<td>0.5 ml</td>
</tr>
<tr>
<td>120</td>
<td>5 ml</td>
</tr>
<tr>
<td>150</td>
<td>480 mg tablet</td>
</tr>
<tr>
<td>180</td>
<td>Start full prophylactic or therapeutic dose.</td>
</tr>
</tbody>
</table>
Avoid giving the following medicines together:

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

<table>
<thead>
<tr>
<th>Age Range</th>
<th>Red Flags</th>
</tr>
</thead>
</table>
| Birth to 3 months | • Failure to alert to environmental stimuli  
                     • Rolling over before 2 months (hypertonia)  
                     • Persistent fisting at 3 months            |
| 4 to 6 months   | • Poor head control  
                     • Failure to smile  
                     • Failure to reach for objects by 5 months   |
| 6 to 12 months  | • No baby sounds or babbling  
                     • Inability to localise sounds by 10 months |
| 12 to 24 months | • Lack of consonant production  
                     • Hand dominance prior to 18 months (contralateral weakness)  
                     • No imitation of speech and activities by 16 months |
| Any age         | • Loss of previously attained milestones                                  |
APPENDIX: Six Gross Motor Milestones

Windows of achievement for six gross motor milestones

APPENDIX: **ARVs Paediatric Dosing Chart**

Note: Higher doses of Lop/r may be required when co-administered with enzyme-inducing medicines such as NVP, EFV; n/r = not recommended.
(Note: Pediatric Dosing Chart on preceding page was adapted from: International Center for AIDS Care and Treatment Programs, Global AIDS Program, Baylor International Pediatric AIDS Initiative, Pediatric Antiretroviral Dosing in Resource-Limited Settings, Updated November 2006. Available at: http://www.cdc.gov/globalAIDS/pa_pmtct_pediatric.htm.)
APPENDIX: Early Infant Diagnosis Algorithm

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

- a POC NAT to provide testing closer to the point of care can be used.
- bStart ART, without delay. At the same time, retest to confirm infection.
- cThe risk of HIV transmission remains as long as breastfeeding continues.
## APPENDIX: Spontaneous Adverse Drug Reaction Report Form

**Medicines Control Authority of Zimbabwe**

### Spontaneous Adverse Drug Reaction Report (ADR) Form

<table>
<thead>
<tr>
<th>MCAZ Reference Number (MCAZ use only)</th>
<th></th>
</tr>
</thead>
</table>

**Patient Details (to allow linkage with other reports)**

<table>
<thead>
<tr>
<th>Clinic/hospital Name:</th>
<th>Clinic/Hospital Number</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient Initials:</td>
<td>VCT/OITB Number</td>
</tr>
<tr>
<td>Date of Birth:</td>
<td>Weight (Kg)</td>
</tr>
<tr>
<td>Age:</td>
<td>Sex:</td>
</tr>
<tr>
<td>Height (meters):</td>
<td></td>
</tr>
</tbody>
</table>

### Adverse Reaction

<table>
<thead>
<tr>
<th>Date of Onset:</th>
<th>Duration:</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Less than one hour</td>
</tr>
</tbody>
</table>

**Description of ADR and/or therapeutic failure or lack of effectiveness**

<table>
<thead>
<tr>
<th>Serious:</th>
<th>Yes □</th>
<th>No □</th>
</tr>
</thead>
</table>

**Reason for Seriousness**

<table>
<thead>
<tr>
<th>□ Death</th>
<th>□ Life-threatening</th>
</tr>
</thead>
<tbody>
<tr>
<td>□ Hospitalization/prolonged</td>
<td>□ Disabling</td>
</tr>
<tr>
<td>□ Congenital-anomaly</td>
<td>□ Other medically important condition</td>
</tr>
</tbody>
</table>

### Relevant Medical History

#### Relevant Past Drug Therapy

#### Outcome of ADR

<table>
<thead>
<tr>
<th>Recovered</th>
<th>Not yet recovered</th>
<th>Fatal</th>
<th>Unknown</th>
</tr>
</thead>
</table>

### Current Medication

<table>
<thead>
<tr>
<th>Generic Name</th>
<th>Brand Name</th>
<th>Batch Number</th>
<th>Dose</th>
<th>Indication</th>
<th>Date Started</th>
<th>Date Stopped</th>
</tr>
</thead>
</table>

#### Concomitant (Other) drugs taken & Dates/period taken:

<table>
<thead>
<tr>
<th>Name of drug:</th>
<th>Dated started</th>
<th>Date stopped</th>
</tr>
</thead>
</table>

#### Suspected drug(s), if known:

#### Laboratory tests results:

**Reported by**

<table>
<thead>
<tr>
<th>Forename(s) &amp; Surname:</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Designation:</td>
<td></td>
</tr>
<tr>
<td>Address:</td>
<td></td>
</tr>
<tr>
<td>Signature:</td>
<td>Date:</td>
</tr>
</tbody>
</table>

**Send to:** The Director-General, Medicines Control Authority of Zimbabwe

106 Baines Avenue, P O Box 10559, Harare

**Tel:** +263-4-708255 or 792165, **E-mail:** mcaz@mcaz.co.zw, **website:** www.mcaz.co.zw

**NB.** This form may be completed for any ADR related to medicines or medical devices
APPENDIX: Medicinal/Pharmaceutical Product Defect Form

Medicines Control Authority of Zimbabwe

PHARMACOVIGILANCE AND CLINICAL TRIALS DIVISION

REPORT ON MEDICINAL (PHARMACEUTICAL) PRODUCT DEFECT OR PROBLEM

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

<table>
<thead>
<tr>
<th>1. Product Name (Brand and Generic)</th>
</tr>
</thead>
<tbody>
<tr>
<td>6. Batch Number</td>
</tr>
<tr>
<td>8. Name and Address of Manufacturer</td>
</tr>
<tr>
<td>9. Name and Title of Reporter</td>
</tr>
<tr>
<td>10. Your Practice Location and Address of Hospital, Clinic, Retail Surgery etc.</td>
</tr>
<tr>
<td>11. Phone Number</td>
</tr>
<tr>
<td>13. If requested will the actual product involved be available for examination by MCAZ.</td>
</tr>
<tr>
<td>14. Signature of Reporter</td>
</tr>
<tr>
<td>16. Defects/Problem Noted or Suspected (see a-j below)</td>
</tr>
</tbody>
</table>

NATURE OF DEFECT OR PROBLEM

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

Return To: The Director-General
Medicines Control Authority of Zimbabwe
106 Baines Avenue
P O Box 10559
Harare
Tel: +263-4-736081/234/45, 708255 or 792165
Email: mcaz@mcaz.co.zw

For Office Use Only
Report Number:
Date Received:

Rev 2_March 2015
APPENDIX: Medication Error Form

Medicines Control Authority of Zimbabwe

PHARMA COVIGILANCE AND CLINICAL TRIALS DIVISION

MEDICATION ERROR FORM

<table>
<thead>
<tr>
<th>Date of event:</th>
<th>Type of Facility:</th>
<th>Location of event:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Times of event:</td>
<td>Govt / Private</td>
<td>Ward</td>
</tr>
<tr>
<td></td>
<td>Hospital Pharmacy</td>
<td>Casualty</td>
</tr>
<tr>
<td></td>
<td>Clinic Others</td>
<td>Clinic</td>
</tr>
</tbody>
</table>

Please describe the error: description/sequence of events and medical/nursing care or management done:

Immediate action or intervention done:

Corrective action taken on the error:

Did the error reach the patient? Yes No

Was the incorrect medication, dose or dosage form administered to or taken by the patient? Yes No

Describe the direct result on the patient (e.g., death, type of harm, additional patient monitoring):

**ERROR OUTCOME CATEGORY (SELECT ONE)**

- NO ERROR
- ERROR, NO HARM
- ERROR, HARM
- ERROR, DEATH

**INDICATE THE POSSIBLE ERROR CAUSE(S) AND CONTRIBUTING FACTORS**

Inexperienced personnel
Wrong dose administered
Medication administration record not accurately documented
Failure to adhere to work procedures

Which category made the error?

Doctor
Pharmacy
Nurse
Pharmacist Assist.
Clinical Officer
Others (specify):

Which category detected the error or recognized the potential error?

Doctor
Pharmacy
Nurse
Pharmacist Assist.
Clinical Officer
Others (specify):

If available, please provide patient’s particulars—no patient identifiers are needed

<table>
<thead>
<tr>
<th>Age</th>
<th>Gender</th>
<th>Product description</th>
<th>Intended product</th>
<th>Product administered in error</th>
</tr>
</thead>
</table>

<table>
<thead>
<tr>
<th>Medication brand</th>
</tr>
</thead>
</table>

<table>
<thead>
<tr>
<th>Generic name</th>
</tr>
</thead>
</table>

<table>
<thead>
<tr>
<th>Dose, frequency, duration, route</th>
</tr>
</thead>
</table>

<table>
<thead>
<tr>
<th>Manufacturer</th>
</tr>
</thead>
</table>

<table>
<thead>
<tr>
<th>Dosage form</th>
</tr>
</thead>
</table>

<table>
<thead>
<tr>
<th>Strength</th>
</tr>
</thead>
</table>

<table>
<thead>
<tr>
<th>Type and size of container</th>
</tr>
</thead>
</table>

Reported by

<table>
<thead>
<tr>
<th>Name</th>
</tr>
</thead>
<tbody>
<tr>
<td>Address</td>
</tr>
</tbody>
</table>

| Designation: |
| Email address: |

| Contact number: |
| Signature: |
| Date: |

Rev 0 July 2016