Republic of Namibia

Ministry of Health and Social Services
Directorate of Special Programmes

National Guidelines for Antiretroviral Therapy
Fifth Edition 2016

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FOREWORD

Namibia has a generalized HIV epidemic, with HIV primarily being transmitted through heterosexual transmission. The first case of HIV was reported in 1986 and since then the prevalence has continued to rise and reached a peak in 2002. To date, it is estimated that about 220,000 Namibians are living with HIV. The HIV burden is much higher among pregnant women with prevalence rate of 16.9%. The Government of Namibia is committed to progressively provide access, on a sustained and equal basis, to affordable, quality and effective antiretroviral therapy and prophylaxis for the prevention of opportunistic infections, to all persons who are in need as stipulated in the National HIV policy of 2007.

Therefore, the Ministry of Health and Social Services (MoHSS) has established a strategy to ensure that treatment guidelines are continuously updated and brought in line with the latest WHO guidelines which will ensure quality of treatment, care and support for people living with HIV. The perpetual search for more efficient, safe and easy to administer treatment regimens for both adult and children will greatly contribute to the achievement of an AIDS free generation in Namibia.

In 2015 the Joint United Nations Program on HIV and AIDS (UNAIDS) developed the 90-90-90 targets to be achieved by 2020 with the aim of ending AIDS epidemic globally by 2030. Namibia is committed and is strongly focused on attaining the UNAIDS aspirational goals by 2020. For the country to end the HIV epidemic, we need to test 90% of all the people who are estimated to be HIV positive and let them know their status, provide antiretroviral therapy (ART) to 90% of all those who test HIV positive and retain them on treatment so that 90% of all those on treatment get their viral load suppressed by 2020.

As part of the overall Prevention Package of HIV transmission, the Ministry of Health and Social Services has been providing ART in Namibia's public health facilities. I urge other partners such as those dealing with Orphans and Vulnerable Children, the Network of People Living with HIV, non-governmental organizations, community-based organizations, other line Ministries, and the private sector to continue giving support to communities and individuals that have been affected by this disease.

The Ministry will continue to revise, update and formulate other editions of these guidelines as more information and scientific evidence become available. The Ministry acknowledges the collaboration and support that has been received from our development partners and all our stakeholders.

Dr. Bernard Haufiku,

Minister, MP

PREFACE

The National Policy on HIV/AIDS 2007 and the National Strategic Framework for HIV and AIDS emphasise the need to offer continuum of HIV care to people living with HIV and their families, which is a comprehensive package of HIV prevention, diagnosis, treatment, and care and support services. In 2003, government introduced provision of free Anti-retroviral therapy (ART) and Prevention of Mother to Child Transmission (PMTCT) to the public. To date, 93% of patients that have been enrolled into the ART program and they are living healthy, normal productive lives thus contributing to the economy of the country.

In order to provide quality of care to the Namibian people living with HIV, The Ministry of Health and Social Services (MoHSS), has been for the past 13 years updating the ART guidelines and this is the 5th edition. Since the introduction of the 4th Edition of the Namibian guidelines, several significant developments have occurred in the HIV field and in June 2016, World Health Organization (WHO) has released new guidelines. The MoHSS has therefore revised the ART guidelines to include new scientific evidence and to conform to the latest WHO guidance. The Fifth Edition of the National Guidelines addresses clinical, operational and programmatic aspects of using ARV medicines for HIV treatment as well as for prevention.

Major changes in these guidelines include the following:

- An expansion in the eligibility criteria by treating all people living with HIV regardless of their clinical and immunological status.
- Guidance on the management of Pre-exposure Prophylaxis (PrEP) for people with a substantial high risk of contracting HIV.
- Special emphasis is put on the use of fixed dose triple-ARV combination as first line for adults and adolescents and routine viral load monitoring as the preferred method of monitoring HIV treatment response.
- Differentiated Care chapter which includes Community ART Delivery models has been added as a measure to promote 'patient centred' care considering the different needs of PLHIV.

The Ministry would like to acknowledge all the participants in the revision of these guidelines. Special appreciations go to our Development Partners such as President's Emergency Plan for AIDS Relief (PEPFAR), Joint United Nations Program on HIV and AIDS (UNAIDS), Line Ministries, Nongovernmental Organizations, PLWH and all other stakeholders. I encourage and urge health care professionals and all community health care workers to familiarise themselves with these guidelines in order to provide quality care to our people.

PERMANENT SECRETARY
06 DEC 2016
REPUBLIC OF NAMIBIA
MINISTRY OF HEALTH AND SOCIAL SERVICES

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Dr. Andreas Mwoombola

Permanent Secretary

LIST OF ABBREVIATIONS

3TC	Lamivudine
ABC	Abacavir
AIDS	Aquired Immune Deficiency Syndrome
ALT	Alanine aminotransferase
ANC	Ante natal care
ART	Anti retroviral therapy
ARV	Antiretroviral
AST	Aspartate aminotransferase
ATV	Atazanavir
AZT	Zidovudine
BD	Twice Per Day
BMI	Body Mass Index
CD4	Cluster of Differentiation 4
CVR	Cenicriviroc
CMV	Cytomegalovirus
CPT	Cotrimoxazole Preventive Therapy
CrAg	Cryptococcal Antigen
CrCl	Creatinine Clearance
CSF	Cerebrospinal Fluid
CXR	Chest X-Ray
d4T	Stavudine
ddC	Zalcitabine
Ddl	Didanosine
DNA	Deoxyribonucleic acid
DTG	Dolutegravir
DVT	Deep Vein Thrombosis
EFV	Efavirenz
ELISA	Enzyme-linked immunosorbent assay
ENF	Enfurvitide
ETR	Etravirine
ePMS	Electronic Patient Monitoring System
eMTCT	Elimination of Mother-to-Child Transmission
EVG	Elvitegravir
FBC	Full Blood Count
FTC	Emtricitabine
GMP	Growth Monitoring and promotion
Hb	Haemoglobin
HBsAg	Hepatitis B surface antigen
HBV	Hepatitis B Virus
HCWs	Health Care Workers
HIV	Human Immunodeficiency Virus
HPV	Human Papilloma Virus
ICU	Intensive Care Unit
IDV	Indinavir
IM	Intramuscular

H	Isoniazid (INH)
IPT	Isoniazid Preventive Therapy
INSTI	Integrase Strand Transfer Inhibitor (Integrase Inhibitor)
IRIS	Immune Reconstitution Inflammatory Syndrome
IUCD	Intra Uterine Contraceptive device
IV	Intra venous
IVI	Intra venous injection
LFT	Liver function test
LPV/r	Lopinavir boosted with ritonavir
LPV/RTV	Equal doses of LPV and RTV
M	Months
MAC	Mycobacterium avium complex
MOTT	Mycobacterium other than tuberculoses
MUAC	Middle Upper Arm Circumference
MVC	Maraviroc
NAT	Nucleic Acid Test
NEMLIST	Namibia Essential Medicine List
NIP	Namibia Institute of Pathology
NVP	Nevirapine
NRTI	Nucleoside reverse transcriptase inhibitor
NNRTI	Non-Nucleoside reverse transcriptase inhibitor
OD or od	Once daily
Ols	Opportunistic infections
PCP	Pneumocystis jiroveci (carinii) pneumonia
PCR	Polymerase chain reaction
PI	Protease Inhibitor
PMTCT	Prevention of Mother-to-Child Transmission
PLHIV	People living with HIV
PML	Progressive multifocal leukoencephalopathy
PO	Per os (by mouth)
RAL	Raltegravir
RNA	Ribonucleic acid
RTV	Ritonavir
SJS	Steven Johnson's Sydrome
SMZ	Sulfamethoxazole
STAT	Immediately
STIs	Sexually Transmitted Infections
sdNVP	single dose Nevirapine
TAF	Tenofovir Alefenamide Fumerate
TB	Tuberculosis
TDF	Tenofovir Disoproxyl Fumerate
TDS or tds	Three times per day
TEN	Toxic epidermal-necrolysis
TMP	Trimethoprim
ULN	Upper limit of normal
VL	(HIV) Viral Load
VZV	Varicella zoster virus
WBC	White Blood Count

WHO	World Health Organization
W	Weeks
XTC	Either 3TC (lamivudine) or FTC (Emtricitibine)

TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

EXECUTIVE SUMMARY

	INTRODUCTION
Background	The Fifth Edition of the National Guidelines for Antiretroviral Therapy include the most recent scientific evidence and best practices as well as guidance from WHO. The standardized guidelines address clinical, operational and programmatic aspects of using ARV medicines for HIV treatment as well as for prevention. Some of the major operational areas are: adherence to ART; retention in care; human resources, models of differentiated care which include patient-centred care and integrating ART with TB treatment, antenatal care and maternal and child programs; laboratory services and medicine supply.
Intended Users	Treatment guidelines are intended for use by national HIV program managers, clinicians and other health service providers in both public and private sectors, managers of laboratory services, people living with HIV and community based organisations, national HIV treatment and prevention advisory bodies as well as international and bilateral agencies that provide financial and technical support.
Chapter 1: ANTIRETROVIRAL THERAPY FOR ADULTS	
Re-testing for HIV prior to ART Initiation	All newly diagnosed HIV positive patients should be re-tested for HIV to verify their HIV positive status prior to enrolment for treatment.
When to start antiretroviral therapy in adults	All HIV positive adults irrespective of CD4 counts, WHO stage are eligible to start ART (Treat All). Patients should be initiated on ART immediately when they are ready, either on the same day or as soon as possible within one week.
First-line ART for adults **(including adolescents ≥ 10 years old and weigh at least 35 kg), pregnant and breastfeeding women, adults with TB disease and adults with HBV coinfection**	Preferred: TDF + FTC (or 3TC) + EFV (once daily FDC) Alternate: ABC + 3TC + EFV (or NVP) AZT + 3TC + EFV AZT + 3TC + NVP TDF + FTC (or 3TC) + NVP
Second-line ART for adults **(including adolescents ≥ 10 years old and weigh at least 35 kg), pregnant and breastfeeding women, adults with TB disease**	Preferred: AZT/TDF/3TC/ATV-r (Where standard first line regimens were used) Alternative: AZT /TDF/3TC/LPV-r AZT/TDF/3TC/LPV/RTV (HIV/TB co-infection)
Third line ART for adults and adolescents	All patients failing second line regimens should undergo HIV resistance testing following consultation with an HIV specialist in order to select the most effective regimen.
Viral load monitoring	Routine viral load (VL) monitoring is recommended to facilitate earlier detection of treatment failure. All patients initiating therapy will routinely have a viral load assay done at 6 and 12 months after beginning therapy and every 12 months thereafter (every 6 months for children/adolescents ≤19 years). VL assays are also recommended for patients already on treatment who are showing evidence of immunologic and or clinical failure. Facilities which have very limited access to transportation of laboratory specimens and cannot ensure that blood specimens will reach NIP within 6 hours should contact the nearest NIP lab and make arrangments to facilitate this. Noting that the plasma VL is still the "gold standard" and should be done wherever possible, another alternative is now available: collecting dried blood spots. Clinicians should be aware that the result has a level of detection of 1000 copies/ml, and hence will be useful to determine if a patient is

	failing treatment, but not to determine if the patient is fully virologically suppressed.
TB screening and IPT	All PLHIV should be screened for TB including asking about TB exposure/contact history at each encounter with a health worker or visit to a health facility. TB-IPT is very effective in preventing TB disease in individuals who have latent TB infection. **To be eligible for TB-IPT the HIV-positive individual must:** • Have no symptoms or signs of TB – such as cough, fever, weight loss, night sweats, fatigue, blood in sputum, chest pain, diarrhoea, shortness of breath, enlarged lymph nodes, loss of appetite (*NB: TB-IPT should not be given to patients who are unwell and where there is no explanation of the illness*) • No current history of alcohol misuse • Have no history of active liver disease, liver insufficiency, or jaundice • Have no history of hypersensitivity to isoniazid • Have no history of exfoliative dermatitis • Be motivated for TB-IPT after being educated about the benefits, possible side-effects and risks.
Use of Xpert MTB/RIF	Xpert MTB/RIF should be used rather than conventional microscopy, culture, and drug susceptibility testing as the initial diagnostic test in adults and children suspected of having HIV-associated TB
Urine dipsticks no longer recommended for monitoring TDF renal toxicity	A systematic review found no evidence in the use of uring dipsticks for estimating renal toxicity in patients with HIV on TDF in the absence of laboratory capacity. Therefore, urine dipsticks is no longer used for monitoring TDF-associated renal toxicity
Chapter 2: PREVENTION OF MOTHER TO CHILD TRANSMISSION OF HIV	
Background	The goal of ART for HIV positive pregnant women is three-fold: to restore and maintain the mother's immune function and therefore general health; secondly, to prevent transmission of HIV during pregnancy, labour, delivery and during breastfeeding; Thirdly resulting reduction in VL reduces the risk of HIV transmission/re-infection
Retesting of HIV negative women during pregnancy and breast-feeding period	Health workers should retest previously HIV-negative women as follows: • first ANC visit • after 3 months and at 36 weeks (unless already tested negative at 32-35 weeks) • 6 weeks post-natal and • 6 monthly during the breastfeeding period
Viral Load algorithm for Pregnant & Lactating Women	For women already on ART: • Check the most recent routine VL to ascertain if the VL is suppressed. o If a VL was not done within the last 3 months, repeat it at the first ANC visit and provide adherence counseling. o If the VL was/is >1000 copies/ml, intensive adherence counseling should immediately be done and the VL should be repeated in 6 weeks and every 3 months until delivery, then at 6 weeks post-partum, and thereafter every 3 months until end of breastfeeding period. For women initiating ART during pregnancy, or in the breast-feeding period • Do VL 3 months after initiation, then 3-monthly until delivery, then 6 weeks post-partum, and thereafter every 3 months until the end of the

	breastfeeding period The above VL monitoring schedule will help to determine whether or not and when her breastfeeding infant can discontinue nevirapine prophylaxis. **At the end of breastfeeding, the viral load monitoring schedule should revert to the non-pregnant adults.**
Definition of high-risk infants	**High risk infants** are defined as those: • born to women with HIV infection who have received less than 4 weeks of ART at the time of delivery; or • born to women with HIV infection with viral load >40 copies/ml in the 3 months prior to delivery if VL measurement is available or • born to women with new HIV infection during pregnancy, breast-feeding or post-partum period
Definition of average risk infants	Infants of all pregnant or breastfeeding women who do not fit into the above high risk category
Management of higher-risk infants	**Higher risk infants qualify for the following PACKAGE OF CARE:** • Nucleid Acid Test (NAT) DBS within 48 hours of birth after the infant's first bath, and labelled as a "fast-track" birth test with the name and telephone number of the district point person • Dual infant prophylaxis to be given for the first 6 weeks of life as described below • Intensified tracking including: o maternity facility to record in a designated register the mother's contact details, a treatment supporter's contact details, anticipated PHC clinic to attend in 2 weeks for birth test result, anticipated PHC clinic to attend in 6 weeks o point person in the district designated to review the maternity facility higher risk infant register on a weekly basis, follow-up with NIP for the results, and inform both the 2-week and the 6-week clinic of results. If result is positive, additionally contact the mother to say the result of the birth test is ready and she should come to the clinic (confirm which clinic) o NIP to immediately notify the point person for any positive NAT result
Infant prophylaxis for higher risk infants	**Infants prophylaxis for first 6 weeks** **NVP plus AZT** for 6 weeks **Infants prophylaxis after 6 weeks of age** **If breastfeeding** *AND* mother's VL ≥40 or unknown, continue with NVP daily **If NOT breastfeeding** since birth or in last 4 weeks, *OR* mother's VL<40, discontinue infant prophylaxis
Infant prophylaxis for average risk infants	**Infant prophylaxis for first 6 weeks** NVP for 6 weeks **Infants prophylaxis after 6 weeks of age** **If breastfeeding** *AND* mother's VL ≥40 or unknown, continue with NVP daily **If NOT breastfeeding** since birth or in last 4 weeks, *OR* mother's VL<40, discontinue infant prophylaxis

Chapter 3: ANTIRETROVIRAL THERAPY FOR INFANTS, CHILDREN AND ADOLESCENTS

Early infant diagnosis of HIV	• All HIV exposed infants should have a NAT test done at 6 weeks of age. Higher risk infants should have a birth NAT test as described in Chapter 2. If the infant was tested and confirmed to be positive using NAT at or immediately after birth, there is no need to repeat NAT at 6 weeks or later. • An HIV-exposed infant who did ***not breastfeed*** and who tests HIV NAT negative at 6 weeks should have a HIV rapid test done at **9 months.** If the RT result is negative, this confirms HIV negative status. If the RT result is positive, an HIV NAT should be done to determine if the infant is truly HIV positive • Breastfeeding HIV-exposed infants who initially tested HIV negative at 6 weeks of age should also have a rapid test done at **9 months of age.** If the result is positive a HIV NAT test should be done to determine if the infant is truly HIV positive. If the results of the RT or the HIV NAT are negative, a repeat RT should be done 3 months after the last exposure to breast milk and, if HIV status of the infant is in doubt, it should be repeated at 18 months.
When to start ART	ALL children and adolescents are eligible for ART and should be initiated on ART irrespective of CD4 count and clinical stage.
Which ARVs to initiate in infants and children	• birth to <2 weeks: AZT/3TC/NVP – given until the infant is 2 weeks old at which time NVP should be changed to LPV/r • 2 weeks to <3 months old: AZT/3TC/LPV/r – until the child is 3 months old at which time AZT should be changed to ABC • 3 months to 2 years old or <10 kg: **ABC/3TC/LPV/r** [ABC/3TC as a once daily dose, LPV/r given twice daily] • 3 years to <10 years or <35 kg ABC/3TC/EFV If had NVP eMTCT/PMTCT, give ABC/3TC/LPV/r
CHAPTER 4: CARE AND SUPPORT FOR ADOLESCENTS LIVING WITH HIV	
Promoting the uptake of services	• The Child Care and Protection Act has made provision for adolescents aged 14 years upwards to access medical services including HTS without parental consent. This is envisaged to facilitate voluntary uptake of HTS among adolescents and subsequent linkage to treatment, care and support. • Approaches recommended to educate, inform and mobilize adolescents for HTS include: ○ Purposefully organized and targeted HTS campaigns. This could be facility or community-based outreach activities; including schools/colleges. ○ 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 as per AFHS guidelines which includes flexibilities in clinic opening times.
Managing the transition of adolescence to adulthood	• Adolescents are in transition from childhood to adulthood and it is a difficult period as they experience physical as well cognitive changes • To facilitate adherence and retention in care, it is essential to screen for and treat mental health problems.
CHAPTER 5: PRE-EXPOSURE PROPHYLAXIS (PrEP)	
Definition of PrEP	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 block or prevent the acquisition of HIV. Oral PrEP should be offered as part of the 'Combination Prevention' package that includes HIV Testing Services (HTS), male and female condoms, lubricants, ART for HIV-positive partners in sero-discordant couples, voluntary medical male circumcision (VMMC) and STI prevention and management.
Eligibility criteria for PrEP	Any sexually active HIV-negative person at substantial risk of acquiring HIV. Those at high risk include but not limited to the following: • HIV negative people in serodiscordant relationships with a partner who is not confirmed as virologically suppressed (VL <40 copies/ml) • All HIV negative people in sero-discordant relationships, regardless of VL of the

	partner, who want to conceive • Those with HIV-positive sexual partner(s) who are not confirmed virologically suppressed • Partner(s) of unknown HIV status • Recent/ recurrent STIs • Multiple and/ or concurrent sexual partners • History of inconsistent or no condom use • Sex workers • Recurrent PEP users • History of sex whilst under the influence of alcohol or recreational drugs.
Contraindications for PrEP	• HIV positive • Evidence or suspicion of HIV primary infection (characterized by a flu-like illness) • Suspicion that person might be in window period following potential exposure • Adolescents <35kg or <15 years who are not Tanner stage 3 or greater (should not get TDF) • Abnormal CrCl<60ml/min • TDF should not be co-administered with other nephrotoxic medications, for example, aminoglycosides • Unwilling or unable to return for 3-monthly HIV testing, counselling and safety monitoring visits • Known allergies to any of the PrEP drugs • Unwilling to get tested for HIV
PrEP ARV Regimen	Daily oral tenofovir/emtricitabine (TDF/FTC 300mg/200mg) or TDF/3TC as FDC is preferred
When to Stop PrEP	PrEP should be stopped when: • Whenever an HIV test is positive • At client's request • For safety concerns/ side effects (CrCl<60ml/Min) • If risks of PrEP outweighs benefits
CHAPTER 6: POST-EXPOSURE PROPHYLAXIS (PEP)	
PEP regimen	Tenofovir 300 mg daily + emtricitabine 200mg (or lamivudine 300 mg) FDC once daily for 28 days In case of high risk exposure; it is recommended to add a third ARV. Expanded regimens include the basic regimen (TDF+FTC[or 3TC]) plus one of the following for 28 days: O Atazanavir 300 with ritonavir 100mg QD (preferred) O Efavirenz 600 mg once nightly. O Lopinavir 400mg plus ritonavir 100mg twice daily. For children less than 10years of age or <35 kg, give ABC plus 3TC plus LPV/r. Use AZT as an alternative when ABC cannot be used.
Procedures for PEP following occupational exposure	• Draw baseline laboratory tests: HIV testing (with consent), HBsAg and Ab, and creatinine. If HIV negative, PEP should be initiated promptly, preferably within 1 - 2 hours post-exposure and especially if the source patient is HIV-positive or the patient's HIV status is unknown. • For those whose results are positive for HIV, PEP should be discontinued immediately, and the clients linked into care for treatment • Workers who are HIV-negative at baseline should repeat HIV-antibody tests at 6 weeks, 12 weeks, and 6 months
Comprehensive management of rape survivors	• PEP regimens: Give expanded PEP regimens as above • Presumptive STI prophylaxis cefixime 400 mg or ceftriaxone 250 mg IM STAT plus metronidazole 2 gram STAT plus azithromycin 1g STAT (adults) • Emergency contraception within 72 hours: norgestrel 0.5mg (500 mcg) and ethynyl oestradiol 0.05mg • Hepatitis B immunoglobulin and hepatitis B vaccination should be started as soon as possible if the patient is not already immune • A tetanus booster should be given. • Counselling, medico-legal assessments

CHAPTER 7: DIFFERENTIATED CARE	
Definition of Differentiated Care	Differentiated care is a **client-centred approach** that simplifies and **adapts HIV services** across the cascade to reflect the preferences and expectations of various groups of people living with HIV (PLHIV) while reducing unnecessary burdens on the health system. By providing differentiated care, the health system can refocus resources to those most in need

Models of ARV Delivery in Namibia	• **Facility-based models**
	  ○ Standard care (Main ART and NIMART sites)
	  ○ Fast-track ART refills model
	  ○ ART Adherence Groups (including Teen clubs)
	• **Out of facility models**
	  ○ ART Outreach models
	  ○ Community ARV Refill Groups (CARGs)

INTRODUCTION

Namibia has the tradition of revising its treatment guidelines regularly in keeping with new advances in the diagnosis and treatment of HIV and AIDS. The First Edition of the National Guidelines for Antiretroviral Therapy was developed in 2003 and this is the Fifth Edition which was newly revised in order to include the most recent scientific evidence and best practices as well as guidance from WHO. The standardized guidelines address clinical, operational and programmatic aspects of using ARV medicines for HIV treatment as well as for prevention. Some of the major operational areas are: adherence to ART; retention in to care; human resources, models of differentiated care which include patient-centred care and integrating ART with TB treatment, antenatal care and maternal and child programs; intergrating screening for mental health conditions into ART, laboratory services and medicine supply. Treatment guidelines are intended for use by national HIV program managers, clinicians and other health service providers in both public and private sectors, managers of laboratory services, people living with HIV and community based organisations, national HIV treatment and prevention advisory bodies as well as international and bilateral agencies that provide financial and technical support.

Major changes in these guidelines include an expansion in the eligibility criteria by Treating All people living with HIV regardless of their clinical and immunological status including all HIV infected pregnant and breastfeeding women, all children and adolescents and HIV/HBV co-infected persons. An accelerated initiation of ART is recommended and especially among pregnant and breast- feeding women to reduce the risk of mother to child transmission of HIV and for the mother's own health. The guidelines also provide guidance on the management of Pre-exposure Prophylaxis for people with a substantial high risk of contracting HIV. Special emphasis is put on the use of fixed dose triple-ARV combination as first line for adults and adolescents and routine viral load monitoring as the preferred method of monitoring HIV treatment response The new ARV regimens provided for all ages have proven to be effective, with fewer side effects and most are simpler in administration. A new chapter on 'Differentiated Care' which includes Cmmunity ARV Delivery models has been added as a measure to promote 'patient centred' care considering the different needs of PLHIV.

To promote early diagnosis of HIV infection and facilitate lifelong adherence to therapy, a favorable environment is essential. The following considerations still remain essential for the provision of ART:

- Easy access, including mobile and outreach services for counseling and testing for early diagnosis of HIV infection to ensure timely access to therapy.
- Understanding of the epidemic as it evolves in order to inform the response (Know your epidemic-Know your response)
- Identification of sufficient resources for treatment and care on a long-term basis through the public sector and through public-private partnerships.
- Continuous patient counseling in order to ensure full understanding of ART, the importance of treatment adherence, timing of medication intake in relation to meals, recording and reporting of adverse events associated with the intake of ARV medicines, and monitoring and management of medicine resistance.
- Follow-up counseling of the patient and review of his/her environment to ensure continued psychosocial support and to enhance adherence to treatment.
- Capacity to recognise and appropriately manage common HIV-related illnesses, opportunistic infections and adverse reactions to antiretroviral medications (ARVs).
- Reliable laboratory monitoring services including routine haematological and biochemical tests for the detection of medication toxicity and response to therapy.
- Assurance of an adequate supply of quality medications, including medicines for treatment of opportunistic infections and other HIV-related illnesses.
- Availability of trained interdisciplinary health care teams, including doctors, pharmacists, nurses, social workers, and counselors. These teams should, where possible, closely collaborate with support groups and communitybased organisations (CBOs) for persons with HIV and their caregivers.
- Community involvement through awareness creation, mobilization, referral linkages and other collaborations.
- Availability of a system for training, continuous education, monitoring and feedback on safe and effective management of HIV-related disease and ART.

- Availability of appropriate care, support services and referral mechanisms in case of treatment failure.
- Keeping up with new scientific evidence on treatment and best practices as well as with the updates of WHO HIV and Hepatitis guidelines.

The cost of ARVs has continued to decrease over the last years through initiatives of the pharmaceutical industry. In addition to public health services, increasing numbers of persons with HIV-related diseases have access to treatment through medical aid schemes or other private sector initiatives.

These guidelines have enabled health care providers to provide standardised care and treatment to people living with HIV(PLHIV) over the last thirteen years and will continue to do so with the revised editions of the guidelines. The guidelines will continue to be regularly updated to incorporate new developments as they occur.

ART does not cure HIV, but it has transformed a potentially fatal disease into a chronic manageable condition. The most important emphasis in curbing the pandemic remains the prevention of primary HIV infection.

IMPLEMENTATION OF THE FIFTH EDITION OF THE NATIONAL GUIDELINES FOR ANTIRETROVIRAL THERAPY

This Fifth Edition of the National Guidelines for Antiretroviral Therapy includes several changes from the Fourth Edition. In order for these revised guidelines to be implemented with minimum disruption to patient care, a smooth transition from the Fourth edition to the Fifth edition of the guidelines is essential. It is important to ensure continuous supply of medicines from the central medical store to the patient with minimal wastage of ARVs due to expiriesy. Experience garnered from changes in other treatment guidelines have shown that some prescribers are eager to transition patients to newer regimens, without considering their availability at the central medical stores. . This may cause disruption to patient care as well as the pharmacy supply system.

Implementation of the 5th edition of the National Guidelines for Antiretroviral Therapy will entail an increase in storage and dispensing of ARVs as more patients will qualify for ART services and such as there is need to continue to decentralize ART services to PHC level and further into the community. Standardisation of dispensing practices at the different service points allows predictable consumption and demand which leads to an uninterrupted ARV supply. This will also allow monitoring of critical adherence-related indicators such as on-time pill pick up of ARVs.

CHAPTER 1: ANTIRETROVIRAL THERAPY FOR ADULTS

1.1 Assessment of HIV-positive adults

In the public sector, HIV-positive individuals should be referred to the nearest ART or NIMART site or, in cases of pregnancy, to the nearest antenatal clinic (ANC) providing ART as a matter of urgency. The MOHSS recommends re-testing of all newly diagnosed HIV positive patients to verify their HIV positive status prior to enrolment for treatment. At the clinic, re-testing for HIV will be done. Upon confirmation of a positive result, the patient will be enrolled for treatment. Enrolement for treatment implies patient registration, assignment of a unique ART number, and opening of a patient care booklet. At this juncture the patient will undergo a complete medical history, physical examination, and appropriate baseline laboratory tests, review of social eligibility criteria, rule out the presence of opportunistic infections and determine readiness to start ART. Patients should be initiated on ART immediately when they are ready, either on the same day or as soon as possible within one week.

Data for all patients will be entered into the Electronic Patient Monitoring System (ePMS), an information system used for patients enrolled in HIV care and treatment to assist with follow-up tracking and record-keeping for overall programme management.

In the private sector, HIV-positive individuals should be assessed similarly by their health care providers and started on ART according to these guidelines, preferably by a trained HIV clinician. For more detailed guidelines for management of HIV-positive adolescents, refer to Adolescent care and support (Chapter 3).

1.2 When to start antiretroviral therapy in adults

All HIV positive adults irrespective of CD4 counts or WHO stage are eligible to start ART (Treat All). Patients should be initiated on ART immediately when they are ready, either on the same day or as soon as possible within one week.

1.3 Adherence

1.3.1 Importance of adherence

ARV medication adherence is absolutely vital for the success of ART. Very high levels of adherence, taking at least 95% of prescribed doses, are required to achieve sustained suppression of HIV replication over time. Adherence is promoted by proper ongoing support and counseling. Adherence is also promoted by prescribing simplified, well-tolerated regimens involving as few pills as possible, administered no more than two times per day.

The goal of ART is to achieve sustained and optimal viral suppression. It is essential for a patient to take medication correctly every day. However patients may forget occasionally. They need to be counseled in advance about what to do should this happen, as part of their pre-initiation counseling. The advice should be as follows:

If a patient misses a dose of antiretrovirals, he/she should **take the missed dose as soon as it is remembered**. If it is more than 2 hours until the next dose is due, he/she takes the missed dose immediately when rememberd, the next dose at the usual time and continue with the normal schedule. If it is less than 2 hours until the next dose is due, he/she should take the missed dose immediately it is rembered, should omit the next dose and continue with the normal schedule.

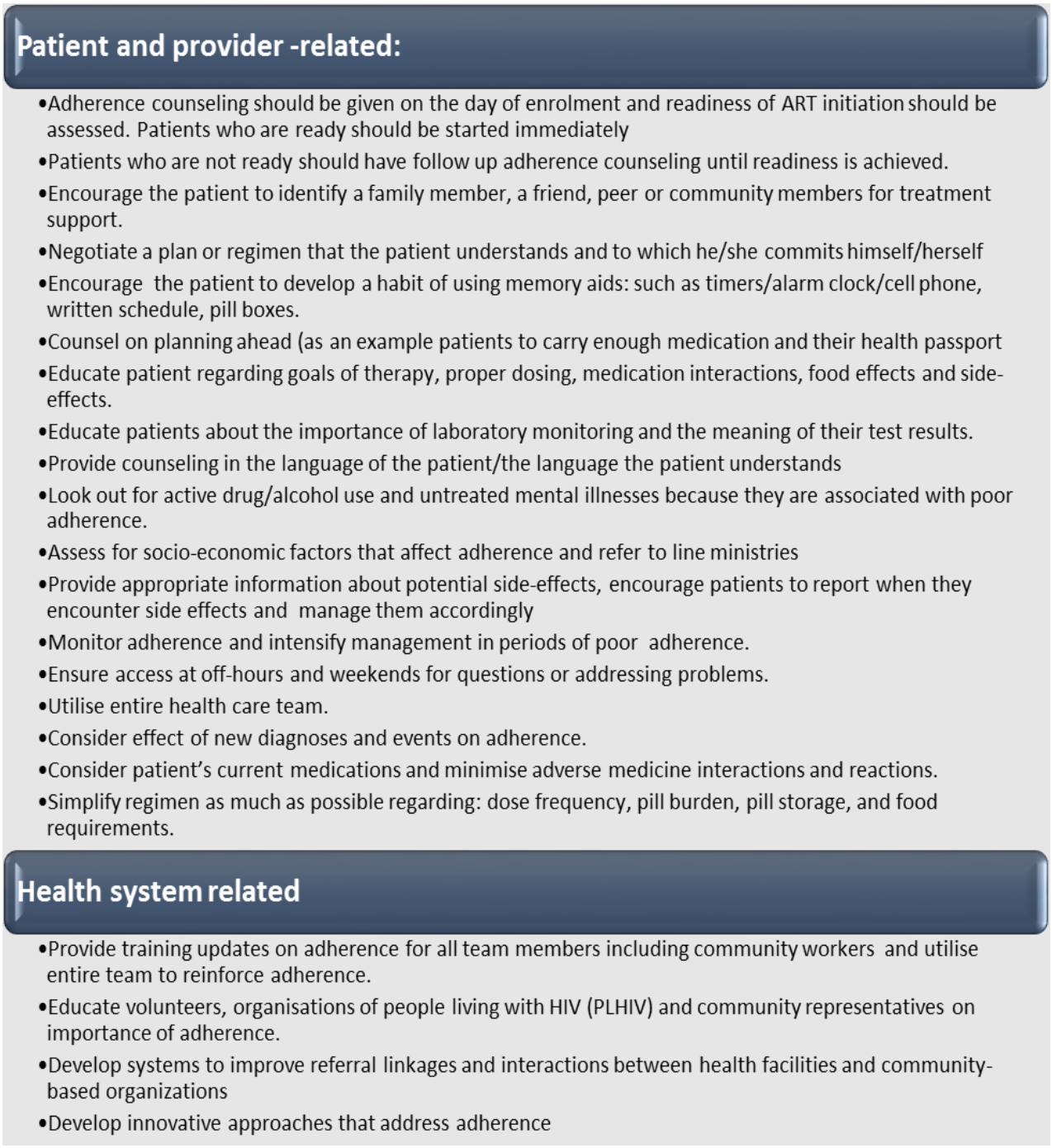
1.3.2 Methods to achieve readiness to start ART and maintain adherence

Before a patient starts ART, it is important to have detailed discussions with them about their willingness and readiness to initiate ART, the ARV regimen, dosage and scheduling, the likely benefits and possible adverse effects and the required follow-up and monitoring visits.

The choice to accept or decline ART ultimately lies with the individual person or his or her care giver, and if they choose to defer initiation, ART can be offered again at subsequent visits. If there are mental health, substance use or other problems that are major barriers to adherence, appropriate support should be provided, and readiness to initiate ART should be reassessed at regular intervals. A wide range of patient information materials as well as community and peer support can enhance the patient's readiness and decision to start therapy. People starting treatment and care givers should understand that the first ART regimen offers the best opportunity for effective viral suppression and immune recovery, and that successful ART requires them to take the medications exactly as prescribed. They should be informed about possible adverse effects most of which are are temporary and manageable. People receiving ART and their care givers should also be asked regularly about any adverse events, other medications they are taking, including herbal remedies and nutritional supplements. Herbal remedies and other nutritional supplements should be discouraged as they are likely to interfere with the way ARV medicines work.

People receiving ART should understand that while the ARV medicines reduce the risk of HIV transmission, they cannot be relied upon to fully prevent other people from acquiring infection. They should be given advice on safer sexual practices (including condom use) and avoidance of other high-risk activities, such as sharing of injecting equipment to prevent transmitting HIV to other people. In order to achieve maximum readiness for ART, there should be a coordinated effort involving the patient, physicians, pharmacy staff, nurses, other health care providers and persons within the immediate environment of the patient. Once therapy has begun, continued monitoring of adherence and ongoing patient education is essential. Ongoing attention to, and reinforcement of, adherence throughout the entire course of ART is an essential part of any successful therapy program. Patients should receive care at points nearest their home. It is however essential to consider the patients' preferences as this may have impact on adherence. Patients should not be denied care or medication refills if they are away from home and need to attend another care point.

Figure 1.1: Methods to achieve readiness to start ART and maintain adherence



1.3.3 Re-starting ART in patients who "default" and "Lost to Follow up".

Interruption of ART may result in viral load rebound and clinical progression of HIV. Any patient who misses their clinic visit and interrupts treatment is defined as a "defaulter". Any patient who interrupts treatment for 90 consecutive days or more is defined as "lost to follow up". He/she should be traced, linked back to care and interviewed to uncover and understand the reasons behind the treatment interruption and to determine if the interruption was intentional or unintentional. Efforts should be made to correct the circumstances leading to the lapse in treatment. Each case of lost to follow up, once returning to care, should be carefully evaluated by an ART team before continuing treatment. Patients who are continuing treatment should receive progressive adherence counseling and close follow-up

For those patients who are not yet committed after an interruption of treatment, a trial period with frequent counseling and clinic visits should be scheduled. The healthcare team should as much as possible try to reinstate treatment within a short time. During the trial period, continue with multivatimins and cotrimoxazole prophylaxis as approriate. Patients who return after being lost to follow-up should be assessed and managed for any co-infections.

Facilities, as a routine practice, should print out on a weekly basis a list of patients who missed their appointments and contact the individuals. Health facilities should collaborate with community based organisations operating in their catchment areas to facilitate tracing of lost to follow-up patients. Facilities should include defaulter tracing activities as part of all service provision approaches.

1.4 Social considerations for starting ART in Namibia

The Ministry of Health and Social Services considers social criteria prior to starting ART. Meeting social eligibility criteria is necessary but should not be an obstacle for accessing ART. The intention of these considerations is to maximise adherence, reduce the risk of treatment failure and the development of resistance. Social considerations should not be used to deny any person treatment.

The social considerations that support better adherence to treatment include the following:

- Having a fixed home address
- Having ready access to a designated treatment centre for follow-up.
- Not abusing alcohol or willingness to stop taking alcohol.
- Mentally stable
- Being committed to:
  - Lifelong treatment with ART.
  - Strict adherence to treatment.
  - Allowing home visits if indicated.

1.4.1 Treatment supporters

A treatment supporter is someone at home, in the community, or at the workplace, who can accompany the patient to visits and assist with daily adherence to ART. The MoHSS advises that it is desirable for all patients to have a treatment supporter. Absence of a treatment supporter, however, should not be a reason to deny treatment to a patient. Where possible, patients who are unable to identify a treatment supporter may benefit from connection with a community-based organisation or support groups to assist with treatment support. Each case should be evaluated on its own merit.

1.5 Antiretroviral medications

There are currently six classes of antiretroviral agents*:

- **Nucleoside/or Nucleotide Reverse Transcriptase Inhibitors (NRTIs).** These medications inhibit the transcription of viral RNA into DNA, which is necessary for reproduction of the virus. The class includes tenofovir disoproxyl fumerate (TDF), tenofovir alefenamide fumerate (TAF)., zidovudine (AZT), lamivudine (3TC), didanosine (ddI), stavudine (d4T), abacavir (ABC) , zalcitabine (ddC) and emtricitabine (FTC).
- **Non-Nucleoside Reverse Transcriptase Inhibitors (NNRTIs).** These medications are of a chemically different class from NRTIs, but also inhibit transcription of viral RNA into DNA. The class includes nevirapine (NVP), efavirenz (EFV), etravirine (ETV), rilpivirine (RPV) and delavirdine (DLV).
- **Protease inhibitors (PIs)**: These medications act on the viral enzyme that cuts long chains of virally produced amino acids into smaller proteins. The class includes lopinavir (LPV), indinavir (IDV), nelfinavir (NFV), saquinavir (SQV), ritonavir (RTV), atazanavir (ATV), fosamprenavir (FPV), tipranavir (TPV) and darunavir (DRV).

- **Integrase strand transfer inhibitors (INSTIs):** These medications prevent the newly synthesized viral DNA from integrating into the host cell DNA. This class includes the following medicines: raltegravir (RAL), Elvitagravir(EVG)and dolutegravir (DTG),
- **Entry inhibitors**: This class consists of CCR5 co-receptor antagonist which prevents the virus from attaching to the host cell CD4 co-receptor CCR5. This class includes maraviroc (MVR) and Cenicriviroc (CVR).
- **Fusion inhibitors:** These medications block the virus from being able to merge with the host cell (i.e. CD4 cell) after binding. The only currently available fusion inhibitor is enfuvirtide (ENF).

**Not all of these medications are currently available in Namibia. The comprehensive list at the time of this printing is given here for completeness.*

1.6 ART regimens

Recommended ART regimens consist of a combination of 2-3 NRTIs plus an NNRTI or PI. For individuals who cannot tolerate the recommended regimens or who experience failure on the second line regimens, an HIV specialist should be consulted.

Examples and explanations of regimens which are NOT recommended:

- Regimens containing both NVP and EFV – antagonism.
- Regimens containing AZT after d4T failure and vice versa – cross resistance.
- Regimens containing EFV after NVP failure and vice versa – cross resistance.
- Regimen containing both TDF and ABC, no additive antiviral effect

1.7 Recommended ART regimens in Namibia

The first line and second line ART regimens for adults, adolescents ≥ 10 years who weigh at least 35 kg, and pregnant and breastfeeding women are listed in Tables 1.1 below respectively.

Table 1.1: Recommended First Line ART regimens in Namibia

1st line ART	Preferred 1st line Regimens	Alternative 1st line Regimens[2]
Adults (including adolescents ≥ 10 years old and weigh at least 35 kg), pregnant and breastfeeding women, adults with TB disease and adults with HBV coinfection	TDF + FTC (or 3TC[1]) + EFV (once daily FDC)	ABC + 3TC + EFV (or NVP2) AZT + 3TC + EFV AZT + 3TC + NVP3 TDF + FTC (or 3TC) + NVP

**In circumstances where a patient develops a significant EFV related neuropsychiatric side-effects, the dose of EFV can be reduced to EFV 400 can be provided or a FDC combination containing EFV 400mgs can be provided when available, after consultation with HIV specialist or a clinical mentor. Note: EFV400 mg is not yet indicated in HIV patients being treated for TB or are pregnant women.*

[1] TDF/FTC/EFV is more preferred regimen to TDF/3TC/EFV, hence TDF/3TC/EFV will be progressively replaced with TDF/FTC/EFV.

[2]Alternative regimens should only be used if the preferred first line regimen is not an option. In an event that NNRTIs can not be used as 3rd ARV, a PI can be considered after consultations with an HIV specialist or clinical mentors.

[3]NVP should not be initiated in women with a CD4 count of >250 or men with a CD4 count of >400. Due to metabolism issues, nevirapine treatment is always initiated as once daily therapy for the first 14 days, and then it is increased to twice daily

A clinician who wishes to initiate a patient on TDF-based regimen should first calculate the creatinine clearance (see Figure 1.2)

Figure 1.2: Formula for the calculation of creatinine clearance in adults and adolescents ≥18 years old

The formula to calculate the creatinine clearance in men is as follows:

$$\frac{\text{(140-age in years) x weight in kg x 1.22}}{\text{Serum creatinine in micromoles/L}}$$

Multiply the answer above by 0.85 for creatinine clearance in women

Note: If the creatinine clearance at baseline is <60ml/minute an alternative to TDF should be included in the ART regimen unless the patient is co-infected with HBV.

Pregnant women require immediate initiation of ART in order to provide optimal HIV prevention for their infants. In addition, these guidelines make provision for "same day" start for other patients. For this reason, a decision to initiate TDF should be based on a normal result of a urine dipstick while waiting for the creatinine clearance result. In case proteinuria and or glycosuria are detected, an alternative to TDF should be initiated while awaiting the creatinine clearance.

TDF can still be used in specific patients with renal insufficiency when its use is unavoidable (e.g. hepatitis B co-infection) but should be carefully monitored and the dosage should be adjusted according to the recommendations concerning use of TDF in renal failure in Table 1.2 below. Appendix 5 also details the appropriate dose adjustment for other NRTIs in case of renal failue.

Table 1.2: Recommendations for Tenofovir Dose Adjustment in Patients with Altered Creatinine Clearance[1]

Creatinine Clearance (ml/min)	Recommended Dosing of TDF 300 mg
≥50	Every 24 hours
30-49	Every 48 hours
10-29	Twice a week
≤ 10	No recommendation available owing to a lack of pharmacokinetic data in this population
Hemodialysis patients	Every 7 days or after a total of 12 hours of dialysis (administer following completion of dialysis)

[1] *Joel E. Gallant, MD, MPH (2005).Tenofovir and Renal Function: A Guide for Clinicians*

Tabla 1.3: Recommended second line ART regimens in Namibia

Target population	Regimen	Remarks
HIV+ adults	Preferred: AZT[1]/TDF/3TC/ATV-r	Where standard first line regimens were used
HIV+pregnant and breastfeeding women	Alternative: AZT /TDF/3TC/LPV-r[2]	
HIV/TB co-infection	AZT[1]/TDF/3TC/LPV/RTV	Increase dose of RTV: i.e., LPV/RTV 400mg/400mg[2]

it is safe to use AZT unless the current Hb<8gm/dl. **For patients with true previous AZT toxicity, consult HIV specialist. If a patient has anaemia with Hb < 8gm/dl consult a HIV specialist/clinical mentor.**

[2]***This regimen is poorly tolerated in some patients due to gastro-intestinal tract (GIT) side effects. Discuss management options with an HIV specialist.*** **ATV-r is currently the preferred PI in Namibia.**

Third line ART for Adults and Adolescents

Third line regimens are complicated, very costly and should only be implemented following the recommendation and close supervision of an HIV specialist. All patients failing second line regimens should undergo HIV resistance testing following consultation with an HIV specialist in order to select the most effective regimen.

1.8 Sexual and Reproductive Health considerations

1.8.1 Contraception

The use of barrier contraception methods is recommended for all male and female patients receiving ART in order to reduce the risk of transmission of STIs and HIV, even when both partners are HIV-positive (it is possible for a person with a resistant strain of HIV to infect his/her partner with the resistant strain).

To minimise the risk of unintended pregnancies, an additional highly effective contraceptive method is recommended for all women of childbearing age. Reversible contraceptive methods include an intrauterine contraceptive device (IUCD), injectable progesterone-based contraceptives (depo-medroxyprogesterone acetate, DMPA).

Permanent contraceptive methods include bilateral tubal ligation for women and vasectomy for male partners – client education must be provided and written informed consent must be obtained from clients prior to undergoing these procedures.

There is a potential for reduced efficacy of long-acting progestogen-only implants when a woman is also on ART containing EFV. Nevirapine, efavirenz and all the ritonavir- boosted PIs affect blood concentrations of oral contraceptives and women receiving these medications should use additional contraceptive methods. Dual protection (use of condom + any other contraceptive method) and planning of pregnancies should be adequately addressed..

Refer to the eMTCT section for more detailed guidance regarding reproductive considerations for HIV-positive individuals who intend to have children (See Part 2).

1.8.2 Cervical Cancer and HIV

Globally and in Namibia, cervical cancer is among the most common cancers among women. HIV positive women are at higher risk of:

- Infection with Human Papilloma Virus (HPV), the causative agent for cervical cancer.
- Having pre-cancerous lesions (2-6 times) depending on degree of immune suppression
- Developing cervical cancer
- Early progression to invasive cancer
- Presenting with late disease with poor prognosis

As part of clinical monitoring annual cervical cancer screening is recommended for all HIV infected sexually active women.

All women with abnormal screening results should be referred for further evaluation and treatment as appropriate. Cervical Cancer screening should be integrated into the HIV care and treatment clinics in order to ensure convenience to clients and early diagnosis of pre-cancer lessions.

1.9 Reasons for changing antiretroviral therapy

Studies have shown that first line regimens give patients the best chance of long-term treatment success. ART may need to be changed due to therapy failure or medication toxicity, but there must be a very strong clinical justification for doing so.

1.9.1 Changing due to toxicity (ARV substitution)

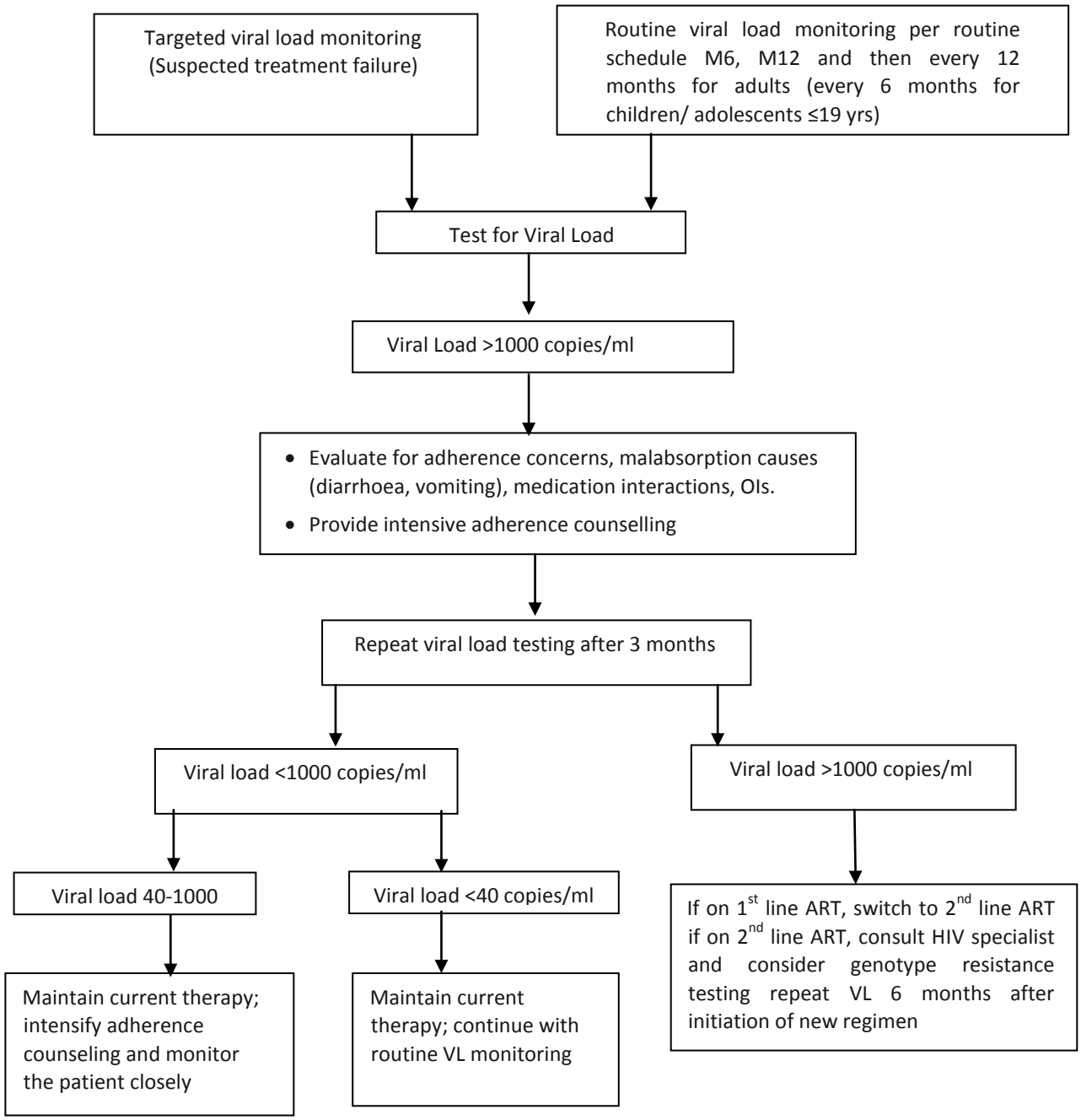
If a change in ARV regimen is needed because of drug- induced toxicity., the offending medicine can be replaced with another medicine that does not have the same level of side-effects. This is further discussed in Section 1.13. When it is not possible to identify the offending medication, discussion with an HIV specialist is recommended.

1.9.2 Changing due to treatment failure (ART Regimen Switch)

Treatment failure can be suspected clinically from patient's history and physical examination, immunologically from CD4 counts, and virologically by measuring viral loads. Clinical evidence of failure is indicated by HIV disease progression (e.g. emergence of new opportunistic infections) in a patient who had been clinically stable. Virological failure is defined as a viral load >1,000 copies/ml 6 months after starting ART or viral rebound to >1,000 copies/ml on two consecutive measurements after a period of viral suppression. Routine viral load testing as described in Section 1.11.3 is recommended for treatment monitoring in order to facilitate earlier detection of virological failure.

An algorithm for evaluating suspected treatment failure is shown in Figure 1.3 below.

Figure 1.3: Algorithm for evaluating suspected treatment failure



Before any change is made due to failure, the circumstances contributing to the failure (e.g. poor adherence, medication interactions, malabsorption) should be thoroughly investigated and corrected before a new regimen can be started. Each case should be discussed with colleagues and/or an HIV specialist.

In the absence of ARV resistance testing, the WHO recommends that the entire regimen be changed from a first to a second line combination regimen in the case of treatment failure. The second line ART regimen should include at least two new ARVs, with at least one from a new class of antiretrovirals.

After a switch from first line to second line or from second line to third line, a VL should be done after 6 months to assess response to treatment, followed by routine yearly viral load testing.

Although management of patients would be easier if resistance testing was done prior to selection of a second line regimen, this is costly and **should not** be done routinely. However resistance testing is essential for patients who have failed a second line regimen and a third line regimen is needed. An HIV specialist must give approval for this on an individual patient basis, and in any case should be consulted for further management of the patient. Ordering an HIV genotype resistance test should be done using the specific form for that purpose (See Appendix 18. On this form, patient's medication history, the indications for doing the test and the name of of the authorized HIV specialists who attended to the patient should be specified. Without a fully completed form, the Namibia Institute of Pathology (NIP) laboratory will not accept the sample for testing.

Interpreting results of resistance testing is complex and should be analysed in conjunction with the ART history of the patient, noting that the test may only provide information about resistance to the current regimen the patient is on.

1.9.3 Elimination of use of d4T based regimens

d4T is no longer a preferred ARV due to its well-documented long term intolerable side effects. **No new patients should be started on d4T and all patients currently on d4T MUST be assessed for transition to another NRTI as per guidance below.**

1.9.4 Transitioning adults to the new first line Fixed-dose Combination formulation

In order to take advantage of the new and now preferable daily dose Fixed Dose Combination (FDC) formulation preferred first line regimen it is important to consider whether the patient has virologic suppression on the current regimen before making a change. It is recommended that HCWs identify adults currently on AZT- and d4T -based first line regimens, and those on NVP as first line. HCWs should then carefully assess whether or not the patient is eligible for a direct substitution or if a regimen switch is required.

. Non-thymidine analogues (e.g. ABC and TDF) are interchangeable because their mutation patterns are similar.. However changing from a thymidine analogue (eg AZT) to a non-thymidine analogue or *vice versa* in the presence of virologic failure could compromise future 2nd line options – it would be essentially introducing one new ARV into a failing regimen. For this reason, results of the most recent viral load should be reviewed to inform the appropriate regimen change. If the most recent VL is more than 6 months previously, it should be repeated.

If a patient's VL is <40 copies/ml and in the absence of specific toxicities experienced by the patient, the following regimen changes are appropriate:

- ***From*** (d4T or AZT) + 3TC + (NVP or EFV) ***to*** TDF + FTC(or 3TC) + EFV

If the patient's VL is ≥40 copies/ml and in the absence of specific toxicities experienced by the patient, ARV regimens should be as follows:

- ***From*** d4T/3TC/NVP ***to*** AZT/3TC/NVP (this is a fixed dose combination given BD – do not change the NNRTI to EFV)

- If on AZT/3TC/NVP do not change the regimen.

Table 1.4 provides further details on the management of patients whose VL is ≥40 copies/ml.

Table 1.4: Transitioning safely to the preferred first line regimen

Current ARVs	VL within last 6 months	
	VL<40	VL≥40
d4T/3TC/NVP	Change to TDF/ FTC/EFV	Change to AZT/3TC/NVP FDC while intensifying adherence counseling and follow-up, and evaluating for treatment failure and possible 2nd line if VL remains>1000 copies/ml2
d4T/3TC/NVP but previous AZT toxicity[1]	Change to TDF/ FTC/EFV	Confirm if truly previous AZT toxicity1. If yes, keep on d4T/3TC/NVP while intensifying adherence counseling and follow-up, and evaluating for treatment failure and possible 2nd line if VL remains>1000 copies/ml. If not true AZT toxicity, manage as above2
AZT/3TC/NVP	Change to TDF/ FTC/EFV	Continue AZT/3TC/NVP FDC while intensifying adherence counseling and follow-up, and evaluating for treatment failure and possible 2nd line if VL remains >1000 copies/ml2
TDF/3TC/NVP	Change to TDF/ FTC (or 3TC)/EFV	Change to TDF/FTC(or 3TC)/EFV

1.10. Clinical monitoring of PLHIV

1.10.1 Baseline clinical assessment

The baseline medical history should be recorded in the standardised patient care booklet and should include essential demographic characteristics; the past medical history including major illnesses (e.g., tuberculosis), hospitalisations and surgeries; the length of time since the diagnosis of HIV infection; current medications; and any active symptoms. In the case of women, date of last menstrual period, current or planned pregnancy and access to contraceptive services should be reviewed.

The baseline physical examination should also be recorded in the patient's file, including vital signs, weight, and detailing of any abnormalities of the eyes (including fundi, if possible), oropharynx, lymph nodes, lungs, heart, abdomen, extremities, skin, genital tract and nervous system.

1.10.2 Clinical monitoring during follow-up visits

Once ART has started, a reasonable schedule for clinical monitoring includes follow-up visits two and six weeks after initiation (which will also be useful to evaluate and reinforce adherence to antiretroviral therapy), and a minimum of every three months thereafter until stable (including clinical and laboratory monitoring). Regular visits with trained nursing staff, which can be combined with medication dispensing, are encouraged to monitor and reinforce adherence and identify problems requiring referral. At each visit, inquiries should be made with respect to the following 3 aspects of ART:

1. Is ART adherence ≥95%? If not, find out why not and discuss what steps can be taken to improve adherence.
2. Are there any new symptoms that may be related to medication side-effects?
3. Are there any new symptoms that may be related to HIV disease progression or opportunistic infections? The development of significant opportunistic infections (OIs) while on ART may indicate clinical failure, but early in treatment may also be attributable to Immune Reconstitution Inflammatory Syndrome (IRIS) (see section 1.18)

[1] *patients who were anaemic at start of ART may have initiated treatment with d4T, however these patients do not have "AZT-induced anaemia" and it is safe to use AZT unless the current Hb<7.5. For patient with true previous AZT toxicity, and who have significant side effects caused by d4T, consult HIV specialist.*

[2] *If VL remains 40-1000 copies/ml, continue to counsel on and re-enforce good adherence but do not transition to TDF/FTC/EFV unless VL falls below 40 copies/ml and do not routinely switch to 2nd line unless the VL rises to >1000 copies/ml.*

Patients should be informed about the symptoms of ARV toxicities and when to seek care. Clinical evaluation of the effectiveness of ART is important, and patients should have relevant physical examinations. WHO Clinical Treatment (T)-staging should be done and recorded for patients on treatment using the standard WHO Clinical Staging list. The long-term basic parameters examined and documented should include:

- The patient's perception of how he/she is doing on therapy.
- Changes in body weight over the course of therapy.
- Changes in the frequency or severity of HIV-associated symptoms (fevers, diarrhoea).
- Physical findings, such as signs of Immune Reconstitution Inflammatory Syndrome (e.g., lymph node swelling), signs of immune improvement (e.g., regression of Kaposi's sarcoma lesions or molluscum contagiosum), signs of HIV-related disease progression (e.g., oropharyngeal and/or vulvovaginal candidiasis, etc.), or signs of medication toxicities (rash, lipodystrophy).

1.11 Laboratory Monitoring of PLHIV

1.11.1 Routine laboratory monitoring

Specific laboratory investigations are recommended as the basic level of care that is necessary to safely start ART. Laboratory tests are also needed to monitor response to treatment and to identify potential toxic reactions which might trigger changes in ARV regimens according to the national guidelines. These tests should be performed at the initial clinic visit and at follow-up as indicated in Table 1.5 below. Experience in some sites has shown that laboratory results are often not available at the time patients are seen for their follow-up visits, causing delays in taking appropriate management decisions for the patient. Sites should therefore implement Point of Care testing where feasible and/or schedule patient visits in a way that allows for the patient to receive results in a timely fashion. Efforts should continue to improve laboratory specimen handling as well as access to results and improved turn-around time (TAT) by increasing access to testing and availability of terminals or SMS printers at health facilities.

Table 1.5: Laboratory assessment for adults for ART initiation and monitoring

Phase of HIV management	Tests	Frequency
At initial clinic visit	CD4	Once
	HBsAg	Once; if positive, repeat after 6 months. If HBsAg is reactive, then the lab will automatically do ALT
	CrAg[1]	Once if CD4<200
	Hb	Once
	CrCl	Once
	Urine dipstick[2]	Once
Treatment monitoring	VL	6 M, 12 M (then every 12 months)
	CrCl	6 W, 6 M, 12 M (then every 12 months) if on TDF
	Hb	2 W, 6 W, 3 M if on AZT. No need to repeat Hb after three months if there is no anemia.
HBsAg positive	ALT	2 W, 6 W, 3 M (then every 6 months if the second HBsAg remains positive)
Suspected treatment failure	VL	repeat VL after 3 months of good adherence to treatment and once OIs are excluded
Virological failure	1) CD4[3]	after three months of suspected virologic failure
	2) HIV Drug Resistance	Before Switching to a 3rdline regimen all ages

Secondary fluconazole prophylaxis following cryptococcal meningitis	CD4[4]	6-monthly while on fluconazole prophylaxis until 2 consecutive values >200 cells/mm[3]

[1] *CrAg: plasma Cryptococcal Antigen: lab will do this automatically for patients with CD4<200*

[2] *note particularly urine protein and glucose*

[3] *Check CD4 count to assess immunological status and inform clinical management (eg. assess for possible OIs)*

[4] *Check CD4 count to determine when fluconazole prophylaxis can safely be stopped*

Other laboratory tests may be indicated based on the suspicion of a medication toxicity (such as signs of liver toxicity or rash with NVP, signs of glucose intolerance if on PIs, etc) or clinical disease progression.

Additional baseline and routine laboratory monitoring may be needed if the patient has existing co-morbidities such as diabetes.

Appendix 3 provides a summary of the routine monitoring laboratory tests to be done based on the ARV regimens used.

1.11.2 CD4 Lymphocyte counts

CD4 levels are important markers of immune function. CD4 testing is recommended at baseline to determine degree of immune suppression.

Because viral load is a more sensitive and an earlier indicator of treatment failure, Namibia has transitioned to routine viral load monitoring rather than CD4 count for treatment monitoring. However if a patient has virologic failure or shows signs of clinical deterioration, a CD4 count should be done.

1.11.3 Plasma HIV-RNA levels (viral load)

Routine viral load (VL) monitoring is recommended to facilitate earlier detection of treatment failure. VL levels should reach undetectable levels by 6 months of therapy in fully adherent patients. All patients initiating therapy will routinely have a viral load assay done at 6 and 12 months after beginning therapy and every 12 months thereafter (every 6 months for children/adolescents <19 years).

The aim is to identify patients who are having suboptimal responses to ARV therapy earlier and whose immunologic and clinical responses may not have deteriorated at this stage. These patients persistently have VLs > 40 copies per ml. Such patients must undergo intensive adherence counseling and support to avoid further failure, to achieve viral suppression and to prevent the emergence of ARV resistant virus and the necessity to switch to second line treatment. In addition, routine viral load measurements will allow analysis of the ART program at the population level.

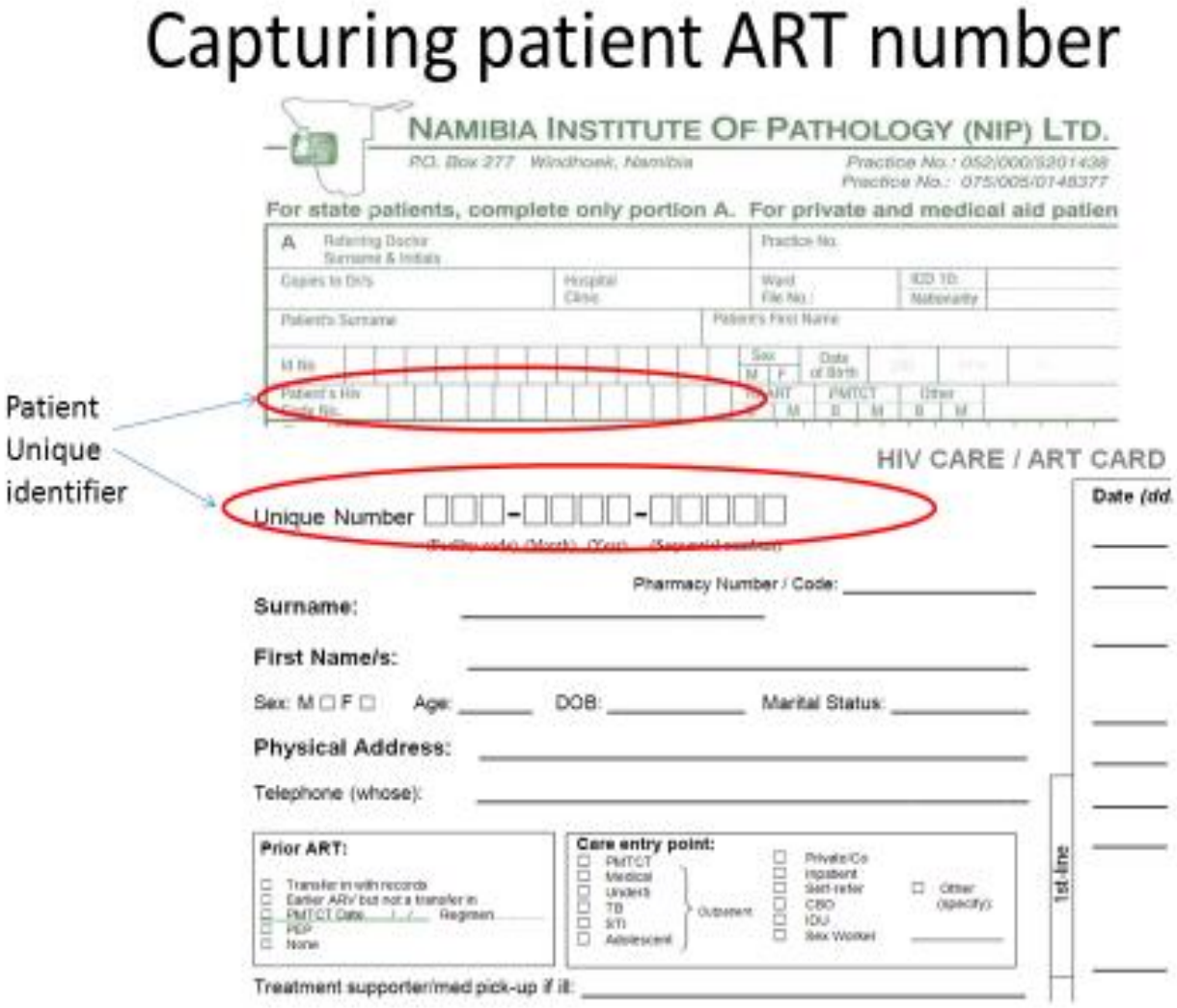
VL assays are also recommended for patients already on treatment who are showing evidence of immunologic and or clinical failure. The test should be repeated in this category of patients 6 months after changing therapy, to evaluate response to the new regimen and to evaluate the level of adherence in this group of patients.

Regions and districts must be made aware that to ensure validity of VL results, blood specimens must reach NIP laboratories **within 6 hours**. Due to reduced validity of results from old specimens, specimens reaching the laboratory for processing after 6 hours will be rejected. At a minimum, samples need to be spun down and separated within that critical period. For districts and facilities which do not have easy access to an NIP lab, alternative arrangements should be made with an NIP lab or NIP visiting sites on specified days. HCWs should use the SOPs for processing of samples at facility level. Facilities will determine the time that specimens will be drawn (e.g. 8-12 am) to ensure that samples get to the lab within 6 hours.

Noting that the plasma VL is still the “gold standard” and should be done wherever possible, another alternative is now a available if there are no other options. That is VL testing through collecting dried blood spots. Clinicians should be aware that the result has a level of detection of 1000 copies/ml, and hence will be useful to determine if a patient is failing treatment, but not to determine if the patient is fully virologically suppressed. HCWs should ensure that ALL DBS card circles a completely filled and samples dried properly before packaging. In addition, the Laboratory request form should **clearly indicate** that this is an HIV Viral Load test.

HCWs are required to capture the **12 digits patient ART Unique Number** on the Laboratory form for ALL HIV Viral Load requests as per below.

Figure 1.4: Laboratory Request Form



1.12 Adverse Reactions Associated with Antiretroviral Medicines

No medicine is 100% safe. Antiretrovirals, like other medicines, may cause adverse reactions (AR). This section provides information on the ARs associated with ARV medicines, and the recommended clinical response. Like all medication toxicities, antiretroviral toxicities are categorized according to severity. The categories are: mild (grade 1), moderate (grade 2), severe (grade 3), life-threatening (grade 4) and death related to the adverse reaction (grade 5).

Some toxicities are class-related while others are related to one particular ARV. The frequency and severity of class related toxicities also vary among medicines within the same class. **Clinicians working with patients on ART should**

be aware of the common and serious adverse reactions associated with these medications and to immediately report any medicine adverse reactions to the Therapeutics Information and Pharmacovigilance Center (TIPC) using the appropriate form. See Appendix 9 for the Adverse Medicine Reaction Reporting Form. Some serious ART-related toxicities are summarised in Table 1.6 below along with ART management recommendations. Management of specific toxicities is in the following section.

1.13 Management of Adverse Medicine Reactions (AMRs) associated with ART

1.13.1 Renal Insufficiency

TDF is included in the preferred first line regimen. The most important side effect of TDF is nephrotoxicity and declining renal function, although the incidence of these complications is relatively rare. TDF nephrotoxicity is characterized by proximal tubular cell dysfunction (indicated by proteinuria or glycosuria) that may be associated with acute kidney injury or chronic kidney disease. Creatinine clearance must be calculated for each patient before starting TDF and regularly monitored during therapy**.** The formula for this calculation is given in Figure 1.2. It is considered safe to continue using normal TDF dose in a patient who remain with creatinine clearance above 50 . Patients with deteriorating renal function TDF should be replaced with alternative ARV , except in case of hepatitis B/HIV co-infection whereby dose adjustment is recommended (See appendix 5)

Neuropsychiatric Changes

Patients started on efavirenz may report abnormal dreams, symptoms of depression, suicidal ideation, dizziness, sense of being off balance and sometimes mental confusion. Most of these complaints are not severe and usually self-limiting, without the need to discontinue ART. However, in case of new onset depression, psychiatric illness or suicidal ideation replace the EFV with NVP

Gynecomastia

Patients present with significant enlargement of breasts and painful breast tissue. This may happen in patients taking EFV or PIs. If this happen stop the EFV to NVP, if on PIs consult the HIV specialist/mentor.

Rash

Rash is a common reaction following initiation of ART. The frequency of rash is estimated at 20% in patients starting NVP-based ART, and 4.6% in those starting EFV-based ART. EFV-induced rashes are generally mild to moderate. Like NVP, EFV and RAL may also provoke severe and life-threatening rashes such as Stevens-Johnson Syndrome (SJS), Toxic Epidermal Necrolysis (TEN), and Erythema Multiforme Major.

Abacavir (ABC) , Raltegravir (RAL) and Dolutegravir (DTG) also causes hypersensitivity reactions. Any rash in a patient on ABC, RAL and DTG could be part of a life-threatening hypersensitivity reaction seen in approximately 5% of patients starting ABC. Patients with rashes on ABC, RAL and DTG need immediate careful evaluation. Symptoms become worse with continued use and include fever, skin rash, malaise, nausea, vomiting, diarrhea, abdominal pain, dyspnea, arthralgia, headache, myalgia, chills and respiratory symptoms. The average onset of reaction is within 9 days of initiation of ABC and within hours after rechallenge.

Rash is also commonly seen in patients taking cotrimoxazole and other non-ARV medicines used in conditions related to HIV disease.

Rashes should be categorized according to the criteria in section 1.12 above, because the management of the rash depends on its severity. Figure 1.5 below summarises recommendations for the management of rash due to specific ARVs.

Figure 1.5: Recommendations for the management of ARV-induced rash

For patients initiated on EFV-based ART

- **When a mild or moderate rash associated with EFV occurs and it does not resolve on observation or following antihistamine therapy, replace EFV with ATV/r** .
- **When a severe or life-threatening rash associated with EFV occurs, stop all treatment at the same time. After resolution of the rash, replace EFV with ATV/r or another PI. Do not replace with NVP.**

For patients initiated on NVP-based ART

- **When a mild or moderate rash associated with NVP**
  - Measure ALT and check for signs of hepatitis
  - **Do not escalate dose of NVP(if the rash happens within two weeks of ART initiation),** continue "lead-in" dose once daily for a further week.
  - Provide supportive treatment (antihistamine) and advise patient to return before one week if rash worsens.
- When rash has resolved after 1-2 weeks, there is no sign of hepatitis and ALT<5xULN
  - Escalate dose to 200mg bd (or appropriate paediatric dose)
- **When rash does not resolve on observation for 2 weeks or does not respond to antihistamine therapy, replace NVP with EFV. The replacement may be immediate.**
- **When a severe or life-threatening rash associated with NVP occurs, stop all treatment. After resolution of the rash, replace NVP with ATV/r or another PI. Do not replace with EFV**

For patients on ABC, RAL and DTG

- **Any rash in a patient on abacavir requires immediate clinical evaluation.**
- **If rash is suspected to be due to ABC, replace ABC with another NRTI**
- **If rash is suspected to be due to RAL and DTG, replace with non intigrase inhibitor (INSTI) ART**
- **Patients should not be rechallenged with ABC, RAL and DTG if there is suspicion of hypersensitivity reaction.**

1.13.2 Hepatotoxicity

Both EFV and NVP may cause severe or life-threatening hepatotoxicity, although hepatotoxicity occurs at a higher frequency with NVP than with EFV, and with an earlier onset, usually within 2 weeks of starting treatment. PIs can also cause hepatotoxicity. Some PIs (e.g. atazanavir/ritonavir and indinavir/ritonavir) may result in the development of unconjugated hyperbilirubinaemia with normal ALT levels. This generally does not require treatment.

The risk of developing hepatotoxicity is higher when NVP-based ART is initiated in an ART naïve patient with a high baseline CD4 count: ≥250 and ≥400 cells/mm^3 in females and males respectively. Other risk factors include pre-existing liver dysfunction, hepatitis-B or C co-infection, and concomitant administration of ARVs with other potentially hepatotoxic medicines e.g. anti-tuberculosis medicines.

Figure 1.6: Recommendations for the management of ARV-induced hepatotoxicity

For patients on any ARVs causing hepatotoxicity

- Stop or substitute relevant hepatotoxic medications in symptomatic patients if ALT is more than 5 times the upper limit of normal, and consult a specialist physician for further management.
- If the ALT is more than 10 times the upper limit of normal in asymptomatic patients, stop all medications immediately.

1.13.3 Haematologic toxicity

Anaemia, leucopaenia, lymphopaenia and thrombocytopaenia are found in 30% to 40% of patients with HIV. As the most common condition is anaemia, all patients have Hb done before intitating ART. Zidovudine (AZT) can be bone marrow toxic, resulting in anaemia, neutropaenia, or both. The use of AZT as an alternative first-line treatment should be avoided in patients with baseline Hb < 8gm/dl. Patients initiating AZT require Hb to be monitored for the first 3 months, the time when AZT-induced anaemia is most likely to occur. (See table 1.6). If Hb drops at all, refer to doctor for evaluation. Doctors should investigate for any other causes of anaemia. If the drop is >10% but <25%, repeat Hb in one week. If the drop is ≥25%, substitute with another NRTI.

Patients on AZT:
AZT should be substituted immediately if Hb falls below 8 gm/dl or drops by more than 25%.

1.13.4 Lactic acidosis

This is a life-threatening complication of ART (mortality approaching 50% in early studies) and can be difficult to recognize as clinical symptoms are non- specific. Clinicians must have a high index of suspicion for lactic acidosis, especially in patients who have been on NRTIs for a prolonged period (>6 months). It has been particularly associated with d4T and ddI use; although it has been reported with most NRTIs (abacavir and tenofovir are exceptions). Co- administration of TDF with some non-ARVs such as tetracycline (antibiotic) and metformin (anti-diabetic) is a risk factor. Additional risk factors include female gender and obesity, chronic HCV, CD4 count <350 cells/mm^3, and nutritional factors such as riboflavin or thiamine deficiencies (HSS Panel 2012a). Patients with lactic acidosis often have had excellent virological and immunological response to their ARVs. The clinical symptoms of lactic acidosis are summarized in Figure 1.7 below.

Figure 10.7: Clinical symptoms of lactic acidosis

• Abdominal Pain	• Hyperventilation	• Liver dysfunction
• Weight loss	• Nausea and vomiting	• Arrhythmias
• Malaise	• Cold extremities	• Cyanosis
• Lethargy	• Hypotension	• Stupor or coma

Lactic acidosis should be suspected in any symptomatic patient having an unexplained acidosis (no evidence of diabetic ketoacidosis, renal failure, dehydration, etc.). Asymptomatic hyperlactataemia is common among patients on ART and requires no treatment. Early intervention can lead to resolution of lactic acidosis. Its management must include immediate discontinuation of ART.

Patients with lactic acidosis may present with acute multi-organ failure, such as fulminant hepatic, pancreatic, and respiratory failure. In addition to the symptoms of metabolic acidosis, lactic acidosis is distinguished by hyperlactataemia:

- pH < 7.25 (normal arterial blood pH ranges from 7.38 to 7.42).
- HCO^3< 21 mEq/L.
- Plasma lactate 2 to 5 mmol/L (moderate).
- Plasma lactate > 5 mmol/L or greater than 2 times the upper limit of normal (severe).

Supportive management within an ICU setting may be lifesaving:

- Hydration.
- Respiratory and/or haemodynamic support to improve tissue perfusion.
- Maintenance of airway patency.
- Delivery of oxygen.
- Monitoring of cardiac rhythm.
- Bicarbonate replacement is controversial and should be avoided.

Recovery from an episode of lactic acidosis can be slow. Continuation of ART following lactic acidosis can only occur after complete resolution and recovery from the acidosis. Modified ART regimens will be required hence consultation with a specialist is essential. See section 1.14 for further details on changing or stopping regimens. Monitor patients monthly for at least 3 months.

1.13.5 Lipodystrophy and lipid abnormalities

Antiretroviral medicines are known to cause lipid abnormalities. The NRTIs and INSTI (RAL) are associated with lipoatrophy and fat accumulation in the abdomen and back, while the PIs and NNRTIs (EFV) and INSTI (RAL, DTG) are associated with abnormalities of lipid levels in plasma. This section provides recommendations on how these abnormalities are managed. Some patients receiving ART can, after several months or even years, develop body changes resulting from the loss of subcutaneous fat in some areas and the abnormal deposition of fat in other areas. Some patients will also develop elevations in cholesterol and/or triglyceride levels. These changes are most commonly associated with protease inhibitor-containing ART regimens with major effect seen in LPV/r combination. However, it has also been seen in patients on all regimens.

For most patients, these changes will be minor, but for some, the cosmetic changes can be extreme – especially when fat is lost from the face resulting in sunken cheeks and temples. For others, the changes can be physically uncomfortable (such as fat loss in the buttocks making sitting uncomfortable, or fat deposition around the neck and upper back making lying down uncomfortable).

Currently there are no recommended treatments for these fat changes other than cosmetic surgery. With respect to lipid changes, patients on protease inhibitors with other risk factors for cardiovascular disease should have their lipids monitored on an annual basis and should be counselled to reduce all possible cardiovascular risks (e.g., stop smoking). If these abnormalities become intolerable, consideration can be given to changing regimens, although this has had variable results in trials. Stopping ARV treatment or substituting can usually halt the process and will sometimes result in a decrease in the fat deposits, but does little to correct fat losses. Patients should be informed of these potential side-effects, with careful emphasis on HIV disease progression if ART is discontinued or delayed.

EFV, too, has been associated with elevation in plasma cholesterol (both total cholesterol and high density lipoprotein cholesterol) and triglycerides. The use of statins is recommended by WHO for individuals with 10 years or more cardiovascular risk exceeding 30% or people with history of cardiovascular disease. (Refer to the Appendix 10 for information on interactions between statins and ARVs).

1.13.6 Pancreatitis

Toxicity resulting in pancreatitis is most commonly associated with the use of didanosine (ddI). It also can be seen with the use of other NRTIs, especially stavudine (d4T). Patients experiencing abdominal or epigastric pain should be informed to report these side effects to the HCWs. These patients should have serum amylase levels measured urgently. Consultation with a specialist physician is recommended if amylase levels are repeatedly above the upper limit of normal (ULN). Didanosine or other potentially offending medicines (d4T) should immediately be stopped if amylase levels are more than 2.5 times ULN. Patients who experience ddI/d4T-related pancreatitis should never receive these ARVs again. See section 1.14 for further details on changing or stopping regimens. High amylase is common in asymptomatic HIV patients and is usually not due to pancreatitis but to sialadenitis (inflammation of the salivary glands).

1.14 Considerations when changing or stopping ART

Substitution of ARVs should not be delayed in cases of severe adverse medicine reactions in order to avoid harm and poor adherence to treatment, which will ultimately lead to drug resistance and poor treatment outcome. When an ARV must be stopped due to intolerance or mild to moderate toxicity, and the offending agent can easily be identified, simple substitution with another ARV in the same class may be done without stopping treatment. For example, a patient taking a TDF-containing regimen who develops renal insufficiency can have the TDF replaced by ABC.

In situations where the adverse reaction is mild or moderate (grade 1 or 2), but the substituting medicine can cause similar reactions, it is advisable to withdraw the causative agent and allow the adverse reaction to resolve before

substituting. If immediate substitution is done the reaction may worsen and both medicines will be lost from the regimen, hence narrowing future treatment options for the patient.

When NNRTIs (NVP or EFV) must be stopped, and the patient is on AZT, patients should discontinue the NNRTI first and continue with the NRTIs at their usual dosage for 14 days. This will decrease the risk of developing NNRTI (cross-) resistance. If the patient is taking either TDF or ABC with an NNRTI, the whole regimen can be stopped at the same time.

If cross-reaction is not expected, then immediate substitution may be made following grade 1 and 2, and higher grade reactions. For example when a patient develops serious CNS symptoms associated with EFV, an immediate replacement with NVP can be made.

Patients with severe life-threatening toxicity on EFV (or NVP), such as symptomatic hepatitis, Stevens - Johnson syndrome or Toxic Epidermal Necrolysis, should stop all medications immediately. When the toxicity has resolved and the patient has recovered, ART can be restarted without using an NNRTI, to avoid recurrence of the toxic event.A regimen that combines 2 NRTIs with a PI can safely be stopped at once.

Table 1.6: ARV-Associated Adeverse Medicine Reaction and Recommended ARV Substitution

Adverse Medicine Reaction	Associated agent(s)	Common signs	Clinical response /ARV Substitution
Potentially fatal adverse effects			
Renal toxicity (renal tubular dysfunction)	TDF	Often asymptomatic, occasionally decreased urine output, Fluid retention, causing swelling in your legs, ankles or feet	If HBV-co-infected, decrease dose of TDF according to the dose adjustment table for renal insufficiency (Appendix 5). If not HBV co-infected, change TDF to ABC
Haematological toxicity (bone marrow suppression: macrocytic anaemia or neutropaenia)	AZT	Dizziness, syncope, palpitations, chest pain, shortness of breath, pale skin, menorrhagia in females, inability to concentrate, cold hands and feet ,	Substitute AZT with TDF if a) within the first 3 months of treatment or b) more than 3 months after start of treatment if recent VL in last 6 months is <40 copies/ml Substitute AZT with d4T if VL unknown or >40 copies/ml, until VL is suppressed
Toxic epidermal necrolysis (TEN) or Steven's Johnsons Syndrome	NVP EFV-less commonly RAL DRV/r	Diffuse, moist desquamation, maculopapular rash involving mucous membranes. Skin peeling leading to formation of painful sores, flu-like symptoms	Stop immediately. Never re-challenge. After resolution, resume ART with a boosted PI instead of an NNRTI
Skin rash with or without hypersensitivity reaction	ABC	Pyrexia and rash, malaise, nausea, headache, myalgia, arthralgia, diarrhea, shortness of breath , systemic anaphylaxis, arthralgia, ,	Stop Immediately. Never re-challenge. After resolution, resume ART with TDF. If cannot use TDF, and if <3 months since start of ART, use AZT or consult an HIV specialist
	RAL		Stop Immediately. Never re-challenge. Substitute with non- INSTI.

Adverse Medicine Reaction	Associated agent(s)	Common signs	Clinical response /ARV Substitution
	NVP EFV-less commonly		For mild to moderate rash, substitute NVP with EFV
Lactic acidosis	All NRTIs (particularly d4T, ddI and AZT)	Gradual onset of nausea/emesis, unexplained weight loss, fatigue, dyspnoea (late) motor weakness, and may include mental status changes and organ failure.	Stop immediately After resolution, check latest VL; if done < 6 mo *prior to* the adverse event and if VL was <40copies/ml, resume ART with TDF; if cannot use TDF, give ABC. If VL was not suppressed, discuss with an HIV specialist
Hepatitis	All ARVs (particularly NVP)	Jaundice , hepatomegaly, elevation of liver enzymes, darkened urine and stool, abdominal pain, diarrhoea, nausea, vomiting & pyrexia	If ALT is >5 times the upper limit of normal, discontinue ART and monitor. After resolution, restart ART, replacing the causative drug.
	DTG		Assess for renal dysfunction if SCr increases by >0.4 mg/dL
Disabling adverse effects			
Peripheral neuropathy	All NRTIs worse w/d4T ddI	Distal extremity painful dysesthesias, allodynia, severe burning pain, pins and needles sensations,	Replacement of d4T with AZT or, if VL<40 in the last 6 months then with TDF Symptomatic treatment
Osteonecrosis/ osteoporosis	Origin uncertain (TDF, PIs?)	Bone pain or tenderness, limited range of motion, joint stiffness, or limping, muscle spasms, progressive bone damage leading to bone collapse, neck or low back pain, loss of height , stooped posture	Manage osteoporosis
Male gynaecomastia	EFV, PIs	Significant enlargement of breasts; painful breast tissue	Substitute EFV with NVP
Neuropsychiatric Changes	EFV,INSTI (RAL, DTG)	Abnormal dreams, Depression, suicidal ideation, or mental confusion	Dreams are usually self-limited, without the need to discontinue ART. New onset depression, psychiatric illness or suicidal ideation replace EFV with NVP
Acute pancreatitis	d4T ddI	Upper abdominal pain which radiates to the back and is exacerbated by the ingestion of food. Abdominal swelling & tenderness, indigestion, steatorrhea, nausea, vomiting & pyrexia	Stop immediately After resolution, check latest VL; if done < 6 mo *prior to* the adverse event and VL was <40 copies/ml, resume ART with TDF; if VL was not suppressed, use AZT and work on adherence.
Long-term adverse effects			
Lipoatrophy and	NRTIs d4T> AZT	Significant loss of subcutaneous fat; abnormal fat distribution	Replace suspected ARV with less toxic agent

Adverse Medicine Reaction	Associated agent(s)	Common signs	Clinical response /ARV Substitution
lipodystrophy	All PIs and EFV INSTI (RAL,DTG)		
Dyslipidaemia	All NRTIs, (d4T worst NRTI) All PIs and EFV DTG	Asymptomatic	Consider replacing the suspected ARV. *NB: currently lipids and cholesterol not monitored routinely in the state sector*
Insulin resistance	All PIs d4T, AZT, ddI	Polyuria, polydipsia, polyphagia, Unexplained weight loss, and fatigue or weakness	Discuss with specialist
Myopathy	AZT, RAL	Muscle pain, weakness, rhabdomyolysis	Do CPK. If elevated stop the ARV and discuss with HIV specialist
Rapidly progressive neurologic weakness	D4T	Ascending muscle weakness similar to Guillaine Barre syndrome	Stop d4T, consult HIV specialist

1.15 Food and medication interactions

Due to the effect of HIV on the immune system, persons infected with HIV are more prone to opportunistic infections than healthy individuals. Furthermore, a low CD4 count and/or high viral load greatly increases one's chances of developing these infections. Antiretroviral therapy provides the body with tremendous benefit in suppressing the viral load thereby increasing the CD4 levels, , and reducing the chances of developing opportunistic infections. Special nutrition considerations must be taken when prescribing ART to clients.

To minimise the negative effects of food-medication interactions and to maximise the benefits of available medications and nutrients, it is important to understand food and medication interactions and how to manage them to improve the health of the client.

Foods and medications can interact in a number of ways that result in both positive and negative health and nutritional outcomes in people living with HIV. Some interactions between medications and food are as follows:

- The effect of certain foods on how medicine works in the body (how medicines are absorbed, metabolised, distributed, and excreted).
- The effect of certain medicine on how food is used in the body –(how nutrients from foods are absorbed, metabolised, distributed, and excreted).
- The side-effects of a medication, which, in turn, can affect food intake and nutrient absorption.
- Side-effects caused by combinations of certain medications and foods.

Most ARVs can be taken with or without food. Proper nutrition management interventions can help alleviate some of these negative effects and can help people living with HIV maintain adequate food and nutrient intake.

1.15.1 The effects of food on medications

Food can enhance or inhibit the absorption, metabolism, distribution, and excretion of medication, and therefore, affect the medication's efficacy and the overall health of the individual. High fatty food increases the bioavailability

of TDF and absorption of PIs. Even if the clinical significance with regard to ARV effectiveness of this is not clear, patients should be counseled to reduce consumption of high fat diet.

1.15.2 Nutrition-related Side-effects of medications and food

Medications may cause side-effects that affect food intake and nutrient absorption in the following ways:

- Side-effects of medication, such as taste changes, loss of appetite (i.e. anorexia), nausea, bloating, heartburn, vomiting and diarrhoea reduce food intake or nutrient absorption.
- Reduced food intake and poor nutrient absorption can lead to weight loss.
- Weight loss leads to further weakening of the immune system.
- A weakened immune system allows HIV to progress to AIDS more rapidly.

However most patients recover quickly and do well on ARV medications.

While ARVs contribute to improved nutritional status, they occasionally create nutritional problems, which require nutritional and other life-style interventions.

- **High blood cholesterol:** Nutritional counseling to reduce dietary fat intake and limiting saturated and trans-fat intake, increase daily vegetable and fruit intake, and regular exercise should be promoted.
- **High triglycerides:** Nutritional counseling to limit saturated and trans- fats intake (low density lipoproteins), moderation in carbohydrate intake and an increase in intake of whole grain cereals, fruits and vegetables. Regular exercise is a vital supportive measure.
- **Peripheral neuropathy:** This is not uncommon condition and is often described as numbness, tingling, burning sensation in the toes, feet, fingers or hands. It might be attributed to HIV, medical treatment or nutritional deficiencies. Thus the cause must be determined in order to provide specific treatment. The condition is usually treatable and reversible. Supplementation with vitamin B is only useful where nutritional deficiency is considered likely.
- **Diabetes:** Some PIs and NRTIs can affect carbohydrate metabolism which may cause insulin resistance and thus, increases patient's risk of developing diabetes. Relevant lifestyle advice should be given.

Proper nutrition management can help maintain food intake, compensate for nutrient losses, prevent weight loss and improve the condition of the patient. Proper nutritional management can also improve adherence to the regimen. When not properly managed, side-effects often lead to the interruption of treatment and contribute to poor adherence. Therefore, nutrition counseling should be provided to all clients on ART from the start of therapy. Health workers and counsellors should provide clients with dietary guidance that is specific to the patient's situation.

1.15.3 Nutrient requirements for people living with HIV

Nutritional assessment, counseling, support, and monitoring are essential components when providing care to HIV patients. Clinical and dietary assessment at enrollment and during management helps in determining additional contributory factors to poor response to therapy. This can promote timely and appropriate interventions. Meal planning should correspond to nutritional requirements of the ARV regimen and should be feasible for clients.

There should be counseling sessions provided by healthcare workers (HCW) to patients and household members if possible, that is directed at helping them to understand the impact of therapy on nutritional status and vice versa. HCWs should also work with patients to identify feasible options.

To provide counseling for clients on antiretroviral therapy, health workers should:

- Always promote and encourage optimal nutrition intake with a variety of foods every day.
- Discuss ART and food interactions with the client before they begin treatment.
- Ask the client about food availability and access at the household level. Address such issues with referrals to community- based projects, or other assistance.
- Use the Food and Medication Intake Form to assist in counseling the client on the importance of food intake with ART.
- Identify medications that have special food interactions

- Identify potential nutrition-related side-effects with ART and provide counseling on management of side-effects.

Malnutrition among PLHIV manifests most commonly as weight loss and wasting in adults. Weight loss among PLHIV occurs due to reduced intake (starvation), malabsorption and sudden increase in energy expenditure, problems with utilization or a combination of these factors. Therefore, a key objective of nutrition, care and support for PLHIV is to prevent weight loss and maintain nutritional status within the normal range.

Good nutrition management can help maintain food intake, compensate for nutrient losses, prevent weight loss and improve the condition of the patient. Proper nutritional management can also improve adherence to the regimen. For these reasons, nutrition counseling should be provided to all clients on ART from the start of therapy.

Increased energy needs

Asymptomatic adult PLHIV require an additional 10% energy foods while symptomatic adult PLHIV require an additional 20-50% depending on disease stage. To achieve the additional energy needs, PLHIV should be counseled and educated on consumption of a variety of foods.

Strategies to meet increased energy requirements of PLHIV include:

- Dietary adjustments and meal plans of regular energy giving foods such as mahangu, maize, rice, potatoes, cassava, wheat.
- Adoption of food preparation methods that add value for example sweetening porridge or adding peanut butter, and frying potato chips raises their energy values several folds.
- Consumption of snacks between meal.

Protein needs

According to WHO, there is insufficient evidence to support increased protein requirements for PLHIV. However, the quality of protein with respect to adequacy of essential amino acids is important. PLHIV should therefore be encouraged to consume foods rich in both animal protein (dried small fish, chicken, Mopani worms, fillet and beef) and plants source protein (soya, lentil seeds, beans, groundnuts and peas).

Micronutrient needs

Adequate micronutrient intake is achievable through consumption of a healthy balanced diet including plenty of fruits and vegetables. Current evidence does not support increased micronutrient needs above 1 Recommended Daily Allowance (RDA) for PLHIV compared to non-HIV infected individuals. Therefore, PLHIV should be encouraged to consume plenty of fruits (such as oranges, mangoes, pawpaw, guava, apples, and baobab) and vegetables (such as spinach, amaranthus, cauliflower).

Water requirement

Water consumption is an integral part of good nutritional practices. A daily fluid intake of 2 litres, equivalent to 8 glasses of about 250 ml is required. PLHIV must take adequate amount of clean and safe water to avoid dehydration and aid transport of nutrients, removal of wastes (such as medication by-products), assist metabolic activities, provide lubrication to moving parts and helps regulate body temperature. In the absence of clean safe water, point-of-use water treatment should be provided to the patients.

Severe acute malnutrition in HIV positive adults

PLHIV are at greater risk of malnutrition (under-nutrition) than non-HIV-infected adults. This manifests as wasting, weight loss and/or reduced immunity and is usually as a result of deficiency in macro- and micronutrients. Prevention or treatment of moderate and severe malnutrition is essential in HIV infected adults. All HIV infected adults attending the ART clinic should regularly undergo nutrition assessment (weight, height, BMI or MUAC) for categorization of their nutritional status. Health care workers should integrate NACS into HIV Clinic care.

Patients who received therapeutic food supplements and have improved nutritional status should be referred and linked to community-based support services through regional councils and other line Ministries.

Furthermore they should be adequately counseled/educated on nutrition using appropriate guidelines. For the management of moderate/severe malnutrition in HIV positive adults refer to Appendix 7.

1.16 Supplements

Traditional therapies and remedies for PLHIV should be discouraged.
Considerations when discussing supplements with clients:

- Multi-vitamins should be used as prescribed by a health worker , they offer most of the micronutrients needed and no extra supplements are necessary.
- Other supplements including traditional herbs and remedies that claim to boost the immune system or cure disease should be discouraged as they have potential adverse medicine interactions with ARVs.

1.17 Prophylaxis for opportunistic infections

1.17.1 Cotrimoxazole Preventive Therapy (CPT)

Daily cotrimoxazole reduces the risk of death and hospitalisation of persons with HIV. In several African countries, different studies have shown that it has reduced overall mortality, hospitalisations, cases of pneumocystis pneumonia, cases of toxoplasmic encephalitis, malaria episodes, bacterial infections including bacterial pneumonia, diarrhoea and bacteraemia, and it may reduce diarrhoea from Isospora sp. Cotrimoxazole also reduces morbidity and mortality in TB patients who are co-infected with HIV.

Cotrimoxazole prophylaxis (two x 400/80mg tablets equivalent to 800/160mg total -daily) is recommended for all adults with HIV who either have WHO Clinical Stage 3 or 4 disease (see Appendix 1) or any WHO clinical stage with a CD4 cell count ≤ 350. The eligibility criteria for initiating CPT has not changed from the previous guideline. Patients with known allergy or those who develop allergy to cotrimoxizole and whose CD4 count is <200 cells/mm^3 should be given Dapsone 100mg once daily as an alternative. .When dapsone (as a substitute for CPT) is being used as PCP prophylaxis, it is only recommended for patients in WHO Stage 4 and/or absolute CD4 count < 200 cells/µL (or CD4 % < 14%), and should be discontinued once a patient achieves a CD4 count of > 200 cells/µL for at least 6 months. Dapsone will contribute to anaemia in most patients, and causes haemolytic anaemia in some patients, so patients should have a baseline Hb before starting dapsone and Hb monitored every 1-2 weeks for the first couple of months.

If a patient started Cotrimoxazole at a CD4 level of > 200 cells/mm3 and developed severe reaction such that desensitization cannot be attempted, then stop cotrimoxizole and do not give Dapsone. If a patient started cotrimoxizole at a CD4 of <200 cells/mm3 and developed severe reaction such that desensitization cannot be attempted, then stop Cotrimoxazole AND give Dapsone 100mgs/day. Discontinue Dapsone when the CD4 count is >200 cells/mm3 for two consecutive determinations 6 months apart

NOTE: *Dapsone is useful to prevent of Penumocystis Jiroveci Pneumonia (PCP) not many other OIs unlike Cotrimoxazole. PCP is commoner at a CD4 levels less than 200 cells/mm3. Moreover, Dapsone has major bone marrow suppressive effects. Hence, the benefit of providing Dapsone to patients with CD4 count more than 200 cells/mm3 will not outweigh the risk of toxicity.*

As previously, HIV-positive pregnant women who are receiveing sulfadoxine/pyrimethamine (SP) for malaria prophylaxis should not be given CPT. During pregnancy, CPT should be initiated irrespective of the gestational age and should continue throughout pregnancy, breastfeeding, and thereafter for life.

Lifelong CPT is recommended for any patient who initiates CPT unless there is a contraindication or clinical indication for discontinuation. In the event of severe renal, liver or BM suppression, discontinue CPT until the clinicial situation has improved.

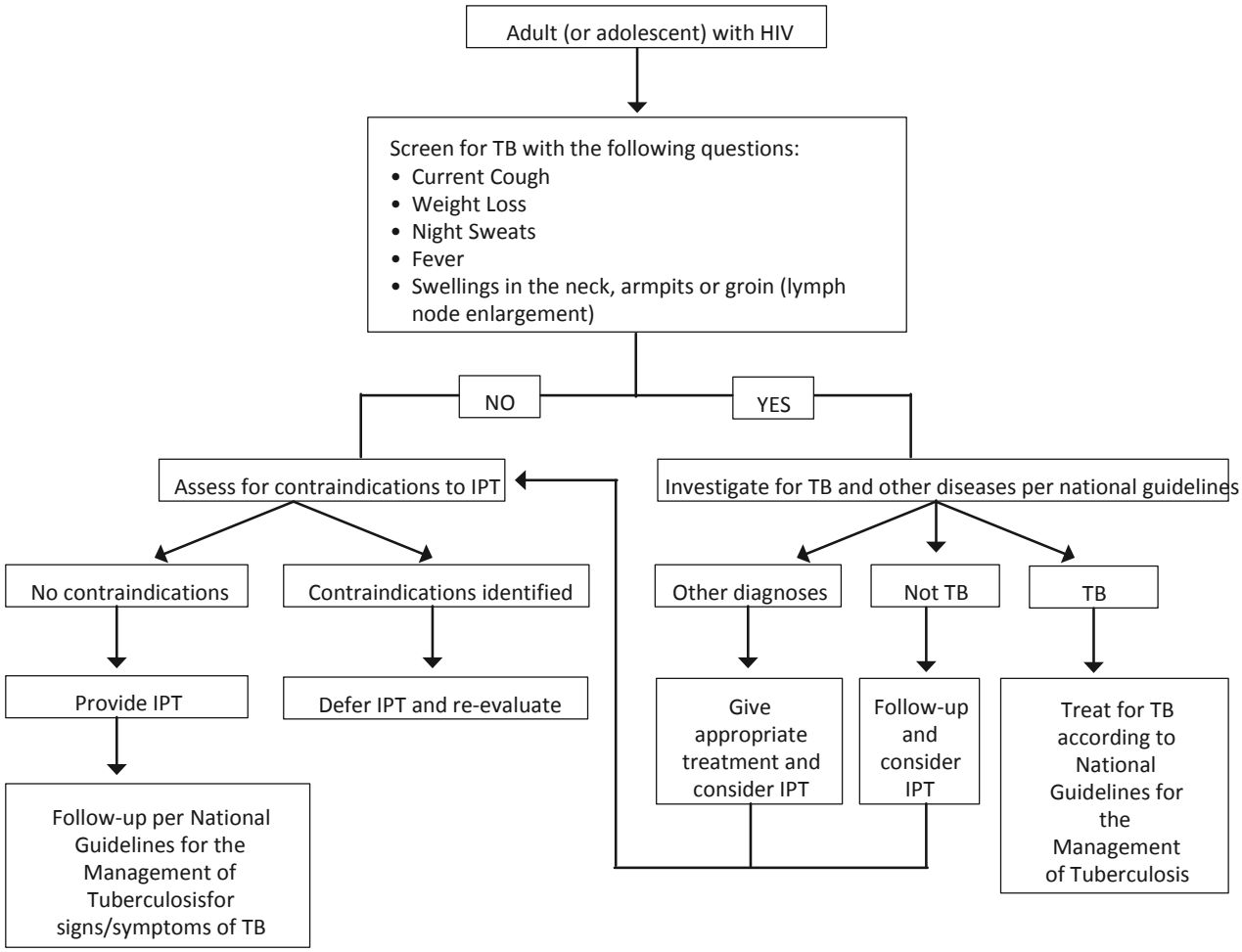
1.17.2 TB screening and Isoniazid (H) preventive therapy for prevention of tuberculosis (TB-IPT)

TB-IPT is very effective in preventing TB disease in individuals who have latent TB infection. Individuals with both HIV infection and latent TB have a 5-10% risk of developing active TB each year, compared to HIV-negative individuals,

whose lifetime risk is 10%. The combination of HIV and TB is one of the major causes of death in Namibia. IPT reduces the risk of TB in HIV-infected patients by at least 60% and, in combination with ART, the risk reduction exceeds 80%.

All people living with HIV should be screened for TB including asking about TB exposure/contact history at each encounter with a health worker or visit to a health facility. See figure 1.8 below for algorithm for TB screening and IPT among adults and adolescents living with HIV.

Figure 1.8: Algorithm for TB screening and TB-IPT among Adults and Adolescents with HIV



Following the strict criteria for TB-IPT eligibility, along with proper monitoring and follow-up, will minimise these risks.

Patients who have signs and symptoms of TB should never be started on TB-IPT.

To be eligible for TB-IPT the HIV-positive individual must:

- Have no symptoms or signs of TB – such as cough, fever, weight loss, night sweats, fatigue, blood in sputum, chest pain, diarrhoea, shortness of breath, enlarged lymph nodes, loss of appetite (*NB: TB-IPT should not be given to patients who are unwell and where there is no explanation of the illness*)
- No current history of alcohol misuse
- Have no history of active liver disease, liver insufficiency, or jaundice
- Have no history of hypersensitivity to isoniazid
- Have no history of exfoliative dermatitis
- Be motivated for TB-IPT after being educated about the benefits, possible side-effects and risks.

In addition HIV-positive persons who are close contacts of patients with infectious TB should receive IPT even if they have completed a previous course of IPT.

Precautions:

- Persons starting TB-IPT must be warned about the possible side-effects of Isoniazid. Isoniazid-induced hepatitis will present with nausea and vomiting accompanied by passing dark urine and/or generalised itching. Peripheral neuropathy manifests as burning, numbness or tingling in feet and/or hands. If these symptoms develop, the patient must stop taking isoniazid and report immediately to the nearest health facility for assessment and management
- Health workers should always check clients for signs and symptoms of hepatitis, neuropathy and skin itching when they come to collect isoniazid.

TB –IPT regimen:

- Isoniazid is given daily for a period of 9 months at a dosage of 300mg/per day.
- Pyridoxine 25 mg daily is administered with the isoniazid to decrease the risk of neuropathy. The risk of developing neuropathy increases in patients also on d4T.
- Temporary TB - IPT interruption, although not ideal, is acceptable, as long as the patient completes a total of 9 months of treatment within a 12 month period. In non-adherent patients, prophylaxis should be discontinued and no further efforts should be made to restart TB - IPT.

Follow up of patients on IPT

Review patients on IPT as appropriate and review/reinforce adherence

- Screen for active TB during each clinic visit using intensive case finding (ICF) form
- Update patient care booklet and TB-IPT clinic register record at every visit and document outcome on completion of therapy
- Monitor for INH adverse effects (co-administer with pyridoxine to minimize adverse events)
    - IPT should be discontinued in symptomatic patients with ALT/AST more than three times the upper limits of normal

Recording and reporting:

All details of the person receiving TB-IPT must be recorded as required in TB-IPT clinic register and in the patient care booklet. In addition either the TB-IPT identity card should be attached to the patient's passport or details of IPT provision should be in the patient's passport. Clinicians should list isoniazid in the list of medications prescribed in the health passport for patients on IPT.

As in the previous guidelines, a 9-month course of TB-IPT is given to each patient. Its efficacy lasts for approximately 1-2 years, after which PLHIV have the same risk of developing TB disease as before the TB-IPT. High risks of reinfection and high susceptibility for TB infection and disease in HIV-positive persons are the cause of this limited efficacy.

1.17.3 Cryptococcal Screening; Pre-emptive treatment and Secondary prophylaxis

Cryptococcal meningitis (CM) is a leading cause of mortality among HIV-infected adults with severe immunosuppression. Early identification of asymptomatic patients and provision of presumptive therapy for patients with a positive cryptococcal antigen test remarkably improves outcomes for these patients. HIV-positive adults with CD4 count <200 cells/mm^3 should be screened for cryptococcal antigenaemia. There are insufficient data to recommend routine cryptococcal screening of HIV-positive children and adolescents, among whom the incidence of CM is much lower.

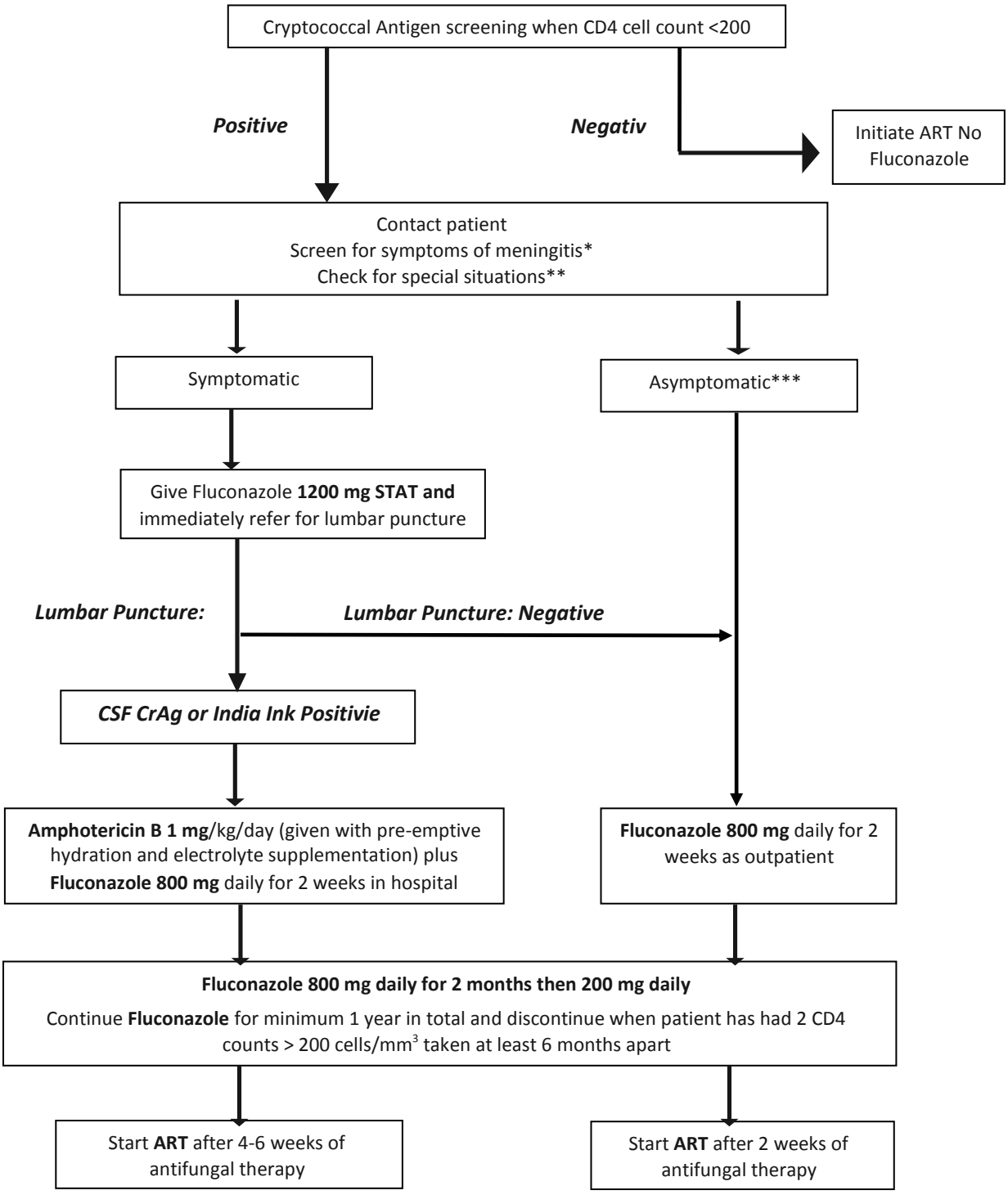
Patients diagnosed with and treated for cryptococcal meningitis should receive secondary prophylaxis with fluconazole 200mg daily for at least one year. This should only be stopped after 2 successive CD4 count results at least 6 months apart are >200 cells/mm^3.

Figure 1.9 shows the current recommended management protocol for HIV-positive patients with positive cryptococcal antigen test.

Timing of ART Initiation in patients with cryptococcal meningitis:

Immediate ART initiation is not recommended in HIV-infected patients with cyptococcal meningitis due to the high risk of IRIS that may be life threatening. ART should be started 4-6 weeks after induction and consolidation anti-fungal regimen.

Figure 1.9: Screening and pre-emptive treatment for Cryptococcal Meningitis



**Symptomatic for meningitis if either of the following present: headache; confusion*

***Special situations include: prior cryptococcal meningitis; pregnancy or breastfeeding mother*

****A lumbar puncture may be considered if available*

1.18 Immune reconstitution

Improvement in a patient's condition in response to antiretroviral therapy (immune reconstitution) is quantitative (CD4 response) and qualitative (antigen/microbe-specific). The clinical impact of immune reconstitution has been demonstrated by:

- The safety of discontinuing prophylaxis for selected OIs.
- The control of several chronic, untreatable opportunistic infections.
- An impressive decline in virtually all HIV-associated complications except lymphomas and liver disease.
- An inflammatory response ascribed to immunologic reactions to selected microbial antigens.

Chronic, relatively untreatable infections that can be controlled with immune reconstitution include molluscum contagiosum, progressive multifocal leukoencephalopathy (PML), cytomegalovirus infections (CMV), cryptosporidiosis, and microsporidiosis. Secondary prophylaxis (suppressive therapy after disease) for opportunistic infections (OIs) may be suspended with adequate criteria for immune reconstitution for virtually all OIs.

1.18.1 Immune Reconstitution Inflammatory Syndrome (IRIS)

This relatively common syndrome results from a dramatic increase in the inflammatory response to antigens from previous, partially treated or latent infections in HIV patients shortly after initiating ART. It usually occurs in the first few weeks after a patient starts therapy. Patients will present with symptoms that suggest worsening of previously diagnosed opportunistic infections or the development of new infections. Although patients with IRIS appear as though ART is failing (clinical deterioration), these patients are actually undergoing robust improvements in their immune systems. Examples of infections or conditions which have been associated with IRIS include tuberculosis, MAC, cryptococcal meningitis, herpes zoster; PML, CMV vitritis, and Kaposi Sarcoma. Recommendations for management vary by pathogen and clinical expression, but most involve medications directed against the pathogen with or without corticosteroids.

1.19 Special populations

1.19.1 People with Tuberculosis and HIV co-infection

Idealy, the patient should receive sevice at one intergrated point of care. The close association between TB and HIV is well-established. TB is the most common opportunistic infection in individuals who are HIV-positive in Namibia. In 2015, a total of 9,944 TB cases were notified with about 98% with known HIV status. The TB/HIV coinfection rate is estimated to be 40% according to the 2015 Global TB Report. ART should be initiated as soon as possible in all HIV/TB coinfected patients with active TB (within 8 weeks after the commencement of TB treatment). HIV-positive TB patients with profound immunosuppression (such as CD4 counts less than 50 cells/mm^3) should receive ART immediately within the first two weeks of initiating TB treatment.

Intensified TB Case-finding (ICF)

All people living with HIV should be screened for TB including asking about TB exposure/contact history at each encounter with a health worker or visit to a health facility and eligible PLHIV should be offered IPT.

TB Infection Control (TB IC)

PLHIV are at high risk of acquiring TB in health care facilities and congregate settings. Each health care facility should have a TB infection control plan for the facility that includes administrative, environmental and personal protection measures to reduce the transmission of TB in these facilities and surveillance of TB disease among workers. A triage system to be put in place to identify patients suspected of having TB and minimize diagnostic delays. Separate people with suspected TB from other patients. Health care workers should be offered HIV testing and counseling and those identified HIV positive should be provided with ART and IPT if they are eligible. Sites should relocate health workers living with HIV to lower risk areas.

TB diagnosis for PLHIV

It is recommended that Xpert MTB/RIF should be used rather than conventional microscopy, culture, and drug susceptibility testing (DST) as the initial diagnostic test in adults and children suspected of having MDR-TB or HIV associated TB.

HIV Treatment

For PLHIV on 1st line ARV with TB No change in regimen

Preferred 1st line ART regimen: TDF + FTC (or 3TC) + EFV

For PLHIV on boosted PI regimen:

Option 1 Substitute rifampicin in the TB treatment with rifabutin

Option 2; If Rifabutin is unavailable or contraindicated, maintain rifampicin in TB treatment and use PI based regimen super boosted with ritonavir:

TDF or AZT + 3TC with LPV/r 400mg+ritonavir 400 mg BD (LPV/RTV)

Note: ATV/r is contra-indicated in patients with TB/HIV co-infection

For patients in whom EFV and super-boosted PI cannot be used

Triple nucleoside regimens: **tenofovir (TDF) + emtricitibine (FTC) (or lamivudine (3TC)) + zidovudine (AZT)**

NB: These combinations are short term and the patient should be switched to a standard regimen two weeks after completing Rifampicin-based TB treatment

If a patient is already on 2nd line ART ***and/or 2nd line Anti TB treament***, discuss management with ***relevant*** specialist.

1.19.2 People with hepatitis B virus (HBV) and HIV co-infection

Prevalence of Hep B in Namibia, is not documented, however it is estimated at 10%.

Patients on ART are at risk for hepatotoxicity due to ART regimens. In addition to the liver damage caused by chronic HBV co-infection. Patients may also experience accelerated liver damage following immune reconstitution (HBV-associated IRIS). All PLHIV should be assessed at enrolment for hepatitis B surface antigen. Lamivudine (3TC) and tenofovir (TDF), have antiviral effects on HBV. And should be used together to effectively suppress HBV replication. Caution should be excercised when stopping ART in HBV/HIV co-infected patients due to risk of rebound Hepatis viral DNA leading to liver damage. It is important to maintain both TDF and XTC when switching regimens due HIV treament failure as HBV resistance to lamivudine develops within two years in 50% of HIV/HBV co infected patients on lamivudine-containing ART without tenofovir. Patients with HIV/HBV coinfection on ART require close monitoring for clinical signs and symptoms of hepatotoxicity and laboratory monitoring of ALT.

All patients in whom HBsAg is reactive (positive) shall have ALT at ART initiation 2, 6, and 12 weeks, and 6-monthly thereafter if the repeat HBsAg result remains positive at 6 months. Elevated ALT arising during therapy may have many causes, and needs to be carefully evaluated for each patient.

Table 1.7: Common causes of liver disease among HIV-positive persons in Namibia

Category of liver disease	General etiology	Specific etiology	Notes
Hepatocellular Disease (ALT or AST)	Medication toxicity	ARV's: NVP>>RTV>EFV NNRTIs and PIs	
	Lactic acidosis with steatohepatitis	NRTIs: d4T>ddI>AZT	
	Acute viral hepatitis	Hepatitis A,B	Self-limited
	Chronic viral hepatitis	Hepatitis B,C	With abrupt withdrawal of TDF or 3TC, or with development of resistance to anti-hepatitis B medicines ALT may rise
	Immune Reconstitution Inflammatory Syndrome	Immunologic response to hepatitis B	If severe may have to stop ART temporarily
	Alcoholic liver disease	Alcoholic steatosis, acute alcoholic hepatitis	Reduce or eliminate alcohol use
Jaundice Bilirubin	Severe liver insufficiency	Any cause	High direct bilirubin, ALT/ AST, low albumin, prolonged prothrombin time, may have ascitis, encephalopathy, GI bleeding
	Severe malaria	Haemolysis rather than hepatitis	High indirect bilirubin with anaemia and positive malaria smear
	Biliary tract obstruction	Common bile duct stones, pancreatitic cancer, mass in prota hepatis	High direct bilirubin, alkaline phosphatase, normal ALT/AST, sonogram helpful
Infiltrative liver disease	Infections	Extra-pulmonary or disseminated TB, MOTT	High alkaline phosphastase, other LFTs nearly normal, hepatomegaly
	Immune Reconstitution Inflammatory Syndrome	Hepatoma, lymphoma, liver metastasis	See section 1.18.1
	Malignancies		Sonogram helpful, liver biopsy diagnostic

1.19.3 People with renal disease

In patients with renal insufficiency or renal failure, ARV dosages need to be adjusted for some medicines on the basis of creatinine clearance (see Appendix 3). Discuss with colleagues or where possible consult with an HIV specialist before starting ART in a patient with renal failure or when renal failure develops in a patient on ART. Figure 1.2 contains the formula for the calculation of CrCl.

1.20 Non-Communicable HIV-associated diseases in Namibia

1.20.1 Common cardiovascular diseases

Non-communicable diseases also affect HIV-infected patients. These diseases include hypertension, diabetes mellitus, and ischaemic and rheumatic valvular heart disease. Generally, cardiovascular conditions particularly pericarditis and dilated cardiomyopathies may be HIV, OI, or medication-related.

Some ARVs, especially PIs, may cause hypercholesterolemia and in the long term could result in premature onset of coronary artery disease or stroke. Therefore, there should be constant screening of such complications of treatment as indicated.

Increased vasculitic events have been noted in HIV patients leading to strokes, peripheral arterial occlusions and other vaso-occlusive events.

At every clinical visit, the patients should be assessed and educated on risk reduction for cardiovascular diseases, by:

- Weight measurements and BMI calculation
- Blood pressure assessment
- Random blood sugar every 6 months for patients with established risk of cardiovascular diseases
- Random Blood cholesteral once a year for all patients on ART and fasting lipogram for at risk patients(PLHIV and Hypertension, PLHIV with Diabetes,PLHIV with history familial dysplidaemia)
- CVD risk reduction counselling- Refer to Namibia Standard Treatment Guidelines (STG) section on Hypertentsion

1.21.1 When to consult

1.21.1.1 HIV specialist/mentor

Good collaboration between general practitioners and HIV specialists/Mentors is essential for the establishment of successful and durable antiretroviral therapy. In the following circumstances consultation with a specialist/mentor is recommended:

- Co-morbid pathologies (hepatitis, renal failure, diabetes, neoplasia, etc.).
- Severe medication toxicities.
- Failure of, or severe toxicity with, first line therapy and consideration of second line therapy.
- Patient failing on second line ART therapy
- Any uncertainties or challenges relating to clinical management of patients

1.21.1.2 MOHSS HIVDR Committee

The MOHSS has established HIV DR Central Clinical Commiteee (HIV DR CCC). This committee reviews and supports the management of all patients with HIV DR. Health Care workers will consult the committee,

- When you have received the genotype HIV resistance results done in consultation with the HIV specialist/ mentor
- When you require receommendation for patients on third line regimens
- When repeat HIV genotyping is deemed necessary (this is an uncommon situation).

CHAPTER 2: ELIMINATION OF MOTHER-TO-CHILD TRANSMISSION (eMTCT)

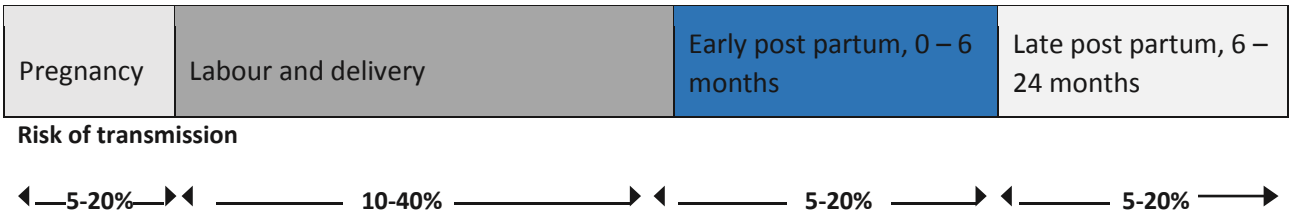
2.1 General Considerations

eMTCT includes 4 main strategies:

1. Primary prevention of HIV infection.
2. Prevention of unintended pregnancy in HIV infected women.
3. Prevention of HIV transmission from HIV infected women to their infants.
4. Provision of comprehensive care to mothers living with HIV, their children and families.

In the absence of antiretroviral medicines and with breastfeeding, published estimated rates of mother-to-child transmission (MTCT) of HIV range from 21% to 43% in various African settings. When it occurs, most transmission takes place during labour and delivery, followed by transmission in the uterus and through breastfeeding, depending on duration. The longer the child is breastfed, the greater the risk of HIV transmission.

Figure 2.1: Timing of mother-to-child transmission with breastfeeding and no ARVs



(Adapted from Bertolli et al., Estimating the timing of mother-to-child transmission of human immunodeficiency virus in a breast-feeding population in Kinshasa, Zaire. J Infect Dis. 1996 Oct. 174(4): 722-6.)

Factors that increase the risk of mother-to-child transmission can be divided into obstetrical, maternal, foetal and viral factors as shown in Table 2.1.

Table 2.1: Factors that increase the risk of mother-to-child transmission

Obstetrical	Maternal	Foetus/Newborn	Viral
• Episiotomy • Invasive monitoring • Instrumental delivery • Rupture of membranes(ROM) >4 hours • Antepartum and intra partum haemorrhage • Amniocentesis	• High viral load • Low CD4 co unt • Advanced disease • Poor nutrition • Breast condition • STIs • New HIV infection • Maternal TB	• Prematurity • Multiple births • Breast feeding • Mixed feeding • Immature gastrointestinal tract • Genetic factors • Immature immune system	• Viral type • Viral resistance

Numerous clinical trials have demonstrated that appropriate use of ARVs can be highly efficacious in reducing the risk of MTCT.

All pregnant women should be offered HIV testing and counselling at their first antenatal visit or subsequent visits if not already tested and have no record of HIV positive results. Health workers should retest previously HIV-negative women as follows:

- first ANC visit
- after 3 months and at 36 weeks (unless already tested negative at 32-35 weeks)

- 6 weeks post-natal and
- 6 monthly during the breastfeeding period

All Pregnant and breastfeeding HIV positive women should be **started on treatment** upon diagnosis or as soon as possible. They should also receive further counselling and clinical care during ANC follow-up, labour, delivery, and breastfeeding period in order to optimize eMTCT as well as the health status of the woman and her infant. Lifelong ARV treatment using an appropriate triple antiretroviral regimen should be provided for all HIV-infected pregnant and breastfeeding women regardless of WHO clinical stage or CD4 cell count and promote safe feeding practices. Infants of mothers receiving ART and who are breastfeeding or on replacement feeding should receive *at least* 6 weeks of infant prophylaxis, as described below.

2.2 Monitoring of viral loads in pregnant and breastfeeding HIV-positive women and HIV-transmission risk for infants

The goal of ART for HIV positive pregnant women is three-fold: to restore and maintain the mother's immune function and therefore general health;secondly, to prevent transmission of HIV during pregnancy, labour, delivery and during breastfeeding; and thirdly resulting reduction in VL reduces the risk of HIV transmission/re-infection. All recommended ART regimens consist of two nucleosides and a potent third medicine to complement it. Because some patients will not tolerate the recommended first line therapy, clinicians providing ART should be familiar with the various regimens.

Monitoring HIV-positive pregnant women is essential in order to achieve the goals listed above. The frequency of VL monitoring is increased in this guideline compared to the previous guidelines in line with the MoHSS commitment to elimintate MTCT and is described below.

For women already on ART:

- Check the most recent routine VL to ascertain if the VL is suppressed.
    - If a VL was not done within the last 3 months, repeat it at the first ANC visit and provide adherence counseling.
    - If the VL was/is >1000 copies/ml, intensive adherence counseling should immediately be given and the VL should be repeated in 6 weeks and every 3 months thereafter until delivery, then at 6 weeks post-partum, and thereafter every 3 months until end of breastfeeding period.

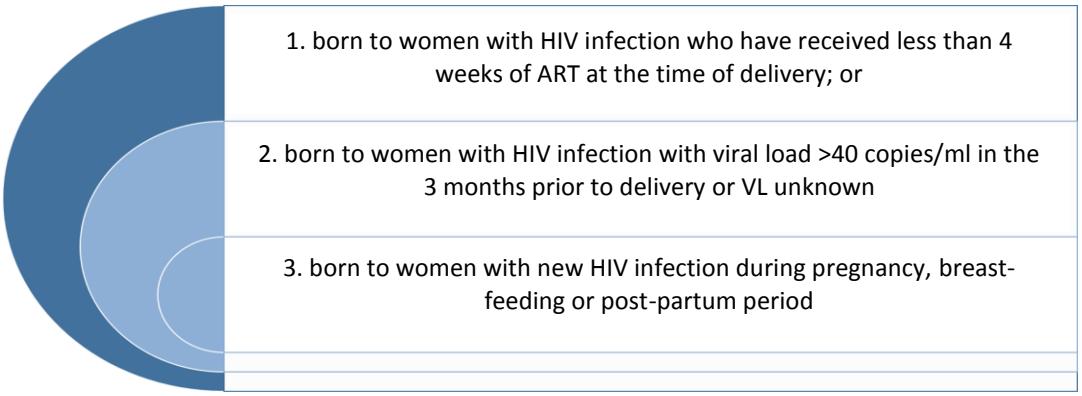
For women initiating ART during pregnancy, or in the breast-feeding period:

- Do VL 3 months after initiation, then 3-monthly until delivery, then 6 weeks post-partum , and thereafter every 3 months until the end of the breastfeeding period

The above VL monitoring schedule will help to determine whether or not and when her breastfeeding infant can discontinue nevirapine prophylaxis. **At the end of breastfeeding, the viral load monitoring schedule should revert to the non-pregnant adults.**

Risk stratification for HIV exposed infants is important to differentiate the management of infants with high-risk of HIV transmission compared with those with standard risk. Figure 2.2 below defines high-risk infants for HIV infection in Namibia.

Figure 2.2: Definition of Higher-risk Infants for HIV infection



Higher risk infants qualify for the following 3-pronged PACKAGE OF CARE:

1. HIV Nucleic Acid Test (NAT) test dried blood spot (DBS) within 48 hours of birth after the infant's first bath, and labelled as a "fast-track" birth test with the name and telephone number of the district point person
2. Dual infant prophylaxis to be given for the first 6 weeks of life as described in table 2.2 below
3. Intensified tracking including:
   - maternity facility to record in a designated register the mother's contact details, a treatment supporter's contact details, anticipated PHC clinic to attend in 2 weeks for birth test result, anticipated PHC clinic to attend in 6 weeks
   - point person in the district designated to review the maternity facility high risk infant register on a weekly basis, follow-up with NIP for the results, and inform both the 2-week and the 6-week clinic of results. If result is positive, additionally contact the mother to say the result of the birth test is ready and she should come to the clinic (confirm which clinic)
   - NIP to immediately notify the point person for any positive NAT test result

Table 2.2: Classification of infant risk and implications for infant prophylaxis regimen

Classification of risk	Risk criteria	Infant prophylaxis for first 6 weeks	Infant prophylaxis after 6 weeks of age
Higher risk of HIV transmission to infant	-Born to women with HIV infection who have received **less than 4 weeks of ART at the time of delivery;** or -Born to women with HIV infection with **viral load >40 copies/ml in the 3 months prior to delivery** if VL measurement is available or -Born to women with **new HIV infection** during pregnancy, breast-feeding or post-partum period	NVP **plus AZT** for 6 weeks	**If breastfeeding AND mother's VL = 40 or more or unknown**, continue with NVP daily **If NOT breastfeeding since birth or in last 4 weeks, OR mother's VL<40**, discontinue infant prophylaxis
Average risk of HIV transmission to infant	All pregnant or breastfeeding women who do not fit into the high risk category	NVP for 6 weeks	

A daily fixed-dose combination of TDF + FTC (or 3TC) + EFV is recommended as first-line ART for pregnant and breastfeeding women, including women in their first trimester of pregnancy.

Infants Prophylaxis:

Infants should be managed according to risk-stratification (See table 2.2 above)

Infants who present to care more than 72 hours of age and who are breastfeeding should receive infant ARV prophylaxis. However if they are not breastfeeding, ARV prophylaxis will offer them protection and should not be given. All infants should be assessed for risk of HIV transmission and those who are higher risk and present more 72 hours should have a "birth" HIV test as soon as possible.

Simplified infant NVP and AZT dosing recommendations are given on Table 2.3. If NVP causes toxicity in the infant (or if NVP is not available), 3TC can be substituted only after discussions with an HIV specialist.

Table 2.3: Simplified infant NVP and AZT dosing recommendations

Infant age	Dosing of NVP (10mg/ml)	Dosing of AZT (10mg/ml)
Birth to 6 weeks		
Birth weight 2000-2499 gm	**10 mg once daily** (1 ml of syrup once daily)	**10 mg twice daily** (1 ml of syrup twice daily)
Birth weight ≥ 2,500 gm	15 mg once daily **(1.5 ml of syrup once daily)**	15 mg twice daily **(1.5 ml of syrup twice daily)**
>6 weeks to <6 months	20 mg once daily **(2 ml of syrup once daily or half a 50 mg tablet once daily)**	No dose established for prophylaxis; use treatment dose 60 mg twice daily **6 ml of syrup twice daily or a 60 mg tablet twice daily**
6 months to <9 months	30 mg once daily	NA
9 months to 4 weeks beyond the end of breastfeeding	40 mg once daily	NA

Source: WHO 2016 Consolidated Guidelines on the Use of ARV drugs for Treating and Preventing HIV Infection

For infants weighing <2000 gm 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.

2.3 Use of ARVs during pregnancy and breastfeeding according to 3 clinical scenarios

2.3.1 Scenario 1: HIV infected pregnant women already on ART during current pregnancy

If a woman becomes pregnant while receiving ART the woman should remain on her current ART regimen unless there is a reason to change it such as side effects or virologic failure. This includes maintaining TDF and EFV in women who were already taking TDF and EFV as previous concerns about use of TDF and EFV in pregnancy have been largely relieved by a volume of accumulated pregnancy data.

It is important to check the most recent routine VL to ascertain if the VL is suppressed. If a VL was not done within the last 3 months, it should be repeated at the first visit and adherence counseling should be done. If the VL was/is >1000 copies/ml, intensive adherence counseling should immediately be done and the VL should be repeated in 6 weeks and every 3 months thereafter until end of breastfeeding period. This will help to determine whether or not and when her breastfeeding infant can discontinue nevirapine prophylaxis. At the end of breastfeeding, the viral load monitoring schedule should revert to the non-pregnant adults.

ARVs should be continued as usual during labour and the postpartum period.

Discontinuing treatment during pregnancy or breastfeeding increases the risk of MTCT and compromises the health of the mother. Nurses should consult a medical officer if ART in a pregnant or breastfeeding woman needs to be switched or interrupted.

Infant Prophylaxis:

Infants should be managed according to risk-stratification and relevant dosages (See tables 2.2 and 2.3 above)

2.3.2 Scenario 2: All HIV positive pregnant and breastfeeding women (known or newly diagnosed) not currently on ART

All pregnant women testing positive for HIV must be initiated on lifelong ART on the day of diagnosis or as soon as possible. The use of ARV therapy during pregnancy will improve the health of the mother and substantially decrease the risk of transmission of HIV to the infant.

Known positives not on ART or women diagnosed HIV positive during pregnancy

All women newly tested HIV positive during pregnancy and the known HIV positive not currently on ART (usually first ANC visit) should be initiated on lifelong ART on the same day of ANC visit.

Women diagnosed HIV positive during labour, after delivery or breastfeeding period

All women newly tested HIV positive during labour, after delivery (immediately postpartum) or during breastfeeding period including the known HIV positive not currently on ART should be initiated on lifelong ART on the same day of diagnosis or clinic visit.

Women initiating ART in labour and delivery may have an increased risk of transmission to their infants as they do not have the benefits of ART when initiated before or in early pregnancy.

ARV regimen for newly diagnosed and known HIV positive pregnant and breastfeeding women not currently on ART treatment

The preferred first line regimen: Tenofovir + Emtricitabine (or Lamivudine) + Efavirenz (TDF + FTC [or 3TC] + EFV)

The dosages for the preferred first line ART regimen in pregnant women are the same as in other adults and are given in Appendix 4.

ARVs should be continued as usual during labour and the postpartum period and beyond. HCWs should remember to check the VL after 3 months of ART.

Table 2.4: Alternative ARV regimens

	Special conditions	Alternative Regimen
1.	Significant psychiatric co-morbidity	**TDF+FTC [or 3TC]+ NVP**(do not use NVP if CD4≥250 cells/mm^3 due to risk of hypersensitivity including severe rash or hepatotoxicity or if on treatment for active TB in which case LPV/r should be considered instead of NVP)
2	Renal insufficiency (CrCl<60ml/min)	Preferablely **ABC+ + 3TC + EFV**
3	Significant psychiatric co-morbidity and Renal insufficiency	**ABC+3TC+NVP** **(**note CD4 restrictions above in 1)
4	If significant psychiatric co-morbidity and CD 4 ≥ 250cells/mm3 or previously had PMTCT that included sdNVP (either sdNVP alone or as part of Option A),	**TDF+ FTC [or 3TC]+ ATV/r**

if **ABC is contraindicated, consult HIV specialist or a clinical mentor**

Initiating ART in HIV Positive Pregnant Women

- A pregnant/ breastfeeding woman should be offered to initiate lifelong ART on the same day she tests positive for HIV at ANC/maternity or during breastfeeding period.
- All HIV infected pregnant/breastfeeding women should be:
    - Screened for active TB– if TB suspected investigate before initiation of ART
    - Assess for other contraindications before initiating ART.
- Ensure patient is counselled and given appropriate information on the importance of ART for her own health and prevention of vertical transmission, adherence, side effects and follow-up care.
- Do physical examination and WHO clinical staging. Collect blood samples for CD4 count and other baseline assessments.
- Initiate the preferred first line regimen (or an alternative if there is a known contraindication to the preferred first line) giving the patient a 4 week prescription – do not wait for baseline lab results
- A decision to initiate TDF should be based on a normal result of a urine dipstick while waiting for the creatinine clearance result. In case proteinuria and or glycosuria are detected (grade 3+ or 4+ on dipstick), an alternative to TDF should be initiated while awaiting the creatinine clearance result.
- Make appointment in 2-weeks time for review of laboratory results and for substantive intensive counselling on adherence and side effects.
    - Note that during pregnancy it is particularly important to accelerate ART initiation in view of the urgent need to reduce the risk of transmitting HIV to the baby.
- Follow up and patient laboratory monitoring should be in line with ANC and PNC care services and the general ART patient's recommendations as indicated in Appendix 3. It is of paramount importance that the routine VL is done is done every 3 months after initiation until delivery, at 6 weeks post partum, and every 3 months until end of breastfeeding period. If viral load is not surpressed, (≥40 copies/ml),she should have intensive adherence counseling and a repeat VL after 6 weeks. This will help to determine whether or not and when her breastfeeding infant can discontinue nevirapine prophylaxis.

Social considerations and treatment supporter

Social considerations and treatment supporter are important for people on ART including HIV positive pregnant and lactating women BUT should not be a reason to deny or delay treatment to an HIV positive pregnant or lactating woman. Social concerns should be assessed and challenges addressed during subsequent counselling sessions. It is important to encourage pregnant women initiated on ART to bring their partner or another treatment supporter during the next follow up visit. Where possible, patients who are unable to name a treatment supporter on their own may benefit from connection with a community-based organisation , a home-based care agency or PLHIV support group to assist with treatment support.

Infant prophylaxis:

Infants should be managed according to risk-stratification and relevant dosages (See tables 2.2 and 2.3 above)

2.3.3 Scenario 3: HIV positive pregnant or breastfeeding women who refuse to commit to or who intrupt life-long ART

Refusal to commit to life long treatment: An HIV positive pregnant or breastfeeding woman may refuse initiation of lifelong ART after being given all the necessary information and reasonable counselling on the importance of taking ART for life. In this case, the woman should be counselled to take triple ARV treatment starting at the time of diagnosis, continued intrapartum and through childbirth if not breastfeeding or until 4 weeks after cessation of all breastfeeding in order to protect her child.

Interruption due to toxicity, stock outs or other factors: When a mother receiving ART interrupts treatment while pregnant / breastfeeding, it is important to determine an alternative ART regimen or solution, and counsel her on the need to continue treatment without interruption.

It is important to conduct WHO clinical staging, CD4 count test and other investigations as part of baseline assessment..

All efforts should be made to continuously counsel women who refuse or interrupt lifelong ART on the importance of continuing ART for life. If a woman maintains her desire to stop ART after cessation of breastfeeding or conditions, her interests should be respected. This position should be revisited from time to time as the woman may decide to opt back into treatment and therefore guidelines for management of treatment interruption should be followed.. Most women will be on an EFV-based ART regimen. If the NRTIs include TDF or ABC, the whole regimen can be stopped immediately.

If the NRTIs include AZT or d4T it is important to stop the EFV first and continue the AZT/3TC or d4T/3TC for an additional 2 weeks due to the long half life of EFV. This will prevent development of resistance to EFV and therefore enable EFV to be safely used in the future for that patient. Properly counsel the woman on the importance of continuing with HIV chronic care and support to ensure timely re-initiation of ART.

Nurses should consult a medical officer if ART in a pregnant or breastfeeding woman needs to be interrupted or stopped.

2.3.3.1 Which regimen to start for HIV positive pregnant or breastfeeding women who refuse to commit to or interrupt lifelong ART.

What to Start

Mother:

Same regimens and considerations as in Scenario 2. Please see above.

Infant prophylaxis:

Infants should be managed according to risk-stratification and relevant dosages (See tables 2.2 and 2.3 above)

2.4 Infant feeding recommendations

Mothers who are known to be HIV uninfected or whose HIV status is unknown should exclusively breastfeed their infants for the first 6 months of life and then introduce appropriate complementary foods while continuing to breastfeed for 24 months or beyond.

Mothers with unknown HIV status should be offered HIV testing and counseling. Breastfeeding mothers with a negative HIV status should be encouraged to test regularly preferably at a 6 month interval and to practice safer sex. Partner involvement at this stage is encouraged and is an opportunity to provide partner testing if not previously done.

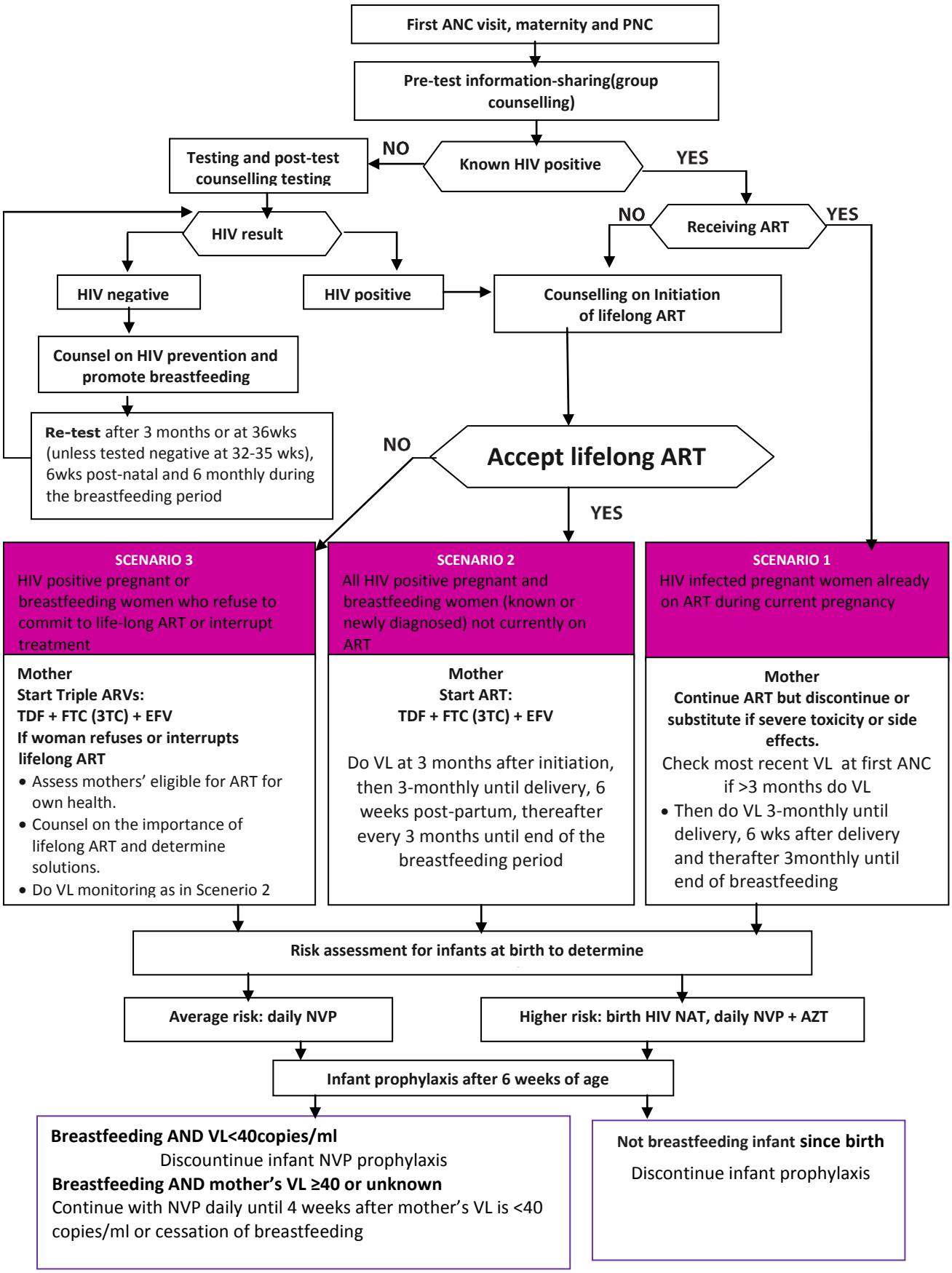
Mothers known to be HIV infected and whose infants are HIV uninfected or of unknown HIV status should breastfeed their infants exclusively for the first 6 months of life. Thereafter, introduce appropriate complementary foods and continue breastfeedingfor at least 12 months. Mothers are encouraged to breastfeed for at least 24 months (similar to the general population) while being fully supported for ART adherence.

When infants and young children are known to be HIV infected, stop nevirapine and initiate pediatric ART as per the guidelines. Mothers should be counselled to breastfeed exclusively for the first 6 months of life and then introduce appropriate complementary foods while continuing to breastfeed for at least 24 months while being fully supported for ART adherence

Table 2.5: Summary of infant feeding recommendations

	Mothers who are known to be HIV uninfected or whose HIV status is unknown	Mothers known to be HIV infected and whose infants are HIV uninfected or of unknown HIV status	Infants and young children known to be HIV infected
<6 months	Exclusive breastfeeding from birth until 6 months	Exclusive breastfeeding from birth until six months, with ARVs.	Exclusive breastfeeding from birth until six months.
≥ 6 months	Introduce appropriate complementary foods at 6months and continue to breastfeed for at least 24 months.	Introduce appropriate complementary foods at 6 months and continue breastfeeding for at least 24 months, continuing maternal ART and (if applicable) infant ARV prophylaxis	Introduce appropriate complementary foods at 6 months and continue to breastfeed for at least24 months, with mother and child on ART

Figure 2.3: Algorithm for use of lifelong ART in eMTCT at ANC, Maternity and PNC



NB: If baby seen >72 hours after birth and NOT breastfeeding DO NOT initiate prophylaxis

2.5 Clinical monitoring during pregnancy, labour, delivery and breastfeeding for women on ART

2.5.1 Baseline Clinical Assessment

The Baseline medical history should include:

- Essential demographic characteristics
- Gestational age
- Obstetric and gynaecological history (including eMTCT/ PMTCT)
- Past medical history including major illnesses, hospitalisations and surgery
- Length of time since the diagnosis of HIV infection and if already on ART most recent viral load
- Current medications and known allergies including those related to ARVs
- Review of symptoms (including screening for TB)
- Psychosocial history and sexual risk assessment
- Family testing and counselling history for HIV (e.g. have partner and other children received HIV counselling and testing?)

The baseline physical examination should include: vital signs, weight, gestational age and height, and should detail any abnormalities of the:

· Eyes	· Oropharynx
· Lymph nodes	· Lungs
· Heart	· Abdomen
· Extremities	·Nervous system
· Genital tract	

Once ART has commenced, clinical monitoring must include follow-up visits at two and six weeks after initiation and monthly thereafter. As much as possible the follow up visits should coincide with antenatal care visits.

These Antenatal clinical monitoring visits should include:

- All physical examinations in the baseline exam as outlined above
- ANC care
- Assess adherence to medication
- ART refill
- Assess toxicity
- On-going counseling
- Follow up or advise on partner HIV testing and counselling
- Monitor viral loads every 3 months
- Refer patient to community based support services or PLHIV groups
- Importance of returning to the same clinic after delivery to continue ART services
- Importance of bringing infant for HIV NAT test at 6 weeks of age
- Advise on importance of bringing ART to all follow up visits and to maternity
- Advise on importance of having a treatment supporter
- Importance of informing health care provider of intention to change facilities

During delivery:

- ART should be continued during labour and after delivery
- Health care providers should adhere to infection control procedures, avoid invasive procedures, e.g., artificial rupture of membranes, episiotomy, fetal scalp monitoring, and minimise trauma if assisted delivery is required.

- Caesarean section should not be routinely offered to HIV positive mothers unless they have another medical indication for surgical delivery.

Postpartum services for HIV positive women and post natal services for babies should include:

- Confirm that mother is on ART
- Confirm most recent VL result within the last 3 months
- Confirm ART adherence; provide adherence counseling if VL is not suppressed or mother is non adherent
- Determine risk stratification of the infant and provide a birth NAT test within 48 hours (after the first bath) for all high risk infants
- Counsel and support mother on exclusive breastfeeding
- Immediately initiate nevirapine or dual (NVP plus AZT) prophylaxis for neonates for the first 6 weeks according to risk stratification
- At six weeks of age, initiate cotrimoxazole
- At six weeks, test baby for HIV (NAT); re-test with rapid test at nine months, 4 weeks after the cessation of breastfeeding
- When an HIV-exposed child reaches 18 months of age, records should be scrutinized to determine if the last HIV test, if negative, was conclusive and could determine HIV status. If in doubt, for example, if it is possible the mother may have continued breastfeeding longer than originally stated, repeat the RT at that time.
- Advise mother that she remains on ART for life
- Advise mother to retain baby in continued care and support until final HIV outcome of the infant is known
- Discuss and provide advise on family planning options
- Encourage male partner to participate in follow up visits and seek testing
- At six weeks and annually thereafter, screen for cervical cancer

For further management of HIV exposed infants, refer to Chapter 3.

Patients should be assessed at each visit which should include clinical monitoring, medicine dispensing and/or refill, lab monitoring as per schedule, and reinforcement of adherence, and identifying problems requiring referral. At each visit the health worker must assess adherence to treatment, and note any new symptoms that may be related to medicine side-effects, HIV disease progression, or opportunistic infections.

2.5.2 Clinical monitoring for toxicities and effectiveness of ARVs in pregnant women

Patients should be informed about the symptoms of ARV medicines side-effects/toxicities and should be educated regarding the need to seek care. Clinical evaluation of the effectiveness of ART is important. The basic parameters examined and documented should include:

1. The patient's perception of how she is doing on therapy.
2. Changes in body weight over the course of therapy/pregnancy.
3. Signs of immune reconstitution inflammatory syndrome.
4. HIV-related disease progression.
5. Signs of medicine toxicities.
6. Improvement in symptoms and quality of life.

2.5.3 Lab Assessment for ART initiation and treatment monitoring in eMTCT

Baseline assessment for pregnant women

For all HIV-positive pregnant women the following laboratory assessments will be done as part of routine ANC work up:

Hb HBsAg RH factor

RPR

Creatinine clearance CD4 count

Patients with a normal urinalysis can be initiated on TDF based regimen while waiting for creatinine clearance results. If the creatinine clearance result is <60 ml/min, an alternative to TDF should be initiated while awaiting the creatinine clearance result.

Refer to Appendix 3 for the detailed schedule of laboratory tests to be performed for each different ART regimens.

Lab Assessment for ART initiation and treatment monitoring in eMTCT: refer to the table below,

Table 2.6: Lab Assessment for ART initiation and treatment monitoring in eMTCT

Phase of HIV management	Tests	Frequency
ART initiation	Hb CD4 Cr Cl Urine dipstick HBsAg	Once Once (baseline only) Once Once Once, if positive – repeat after 6 months to confirm if chronically infected (lab will do an ALT automatically if HBsAg reactive)
Treatment monitoring	VL CrCl Hb	M6,12 (then every 12 months) 6w, ,6M,12M (then every 12 months) if on TDF 2w, 6w, M3 **if on AZT**
HBsAg positive	ALT	ART initiation, 2w, 6w, M3 (then every 6 months if 2nd HBsAg positive)
Suspected treatment failure	VL	Anytime after the first 6 months of ART provided non-adherence and OIs excluded
Virological failure	1) CD4 2) HIV Drug Resistance	1)Every episode of virologic failure 2) Before Switching to a 3rdline regimen all ages

Refer to Appendix 3 for the detailed schedule of routine laboratory tests to be performed for each different ART regimens.

2.6 Management of pregnant HIV-positive women with concurrent diseases

2.6.1 Tuberculosis

All HIV infected individuals including pregnant and lactating women with active TB should start ART . TB in pregnant women is associated with prematurity, low birth weight, and perinatal tuberculosis; it has also been associated with an increased risk for mother-to-child transmission of HIV among HIV-positive pregnant women. A pregnant woman should be advised that successful treatment of TB with the standard regimen is important for successful outcome of pregnancy.

All HIV infected pregnant women should be assessed for TB signs and symptoms at each visit and those presenting with any of the following: cough, fever, night sweats, weight loss, enlarged lymph nodes should be evaluated for active TB. If none of these exist, assess for contraindications for IPT.

If active TB is confirmed, TB treatment is started first before initiation of ART. The first line anti-TB medicines are safe for use in pregnancy except streptomycin which is ototoxic to the foetus and should generally not be used during pregnancy. ART should be started as soon as TB medications are tolerated.

The preferred ART regimen for HIV pregnant women with TB co-infection is TDF + FTC (or 3TC) + EFV. **NVP should NOT be used**.

If EFV is contraindicated, a triple NRTI regimen (e.g. AZT+3TC+TDF or AZT+3TC+ABC) can be used for the duration of the TB treatment. The option of giving 2 NRTIs with "super-boosted" Lopinavir (400 mg lopinavir + 400 mg ritonavir) while on TB therapy is unlikely to be tolerated by pregnant women and therefore is not recommended.

See Figure 1.7, section 1.17.2 for TB screening algorithm in patients with HIV.

2.6.2 Hepatitis B

Viral hepatitis is an increasing cause of morbidity and mortality among people living with HIV, including those on ART. All HIV positive people including pregnant women should have an HBsAg test as part of routine care.
Lamivudine and tenofovir have an antiviral effect on HBV. The combination of these medicines reduces the development of viral resistance of HBV.

All ARV medicines are potentially hepatotoxic. Among the NNRTIs, efavirenz is the best tolerated in patients with HBV.

Pregnant women with Hepatitis B should be initiate or continued on**: TDF + FTC (or 3TC) + EFV** ALT should be checked according to the schedule in Table 1.6.

Infants of mothers who are Hepatitis B surface Antigen positive (HBsAg) must receive Hepatitis B immunoglobulin and Hepatitis B vaccine within 24 hours of birth.

For more information, see section 1.19.2

2.6.3 Renal disease

In patients with renal failure, ARV dosages need to be adjusted for some medicines on the basis of creatinine clearance (see appendix 5).

Consult with a specialist physician before starting ART in a patient with a creatinine clearance <60ml/min or when renal failure develops in a patient on ART..

2.6.4 Anaemia in pregnancy

Anaemia is the most common medical disorder in pregnancy. It is important that appropriate measures are taken to prevent and treat anaemia in pregnant women. The Ministry of Health and Social Services (MoHSS) recommends that all pregnant women should have a haemoglobin level of 12.0 g/dl or more upon reaching full term .

Recommended Action
Women with Hb below 10.0 g/dl while receiving adequate doses of Pregamol (Iron and Folic acid supplement) should be recommended for further investigation and referred to the medical doctor. All pregnant women should have Hb estimation at 36 weeks irrespective of the Hb level during the course of pregnancy.

- **If Hb is more than 12.0 g//dl.**
  - Give standard pregamal prophylaxis 1 tab daily until 6-8 weeks after delivery.

- **If Hb level is between 10.0-12.0 g/dl**
  - Determine the possible cause clinically

- Advise on diet
- Give oral Pregamal 1 tab twice per day
- Repeat Hb after two months or at 36 weeks

- **If Hb level is less than 10.0 g/dl**
  - Take history; take blood specimen for Full Blood Count (FBC) with differential and reticulocyte count
  - Collect stool specimen for microscopy
  - Inform the medical doctor in charge about results to determine the type of anaemia
  - Treat the cause of aneamia, give advice on diet and give oral pregamal 1 tab three times per day if underlying cause is iron deficiency anaemia.
  - Repeat Hb two weeks after initiation of treatment (in iron deficiency anaemia Hb rises by at least 1 g/dl per week when adequate dose of iron is administered).
  - If there is no improvement consider further investigations.

Blood transfusion may be considered:

- In patients who show signs of cardiac decompensation
- Any patient with Hb ≤ 6.0 g/dl

If an HIV-positive woman is on AZT-based ART, Hb should be monitored at the clinic 2 weeks after initiation of AZT based ART and then monthly. If the Hb falls below 8g/dl or drops by more than 25% from the baseline level, another NRTI should be substituted for AZT.

2.7. When to consult a specialist

In the following circumstances, consult a specialist:

- Combined pathologies (renal failure, diabetes, neoplasia, etc.).
- Severe medicine toxicities.
- Pregnant women receiving any other regimen than the recommended ones.

2.8. Reproductive considerations when one or both sexual partners are HIV positive

The success of ART has resulted in HIV- infected people living longer healthier lives and therefore having to make informed reproductive choices. However, it is important that those planning to have children do so carefully in consultation with health care providers to minimize the risk of infection to the sexual partner and their child. The first step towards addressing the issues of fertility and childbearing is to regularly and repeatedly raise these with HIV-positive patients, to understand their desires and related health care needs. Use of family planning services is important to avoid unplanned and unwanted pregnancies. Adherence to ART is critical to ensure suppressed viral load before getting pregnant.

If a Couple Wishes to Have a Child:

- Determine HIV status of both sexual partners – HIV counselling and testing is a prerequisite if the HIV status of both partners is not known.
- Counsel on the risks of MTCT
- Discuss alternatives e.g. adoption
- Advise on use of family planning services including condoms
- Check CD4 or viral load (if on ART), screen for syphilis, other STIs, check haemoglobin and screen for cervical cancer (female)

- Identify and manage co-morbidities. For conditions with short-term management (e.g. TB or acute infections), recommend delay in attempts at conception until treatment is completed.

HIV Sero-Concordant Couple (Female and Male HIV-infected):

- **If both partners are on ART:**
  - Assess adherence and check for most recent viral load (repeat if not done within last 6 months). If viral load is suppressed (<40 copies/ml) in both – advise couple on peri-ovulatory unprotected sexual intercourse (between days 10 and 18 of her menstrual cycle) for 3 months. Emphasise consistent use of condom outside this period.
  - If viral load is not suppressed (≥40 copies/ml) in either partner, evaluate the patient(s) for inadequate adherence and other causes of failure and possible 2nd line treatment if VL>1000 copies/ml. Advise a delay in conception until the VL is <40 copies/ml.

- **If one or both partners are not on ART:**
  - Initiate ART according to guidelines if either one or both partners are not on treatment
  - Check viral load in both after 3-6 months. If viral load is suppressed (<40copies/ml) in both – advise couple on peri-ovulatory unprotected sexual intercourse (between days 10 and 18 of her menstrual cycle) for 3 months. Emphasise consistent use of condom outside this period.
    - If viral load is not suppressed (≥40 copies/ml) evaluate the patient(s) for inadequate adherence and other causes of failure and possible 2nd line treatment if VL>1000 copies/ml. Advise a delay in conception until the VL is <40 copies/ml.

HIV Sero-discordant Couples (Male HIV-positive) :

- **If not on ART-** start treatment as soon as possible and check viral load after 6 months
- **If on ART** – assess adherence and check most recent viral load (repeat if not done within last 6 months)
  - If man's viral load is suppressed (<40 copies/ml):
    - Check the woman's
      - HIV antibody test (repeat if not done within last 3 months)
      - Creatinine clearance
    - If confirmatory antibody test is negative and CrCl is normal, provide PrEP (TDF +FTC (or 3TC)) to the woman daily one week prior to and until one month following the period of exposure. Monitor woman's CrCl every 3 months.
    - Advise the couple on peri-ovulatory unprotected sexual intercourse (between days 10 and 18 of her menstrual cycle) for 3 months. Emphasise consistent use of condom outside this period.
      - If male's viral load is not suppressed (≥40 copies/ml) evaluate the patient for inadequate adherence and other causes of failure and possible 2nd line treatment if VL>1000 copies/ml. Advise a delay in conception until the VL is <40 copies/ml.
        - **If woman conceives:** Repeat HIV testing during pregnancy and breastfeeding period is important with appropriate management if she becomes infected.

HIV Sero-discordant Couples (Female HIV-positive):

- **If woman not on ART-** start treatment as soon as possible and check viral load after 3 -6 month.
- **If woman on ART** – assess adherence and check most recent viral load (repeat if not done within last 6 months).
  - Re-check male partner's HIV antibody test.

- If negative, advise ejaculate collection using a cup and draw ejaculate up into a syringe. Woman should then do self-intra-vaginal insemination. This method avoids exposure of the male partner to acquiring HIV infection and is therefore the safest method.
- If woman's viral load is suppressed (<40 copies/ml) and the couple is unable or unwilling to use the artificial insemination method described above,
  - Check the man's
    - HIV antibody test (if not done already)

    - Creatinine clearance
  - If confirmatory antibody test is negative and CrCl is normal, provide PrEP (TDF + FTC (or 3TC)) to the man daily one week prior to and until 3 months following the period of exposure. Monitor CrCl every 3 months.
    - Advise the couple on peri-ovulatory unprotected sexual intercourse (between days 10 and 18 of her menstrual cycle) for 3 months. Emphasise consistent use of condoms outside this period.
- If woman's viral load is not suppressed (≥40 copies/ml) evaluate the patient for inadequate adherence and other causes of failure and possible 2nd line treatment if VL>1000 copies/ml. Advise a delay in conception until the VL is 40 copies/ml.

Where there is a sero-discordant couple that mutually desires a pregnancy and the fertility procedure involves high HIV risk to the HIV negative partner, targeted counseling and appropriate options should be presented to the couple with their acknowledgement that they understand the process and risk of transmission to the negative partner.

CHAPTER 3: ANTIRETROVIRAL THERAPY FOR INFANTS, CHILDREN AND ADOLESCENTS

Many of the goals of HIV care and treatment in children and adolescents are similar to those in adults and are listed below:

- Undetectable viral load
- Durable suppression of HIV replication
- Restoration and/or preservation of immune function
- Reduction of HIV related morbidity and mortality
- Preservation of normal growth and development
- Safe and effective HIV disclosure to the child
- Improvement in quality of life for child and family
- Successful transition to adolescents and adult HIV care

Preservation of normal growth and development, the need for disclosure of child's HIV status, and successful transition to adult HIV care are unique to pediatrics. In order for ART to be considered a success, growth and development must be monitored carefully and taken into consideration when managing such patients.

3.1 The natural course of HIV disease in children

Children may be infected with HIV during pregnancy, during delivery, or postnatally (through breastfeeding). Left untreated, the mortality rate from HIV/AIDS is approximately 30% by age 1 year, 50% by age 2, and 60% by age 3. The mortality rate from untreated HIV/AIDS is highest at < 18 months of age.

HIV RNA levels in perinatally infected infants are generally low at birth (i.e. <10,000 copies/ml), increase to high values by age 2 months and then decrease slowly after the first year over the next few years of life. This pattern probably reflects the lower efficiency of an immature but developing immune system in containing viral replication and possibly a greater number of HIV-susceptible cells in younger children.

CD4 T-lymphocyte counts and percentage values in healthy infants who are not infected with HIV are considerably higher than those observed in uninfected adults and slowly decline to adult values by age 5 years. A paediatric immunological classification system for HIV infection has been developed that includes age-related definitions of immune suppression (seeTable 3.1). Although the CD4 absolute number that identifies a specific level of immune suppression changes with age, the CD4 percentage that defines each immunologic category is less variable. CD4 values at base-line will be used to assess the level of immunosuppression among HIV-infected children.

Table 3.1: HIV Paediatric immunological classification

Classification of HIV associated immunodeficiency	Age related CD4 values			
	≤11 months (%)	12 – 35 months (%)	36 – 59 months (%)	≥ 5 years (cells/ mm^3)
Not significant	>35	>30	>25	>500
Mild	30-35	25-30	20-25	350-499
Advanced	25-29	20-24	15-19	200-349
Severe	<25	<20	<15	<200 or <15%

Note: CD4 cell values can vary considerably with minor infections and immunizations, and are therefore best measured when patients are stable.

As with adults, progression of clinical HIV disease is determined through classification of associated illnesses and conditions into 4 clinical stages (See Appendix 2). These are similar to adult staging classification, however they include some conditions specifically targeting children such as stunting, unexplained parotid enlargement, symptomatic lymphoid interstitial pneumonitis, and others. Although the WHO clinical stage is not an eligibility criterion for children for ART initiation, it is important to be aware of and to record the child's stage of disease and to recognize co-existing conditions which need treatment.

3.2 Diagnosis of HIV infection in children

3.2.1 Early infant diagnosis of HIV using diagnostic HIV-1 Nucleic Acid Test (NAT)

As a result of the programme for elimination of mother-to-child transmission (eMTCT), a large number of HIV-exposed infants are being identified who require follow-up care and HIV diagnosis. It is important to identify young infants with HIV infection and enrol them in HIV care early because of the high mortality from untreated HIV in this age group. It is also important to promptly identify young infants who are not HIV-infected in order to reassure their parent(s), discharge them from costly follow-up, and to measure the overall effectiveness of the eMTCT programme.

The polymerase chain reaction (PCR) test can reliably and accurately detect HIV DNA or RNA from whole blood or from a dried blood spot (DBS) specimen at an early age. This test detects the genetic material of HIV rather than of anti-HIV antibodies, and therefore is not affected by the trans-placental transfer of maternal anti-HIV antibodies, unlike the HIV antibody tests. NIP has recently replaced the DNA PCR test for a NAT test that identifies both HIV DNA (deoxyribonucleic acid) and RNA (ribonucleic acid). For this reason, the infant testing can best be described as NAT. As with DNA PCR, NAT specimens are collected using the dried blood spot (DBS) methodology. **A positive initial NAT followed by a repeat positive NAT confirms true HIV infection in the child.**

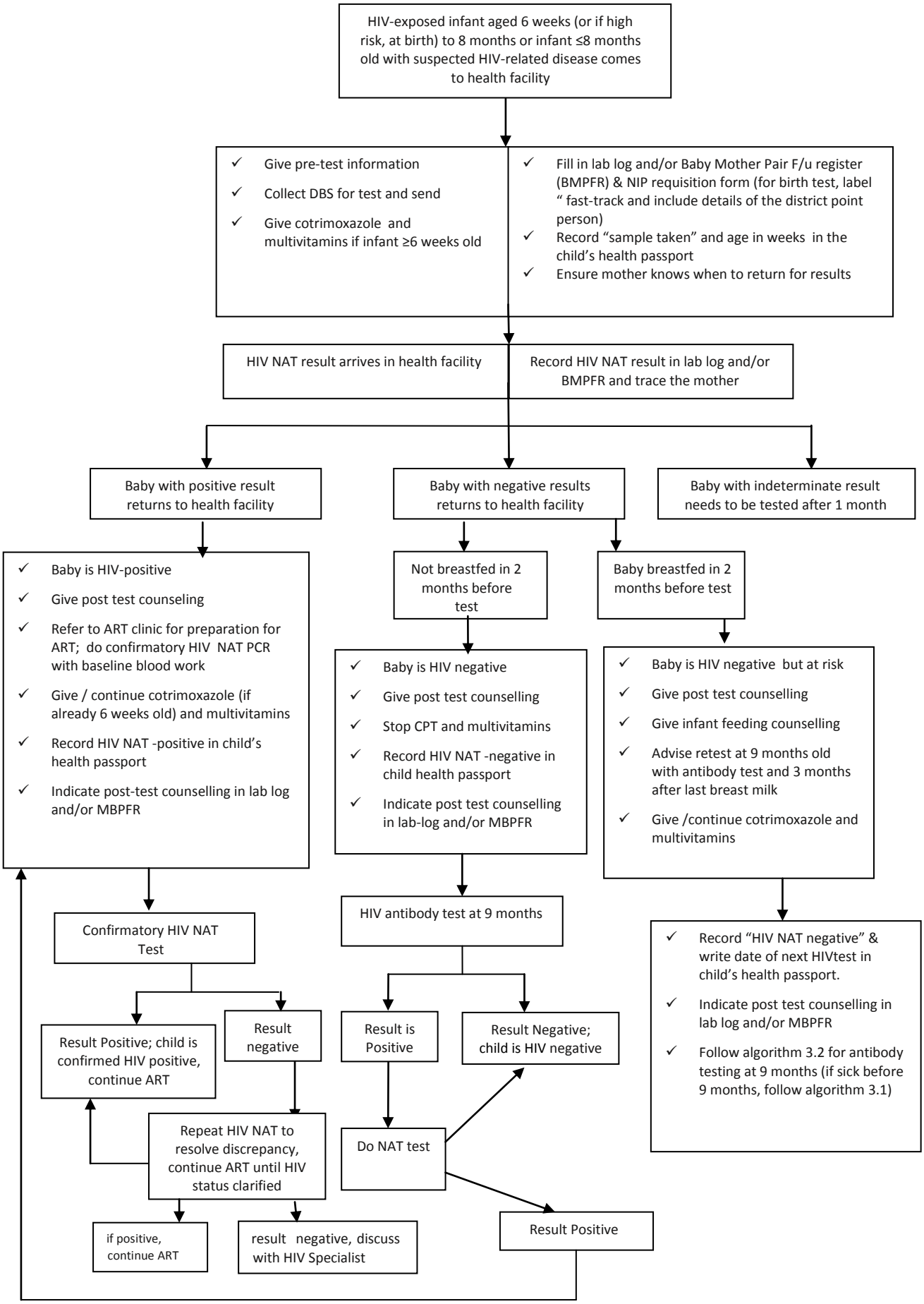
An HIV-exposed infant who did ***not breastfeed*** and who tests HIV NAT negative at 6 weeks should have a HIV rapid test done at **9 months** of age to coincide with a routine visit for measles immunisation. If the RT result is negative, this confirms HIV negative status. If the RT result is positive, an HIV NAT should be done to determine if the infant is truly HIV positive. If the result is discordant, follow the standard algorithm for resolution of status.

Breastfeeding HIV-exposed infants who initially tested HIV negative at 6 weeks of age should also have a rapid test done at **9 months of age.** If the result is positive a HIV NAT should be done to determine if the infant is truly HIV positive. If the results of the RT or the HIV NAT are negative, a repeat RT should be done 3 months after the last exposure to breast milk. The infant should remain on cotrimoxazole and multivitamins until confirmed HIV negative. Infant prophylaxis with either NVP or NVP/AZT should be give as per Chapter 2 of guidelines.

WHO has recommended the addition of NAT at birth (birth PCR) to identify HIV infection early in HIV-exposed infants. As discussed in Chapter 2 of the guidelines, infants classified as having high risk of HIV infection will receive a special package of care including being offered an HIV test within 48 hours of birth. Active tracing of infants found to be positive by birth testing is critical to ensure initiation of ART on time and to save lives.

The algorithm for diagnostic HIV NAT testing is summarised in Figure 3.1.

Figure 3.1: Algorithm for early infant diagnosis of HIV using diagnostic Nucleic Acid Test (NAT)



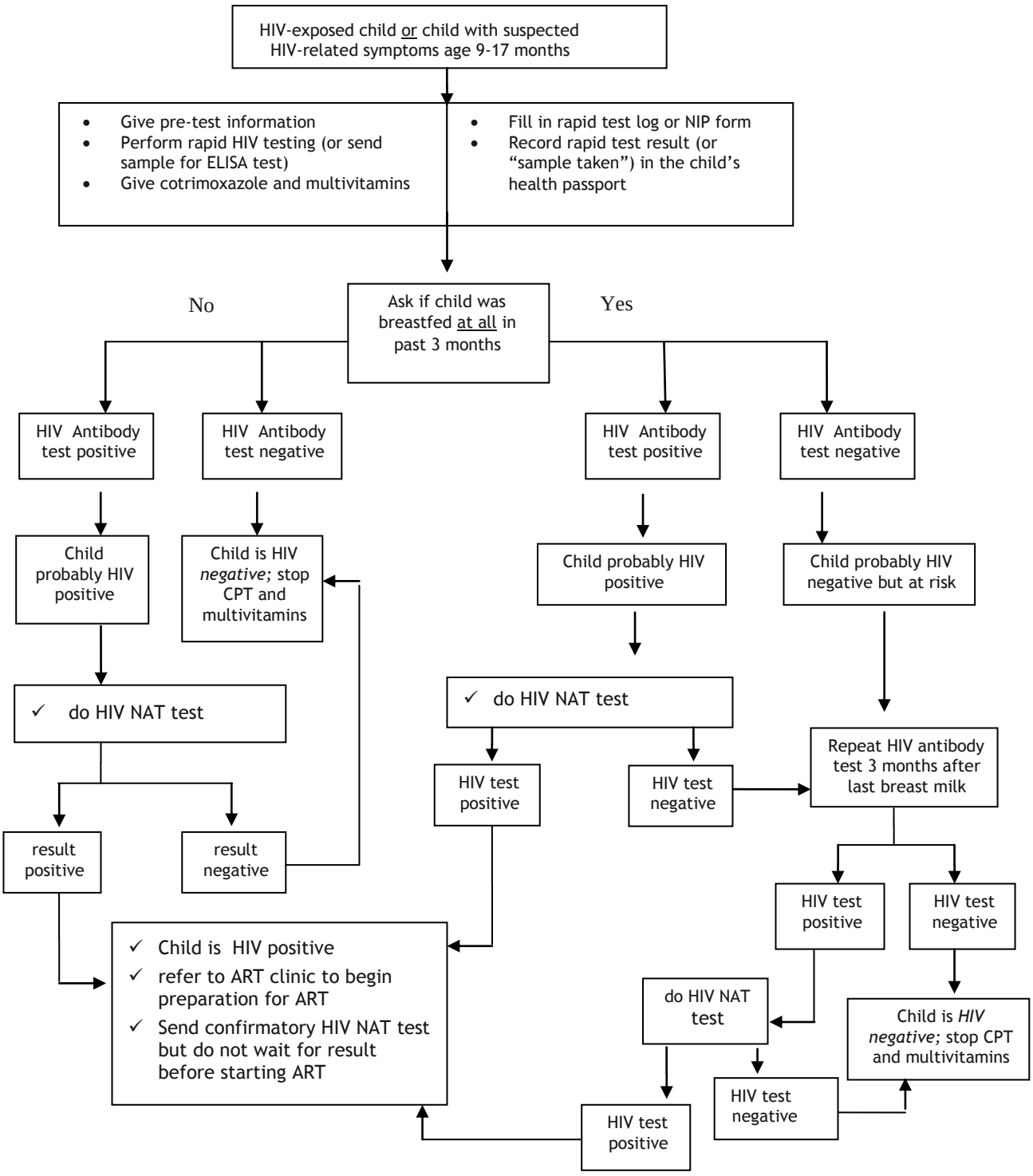
3.2.2 HIV antibody testing

As with adults, HIV antibody testing gives definitive results for diagnosis of HIV infection in children ≥18 months old. While rapid HIV testing or ELISA (enzyme-linked immunosorbent assay) can be used, rapid testing is preferred in our setting. As such this is the recommended testing approach for the diagnosis or exclusion of HIV in this age group. It is important to remember that HIV-exposed children ≥18 months old who have had prolonged breastfeeding would need to have a negative HIV antibody test result at least 3 months after breastfeeding is discontinued to exclude HIV infection.

Antibody testing for HIV diagnosis is less useful in infants because passively transferred maternal anti-HIV antibodies may persist and be detected in a child up to 18 months of age. To determine HIV-exposure status of an infant, a positive RT done within the first four months of age will reliably indicate HIV-exposure. However to determine the HIV-exposure status of a 4-17 month old infant, ideally the biological mother should be tested for HIV. If the biological mother is not available, then the infant should be screened with a RT.

The algorithm for HIV diagnosis using rapid testing (or ELISA) is outlined in Figure 3.2 for infants 9-17 months of age who are HIV-exposed and/or who show signs or symptoms consistent with HIV-related disease. In summary: following HIV antibody testing at 9 -17 months of age, diagnosis of HIV infection may be excluded if the child's test is negative and there has been no breastfeeding for the past 3 months, in that case there is no need to do further HIV testing. If the child tests antibody positive before 18 months of age, an HIV NAT should be performed to determine if child has HIV infection.

Figure 32: Algorithm for diagnosis of HIV in children using HIV antibody testing



3.2.3 Criteria for diagnosis or exclusion of HIV

HIV-positive children

Parent(s) should be counseled and a child should be clinically managed as being HIV-positive if:

- HIV NAT test is positive at any age, or
- HIV antibody test is positive (initial and repeat RT) at ≥ 18 months, regardless of symptoms, or
- HIV antibody testing is positive at an earlier age, e.g. 14 months, and there are signs and symptoms suggestive of HIV-infection. In this case the infant should have an HIV NAT test for confirmation, but counseling and baseline blood testing can be done while awaiting the result.

Children who are confirmed HIV positive by HIV NAT or HIV antibody testing at an early age should be evaluated for ART immediately due to the high mortality rate in young children (see Section 3.4). Indeed, all children are eligible to start ART once HIV infection is identified by HIV NAT (if <18 months old) or rapid test (if ≥18 months old irrespective of immune status or clinical stage). Counseling of parents and/or caregivers should begin as soon as a child is found to be HIV positive with a view to actually starting ART preferably in one week. **It is important that the main parent/caregiver select a treatment supporter in case he/she becomes ill, for example, and another person needs to give medication to, and care for, the child.**

Children who test HIV positive in early infancy with HIV NAT should have a confirmatory HIV test done, because otherwise life-long treatment will be given on the basis of a single blood test. A repeat HIV NAT (confirmatory test) must therefore be done for HIV-positive infants <18 months old at the same time as the baseline blood tests are taken, however ART should be commenced based on the first result - **do not wait for the results of the confirmatory HIV NAT to initiate ART.** If the confirmatory test is positive, there is no need to ever repeat a diagnostic HIV test.

For children ≥18 months of age diagnosed with HIV by RT, a repeat RT should be done before starting ART.

Serologic and/or NAT reversion can occur in HIV positive children who start ART early and whose viral load is persistently maximally suppressed (target not detected) through excellent adherence. This means that standard antibody tests (RT) and/or the NAT give negative results while the child is actually HIV positive. If ART is discontinued in that child, the HIV viral load will rebound and the child can become ill. *It is important for all health care workers and counselors to be aware of this phenomenon to ensure that no child is inadvertently taken off treatment in the mistaken belief that the child is no longer infected with HIV.*

In the rare event that a child was diagnosed HIV positive on the basis of a single HIV NAT (no confirmatory NAT result is found), a detectable viral load test result can serve as the confirmatory test. If all viral load results are undetectable (target not detected) in such children, and the HIV diagnosis is in doubt, **do not stop ART.** Consult an HIV specialist before taking further action.

HIV-negative HIV-exposed infant

The parent(s) should be counseled that their infant is HIV-negative and the child can be discharged from HIV follow-up if:

- **Diagnostic HIV NAT is negative and the child has not been breastfed for the preceding 2 months or**
- **HIV antibody test is negative and the child has not been breastfed for the preceding 3 months.**

HIV-exposed children in whom HIV infection has been excluded by one HIV NAT test, should have an antibody test (preferably rapid test) at 9 months of age. Health workers should therefore make a note in the child's health passport to that effect. The child should then conveniently be tested when the child attends any clinic doing rapid HIV antibody testing at 9 months ideally coinciding with the measles immunisation. (see section 3.2.1)

When an HIV-exposed child reaches 18 months of age, records should be scrutinized to determine if the last HIV test, if negative, was conclusive and could determine HIV status. If in doubt, for example, if it is possible the mother may have continued breastfeeding longer than originally stated, repeat the RT at that time.

3.3 Prevention of opportunistic infections in children

3.3.1 Cotrimoxazole preventive treatment

Cotrimoxazole (sulfamethoxazole (SMZ) plus trimethoprim (TMP)) has been shown to have protective effects against pneumocystis pneumonia, and other bacterial and parasitic infections, including malaria. It is recommended to initiate cotrimoxazole preventive therapy (CPT) for all HIV-exposed children from the age of 6 weeks and only discontinue if the child is proven to be HIV negative according to the criteria mentioned in section 3.2.3.2 above.

All HIV positive children and adolescents at whatever age they are diagnosed should receive CPT and should continue on it for life unless there is a contradiction or clinical indication for discontinuation.

Table 3.2: Recommended oral doses of cotrimoxazole for Cotrimoxazole Preventive Therapy

	Once daily cotrimoxazole dosage (SMZ/TMP)		
Weight (kg)	**Suspension (200/40mg)/5ml**	**Tablets 400/80 mg**	**Tablets 800/160mg**
3-5.9 kg	2.5 ml	-	-
6-13.9 kg	5 ml	½ tablet	-
14-24.9 kg	10 ml	1 tablet	½ tablet
≥25 kg	-	2 tablets	1 tablet

3.3.2 TB screening and isoniazid preventive therapy (TB-IPT) for children

Children and adolescents with HIV should be screened for TB including asking about TB exposure/contact history at each encounter with a health worker or visit to a health facility; eligible children and adolescents with HIV should be offered IPT (see Figure 3.3 below for algorithms for TB screening and IPT among children and adolescents with HIV).

TB Screening Questions for Children:

- Poor weight gain defined as reported weight loss, very low weight (weight-for-age < -3 z-score), underweight (weight-for-age < -2 z-score), confirmed weight loss >5% since last visit, or growth curve flattening
- Fever
- Current Cough
- Lymph node enlargement
- Contact with person with confirmed or presumptive infectious TB.

If the answer to any of the screening questions is “Yes”, investigations for TB and other diseases is required; patients who have signs and symptoms of active TB, should never be started on TB-IPT.

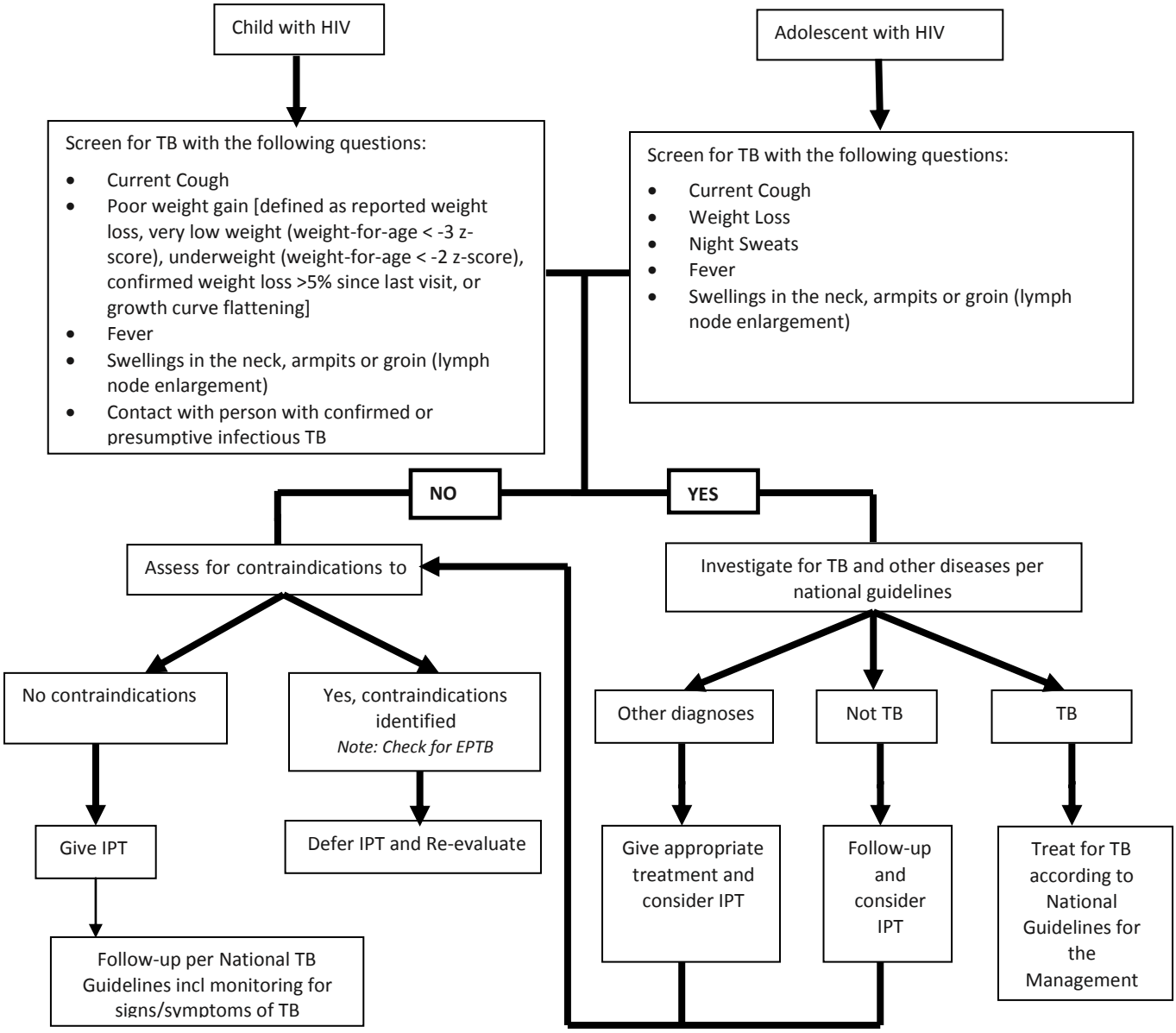
For all children <5 years old (whether HIV positive or negative) and all HIV-positive children and adolescents (regardless of age) who have had contact with someone with infectious TB, and infants born to mothers with untreated pulmonary TB disease, supervised isoniazid preventive therapy (TB-IPT) should be given once active TB disease has been excluded.

All HIV-positive children and adolescents in whom active TB has been excluded are eligible for a 9-month course of TB-IPT, whether there has been a documented exposure to active TB or not.

In addition, even if a child has already taken a course of TB-IPT and is subsequently -exposed to a patient with infectious TB, another course of IPT should be given after every episode of exposure.

Answers to the TB screening questions and follow-on evaluations/decisions should be recorded in the appropriate page of the pediatric patient care booklet.

Figure 3.3: Algorithm for TB screening and TB-IPT among Children and Adolescents with HIV



The isoniazid dosage for children is 10 mg/ kg (range: 7-15 mg per kg; maximum 300mg) daily. See table 3.3 below for simplified weight-based dosing for children. The recommended duration of IPT treatment is 9 months.

Table 3.3: Simplified paediatric weight-based dosing for isoniazid

Weight (kg)	Once daily dose (mg)	Number of 100mg isoniazid tablets per dose
4 - 6.4 kg	50	½ tablet
6.5 - 9.9	100	1 tablet
10 - 13.9	150	1½ tablets or ½ of a 300 mg tablet
14 - 19.9	200	2 tablets
20 - 24.9	250	2½ tablets
≥ 25	300	3 tablets or one adult 300mg tablet

Pyridoxine should be given along with isoniazid to prevent isoniazid associated neuropathy in children from 5 years of age. The dose of pyridoxine is 12.5mg/day (1/2 tablet) for children 5-11 years old and 25mg/day for children ≥12 years old.

3.4 ART in children and when to start

3.4.1 Response to ART in children

The immunological response to ART in children with HIV is better than in adults. Children restore their CD4 cell counts and percentages better and more rapidly than adults, even in late stages of HIV-1 infection. Moreover, normalisation of CD4 cell count in HIV-1-infected children taking ART is age-independent.

Early studies suggested that virological success with undetectable viral loads may be more difficult to achieve in children. However newer evidence suggests that viral suppression was initially achieved in >80% of treatment-naïve children in resource poor settings, similar to the responses seen in adults. In Namibia routine virological testing is the preferred approach to monitoring treatment response.

3.4.2 Counseling prior to starting ART

Children are dependent on their parents/caregivers for managing their ARV administration and for overall care and support. Therefore careful discussion about the illness and adherence counseling for the primary caregiver and at least one other treatment supporter should be done from the outset. Some parents may themselves be infected with HIV or may have other health or social challenges which might put maintenance of the child's care at risk, so there needs to be a "back-up" system in place. It is important for children to initiate treatment as soon as possible and preferably within one week after diagnosis of HIV, therefore counseling sessions should start immediately upon diagnosis. During counseling sessions it is very important to fully assess, discuss and address issues to do with adherence with caregivers and, if of appropriate age, with the children themselves. This is always essential, and can be particularly challenging if an HIV-infected child does not have any signs of HIV disease. Caregivers should be informed that at the start of ART, there is a need for more frequent visits, but that the frequency of visits will decrease once the child is stable on treatment.

Furthermore, HCWs should ask the caregiver which health facility would be most convenient for him/her to access HIV services for the child. Every effort should be made to enable caregivers and children to attend the same health facility.

3.4.3 When to start ART and which ARVs to use in children and adolescents

ALL children and adolescents are eligible for ART and should be initiated on ART irrespective of CD4 count and clinical stage.

The choice of ARVs in children depends upon age, weight, previous eMTCT/PMTCT nevirapine exposure and co-morbidities. Children who have had NVP as part of eMTCT/PMTCT may have HIV resistance mutations to NVP. Therefore initiating an ART regimen containing NNRTIs to those children would not be expected to be durable.

The general principles followed in selecting ARVs for children include:

- It is preferable to use an age-appropriate fixed dose combination for any regimen if such a formulation is available
- Oral liquid or syrup formulations should be avoided where possible, especially if dosage volumes are large
- Where children use adult formulations, care must be taken to give the right dosage. Tablets that are not easily split should be cut at the dispensing pharmacy using tablet cutters
- Children must be weighed at each clinic visit and appropriate dose changes made as children grow and gain weight.

3.5. Paediatric ARV Formulations

3.5.1 Available formulations

Many antiretrovirals have liquid formulations and small dose dispersible tablets available for use in children. Although sometimes essential for comprehensive paediatric HIV care, there are some limitations to liquid formulations. They generally require prescription of several bottles and administration of large volumes to the child, sometimes leading to confusion. Care must be taken to mark syringes with a blade or permanent marker at the correct dose for the child. At times the "permanent" mark and the millilitre (ml) scale marks wear off by the end of a month, leading to errors in dosing. Liquid formulations may also have an unpalatable after-taste. In addition some solutions are impractical to use, e.g., lopinavir/ritonavir (LPV/r) syrup can be used for only 6 weeks at room temperature.

Several manufacturers have developed paediatric versions of single ARV and Fixed Dose Combination tablets (FDCs) which are much easier to administer than liquid formulations while still allowing the more accurate dosage required for small children. Most pediatric tablets are scored, crushable and dispersible in water and may be given in appropriate doses to children of all weights including infants as small as 3kg.

Children can be taught to swallow tablets and capsules from an early age, practicing with small sweets. This helps to make adult formulations more available for use by children. In addition, most 'adult' formulation tablets are crushable and capsules can be opened, mixed with a small amount of food and given immediately. One exception to this is LPV/r tablets which must be swallowed whole.

Some of the currently available adult strength FDCs (e.g. combined tablets of abacavir-lamivudine (ABC/3TC) can be split into halves to facilitate dosing in children.

See tables in Appendix 11, 12 and 13 for paediatric dosages of ARVs.

3.5.2. Initiating treatment

The preferred first line ART regimen in children depends upon age, weight, prior eMTCT/PMTCT nevirapine exposure and the presence of co-morbidities. **In this guideline, eMTCT/PMTCT NVP exposure is defined as any duration of NVP prophylaxis given to HIV-exposed infants as part of eMTCT/PMTCT**.

CAUTION:

Abacavir is not yet approved for use in infants <3 months old.
Lopinavir/ritonavir is not approved for use in infants <2 week of age (42 week gestational age).

It is important to initiate ART as soon as possible after the diagnosis of HIV infection is made. In most infants this will be after the birth test or the 6 week HIV NAT test.

Preferred first line ART regimen for infants who initiate at the following ages:

1. birth to <2 weeks: AZT/3TC/NVP (doses and regimen selection may vary with gestational age; seek specialist advice if <42 week gestational age) until the child is 2 weeks old. At that time change NVP to LPV/r
2. 2 weeks to <3 months old:
   i. AZT/3TC/LPV/r – until the child is 3 months old. At that time change AZT to ABC
3. 3 months to 2 years old or <10 kg: **ABC/3TC/LPV/r** [ABC/3TC as a once daily dose, LPV/r given twice daily]
4. 3 to 9 years old ***and*** 10 kg to <35 kg:
   i. NO previous eMTCT/PMTCT NVP exposure:
      - give **ABC/3TC/EFV** [all given together as once daily doses]

   ii. o Previous eMTCT/PMTCT NVP exposure:
      - if 3-5 years old or <15 kg give **ABC/3TC/LPV/r** [ABC/3TC as a once daily dose, LPV/r given twice daily]
      - if 6-9 years old and 15 to <35 kg give **ABC/3TC/[ATV+r]** [ABC/3TC and ATV+r given as a once daily doses]

- ≥35 kg and at least 10 years old : TDF/FTC (or 3TC)/EFV [all given together as once daily doses]

NB: Children generally reach 35 kg by 10-12 years of age. ***Tenofovir should NOT routinely be given to any child <10 years old even if that child weighs ≥35 kg unless the child is co-infected with Hepatitis B (see section 3.8.3).***

Table 3.4 below summarises the preferred first line ART regimens for children and adolescents in Namibia:

Table 3.4: The box below summarises the preferred first line ART regimens for children and adolescents in Namibia

	<2 weeks full term	2 weeks to 2 months	3 – 35 months	3 years to <10 years or <35 kg	[3]≥10 years and ≥35 kg
Preferred	AZT/3TC/NVP[1]	AZT/3TC/LPV/r[1,2]	ABC/3TC/LPV/r	ABC/3TC/EFV If had NVP eMTCT/PMTCT, give ABC/3TC/LPV/r	**TDF + XTC+ EFV^{4}_{600}**
Alternative	Seek specialist advice		ABC/3TC/ATV+r AZT/3TC/ATV+r AZT/3TC/LPV/r	ABC/3TC/EFV AZT/3TC /NVP ABC/3TC/ATV+r[3] AZT/3TC/LPV/r	**TDF + XTC+ EFV^{4}_{400}** AZT + 3TC + EFV^{4}_{600} AZT + 3TC + NVP TDF + XTC + NVP ABC+3TC+NVP (EFV)

[1]Seek specialist advice if the infant is <42 weeks gestational age, remember to change to AZT/3TC/LPV/r when the infant turns 2 weeks old

[2]Remember to change to ABC/3TC/LPV/r when the infant turns 3 months old

[3]ATV-r can be considered in patients who can't take either EFV or NVP. ATV+r preferred if the child is ≥6 years old and ≥15 kg

[4]If a patient is not pregnant or on TB treatment, EFV_{400} can be given.

3.5.2.1 Conditions in which alternative regimens could be considered

If any of the preferred first line ARVs cannot be used, **alternative ARVs are suggested in Table 3.6 below.**

In the rare instance when there is a hypersensitivity reaction to ABC and the child's regimen needs to be changed to AZT, it is important to remember to check that the Hb is ≥8 gm/dl before initiating AZT, and that follow-up Hbs are done at 2 weeks, 6 weeks and 3 months after initiating AZT.

If a child cannot use EFV due to a pre-existing condition (e.g. epilepsy), NVP can be used, but care should be taken to ensure its appropriate and safe initiation. All patients who are initiating ART with NVP should have half of the daily maintenance dose given once daily for the first 2 weeks of treatment while metabolic enzymes are being induced, increasing the dose to twice daily if the child has no signs or symptoms of hypersensitivity. Induction dosing is associated with a lower incidence of NVP rash and hepatotoxicity. If a child develops a MILD RASH with nevirapine, check for nausea & hepatic tenderness, send blood for ALT and continue induction dose for a further week. Counsel caregiver to bring the child back if rash gets worse, and reassess the child in one week.

If a child develops severe neuropsychiatric side effects from EFV, a change to NVP is appropriate. However in that case, initiate NVP with the twice-daily maintenance regimen, and omit the period of induction dosing.

The most frequently experienced side effect from atazanavir (ATV) is indirect hyperbilirubinaemia (jaundice). This does not usually require a regimen change.

Table 3.5: Severe toxicities associated with ARVs and suggested substitutions for children

ARV	Most Frequent or Significant Toxicity	Suggested ARV Substitution
ABC	Hypersensitivity reaction	If <3 months after start of ART, use AZT
TDF	Renal insufficiency (CrCl<60ml/min)	ABC if not HBV co-infected. If HBV co-infected, decrease TDF dose according to dose adjustment table in Appendix 5
AZT	Severe anaemia (<8 gm/dl,)[1] or severe neutropenia (<500 cells/mm3)	If <3 months after start of ART, use ABC. If >3 months, consult HIV specialist
	Lactic acidosis	ABC if < 3 months after start of ART or >3 months after start of ART and VL in last 6 months <40 copies/ml. If VL not suppressed, consult HIV specialist
	Severe gastrointestinal intolerance that prevents ingestion of ARVs (persistant nausea and vomiting)	If <3 months after start of ART, use ABC. If >3 months, consult HIV specialist
EFV	Persistent and severe central nervous system toxicity (severe dizziness, hallucinations, psychosis)	NVP
NVP	Acute symptomatic hepatitis or asymptomatic hepatitis with ALT>5x ULN	EFV[2] if ≥3 years old and ≥10 kg, unless severe hepatitis If <3 years old or < 10 kg, consult HIV specialist
	Severe or life threatening rash (Stevens Johnsons Syndrome (SJS)[3]	Substitute with a PI
LPV/r	GI intolerance, nausea, vomiting, diarrhea elevated transaminase enzymes, hypeglycaemia lipid re-distribution and lipid abnormalities	ATV/r (because this change is being made for toxicity, it can be done at any VL level)
ATV/r	prolonged QT interval leading to potential atrioventricular heart block	LPV/r

[1] *Exclude malaria in areas of endemic malaria*

[2] *EFV may cause hepatitis but much more rarely than NVP. If severe may need to change to LPV/r*

[3] *Hospitalization is required for all patients with SJS*

3.5.2.2 Transitioning children from AZT or D4T to ABC or TDF, from NVP to EFV and from LPV/r to ATV/r

All patients should already have transitioned off d4T, unless there is no other option for specific patients. In order to take advantage of preferable dosing schedules, side effect profiles and mutation sequencing and to allow harmonization with preferred ART regimens for adults, HCWs should identify children and adolescents currently on AZT, NVP or LPV/r and should carefully plan a change to the currently preferred regimens according to the following guidance.

Thymidine analogues (e.g. d4T and AZT) can be considered interchangeable because their mutation patterns are similar. Non-thymidine analogues (e.g. ABC and TDF) are also interchangeable for the same reason. However changing from a thymidine analogue to a non-thymidine analoque or *vice versa* in the presence of virologic failure could compromise future 2nd line options – it would be essentially introducing one new ARV into a failing regimen. For this reason, results of the most recent viral load should be reviewed to inform the appropriate regimen change. If the most recent VL is more than 6 months previously, it should be repeated.
Other principles to note when considering transitioning children from the previous regimens to new regimens:

- ABC/3TC should be given as a daily dose. There is an advantage therefore to changing from NVP to EFV in children using these NRTIs, as EFV is also a daily dose

- if any child cannot change to ABC/3TC because the VL is not suppressed while on a regimen with AZT(or 3TC/NVP, then it is best to keep the child on an FDC containing NVP given bd rather than change the NVP to EFV which would introduce a higher pill burden
- children are only eligible for a change from NVP to EFV if they are ≥3 years old and ≥10kg. If they are <3 years old or <10 kg and are on NVP, they should remain on NVP.
- children are only eligible for a change from LPV/r to ATV+r if they are ≥6 years old and ≥15 kg.

Table 3.6 summarises the guidance on changing regimens described below.

For children ≥10 years old and ≥35 kg: replace ABC/3TC with TDF/FTC as in table 3.6.

Table 3.6: Transitioning safely from previous ART regimens to new preferred regimens

		VL within last 6 months	
No.	**Current Regimens**	**VL<40**	**VL≥40**
	d4T/3TC/NVP but previous AZT toxicity[1]	Change to ABC/3TC + (if ≥3 yrs and ≥10kg) EFV	Confirm if truly previous AZT toxicity[2]. If yes, continue d4T/3TC/NVP as an FDC while intensifying adherence counseling and follow-up, evaluating for treatment failure and possible 2nd line if VL>1000[2]. If not true AZT toxicity, manage as in 1 above
2	d4T/3TC + LPV/r but previous AZT toxicity[2]	Change to ABC/3TC + LPV/r	Confirm if truly previous AZT toxicity[2]. If yes, keep on d4T/3TC + LPV/r while intensifying adherence counseling and follow-up, evaluating for treatment failure and possible 2nd line if VL>1000[3]. If not true AZT toxicity, manage as in 2 above
3	AZT/3TC/NVP	Change to ABC/3TC + (if ≥3 yrs and ≥10kg) EFV	Continue AZT/3TC/NVP as an FDC while intensifying adherence counseling and follow-up, evaluating for treatment failure and possible 2nd line if VL>1000[3]
4	AZT/3TC + LPV/r	Change to ABC/3TC + LPV/r	Continue AZT/3TC + LPV/r while intensifying adherence counseling and follow-up, evaluating for treatment failure and possible 2nd line if VL>1000[3]
5	ABC/3TC/LPV/r	Change to ABC/3TC/ATV/r (if ≥6 years and ≥15 kg)	Continue ABC/3TC/LPV/r while intensifying adherence counseling and follow-up, evaluating for treatment failure and possible 2nd line if VL>1000[3]

[1] *Patients who were anaemic at start of ART may have initiated treatment with d4T, however these patients do not have "AZT-induced anaemia" and it is safe to use AZT unless the current Hb<7.5*

[2] *If VL remains 40-1000 copies/ml, continue to counsel on and re-enforce good adherence but do not transition NRTIs to ABC/3TC unless VL falls below 40 copies/ml and do not routinely switch to 2nd line unless VL rises to >1000 copies/ml.*

3.5.3 Second Line ART

3.5.3.1 When to switch therapy in children

The term "switching" regimens is usually reserved for changing a regimen due to virologic failure rather than for toxicity or other reasons.

Deterioration or lack of improvement in either clinical or immunological criteria is an indication to investigate for possible virologic failure.

Viral load should be done in cases of suspected failure; however a non-suppressed viral load is not necessarily an indication for switching therapy.

The most common cause of virologic failure is non-adherence to therapy. Children who have viral loads >1000 copies/ ml need urgent attention paid to adherence to help determine any factors that negatively impact on adherence. ARV administration should be reviewed in detail, including pill counts, discussion about who administers the medicine routinely and on holidays, when and where, as well as how medication times fit into the family schedule. There are other causes of failure which need to be considered as well such as intercurrent OIs (e.g. TB), incorrect dosage of ARVs, adverse drug-drug interactions, poor absorption of medication and incorrect storage of medication.

The aim is to **earlier** identify children who have suboptimal responses to ARV therapy and whose immunologic and clinical responses may not have deteriorated at this stage. These children persistently have VLs > 40 copies per ml. Such children and their caregivers must undergo intensive adherence counseling and support to avoid further failure, to achieve viral suppression and to prevent the emergence of ARV resistant virus and the necessity to switch to second line treatment.

A viral load result >1000 cells/ml after at least 6 months of ART in a patient whose adherence is good and who has no other explanation for failure (see above) should have a repeat viral load done 3 months after intensive adherence counseling. A persistently high viral load despite good adherence is a reason to consider switching therapy to second line. A switch should only be made if adherence challenges are solved and it is anticipated that adherence to second line will be good.

3.5.3.2 Second line regimens

As a general rule, when considering switching to second line therapy in children, health care workers at the clinic should meet as a group to thoroughly review all aspects of the patient's case. In addition it is recommended that a second opinion from an HIV expert may be sought. Table 20 The preferred second line regimens for children are listed in the table 3.7 below.

Table 3.7: The preferred second line regimens for children

	Age	First-line ART regimen	Second-line ART regimen
PI-based first line	< 3 years	ABC/3TC/LPV/r AZT/3TC/LPV/r	AZT/ABC/3TC/NVP (if did not have eMTCT/PMTCT NVP in past) ***If had eMTCT/PMTCT NVP, do genotype****
	3 – 9 years or <35 kg	ABC/3TC/[ATV+r or LPV/r] AZT/3TC/[ATV+r or LPV/r]	ABC/AZT/3TC/EFV (if never had eMTCT/PMTCT NVP) ***If had eMTCT/ PMTCT NVP, do genotype****
	≥10 and ≥35 kg	ABC/3TC/ATV/r (or LPV/r) AZT/3TC/ATV/r (or LPV/r) TDF/[3TC or FTC]/[ATV+r or LPV/r]	TDF/FTC/AZT/EFV
NNRTI-based first line	<10 years or <35 kg	ABC/3TC/EFV (or NVP) AZT/3TC/EFV (or NVP)	AZT/ABC/3TC/LPV/r if <6 years old or <15 kg AZT/ABC/3TC/ATV+r if ≥6 years old and >15 kg
	≥10 a nd ≥35 kg	ABC/3TC/EFV (or NVP) AZT/3TC/EFV (or NVP) TDF/XTC/EFV (or NVP)	AZT/TDF/XTC/ATV+r
If a child <10 years old who was on LPV/r or ATV+r in first line, and was given NVP for eMTCT/ PMTCT as an infant, an NNRTI should not be used because of possible resistance mutations acquired during the period on NVP. Seek advice of an HIV specialist and do an HIV resistance test (see section 3.5.3.3)* * ATV+r is the preferred PI for children ≥6 years and ≥15 kg. Children who weigh ≥40 kg are eligible for the ATV/r (300mg/100mg) fixed dose combination*			

3.5.3.3 Resistance testing

Resistance testing provides identification of HIV mutations that may have been selected and which might be causing virological failure in a patient who is adhering well to ART. Although management of patients would be easier if resistance testing was done prior to selection of a second line regimen, this is costly and should not be done routinely. However resistance testing is essential for a child or adolescent who has failed a second line regimen and a third line regimen is needed. In addition, children who have been exposed to NVP for eMTCT/PMTCT and have failed a protease inhibitor as a first line regimen, qualify for resistance testing to allow for selection of an effective 2nd line regimen. An HIV specialist can give approval for this on an individual patient basis, and in any case should be consulted for further management of this child.

Eligibility for resistance testing in children who are adhering well to ARVs:

- Virologic failure in the presence of confirmed good adherence on 2nd line ART
- Virologic failure in the presence of confirmed good adherence in children <10 years old who have been on LPV/r (or ATV+r) as part of first line and who have a history of having had NVP as eMTCT/PMTCT in infancy

Ordering an HIV genotype resistance test should be done using the specific "HIV Genotype Resistance Test" form for that purpose. (see Appendix 18) On this form, patient medication history, the indications for doing the test and which of the authorized HIV specialists has been consulted should be specified. Without a fully completed form, NIP will not accept the sample for testing.

Interpreting results of resistance testing is complex and should be analysed in conjunction with the ART history of the child, noting that it may only provide full information about resistance to the current regime the child is on. Mutations selected by a previous regimen that the child was taking may be "archived" (still present but not in high

enough quantity to be detected by the resistance test) and if that ARV is given again, the mutation will become more prominent and the ARV will not be effective. Interpretation of results should be done in consultation with a specialist. The HIV Drug Resistance Central Clinical Committee (HIV DR CCC) meets monthly to review cases and reaches a consensus decision on the way forward in management of specific patient. Particularly if the mutation pattern assessment results in a recommendation for buying out of ARVs not routinely available, it is important that the case is discussed at the HIV DR CCC meeting.

3.6 Clinical assessment and monitoring

Careful clinical assessment and follow-up is essential to managing HIV-infected children and adolescents and to monitoring the effectiveness of ART.

3.6.1 Baseline clinical assessment following confirmation of HIV infection.

This includes:

1. Weight, length or height, and head circumference (for <3 year olds). Plot on growth appropriate growth charts in the Paediatric Patient Care Booklet
2. Assessment of developmental milestones achieved (for <5 year olds) or school performance for school-aged children – record in the Paediatric Patient Care Booklet
3. WHO Clinical Staging
4. Identification of concomitant conditions (e.g., TB screening, other OIs, pregnancy in adolescent girls)
5. Screening for isoniazid preventive therapy (IPT) eligibility
6. Immunisation status
7. Nutritional status including assessment of quality and quantity of intake
8. Detailing of concomitant medications (e.g., cotrimoxazole, traditional medications)
9. Assessment of child's and caregiver's preparedness for therapy. Aim to start ART on same day or within one week.

3.6.2 Routine monitoring of children on ART. This includes:

- Clinical evaluation every 3 months
- Weight, length or height, and head circumference (for <3 year olds). Plot on appropriate growth charts in the Paediatric Patient Care Booklet
- Assessment of developmental milestones achieved (for <5 year olds) or school performance for school-aged children - record in the Paediatric Patient Care Booklet
- WHO clinical staging should be done at each visit using the standard WHO Clinical Staging of HIV in infants and children chart. Since the child is on ART, this staging is termed "T-stage" and it should recorded in the Patient Care Booklet as "T1, T2, T3 or T4" in the column "WHO Clinical Stage"
- Identification of concomitant conditions, especially TB screening
- Screening for isoniazid preventive therapy (IPT) eligibility
- Nutritional status including assessment of quality and quantity of intake
- Evaluation of adherence to ARV therapy and to cotrimoxazole and vitamins. Discuss adherence issues with the child and caregiver(s)
- For children ≥6 years old, enroll in HIV disclosure activities and record at each visit on the appropriate form in the Paediatric Patient Care Booklet . Engage caregiver into discussions about disclosure until full HIV disclosure is achieved. (see section 3.10.3)
- Discussion of symptoms and observation for signs of medicine toxicity or intolerance
- Discussion of symptoms and observation for signs of treatment failure (e.g., poor growth progression, development ofneurological symptoms or poor development, development of new infections)

- Laboratory monitoring as per Table 3.8
- Appendix 3 gives details of the laboratory monitoring required depending on the ART regimen the child is on.

3.6.3 Laboratory monitoring

Table 3.8 below lists routine bioclinical monitoring tests that should be done at different phases of HIV management.

Table 3.8: Baseline and monitoring laboratory tests for children and adolescents prior to and after starting ART

Phase of HIV management	Tests	Frequency
At HIV diagnosis	CD4	Once
	HBsAg	Once. If positive, repeat after 6 months, the lab will autamically do ALT if HBsAg is positive (reactive)
	Hb	Once
	HIV NAT repeat	Once if <18 months old - Do not wait for result to initiate ART
	CrCl	If intend to initiate TDF
	Urine dipstick	If intend to initiate TDF
Treatment monitoring	VL	M 6 (then every 6 months)
	CrCl	6 W, M 6, M 12 (then every 12 months) if on TDF
	Hb	2 W, 6 W, M 3 if on AZT
HBsAg positive	ALT	ART initiation, 2 W, 6 W, M 3 (then every 6 months if the repeat HBsAg is positive indicating chronic HBV infection)
Suspected treatment failure	VL	Repeat VL after 3 months of good adherence and once OIs excluded
Virological failure	CD4[2]	Every episode of virologic failure
	HIV Drug Resistance	Children <10 years old who have been on a PI as part of 1st line with PMTCT NVP exposure in infancy
		At any age, before switching to 3rd line ART

the creatinine clearance calculation for adults is not applicable to children <18 years old. The equation (SCHWARTZ equation) which should be used to estimate creatinine clearance (CrCl) in children from 1 week – 18 years of age is shown in figure 3.4
Check CD4 count to assess immunological status and inform clinical management (eg. assess for possible OIs)

The Swartz equation shown in Figure 3.4 should be used to estimate creatinine clearance (CrCl) in children from 1 week – 18 years of age

Figure 3.4: Creatinine Clearance calculation for use in children <19 years old

SCHWARTZ equation

CrCl (ml/min/1.73m^2) ≈[length (cm) x k x 88.4]/serum creatinine (mmol/l)

k = 0.45 for infants 1 – 52 weeks
k = 0.55 for children 1 – 13 years old
k = 0.55 for adolescent females 13 – 18 years old
k = 0.7 for adolescent males 13 – 18 years old

Ref: Schwartz, GL et. al. A simple estimate of glomerular filtration rate in children derived from body length and plasma creatinine. Pediatrics 1976, 58:259-263

Table 3.9 below gives normal GFR values for children and young adults:

Table 3.9: Normal GFR in children and young adults

Age (gender)	Mean GFR ± SD (ml/min/1.73m3
> 8 weeks and <2 years (males and females)	95.7 ± 21.7
2 - 12 years (males and females)	133 ± 27.0
13 - 21 years (males)	140 ± 30.0
13 - 21 years (females)	126 ± 22.0

Ref: National Kidney Foundation / KDOQI Clinical Practice Guidelines for Chronic Kidney Disease: Evaluation, Classification and Stratification (2002), National Kidney Foundation, Inc

3.7 Children with Tuberculosis (TB) and HIV co-infection

As with adults, tuberculosis occurs more commonly in children with HIV infection than in those without HIV. Children with HIV are more likely to be exposed to and infected with TB than children without HIV because they are more likely to live in households with TB and HIV and are, therefore, more likely to be a close contact of a case of active TB disease. If infected with TB, children with HIV are more likely to develop TB disease. TB screening and preventive therapy to reduce the risk of TB disease following TB exposure and infection are key interventions to reduce the impact of TB among children with HIV.

Children and adolescents with HIV should be screened for TB including asking about TB exposure/contact history at each encounter with a health worker or visit to a health facility; eligible children and adolescents with HIV should be offered IPT. **See section 3.3.2 for algorithms for TB screening and IPT among PLHIV and Section 1.17.2 for more detail regarding TB-IPT.**

TB Screening Questions:

- Poor weight gain o defined as reported weight loss, very low weight (weight-for-age < -3 z-score), underweight (weight-for-age < -2 z-score), confirmed weight loss >5% since last visit, or growth curve flattening

- Fever
- Cough
- Lymph node enlargement
- Contact with person with confirmed or presumptive infectious TB

All children and adolescents with HIV who have signs and/or symptoms suggestive of TB should be evaluated for TB disease including careful history, thorough physical examination, chest radiography and possibly a TST along with any other relevant tests. Bacteriological confirmation should be sought whenever possible. Sputum can be collected from most children using either direct expectoration (older children), gastric aspirates or sputum induction. For a description of specimen collection in children, see the National Guidelines for the Management of Tuberculosis.

Xpert MTB/Rif is the preferred initial diagnostic test over DM and Culture and DST. It is also the preferred test for CSF specimens in patients with possible TBM. Specimens should be sent for mycobacterial culture and Xpert MTB/Rif due to the low sensitivity of smear microscopy.

Remember: a negative Xpert MTB/Rif, DM or culture test result does not rule out TB.

Answers to the TB screening questions and follow-on evaluations/decisions should be recorded in the appropriate page of the pediatric patient care booklet. Please refer to the National Guidelines for the Management of Tuberculosis for help with diagnosing and treating TB in children and adolescents.

3.7.1 When to start ART in HIV/TB co-infected children and adolescents

ART should be started in all HIV-infected children and adolescents with TB disease, including those with drug-resistant TB, irrespective of the CD4 and clinical stage.

If the diagnosis of TB and HIV are made simultaneously, ART should be started in any child or adolescent with active TB disease as soon as possible and within eight weeks of starting antituberculosis treatment. Children with profound immunosuppression (e.g. CD4<50 cells/mm^3) should receive ART immediately, within two weeks of initiating TB treatment as this carries a survival advantage in this group.

HCWs should be aware that starting ART within the first 8 weeks of TB treatment does carry a risk of Immune Reconstitution Inflammatory Syndrome (IRIS). However, there is ample evidence that mortality from delaying the start of ART in TB coinfected children and adolescents greatly outweighs the risk from IRIS (see 3.9 section for the management of IRIS).

3.7.2 ART regimens for children with TB being treated with rifampicin-based regimen

Not all antiretrovirals should be used in combination with rifampicin. Rifampicin increases metabolism of and hence lowers the blood levels of protease inhibitors by approximately 80%, of nevirapine by 30-50%, and of efavirenz by 25%. Given concurrently with rifampicin, nevirapine is probably not as effective and nevirapine resistance can be selected, which may compromise future ARV choices. At standard doses, efavirenz remains effective in the presence of rifampicin. For this reason, efavirenz is preferred for use in children needing rifampicin-based TB treatment if they are at least 3 years old, 10 kg and have not had previous nevirapine for eMTCT/PMTCT.

Giving lopinavir "super-boosted" with ritonavir results in a therapeutic blood level of lopinavir in children on rifampicin. "Superboosting" means adding additional ritonavir to bring the dose of ritonavir equal to that of lopinavir. Atazanavir should not be co-administered with rifampicin. Therefore children on ATV+r should be given LPV/r+R instead until 2 weeks after stopping rifampicin.

If a child or adolescent presents with TB and is not yet on ART, start ART with the following regimens:

2 weeks to <3 months old:

- AZT/3TC + LPV/r + R

3 months to <3 years old or weight <10 kg:

- ABC + 3TC + super-boosted lopinavir/ritonavir (LPV/r + R)
- AZT + 3TC + ABC

NB: Switch to standard ART regimen two weeks after competing rifampicin-based *TB treatment*

9 years old and weight 10 kg to <35 kg

- *If the child has had NO previous eMTCT/PMTCT NVP exposure:* ABC+ 3TC + EFV
- *if the child has had previous eMTCT/PMTCT NVP exposure*
  - ABC + 3TC + super-boosted lopinavir/ritonavir (LPV/r + R) or
  - ABC+3TC+AZT

NB: two weeks after TB treatment is completed, change to the standard ART regimens

≥35 kg and at least 10 years old:

- TDF + 3TC + EFV

If a child is on first line ART and is diagnosed with TB, make the following temporary changes to the ART regimen, always changing back to the standard ART regimen two weeks after completion of TB treatment:

- **If <3 years or <10 kg and already on NVP or LPV/r,** change to ABC + AZT + 3TC
- If on LPV/r give: ABC + 3TC + LPV/RTV

- **If ≥ 3 years old and ≥10 kg and already on NVP**, change NVP to EFV
- **3 - 9 years old *or* 10 kg to <35 kg and already on ATV/r or LPV/r**, give LPV/r with added ritonavir to achieve super-boosted lopinavir/ ritonavir (LPV/RTV) [do not use ATV when on rifampicin for TB as there are significant drug-drug interactions] or if not possible, give ABC + AZT + 3TC.
- **If ≥35kg and at least 10 years old and already on ATV/r or LPV/r,** give LPV/r with added ritonavir to achieve super-boosted lopinavir/ ritonavir (LPV/RTV) or change to TDF + AZT + 3TC

If a child is on second line ART and is diagnosed with TB, make the following temporary changes to the ART regimen , makethe following *temporary changes* to the ART regimen:

If already on 3 NRTIs + EFV: leave unchanged

If already on 3 NRTIs + NVP and ≥ 3 years old and ≥10 kg: change NVP to EFV

If already on any other regimen or <3 years old or <10 kg, consult an HIV specialist and consider discussing TB regimen change with CCRC (Clinical Case Review Committee).

Remember: Two weeks after TB treatment with rifampicin is completed, the child should change to the usual first line regimens, or to the regimen he/she was taking before starting TB treatment if the child has been given a triple NRTI regimen or super-boosted lopinavir/ritonavir.

NB: The use of d4T with isoniazid in TB therapy may result in a greater incidence of peripheral neuropathy. If d4T cannot be avoided, monitor for neuropathy and ensure that they receive pyridoxine. The dose of pyridoxine is 12.5mg/day (1/2 tablet) for children 5-11 years old and 25mg/day for children ≥12 years old. This is an increase in dose compared to the previous guidelines.

3.8 Children with chronic Hepatitis B virus (HBV) and HIV co-infection

3.8.1. Background

The prevalence of chronic HBV among children with HIV throughout Namibia is not known however it is thought to be as high 8-9%. Children who are infected with HBV can clear the infection or can become chronically infected. The likelihood of chronic HBV infection, defined as persistence of HBsAg for at least 6 months, varies by the age at which the child is acutely infected. Chronic HBV develops in 90% of infants infected, 25-50% of 1-5 year olds and 6-10% of older children and adolescents.

Recently HBV vaccinations were included in the routine immunisation schedule for newborns and infants. It is anticipated therefore that the incidence and prevalence of HBV will decrease with time. For further guidance on the possible provision of "catch-up" vaccinations for older children who did not receive HBV vaccination in infancy, await further upcoming MoHSS policy decisions.

3.8.2 Diagnosis of chronic HBV in children

It is important to determine if a child who has one positive HBsAg result is actually chronically infected with HBV or if the infection is acute and will clear with time. A repeat HBsAg done 6 months after the first positive one will allow this distinction to be made. Therefore:

All children and adolescents with one HBsAg positive result should have one repeat HBsAg test done 6 months after the initial positive test.

If the repeat test is positive, the child has chronic HBV infection. Currently TDF has been approved by FDA for use in children > 2 Years. However, there is no appropriate does formulation for children < 10 years or <35 kg in Namibia. If or when the age appropriate dosage formulations of TDF are available for children, MOHSS will issue a circular to guide and direct on proper implementation. Until then all children with HBV/HIV Co-infection receive the currently recommended ART regimens just like those with no HBV co-infection.

If the result of the 2nd HBsAg is non-reactive, it can be concluded that the child does not have chronic HBV infection. If that child was already initiated on TDF/FTC, but is <35 kg or <10 years old, the NRTI backbone should be changed to ABC/3TC after receiving this result.

3.8.3 Management of children with Chronic HBV

Three antiretroviral medicines used in Namibia for HIV also treat HBV: lamivudine (3TC), emtricitabine (FTC) and tenofovir (TDF). Studies in HIV/HBV co-infected children show that giving 3TC as part of an ART regimen without TDF results in a more than 20% per year HBV mutation rate to 3TC. Evidence has also been showing that some 3TC-resistant mutations also result in changes in the HBsAg which cause decreased antigenicity and also allows HBV to escape being killed by HBV vaccination.

Extrapolating from evidence in adults, ongoing HBV infection exposes HIV/HBV co-infected children to liver damage and an increased risk of future hepatic cancer.

For the above reasons, TDF should be included in the treatment of HBV/HIV co-infection in children. The benefits of giving TDF to HBV/HIV co-infected children outweigh the risks of TDF adverse events.

There is little known about the long-term significance of potential side effects of tenofovir such as decreased bone mineralization and renal insufficiency, and hence routine use of tenofovir in children<10 years old and <35 kg is generally not recommended. However in children with HBV/HIV co-infection, the potential benefits of averting selection of HBV mutations and ongoing liver damage outweighs the potential risks of adverse events from giving tenofovir together with lamivudine to these children. Several paediatric formulations of TDF are currently available.

HBV/HIV co-infected children who weigh ***at least 17 kg and are at least 2 years old*** should receive TDF/FTC as part of their ART according to the NRTI dosage schedule Appendix 11. Such children should be routinely screened for renal function.

Children ***<2 years old or <17 kg*** should have the standard preferred first line NRTIs (ABC/3TC) as part of their ART regimen and should transition to TDF/FTC when eligible by age and weight.

3.9 Immune Reconstitution Inflammatory Syndrome (IRIS) in children

IRIS has been observed in children who have initiated ART, especially in those children receiving anti-TB treatment. IRIS is characterised by worsening clinical condition after initial improvement and can manifest with:

- new onset of systemic symptoms such as fever
- worsening of pulmonary infiltrates
- peripheral or mediastinal adenopathy
- expanding CNS lesions

IRIS usually occurs during the first three months of ART treatment. Generally, IRIS is self-limiting, lasting 10-14 days. Treat symptomatically. Some patients may require a short course of steroid treatment for symptom management. Except in rare life-threatening situations, ART should not be discontinued. Close monitoring of the child is essential.

3.10 Monitoring in HIV-infected children, before and after ART initiation

3.10.1 Growth monitoring and nutrition considerations

Malnutrition is common in HIV-infected children and is a major contributor to mortality in both HIV-uninfected and HIV infected children. In HIV infected children, wasting (i.e. low weight for height/length) has been associated with reduced survival, while weight loss has resulted in increased infectious complications in children with HIV. In addition, HIV has been associated with nutritional disorders and impaired immune function. HIV-infected children require more energy and nutrients than non-infected children. They are at higher risk for acute malnutrition and take longer to recover when they become malnourished. It is important that nutritional support is given early in the onset of malnutrition in order to give these children the best chance of recovery. Early nutritional intervention (i.e. nutritional assessment, counseling and support) is recommended as an integral part of the care plan of HIV infected children (WHO, 2009).

3.10.1.1 Growth monitoring

Monitoring growth, nutritional status, diet and nutrition-related symptoms, are critical in the early identification of malnutrition and poor growth. Growth failure may present as only a slight decline in normal growth rate, however if not adequately addressed this could lead to static (unchanging) growth or weight loss. Height (or length in infants), weight and head circumference (in children <3 years old) should be routinely measured, recorded and charted on the appropriate growth charts in the patient care booklet at every visit the child makes to the clinic. This is essential to ensure that doses of medication are escalated along with weight gain and to evaluate whether or not the child is growing and gaining weight normally.

In addition to lack of appropriate diet, HIV and other opportunistic infections can impact optimal growth for a child, leading to poor brain development, growth failure, and severe malnutrition. Other causes of growth failure such as superimposed infection (e.g. TB) and medicine intolerance need also to be considered.

3.10.1.2 Neurological and cognitive development

HIV can interfere with the normal neurological and cognitive development in a child. Therefore it is very important that for children <5 years old, achievement of developmental milestones be monitored and recorded in the child's patient care booklet. A child who is not achieving normal developmental milestones, or indeed who shows signs of regression after having achieved some, should be further assessed. Referral to a physiotherapist / occupational therapist (physical delay) or a social worker (cognitive delay) should be done as appropriate. Screening for normal neurological development need not take much time. A tool such as the one shown in Table 3.10 below offers a quick screen for assessing achievement of developmental milestones.

Table 3.10: Developmental Screening Checklist

Age	Developmental milestone
1 month	Raises head, makes crawling movements, alert to sound
2 months	Holds head at midline, lifts chest off table, smiles socially
4 months	Rolls front to back, laughs
6 months	Sits unsupported, babbles
9 months	Pulls to stand
12 months	Walks alone, uses single words
18 months	Can remove garment, scribbles, uses 6 words, runs
24 months	Can wash hands, jump up, combine words
36 months	Can put shirt on, speech is understandable, can balance on one foot
48 months	Can dress alone, draw a person, use complex speech, hop

3.10.1.3 Nutrient requirements of HIV-infected children

Increased energy needs

HIV infected children have greater energy needs compared to healthy non HIV infected children. The energy requirements of HIV infected children with no symptoms are increased by 10%. During the symptomatic phase without weight loss, energy requirements increase by 20 to 30% over the level of energy intake recommended for healthy non HIV infected children of the same age. When the child is both symptomatic and losing weight, energy requirements increase by 50 to 100% (FANTA 2004; WHO Nutrition 2009).

Strategies to meet increased energy requirements include:

- Dietary adjustments and meal plans of available energy-giving foods such as mahangu, maize, rice, potatoes, cassava, wheat
- Increased frequency of meal intake in a day
- Adoption of food preparation methods that add more energy, for example sweetening porridge or adding nuts and oil during preparation of meals raises their energy values several folds
- Consumption of snacks between meals.

Protein needs

Protein requirements remain the same for children of the same age, sex and physical activity, regardless of HIV status. With an increase in calorie intake through consuming a balanced and complete diet, protein intake tends to naturally increase. If, however, children have pre-existing inadequate protein intake, this needs to be addressed and may require increased protein intake.

Micronutrient needs

Micronutrient needs are the same as for children with or without HIV. Micronutrients found in fruits and vegetables will help the child fight infections by boosting the immune system. Iron, vitamin A, and vitamin C-rich foods are important in the child's development and in the prevention of childhood diseases. Fruits and vegetables are important sources of vitamins and minerals and should be part of a children's diet. The deep colored varieties of vegetables contain abundant amounts of minerals and vitamins that are useful to the immune system. Children require adequate iron from meat, beans, and vegetables such as spinach to prevent anaemia. Vitamin C-rich foods - such as oranges, mangoes, pawpaw, guava, baobab, and tomatoes - help iron absorb faster and more effectively

into the body. In cases of deficiency, the child should take a multivitamin/ mineral supplement daily with the guidance of a health provider. Vitamin A supplementation is provided for all children as part of the Expanded Programme on Immunization (EPI) policy.

Malnutrition in HIV-infected children

Severe malnutrition is a life threatening condition in HIV infected children and requires urgent therapeutic feeding (WHO 2009). For the management of moderate and severe malnutrition in HIV positive children and adolescent, refer to Appendix 8.. Always test malnourished children for HIV.

All children with severe malnutrition are at risk for a number of life-threatening problems and should be treated according to national guidelines before decisions are made on the initiation of ART. However the delay should be minimized.

- The treatment of severe malnutrition should be started at least one week before the introduction of antiretroviral medicines to diminish the risk of serious side effects from the medication
- The initial phase of treatment of severe malnutrition should continue until the child has stabilized and has regained appetite
- A child who is not responding to nutritional management should receive a home visit from a community health care provider to assess the home environment, and should be referred to a doctor for further assessment if there is no improvement after three months.

Prevention or treatment of malnutrition is essential in HIV infected children. All HIV infected children attending the clinic should undergo nutrition assessment of weight-for-height (WFH), weight-for-age (WFA), height-for-age (HFA) and midupper arm circumference (MUAC) to categorize their nutritional status.

Nutrition Assessment, Counseling and Support

Nutrition assessment is an analysis of an individual's medical and diet history, laboratory values, and anthropometric measurements to identify nutritional risk or malnutrition and identify underlying causes so that appropriate nutrition intervention can be planned and initiated.

The nutrition assessment, counselling and support (NACS) is an approach designed to:

1. Provide food and nutrition services as part of care and treatment on an outpatient basis, with strong links to community service
2. Prescribe food to malnourished target individuals for a limited time, based on clear admission and discharge criteria to improve nutrition and health outcomes.

Health workers should encourage mothers and caregivers to routinely bring their children to the facility for assessment and counseled/educated using appropriate guidelines. Any child who is identified as malnourished should receive the therapeutic food products as per the national guidelines.

3.10.2 Adherence and missed doses

Adherence to medication is the single most important factor predicting success of antiretroviral therapy. It should therefore be addressed at each visit to the clinic and in all encounters with health care workers. Pill (and liquid) counts should be routinely done as well as discussions specifically targeting any possible barriers to adherence.

If a child misses a dose of antiretrovirals, he/she should **take the missed dose as soon as it is remembered.** Then determine how long it is until the next dose is due.

1. If it is more than 2 hours before the next dose is due, take the next dose at the usual time and continue with the normal schedule
2. If it is less than 2 hours before the next dose is due, omit the next dose and then continue with the normal schedule.

For example, if a child was due for tablets at 6AM and remembers at 11AM that the dose was not taken, he/she should take that dose immediately and still take the 6PM dose on time. If the child was due for tablets at 6AM and remembers at 5PM, then he/she should take the forgotten dose at 5PM but should omit the 6PM dose, and then go back to the normal 6AM/6PM schedule.

3.10.3 Disclosure of HIV status

Disclosure of HIV status to children is challenging for parents/ caregivers and health care workers alike. However age-appropriate partial or full disclosure is essential if sustained adherence to medication is to be achieved, especially as children grow into young adolescence. When children reach 6 years old, they should be enrolled into specific activities that start the partial disclosure process and HCWs should begin discussions with the caregivers. The ultimate aim is that by the child's 10th birthday, he/she knows his/her HIV status, and that the child should be told in a safe and supportive way.

Before disclosure of HIV status to a child, it is essential that the caregiver(s) are ready for disclosure to take place. There may be concerns about the effect disclosure will have on the child and family, and these concerns need to be discussed and resolved in advance.

Caregivers need to be prepared for any questions that may come from the child at home as they are the ones who live with the child. The whole family may be worried about possible consequences of stigma or ostracism in the community if the family secret emerges, so caregivers need to work through how they will handle or prevent this. To guide this process, there is a list of 17 questions in the pediatric patient care booklet that should be answered to ensure that the most important issues are covered and resolved with caregivers.

Some caregivers are comfortable disclosing HIV status to their children, and HCWs should support them in their efforts, helping them to anticipate issues and questions that will arise. Other caregivers prefer for disclosure to be done by clinic staff and in that case the HCW should ensure that the caregiver is present and agrees in advance with what the child will be told.

Disclosure is a process rather than a single event. It starts with a relationship of trust that caregivers and/or HCWs build with the child in which the child is always told the truth, in a positive and supportive way. At every clinic visit routine age-appropriate discussions with the child should be done concerning their experiences at school, their future plans and why they are taking their medicines. This gives ample opportunity to ensure correct understanding and to detect any problems that may arise. Notes about these discussions should be recorded by the HCW in the HIV disclosure form included in the paediatric patient care booklet.

A booklet called *"Why I take my medicines"* is available in clinics in several local languages and should be used to guide HIV disclosure to children. The booklet helps children understand, with increasing levels of complexity depicted in 5 chapters, why they need to take medicines every day and on time in order to stay healthy. Messages are positive, and the child's understanding should be assessed and re-enforced at every visit. The booklets consist of cartoon illustrations depicting, for example, HIV as "bad guys" and CD4 cells as "soldiers", and also has guidance for HCWs on how best to communicate with the child in an interactive way. Following full HIV disclosure it is important to offer the child an appointment in 2 weeks to ensure that any unanswered questions or worries are resolved early.

Older children and young adolescents should learn the names of their antiretrovirals and should play a major role in remembering to take their medicines on time, still supervised by a care-giver. Health care workers need to ensure that adolescents are equipped with the information they need about the modes of HIV transmission and prevention before they enter into possible sexual relationships.

3.11 When to consult an HIV specialist

Good collaboration between general practitioners and HIV specialists is essential for the establishment of successful and durable antiretroviral therapy in children and adolescents. In the following circumstances it is recommended to consult a specialist, ideally a pediatric HIV specialist:

- Combined pathologies (hepatitis, renal failure, diabetes, tuberculosis, etc.)

- Severe medication toxicities
- Lack of or insufficient clinical response to therapy (as identified by growth and development parameters) or worsening clinical condition
- Immunological or virologic failure of first or second line therapy

CHAPTER 4: CARE AND SUPPORT FOR ADOLESCENTS LIVING WITH HIV

4.1. Overview of Adolescents issues

WHO defines adolescents as children between 10-19 years of age. They may be further classified as younger adolescents (10-14years) and older adolescents (15-19 years). Namibia has adopted this definition for adolescents. Furthermore, Child Care and Protection Act of 2015 in Namibia defines a child as an individual below the age of 18. The Act has further lowered the age of Majority from 21 to 18 years and made provision that an individual at the age of 14 years can get medical procedures and treatment without the permission of a caregiver/parent. Any adolescent from the age of 14 years and upwards can consent to having an HIV testing and initiating ART.

ART coverage among adolescents is 74% among girls and 86% among boys, which is below the national target. The coverage is highest in the age 10-14 with 92% among girls and 94% among boys. There is a sharp decline in the age 15-19 especially among girls at 61% and 76% among boys. The coverage further declines in the age 20-24 with 39% among females and 14% among males. The declining ART coverage with age and corresponding low HIV testing rates indicates challenges in initiation among newly infected adolescents and young adults and retention of patients on ART as they transition into adulthood. Viral suppression is 74% and 70% for adolescent girls and boys on ART respectively which is below the 90% national target. The viral load suppression is higher among the 10- 14 year olds at 73% compared to 63% among the 15-19 year olds. (Namibia Preliminary Report for Adolescent Assessment, 2015)

Namibia developed National Guidelines on Adolescents Living with HIV (ALHIV) in 2012, which outlines the strategic guidelines for the provision of multisectoral services to ALHIV. To meet the objective of delivering comprehensive adolescent-focused clinical HIV services to ALHIV, the following interventions need to be put in place :

4.2.Promoting the uptake of HIV Testing Services

The Child Care and Protection Act made provision for adolescents age 14 years upwards to access medical services including HTS without parental consent. This is envisaged to facilitate voluntary uptake of HTS among adolescents and subsequent linkage to treatment, care and support.

The following approaches are recommended to educate, inform and mobilize adolesents for HTS:

- Purposefully organized and targeted HTS campaigns. This could be facility or community-based outreach activities; including schools/colleges.
- Provider-initiated HTS coupled with other entry services such family planning services, VMMC (Voluntary Medical Male Circumcision) and immunization campaigns
- Ensuring that all health facilities are oriented towards the adolescent friendly health services approach as per AFHS guidelines which includes flexibilities in clinic opening times .

4.3. Treatment, Clinical visit and integrated interventions

ART coverage in Namibia among adolescents is lower compared to the national target. ART should be provided to all ALHIV regardless of their WHO clinical stage and CD4 Count. However, due to complex and multiple factors around adolescence treatment readiness from adolescents and caregivers' side will determine ART initiation.

Normally, the adolescent ART regimen is similar to the regimen used in adults (Refer to the adult ART Regimen in Chapter 1 of this guideline). It is essential to also note that some adolescents living with HIV may be stunted or underweight and hence medicine dosage may require adjustments accordingly (See adult and paediatric, adolescent ART sections).

4.3.1 Clinical Care

Adolescents face many challenges related to their period of age and different biological, physiological , social and behavioural changes that they go through. They prefer some degree of independence to decide whether or not to take their medicines. This forms the basis for closer monitoring and more frequent visits to the health facility. Older adolescents (15-19) adhere less to the medications compared to the younger adolescents (10-14) who generally are still under care giver support. It is recommended that adolescents have 3-monthly visits.(Refer to Namibian Rapid assessment 2015)

4.3.2.Cervical cancer Prevention and screening

It is known that cervical cancer is caused by infection with human papilloma virus (HPV).

It is recommended that HPV vaccine be provided to all sexually active adolescents considering the high risk of cervical cancer among adoescents living with HIV. All girls aged from 9 to 19 years should get HPV vaccine . Adolescents living with HIV who received HPV vaccine may start the cervical cancer screening 3 years after the sexual debut. (MoHSS 2012). The HPV vaccination schedule is a 3 doses schedule with second dose administered 1-2 months after the first dose and third dose given 6 month after the first dose .

It is also recommended that sexually active adolescents should be screened for cervical cancer annually ,especially for those who were not vaccinated during early adolescence phase.

4.3.3 PrEP for adolescents at Risk :

Adolescents at substantial risk of HIV acquisition should be considered for PrEP (See PrEP Chapter).

4.3.4. Screening for STIs

All health care providers should screen all sexually active adolescents for sexually transmitted infections (STIs), and should discuss the importance of prevention and treatment of STIs (Refer to STI Guidelines).

4.3.5. Voluntary Medical Male Circumcision (VMMC)

VMMC should be part of health promotion activities aimed at encouraging the Uptake VMMC services.

4.3 6 Mental health and physchosocial support

Adolescents living with HIV deal with challenges such as loss of loved ones, stigma and isolation, gender-based violence and the responsibility of taking care of oneself in the presence of a chronic illness. Adolescents who suffer from depression are more likely to be non-adherent to their medication and have other self-care issues.

Transition to Adulthood: Adolescents are in transition from childhood to adulthood and it is a difficult period even for those without HIV. They experience physical as well cognitive changes and maturations. 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 often start to default taking their medicines in their adolescence. Health Care workers should anticipate this and discuss it with adolescents and caregivers as part of the treatment plan. In addition, comprehensive sexuality education should be provided as indicated.

To facilitate adherence and retention to care, it is essential to screen for and treat mental health problems. Some of the potential symptoms of an adolescent experiencing depression include the following symptoms: social withdrawal, loss of appetite or increased appetite, difficulty sleeping or too much sleep and poor personal hygiene,

Activities that can help in identifying and addressing mental health and psychosocial issues include:

- Train health providers to screen adolescents for potential symptoms of mental health problems;

- Effective communication skills and building trust between health providers, care givers and adolescents are the first steps towards creating a supportive environment;
- Mental health promoting activities should be incorporated in individual and group activities for adolescent support groups. Examples of mental health promotion activities include:
- Support for Transition to adulthood (prepare the adolescents to take control of their own treatment and be less dependent on caregivers.)

Planning and problem solving skills, treatment literacy, self-confidence and a therapeutic relationship with members of the health care team are important for adolescents on ART to achieve good adherence to therapy as they transition into adulthood. 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.

The following table provides specific goals that should be achieved by adolescents throughout the transition process. Younger adolescents should achieve all Phase 1 goals before transitioning to Phase 2 goals. All goals indicated under phase 2 should be fulfilled prior to transitioning to adult care. For details, refer to Figure 4.1

Figure 4.1: Adolescent Transition implementation goals per age group

Group	Transition Goals
Young Adoloscents 10 -14 years	**Phase 1 Goals** • Full HIV disclosure • Understand disease process • Understand disease markers • Understand prevention measures
Older Adoloscents 15-19 Years	**Phase 2 Goals** • Medication independence • Independent clinic visits • Maintain >95% adherence • Positive living • 2 consecutive undetectable viral load • Orient and enroll in adult ART clinic

Source: (MoHSS 2012a: National Guideline for ALHIV, Annexure C: Adolescent Transition Implementation Algorithm, pg. 51)

4.3.7 Disclosure (stigma and discrimination reduction activities)

Disclosure of HIV status to adolescents living with HIV: It is important to disclose HIV status to adolescents living with HIV (ALHIV) so that they fully understand and engage in their care. Parents and guardians of adolescents should seek support from the clinical team to inform the adolescents of their HIV infection and why they are taking treatment for HIV and or prophylaxis for opportunistic infections. For younger adolescents, disclosure should be a gradual and ongoing process (see section 3.10.3), while for older adolescents full disclosure may be applied with or **without the assistance from their caregivers and is dependent on the readiness of the adolescent.** Health care workers should be cognizant of adolescents' cognitive and emotional development during the disclosure process. Adolescents living with HIV should be empowered to disclose their HIV status to family members, friends or significant others ,safely on a voluntary basis. (MoHSS 2012). Health care providers should purposefully support facility-based and home disclosure. Early disclosure will prevent accidental disclosure; facilitate access to a wide range of care and support services, including sexual and reproductive health and rights (MoHSS 2012)

4.3.8 Sexual and Reproductive Health and Rights:

Adolescents in HIV and ART care should be provided with age and developmentally appropriate sexual and reproductive health services. Discuss with adolescent the advantages of delayed sexual debut, the right to delay marriage and to refuse unwanted sexual advances. Adoloscents should be provided with access to accurate sexual

and reproductive health information, services for STI prevention, diagnosis and treatment and family planning counselling.

For sexually active adolescents dual protection with a condom should also be discussed and safe sex with consistent condom use encouraged. It is important to provide individual family planning counseling and methods to prevent unintended pregnancy; where possible family planning commodities including emergency contraception should be made available in the clinic where the adolescent is receiving ART. If applicable, partner testing and disclosure should be encouraged (MoHSS 2012). Sexually active adolescents should be educated on the benefits of good adherence to treatment and subsequent reduction of HIV transmission risk.

CHAPTER 5: PRE-EXPOSURE PROPHYLAXIS (PrEP)

5.1 Introduction

Pre-Exposure Prophylaxis (PrEP) with oral tenofovir (TDF) or TDF co-formulated with emtricitabine (TDF/FTC) demonstrated substantial HIV prevention benefits in clinical trials. With strong evidence for the efficacy and effectiveness of daily oral PrEP across multiple studies; WHO issued guidance on PrEP use in high HIV incidence settings to people having substantial risk of HIV acquisition (WHO, 2015). 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 block or prevent the acquisition of HIV. Oral PrEP should be offered as part of the 'Combination Prevention' package that includes HIV Testing Services (HTS), male and female condoms, lubricants, ART for HIV-positive partners in sero-discordant couples, voluntary medical male circumcision (VMMC) and STI prevention and management.

5.2 Eligibility Criteria for PrEP

Indications

Any sexually active HIV-negative person at substantial risk of acquiring HIV. Those at high risk include but not limited to the following:

- HIV negative people in serodiscordant relationships with a partner who is not confirmed as virologically suppressed (VL <40 copies/ml)
- All HIV negative people in serodiscordant relationships, regardless of VL of the partner, who want to conceive
- Partner(s) of unknown HIV status
- Recent/ recurrent STIs
- Multiple and/ or concurrent sexual partners
- History of inconsistent or no condom use
- Recurrent PEP users
- History of sex whilst under the influence of alcohol or recreational drugs.

Note: PrEP should always be taken as an additional prevention strategy in combination with a comprehensive prevention package

Contraindications

The following are contraindications of PrEP:

- HIV positive
- Evidence or suspicion of HIV primary infection (characterized by flu-like symptoms)
- Suspicion that person might be in window period following potential exposure
- Adolescents <35kg or <15 years who are not Tanner stage 3 or greater (should not get TDF)
- Abnormal CrCl<60ml/min
- TDF for PrEP should not be co-administered with other nephrotoxic drugs, for example, aminoglycosides
- Unwilling or unable to return for 3-monthly HIV testing, counselling and safety monitoring visits
- Known allergies to any of the PrEP drugs
- Unwilling to get tested for HIV

Note: it is critically important to take a thorough history (particularly sexual) to determine PrEP eligibility. When there is suspicion of HIV primary infection and/or when there is a history of possible recent HIV exposure; PrEP can be deferred for 4 weeks and the client re-tested to ascertain HIV status.

5.3 PrEP ARV Regimen

- Daily oral tenofovir/emtricitabine (TDF/FTC 300mg/200mg) or TDF/3TC 300mg/300mg

Note:

- PrEP may be used intermittently during periods of perceived HIV acquisition risk, rather than continually and lifelong, as is the case with antiretroviral treatment.
- It is important to bear in mind that it takes 7 days of daily dosing PrEP to reach adequate anal/rectal tissue levels and up to 20 days of daily dosing to achieve protective vaginal tissue.
- During this period, other protective precautions must be used, such as abstinence or condoms.
- PrEP medications should be continued for 28 days after the last potential HIV exposure in those wanting to stop taking PrEP.
- These should also be borne in mind in users who stop and start PrEP according to their periods of risk.

Table 5.1: Summary of pre-exposure prophylaxis visits and procedures

Visit	Recommended Procedures
Screening and PrEP initiation	• Assess risk and eligibility --thorough history (sexual) and physical examination • Educate about the risks and benefits of PrEP • Contraceptive counselling and offer services • **Tests**—HIV test, CrCl, HBsAg • Confirm eligibility (including investigation results and creatinine clearance calculation) • Provide STI treatment if indicated • Educate client about PrEP side-effects and management • Educate client about signs and symptoms of acute HIV infection • Discuss with client on the adoption of healthy life-styles such as avoiding alcohol, , tobacco and recreational drugs • Provide condoms and lubricants • Provide one-month TDF/FTC (FDC) prescription and follow-up date • Arrange follow up visit
One-month follow-up	Same as at PrEP initiation visit PLUS: • Assess tolerability, side effects and effective use (adherence) • Actively manage side effects • Contraceptive services • Tests—HIV test, CrCl, • Provide 3 month prescription and follow up date
Four-month follow-up and 3-monthly maintenance visits	Repeat procedures done at one-month follow-up (HTC) • **Tests:** ○ **4th Month**—HIV test, STI symptom screening, CrCl, ○ **3 monthly afterwards**—HIV test, Pregnancy test, HBsAg (at 6 months only) ○ **6 monthly afterwards—CrCl,** STI symptom screening, rapid syphilis test and HIV test

Adapted from South African Guidelines on use of PrEP in persons at risk of acquiring HIV

Note: Condoms and condom-compatible lubrication should be provided, and arrangements made for follow-up. HIV negative men who are 10-49 years old should be referred for VMMC.

5.4 Side effects of PrEP medicines:

PrEP is usually safe, with no side-effects for 90% of users. Minor side effects: 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.

Stopping PrEP

PrEP should be stopped when:

- Whenever an HIV test is positive
- At client's request
- For safety concerns/ side effects (CrCl<60ml/Min)
- If risks of PrEP outweigh benefits

If a client tests HIV positive, discontinue PrEP and refer for enrolment into HIV care.

Notes for Implementing PrEP

- Medical officers and nurses trained to provide ART can provide PrEP
- The PrEP initiation visit should preferably take place on the same day of screeninng
- Review results from baseline investigations and confirm that estimated creatinine clearance is > 60 ml/min.
- Provide STI treatment as required (refer to latest national guidelines).
- Educate the user about potential PrEP side-effects and their management, as well as signs and symptoms of acute HIV infection (and the need to return for urgent HIV testing). HIV testing should be repeated every 3 months.

MOHSS is putting in place a system for recording and reporting PrEP use.

CHAPTER 6: POST-EXPOSURE PROPHYLAXIS (PEP)

6.1. Prophylaxis after occupational exposure to HIV

6.1.1 Introduction

Health care workers have a low but measurable risk of HIV infection after accidental exposure to blood or body fluids from an HIV infected individual. Based on over 3,000 incidents, the average risk of HIV infection after a single percutaneous exposure is 0.3%. As a result, HIV attributable to occupational exposure is an uncommon, but has definite risk. Compliance with infection control recommendations in handling sharps is the mainstay of prevention of occupational HIV infection. Additional prevention strategies now include post-exposure prophylaxis with antiretroviral medicines. The biological rationale for prophylaxis with antiretroviral therapy is that initial virus uptake and antigen processing after inoculation may take a few hours to a couple of days. This presents a window opportunity for therapeutic intervention before virus propagation occurs.

6.1.2 Risk of infection

Factors that increase the risk of sero-conversion include exposure to large inoculums of infected blood (indicated by a deep injury, visible blood on the device, and procedures involving needles placed directly in arteries or veins) and a source patient with advanced HIV infection. If the source patient is unavailable or refuses to be tested, then, considering the high prevalence of HIV in Namibia, PEP is recommended.

Table 6.1: Risk factors for HIV infection in health care workers after percutaneous exposure to HIV-infected blood

Risk factors	Adjusted odds ratio (95% confidence interval)
Deep injury	16.1 (6.1 - 44.6)
Visible blood on device	5.2 (1.8 – 17.1)
Procedures involving needle placed directly in a vein or artery	5.1 (1.9 – 14.8)
Terminal illness in source patient	6.4 (2.2 – 18.9)
Post-exposure use of zidovudine	0.2 (0.1 – 0.6)

Table 6.2: Assessment of exposure risk

Low risk exposure	High risk exposure
Exposure to a small volume of blood	Exposure to large volume of blood or potentially infectious fluids eg. Contaminated blood transfusion
An injury with a solid needle	Injury with a hollow bore needle
Any superficial injury or mucocutaneous exposure	Deep and intensive injury

6.1.3 Recommendations for Post-exposure Prophylaxis

1. Draw baseline laboratory tests: HIV testing (with consent), HBsAg and Ab, creatinine and urine dipstick. Drawing these tests and waiting for the results must not delay starting PEP.
2. TDF 300mg plus FTC 200mg or 3TC 300mg fixed dose combination for 28 days is the recommended ARV regimen for PEP in Namibia.
3. In cases of high risk exposure such as contaminated blood transfusion or injection of a substantial volume of contaminated blood, it is recommended to add a third ARV. The preferred third PEP agent in Namibia at the moment is ATV/r, alternative third agent can be LPV/r, or EFV.

4. For children less than 10years of age, give ABC plus 3TC, add LPV/r if the exposure is high risk exposure. Use AZT as an alternative when ABC can not be used. ATV/r may be used instead of LPV/r if the child is at least 6 years old and weighs at least 15 kg.
5. PEP should be recommended to exposed healthcare workers after occupational exposures (percutaneous or trans-mucous membrane) to blood or other potentially infectious body fluids. For exposures with negligible risk (intact skin contact with blood), PEP is not justified. The exposed health worker has the right to decline PEP without risk of losing eventual compensations if infection develops.
6. PEP should be initiated promptly, preferably within 1 - 2 hours post-exposure. The longer it takes to initiate PEP, the higher the risk of contracting HIV following exposure. PEP is not offered at more than 72 hours after exposure.
7. Considering the importance of early initiation of PEP and the high prevalence of HIV among hospitalised patients, it is recommended to initiate PEP immediately if the source patient is HIV-positive or the patient's HIV status is unknown. If results of the HIV sero-status of the source patient later become available, decisions about discontinuation of PEP can be made on a case-by-case basis.
8. Workers with occupational exposures to HIV should be offered, and should undergo HIV rapid test and if negative, baseline testing for, HBsAg , HBsAb, Creatinine, and receive follow-up counselling and medical evaluation. For those whose results are positive for HIV, PEP should be discontinued immediately, and the clients linked into care for treatment. Workers who are HIV-negative at baseline should repeat HIV-antibody tests at 6 weeks, 12 weeks, and 6 months. Exposed workers should be counselled to observe precautions to prevent possible secondary transmission (for example to their sexual partner or from mother to child) until they are found to be HIV-negative 6 months following the exposure.
9. Monitoring for medication toxicities should include Crcl testing at baseline and 2 weeks after starting PEP. If subjective or objective toxicity is noted, ARV substitution should be considered with expert consultation, and further diagnostic studies may be indicated.
10. Relative contraindications of PEP include significant renal or liver impairment and severely ill workers. When in doubt about the use of PEP, urgent consultation from a specialised physician or referral centre can be sought, but care must be taken that this consult not unduly delay the initiation of treatment when indicated. It may be necessary to begin PEP while awaiting this consultation.
11. Health workers who become infected with HIV should receive appropriate medical care.

6.1.4 PEP regimens

Prophylaxis should be given for 28 days.

Recommended basic regimen:

- Tenofovir 300 mg daily + emtricitabine 200mg (or lamivudine 300 mg) fixed dose combination once daily for 28 days
- Expanded regimens include the basic regimen (TDF+FTC[or 3TC]) plus one of the following for 28 days:

Expanded regimens include the basic regimen (TDF+FTC or 3TC) plus one of the following for 28 days:

- Atazanavir 300 with ritonavir 100mg QD (preferred)
- Efavirenz 600 mg once nightly.
- Lopinavir 400mg plus ritonavir 100mg twice daily.

PEP regimens when the source patient has been on ART:

If the source patient has been on ART and there is reason to believe the regimen is failing (i.e. clinical progression, falling CD4 level, documented elevated viral load), viral resistance should be suspected. In this instance, consideration must be given to the source patient's ART regimen, and ARVs with a different resistance profile should be used for PEP. For example, if the source patient is (or was) on first line therapy with AZT + 3TC + NVP, a basic PEP regimen could include TDF + FTC (3TC) or ABC + 3TC plus ATV/r. Efavirenz should not be used for PEP if there is a possibility that the source patient may be resistant to Nevirapine due to issues of cross-resistance. Where possible, discussion of such cases with an HIV specialist is recommended.

Table 6.3: Summary of PEP recommendations

Exposure	PEP recommendation	Regimen
High risk exposure	Recommended	TDF/FTC (or 3TC)/ATV/r
Low risk exposure	Offer	TDF plus FTC (or 3TC)
Intact skin Low risk fluids HIV- negative source	Do not offer	

6.1.5 Accompanying measures

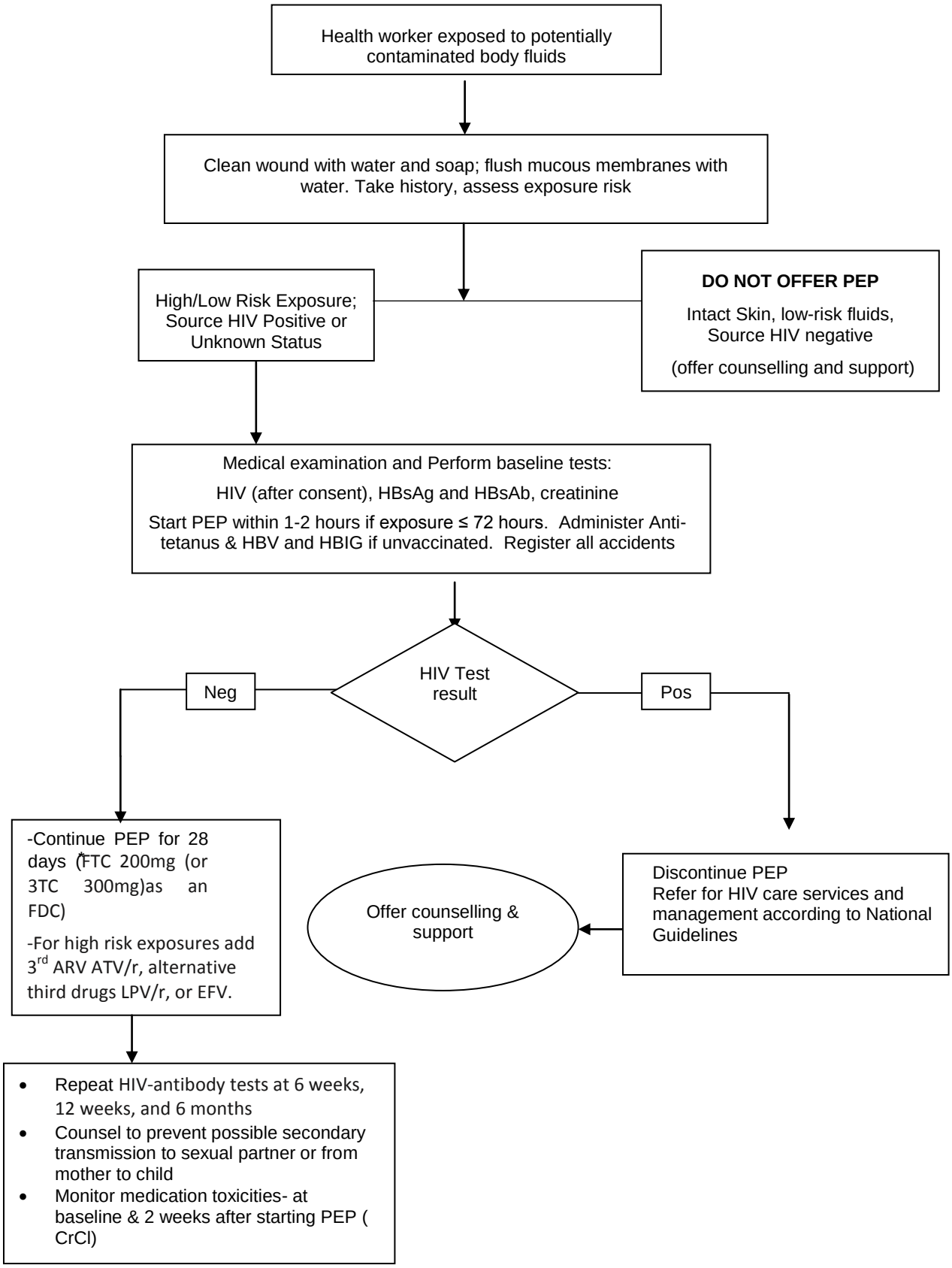
To ensure that the risk of occupational exposure is minimised and PEP is administered according to the guidelines, it is recommended that the following measures be taken at all facilities in the country:

- Infection control committees should be put in place
- Strict attention should be given to the correct handling of sharps and all contaminated materials through standard precautions (e.g., no recapping or bending of needles, disposal of all sharps in solid containers, etc.).
- Staff should be fully informed about the measures to be taken following exposure to a potentially infectious body fluid. Each health facility should establish and disseminate clear procedures to ensure appropriate management following an occupational exposure.
- Monitoring of all potential exposures. For each incident, the facility supervisors should investigate the circumstances and report the findings and measures proposed to avoid reoccurrence to the infection control committee. Risks for support staff (cleaners, porters, etc.) should be minimised. Registration of accidents should be standardised and they should be regularly reported by all relevant health facilities.
- Antiretroviral medications for PEP should be made available on a 24-hour basis (for example through casualty services).
- All employees of health facilities should be vaccinated against HBV and tetanus. Hepatitis B vaccination series with hepatitis B immunoglobulin (HBIG) should also be provided for all unvaccinated, non-immune health care workers following sharps injuries or exposure to infected materials. The risk of transmission of hepatitis B infection following a needle stick injury ranges from 6-30%. Thus, the risk of transmission of hepatitis B from an occupational exposure is significantly greater than the risk for transmission of HIV.

Step 1: First Aid, Immediately clean the wound with soap and water or flush mucous membranes with water (encourage bleeding from the site but do not increase the tissue damage in any way (e.g. do not squeeze or scrub)

Step 2: Type of exposure – determine the type of exposure

Figure 6.1: Algorithm for PEP after occupational exposure



6.2 Prophylaxis after rape

6.2.1 Introduction

All women, men and children presenting to a health facility after being raped should be counselled by the examining health care worker about the potential risks of HIV transmission post-rape. If the rape survivor presents within 72 hours of being raped, post-exposure prophylaxis (PEP) should be offered to prevent HIV transmission.

6.2.2 Issues to be addressed during counseling

The following issues should be addressed during counseling:

- The risk of HIV transmission is not known, but it exists.
- It is important for the survivor to know her/his HIV status prior to starting PEP.
- It is important to start PEP as soon as possible.
- It is the survivor's choice to receive PEP and to have HIV testing.
- For each rape survivor, blood and urine will be taken routinely to screen for syphilis, HIV (unless refused), and existing pregnancy.
- If the possible risk for HIV transmission has been established, the rape has occurred within a period of 72 hours, and the rape survivor is HIV-negative or results are not immediately available, PEP will be offered.
- The efficacy of PEP in preventing HIV sero-conversion in cases of sexual assault is not known.
- The common side-effects of the medicines should be explained, with particular reference to feelings of fatigue, nausea, headache, and flu-like symptoms.
- PEP should be discontinued immediately if the baseline HIV test of the survivor is confirmed to be positive. Even in the absence of on-the-spot rapid testing, this should not take more than 3 days.
- The importance of adherence to treatment should be emphasised.
- Survivors should be counselled to observe precautions to prevent possible secondary transmission (for example to their sexual partner or from mother to child) until they are found to be HIV-negative 6 months following the exposure.

All women who choose to use PEP should undergo pregnancy testing to ensure that pregnant women are identified and then receive appropriate antenatal care. The possibility of HIV transmission to the unborn baby should the woman sero-convert should be discussed.

Survivors presenting more than 72 hours after the rape should be counselled about the possible risk of HIV transmission. It should be explained that it is highly unlikely that PEP started >72 hours after the rape will have impact on preventing HIV infection. Use shared decision-making with the survivor to determine whether HIV post-exposure prophylaxis is appropriate. If a rape survivor becomes pregnant as a result of the rape, she should be counselled on the option of termination of the pregnancy as per provisions of the Abortion and Sterilization Act, 1975 (Act No. 2 of 1975).

6.2.3 Procedures for administering PEP for rape survivors

Voluntary HIV testing (using rapid testing if possible) should be made available and should be performed for all rape survivors, whether or not they are choosing to use PEP. Additionally, tests for syphilis, pregnancy, and hepatitis B antibody should be performed.

It may be difficult to obtain informed consent for HIV testing shortly after the rape. The importance of an HIV test should be explained. All rape survivors who present within 72 hours should be offered a 3-day course of TDF/FTC/ATV/r (alternative third drug can be LPV/r, or EFV). and be given a return appointment at the ARV clinic within three days, during which time either their HIV test results will become available, or they will have been given time to think further about consenting to testing. The remainder of the 28 day PEP regimen should be given at this visit if the survivor is HIV negative.

Survivors who are either known to be HIV-positive or found to be HIV-positive at baseline should be appropriately counselled and referred to an ART-clinic for long-term management of HIV infection.

Relative contraindications to the use of PEP include significant renal or liver impairment. When in doubt about the use of PEP, urgent consultation with a specialist physician or referral centre can be sought, but care must be taken that this consultation does not unduly delay the initiation of treatment when indicated. It may be necessary to begin PEP while awaiting this consultation.

Monitoring for toxicities due to PEP should include liver transaminase (ALT) and creatinine clearance at baseline, and repeated 2 weeks after starting PEP or when symptoms occur. If subjective or objective toxicity is noted, ARV substitution should be considered with expert consultation, and further diagnostic studies may be indicated.

HIV serology should be done at 6 weeks, 12 weeks and 6 months. Rape survivors who become infected with HIV should receive appropriate medical care.

6.2.4 PEP regimen after rape

The recommended antiretroviral regimen following rape is: TDF + FTC (or 3TC) + ATV/r daily for 28 days.

Child survivors of rape who are <10 years old or <35kg cannot use the preferred adult PEP regimen. In such cases, replace TDF with ABC (or AZT if ABC is not readily available) in those children. In addition, for children <3 years old or <10 kg, replace EFV with Lpv/r.

6.2.5 Comprehensive Management

It is strongly suggested that PEP be administered only in the context of a comprehensive support programme for rape survivors. This should encompass the following:

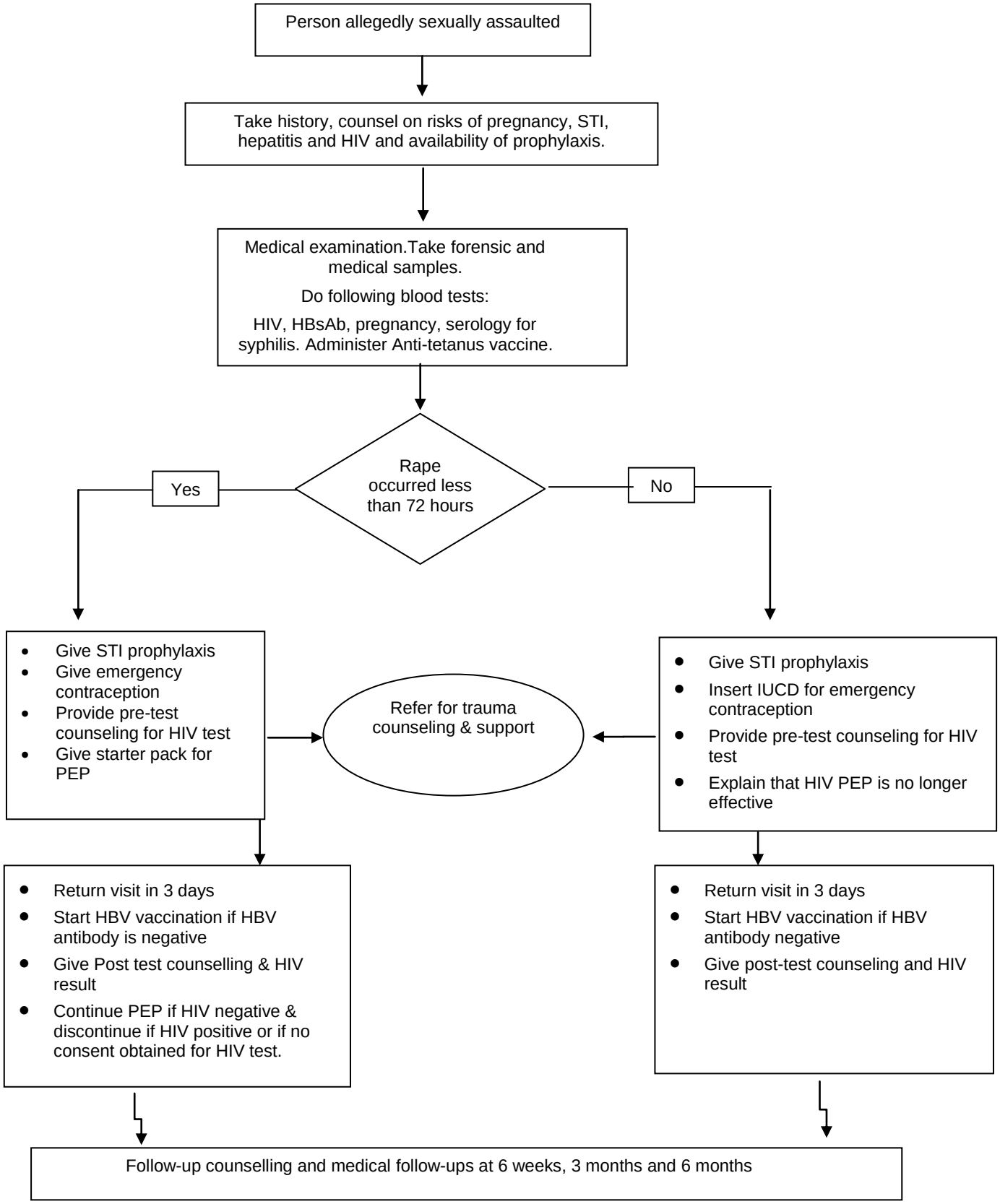
- STI prophylaxis: presumptive prophylaxis should be given in the form of cefixime 400 mg or ceftriaxone 250 mg IM STAT plus metronidazole 2 gram STAT plus azithromycin 1g STAT .
- Emergency contraception within 72 hours: norgestrel 0.5mg (500 mcg) and ethynyl oestradiol 0.05mg (50 mcg) (Ovral) given 2 tablets STAT and 2 tablets 12 hours after the first dose. Another regimen available in the private sector is levonorgestel 2 tablets (or 0.75 mg) STAT. A copper T IUCD can be inserted up to 5 days after the rape.
- Hepatitis B immunoglobulin and hepatitis B vaccination should be started as soon as possible if the patient is not already immune, and no later than 21 days after the incident. If the results of the HBsAb test is non-reactive vaccinate at 0, 1, and 3 to 6 months.
- A tetanus booster should be given.
- Counselling of the rape survivor, identification of support needs, and necessary referrals should be done.
- In cases where rape survivors have severe bleeding, the issue of proper nutrition with regards to foods that are high in iron, folate, riboflavin, vitamin A and vitamin B12 to avoid developing anaemia should be emphasised.
- In subsequent visits, issues relating to stress management should be discussed as part of the support programme. Since stress may cause illness related to physical and mental exhaustion, the survivor should be made aware of stress indicators such as general irritability, trembling, pain in the neck or back and changes in appetite or sleeping patterns.
- Medico-legal assessment of injuries.
- Completion of appropriate registers.

It is recognized that children who experience rape need ongoing, comprehensive support. Where there is any suggestion that a child has been raped, the case should be referred to an experienced paediatrician. Full assessment of physical injuries must be performed, STI prophylaxis will need to be adjusted using paediatric doses, and psychological and emotional support must be initiated systematically.

6.2.6. Post-exposure prophlyaxis in other situations

- **Accidental sexual exposure**. It is recognized that clients sometimes present to health facilities after having had unprotected sex (or 'burst condom') with a partner of known HIV positive status or unknown serostatus. If the client presents within 72 hours, clinicians should offer PEP , but counseling concerning correct condom use and risky behavior is essential. PEP regimen is the same as detailed above. For repeated accidental sexual exposure, counsel the client for PrEP (client to be on TDF/FTC for as long as he/she in on repeated exposure).
- **Accidents.** Where there is exposure to blood or body fluids such as at the scene of a motor vehicle accident or injuries caused by human bites, clinicians should assess the level of exposure risk as detailed in Figure 6.1 and provide the appropriate counseling and PEP regimen.

Figure 6.2: Algorithm for PEP for Rape Survivor



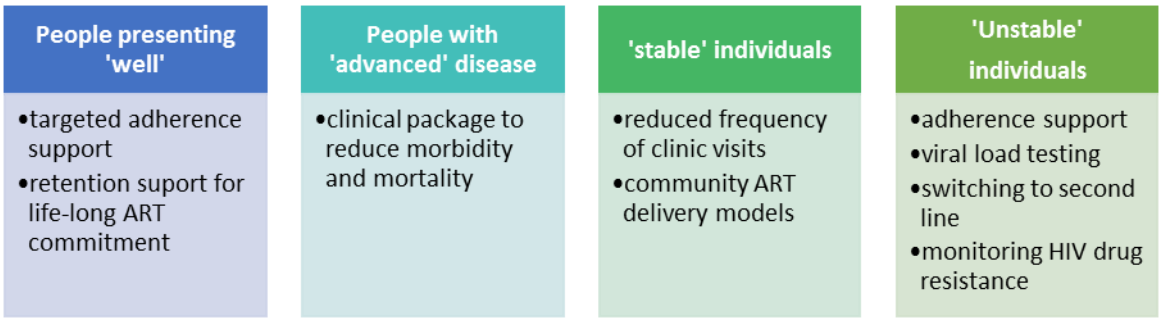
CHAPTER 7: DIFFERENTIATED CARE

7.1 Introduction

This chapter aims at providing guidance to programme managers and service providers on the 'Differentiated Care' models and some key operational and service delivery issues that need strengthening to support comprehensive delivery of HIV and AIDS prevention, care and treatment services. The chapter covers the following areas: differentiated care, models for Community ARV delivery, HIV care providers, adherence and retention in care. It is estimated that the majority of HIV service delivery in countries is 'clinic-based' with a 'one-size- fits- all' approach and yet PLHIV present with different needs. As HIV treatment guidelines evolve through widened eligibility criteria for ART initiation; different sub-populations of PLHIV emerge that require HIV services that are tailor-made to meet their specific needs.

Differentiated care is a **client-centred approach** that simplifies and **adapts HIV services** across the cascade to reflect the healthcare needs preferences and expectations of various groups of people living with HIV (PLHIV) while reducing unnecessary burdens on the health system. The health system can refocus resources to those most in need by providing differentiated care. WHO has grouped four categories of patients that need attention namely: **'well' patients** who present with relatively high CD4 count; people with **'advanced'** disease who require more intense care and regular follow up; **'stable' patients** who are the majority of patients that are already on ART and doing well and hence may require less frequent clinic visits and benefit from community ART delivery services; and lastly the **'unstable'** patients who are already on ART but present with emerging OIs that may require prompt management and possible drug switching to second or third line ARV regimens. Figure 7.1 below summarizes the four groups of patients and the specific interventions they may require.

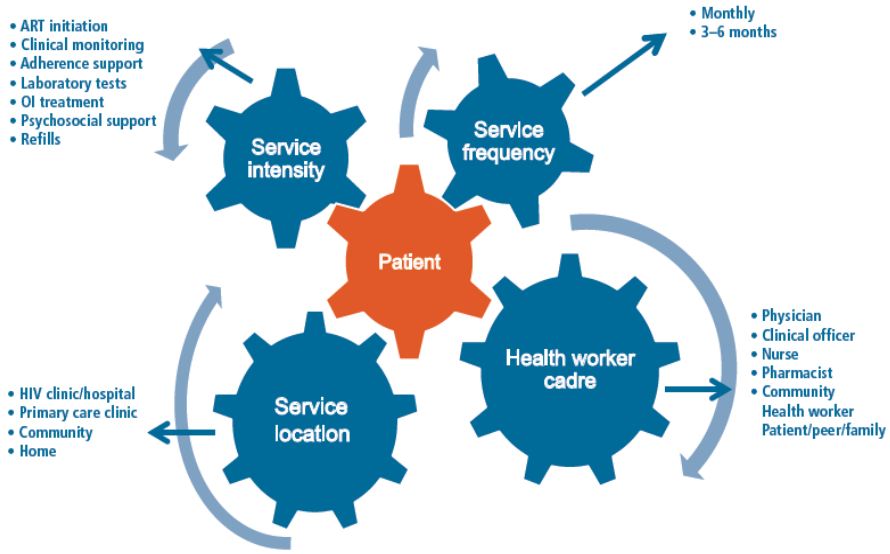
Figure 7.1: Categories of patients presenting for HIV care



It is important to note that people will move between classifications according to their health and circumstances. For example, a stable patient who develops a new OI may need to be considered as unstable until the OI has resolved. People with advanced disease will become stable after a period of time on ARVs.

Many aspects of HIV services targeting these different groups of patients have been discussed in detail in the previous chapters. However, this section will describe the different aspects of care that promote adherence, retention in care along the HIV care cascade including models of care outside the 'standard' HIV service delivery model. The 'Differentiated Care' Framework by WHO includes specific service packages based on care needs and is characterised by four delivery components which are highlighted in the framework below i.e. **the type of services delivered, the location of services, the provider of the services and the frequency of the services.** This frame-work will form the basis of the guidance on 'Differentiated Care' in this chapter.

Figure 7.2: Implementation Framework for Differentiated Care Model



Source: WHO 2015 Policy brief: consolidated guidelines on the use of antiretroviral drugs for treating and preventing HIV infection: what's new.

7.2 Differentiated HIV Service Delivery Models in Namibia

7.2 1 Background and Rationale for Differentiated Care Models in Namibia

Differentiated care and treatment approaches should be applicable in all health care settings based on patient needs, preferences and expectations. In high-volume settings, client sub-groups are likely to be large enough to justify dedicated services. The approaches should increase cost-efficiency by optimizing staff workload and responding to unique patient needs. These models should further improve health outcomes for patients through higher adherence to treatment and retention in care through targeted counseling, peer support, reduced waiting times and reduced congestion at the facility. The approaches will relieve overburdened health-care personnel and enable them to pay more attention to patients who are unwell or unstable.

Namibia is a vast country with sparsely distributed population. Easy access to health care services in general and HIV/AIDS services in particular has been a challenge to many due to long distances to health facilities. People living with HIV (PLHIV) have other challenges such as transport costs, repeated absence from work or schools, and stigma. On the other hand, health facilities are already congested and with the increasing number of PLHIV put on ART services, there is a decrease in the health care provider and patient ratio. These challenges are negatively impacting the quality of health services.

Different models have proved effective in addressing these challenges in different regions including Southern Africa. Decentralization of HIV/AIDS services from tertiary level to primary health care facilities and outreach points has supported differentiation of care. However, this approach did not completely solve challenges related to access to health services. Different community based models such as community ARV distribution points and client led ARV distribution groups have shown positive results in terms of treatment outcomes and cost-savings. Community led approaches also have the added advantage of fostering community ownership and sustainability.

Examples of existing Differentiated Care Models in Namibia:

- **Decentralized ART care to peripheral health facilities:** in this model HIV services are provided by nurses in smaller facilities [NIMART, ART Outreach Services]
- **Decentralized HIV care and ART to Community Based Service points [Okongo Experience]**
- **Facility Based ART Adherence Groups led by expert patients:** Adherence groups established in health facilities can be used as ARV drug distribution platforms reducing the burden on pharmacies. This approach still keeps clients in health facilities.
- Community Based Client Led ARV Distribution Groups: these are self-formed PLHIV support groups whereby one or two people are identified for training, mentoring and support to enable them to collect and distribute ARVs medicine for other members. Health facilities make special arrangements with such groups making sure patient monitoring and data is not compromised.

Countries within the region and including Namibia are implementing different models of HIV delivery. However, facility teams are encouraged to modify or create new approaches that are responsive to the needs of their patients, communities and facility.

7.2.2 Models of ARV Delivery

This section describes the ART delivery models for Namibia which are categorized as follows:

1. **Facility-based models**
    a. Standard care (Main ART Sites and NIMART sites)
    b. Fast-track ART refill model
    c. ART Adherence Clubs e.g. Teen Club, Young Adults Club, Mothers' Club, Men's Club, etc.
2. **Out of facility models**
    a. ART Outreach models
    b. Community ARV Refill Groups (CARGs)

Table 7.1 below summarizes the Differentiated care models in Namibia. The Main ART sites are comprised mainly of hospitals that have the capacity to provide comprehensive HIV prevention, care, treatment and support services. These are referral sites where sick or complicated patients are referred to for further investigations and management. NIMART sites are mainly clinics manned by a nurse in charge trained in ART management and other HIV care providers including health assistants, pharmacists, pharmacy assistants, social workers, and administrative officers (M&E). These sites provide a wide array of services to clients and are supported by mentors in the management of complicated cases. NIMART sites conduct ART outreach visits to hard-to reach communities in order to bring services closest to where people live. Multi-disciplinary teams are expected to conduct regular scheduled visits to community outreach points where both six-monthly clinical reviews are performed alongside 3-monthly ARV refills to clients.

Table 7.1: Characteristics of Differentiated Care Models in Namibia

Model	Criteria	Care Provider	Frequency of visits	Minimum Care Package
Facility-based models				
Standard Care 1a. Main ART Site	Unstable Patients • VL > 50 [with no access challenges] • Patient with OIs and other co-morbidities* • Newly initiating patients • Patients who need close monitoring (malnourished, alcohol abuse, etc.) Stable patients who still prefer to be at the main site	• Doctors • Nurses • Health Assistants • Pharmacists • Pharmacist Assistants • Social Workers • Admin Officers(M&E)	Follow up visit depends mostly on the patient's condition. Follow treatment monitoring schedule for adult & paediatric ART clients] Stable patients can have consultations every 6 months (for children scrutinize growth and development to decide on the frequency of visit) Refill every 3 months	• Clinical consultations • Laboratory Monitoring • Adherence Counseling • Prescription • Refills • Fast-tracking of stable patients • Defaulter Tracing
1b. NIMART site	Unstable patients • VL > 50 [with no access challenges] • Newly initiating patients • Patients who need close monitoring (malnourished, alcohol abuse, etc.) Stable patients who still prefer to be at the NIMART site	• Nurses • Health Assistants • Pharmacists • Pharmacy Assistant • Social Workers • AdminOfficers (M&E)	Follow up visit depends mostly on the patient's condition. Follow treatment monitoring schedule for adult and paediatric ART clients] Stable patients can have consultations every 6 months (for children scrutinize wight and adherence to decide on the frequency of visits) Refill every 3 months	• Clinical consultations • Laboratory Monitoring • Adherence Counseling • Prescription • Refills • Fast-tracking of stable patients • Defaulter Tracing
1c. Fast-track ART Refills model	Stable patients • Virally suppressed (two previous consecutive tests should be < 50) • No OIs • Patients who stayed > 12 months on ART • Patients with	Doctor, Nurse Health assistant HEW Expert patient, CARG leader Pharmacist pharmacist assistant	Refills every 3 months Clinical consultations every 6 months (for children scrutinize weight and adherence to decide on the frequency of visits)	Pill count at facility ARV refills provide CPT Lab tests (Viral Load etc.) Clinical review Pill counts adherence

	challenges related to access to health facilities Not pregnant			counseling TB screening
c. ART Adherence Groups in Health Facilities	Stable patients • Virally suppressed (two previous consecutive tests should be < 50/ml) • No OIs • Patients who stayed > 12 months on ART • Patients with challenges related to access to health facilities Not pregnant	• Peer Educators/ Expert Patients • Community Health Workers • Admin Officers (M&E)	Consultation at health facilities every 6 months (NIMART or Main ART Sites) (for children scrutinize wight and adherence to decide on the frequency of visits) Refill every 3 months (pick up and distribution by group facilitators)	• Peer education • Adherence Counseling • Adherence Support • Refills • Fast-tracking of stable patients • Defaulter Tracing
Out of Facility Models				
2a. ART Outreach Model/ Community ARV Medicine Distribution Points*	Stable patients • Virally suppressed (VL < 50, at least one latest VL taken within a year • No OIs or other co-morbidities that require special care • Patients who stayed > 12 months on ART • Not pregnant Patients with challenges related to access to health care facilities	• Nurses • Health Assistants • Pharmacy Assistants/ Pharmacy Work Hand • Admin Officers (M&E) • Expert Patients • Health Extension Workers • TB Field Promoters at Community TB DOT Sites	Consultation every 6 months at outreach or community based distribution point (for children scrutinize wight and adherence to decide on the frequency of visits) Refill every 3 months	• Clinical consultations • Laboratory Monitoring • Adherence Counseling • Prescription • Refills Defaulter Tracing
2b. Community ARV Groups (CARGs)	Stable patients • Virally suppressed (two previous consecutive tests should be < 50) • No OIs • Patients who stayed > 12 months on ART • Patients with challenges related to access to health facilities Not pregnant	• Clients • Community Based facilitators • Clinical Team facilitates the dispensing of ARV medicines to the clients • M and E	Consultation to health facilities every 6 months (for children scrutinize wight and adherence to decide on the frequency of visits) Refill every 3 months	• Peer education • Adherence Counseling • Adherence Support • Refills Defaulter Tracing

*Health facilities are not the preferred sites for outreach services. Regional and District staff are encouraged to build the capacity of clinic staff and turn the clinics to fully fledged NIMART sites for sustainability of HIV services.

7.2.3 Dispensing ARV medicines:

The following standard practices are recommended for dispensing of ARV across the differentiated care sites:

Routine ARV refills

Unless there are special circumstances, health care workers involved in dispensing of ARVs should dispense 3 months' supply of ARVs to stable patients. Special considerations will be made to clients on a case by case basis (patients who will be at sea or abroad for more than three months) e.g. to migrant workers.

In transit patients

All in transit patients that visit ART sites should be supplied with ARVs ideally for no more than two months at the sites they are visiting.

A patient who is planning to be in-transit at another facility for more than two months should obtain a transfer out letter from the original facility and be officially transferred in to the new facility. This recommendation applies to seasonal workers who stay in an area for several months every year e.g. during the harvesting or planting season. Transit facility should request transfer letter from the original site of service.

Dispensing of extra ARV pills

It has been noted that when patients are given too many extra tablets, they are prone to being dumped, which also complicates monitoring of adherence by pill count. It is therefore recommended that patients be given extra ARV pills for only 2 days.

Other recommendations

- Pill counts should be done routinely for all patients at each encounter with a health worker and the number of remaining pills should be entered in the appropriate data capturing tool and health passport.
- Left over medicines should be discarded if they are soiled, broken or expired; this should also be recorded in the data capturing tool.

7.2.4 Providers of Differentiated HIV Care

In view of the need to further decentralize HIV care and prevention services; it is important to clearly define the roles and responsibilities of HIV care providers. Both health care workers and non-health care workers can be involved in providing HIV services. In Namibia the following health care workers provide HIV services in the differentiated care approaches that involve health facilities and community: Doctors, Nurses, Pharmacists, Pharmacists' Assistants, Health Assistants and Health Extension Workers. Non- health care workers who can provide different aspects of HIV services in the differentiated care model may include but not limited to: PLHIV Support Groups, Expert Patients, Community Health Workers, TB Field Promoters, Community Leaders, Employers, Treatment Supporters, Social Workers, Teachers and Psychologists.

Differentiated models of care will require task shifting between various cadres of health care workers. Adequate training and mentoring will be required to ensure that health workers are functioning within their maximum capacity. Community leaders and volunteers will provide care and support to PLHIV at the community level, in collaboration with Healthcare workers.

Doctors/Nurses in charge of the health institutions are expected to allocate tasks appropriately ensuring each staff member has clearly defined responsibilities, in accordance with the Standard Operating Procedures.

7.2.5 Retention and adherence:

Globally, the scale-up of antiretroviral treatment has been an unprecedented achievement, meeting the UNAIDS goal of reaching 15 million people receiving life-saving ART by end of March, 2015 (UNAIDS, 2015). However, this represents only 41% of all PLHIV, globally. Optimal health, clinical and social outcomes require early diagnosis, timely linkage and initiation of ART, and consistent adherence to ART (Tanser F., 2013). Unfortunately, loss to follow-up at each step of the HIV cascade (e.g., pre-ART and after ART initiation) remains a key challenge for HIV programmes. Systematic reviews (Fox MP, 2010) show that retention rates are estimated to range from as low as 64% to as high as 94% at 12 months after ART initiation. Poor patient retention undermines programme and patient outcomes including the attainment of viral suppression. Multiple barriers to adherence and retention of patients during Pre-ART and while on ART has been documented in literature. Table 7.2 below outlines main barriers to adherence and retention in Namibia and possible solutions.

Table 7.2: Barriers and solutions to improve adherence and retention on ART

Barriers to adherence and retention on ART	Possible Solutions
Health System related	
High direct and indirect costs	• Decentralization of ART services (clinics stocking ARVs) to reduce transport cost due to outreach activities. • Task-shifting
Long waiting period	• Decentralization of services to clinics • Increase HR capacity • Staff capacity building and retention • Longer prescription and dispensing i.e 3 months for stable patients • Infrastructure expansion (more consulting rooms) • Scale-up of integration of services • Expedited roll-out of fast-tracking and community refill groups
ARV stock-outs	• Stock sharing among facilities • Timely ordering
Attitudes of health facility staff	• Use of anonymous suggestion boxes • Regular supervision • Regular employee evaluation • Training on interpersonal skills/sensitization
Use of multiple medicines	4. Use fixed dose formulations 5. Avoid Unnecessary prescriptions (Poly-pharmacy) 6. Replace liquid formulations with dispersible tablets in Paeds
Limited education on ART adherence	1. In-service training and mentoring of HCW 2. Use simplified adherence counselling education/language
Use of medicines with many side effects	• Encourage reporting of adverse effects using the safety yellow form. • Regular review of guidelines, counselling curriculum about side effects. • Prescribers to take note of drug to drug interactions • Clinicians to manage side effects of medication e.g antiemetics etc
Patient related	
Stigma and lack of disclosure	1. Linkage to PLHIV clubs, HEW 2. Intensify children full disclosure process 3. Offer Couple Counselling and testing.
Forgetfulness	• Encourage use of alarm and reminders. • Use of sms reminders for clinical appointments, telephonic tracing • Linkage to community-based health structures e.g HEW and Clubs • Engage treatment supporters
Co-morbid conditions (mental health issues, alcohol, substance abuse)	• Engage treatment supporters • Linkage to other clinical and support services, e.g. Rehabilitation, Social services and psychiatry services
Cultural and religious beliefs	• Sensitization of community leaders, religious leaders and community members. • Address harmful cultural norms
Limited access to care	• Community healthworkers, e.g (organize to collect medication for group of patients) • Community refill groups
Food security	• Linkage to Regional councillor's office • Linkage to income generating activities programs • Backyard gardening • Linkage to social workers

7.2.5.1 Special considerations for Adolescents:

In the ART Clinic, space and time should be created for adolescents. Consider having adolescent-designated clinic days and a room where only adolescents are seen. HCWs should be trained to be adolescent friendly in their approach to adolescents. Provide some group activities for adolescents as they wait to see the HCWs. Start adolescent peer support groups and "teen clubs". Teen-clubs are ideal for promoting knowledge transfer, skill building and sharing of experiences among peers. For more information on psychological support and "Teen Clubs" see MoHSS 2012a:p. 32 -34. During "Teen Club" sessions, facilitators should lead the group to talk about issues and needs of adolescents including topics such HIV treatment literacy, life skills, communication and negotiations, adherence support, substance abuse etc.

The parents and caregivers of adolescents living with HIV require psychosocial support to be able to work together with the HCWs in providing expected guidance and support on key concerns facing adolescents. Provide health education and skills building to parents and emphasize their role during adolescent transitioning to adulthood. Promote bonding and better understanding of adolescent transition among parents. Similarly, knowledge and skills on sexual reproductive health can remove barriers surrounding cultural taboos and increase open dialogue among parents and caregivers. For more information on Guardian clubs see the national guidelines on ALHIV service provision (MoHSS 2012a, 34).

Re-inforce the need for Career planning: Treatment for HIV infection is lifelong and with good quality of care, HIV becomes a chronic disease that, when managed well, will allow the adolescent living with HIV to lead a productive life into adulthood. Discussions about future career goals should be part of clinical care and the transition plan. These could include referral to an appropriate department or office for counseling on career choices so that the ALHIV faces the future with hope and optimism, with the ability to reach their goals, realize their dreams, provide for their families and live productive lives.

It is important to note that adolescents who are perinatally infected may have already been taking on some responsibility for self-care and have experience confronting issues such as disclosure, stigma, and adherence. However, they may be more ill and require a higher degree of clinical monitoring. On the other hand, those who were recently diagnosed may not be as clinically ill, but are just beginning to understand what it means to be diagnosed with HIV. As a result, these adolescents may not be prepared to take on the same responsibilities as the adolescent diagnosed in infancy; even though they may be healthier, they may not follow the treatment plan (page, 17 Toolkit for Transition of Care and Other Services for Adolescents Living with HIV—Training Manual). To facilitate retention and adherence among adolescent living with HIV, the following approaches have been demonstrated to be useful:

- Working to ensure that relationships with health providers are in place to establish partnerships with patients' guardians and adolescents themselves
- Providing home visits to support the ALHIV and their families by health workers, lay counselors and their peers.
- Establishing support groups for ALHIV (page 12, UNICEF – Field Lessons: ALHIV February 2013).

In efforts to improve retention and adherence to ART among adolescents there is need to provide training to health care providers including lay counselors and social workers. The focus on these trainings should be on adherence reinforcement and HIV disclosure and creation of support groups. To complement these trainings, the trainees should be provided with materials, including job aids, an adherence flip chart and a manual on support groups (page18, UNICEF – Field Lessons: ALHIV February 2013). To promote better adherence and retention in care for this vulnerable age group, the following guidance is useful:

- Provide positive feedback to the adolescent for any success in adherence to clinical visits and/or to medications
- Ensure that disclosure is done and positive re-enforcement is given (see section 3.8.3)
- Ensure that adolescents understand the modes of transmission of HIV and are able to describe them
- Continue adult supervision of treatment, including watching the adolescent swallow the medication
- If possible, promote adolescent-friendly services in the clinic by:
    - Scheduling adolescents to be seen on the same day of the week where feasible

- Providing some group activities for the adolescent as they wait to see the HCWs

Table 7.3: Adolescent clinic care model

Clinic model	Patient attendees	Services
Adolescent-only clinic	• Only adolescents who know that they are living with HIV	• Meet weekly or on a 2-4 week basis depending on patient volume • Group education and psychosocial support to be given to small groups while waiting for clinical review • Adolescents should be supervised • Organize parent/guardian sessions during clinical reviews
Adolescent Room	• All adolescents seen by a designated provider team in a specific consultation room	• Pharmacy expedites refills • Cluster adolescents in the afternoon after school • 'Teen club' sessions can be organized before clinical review or on a separate day • Organize parent/guardian sessions during clinical reviews

Source: Modified from National guidelines on Adolescent living with HIV, 2012

APPENDIXES

APPENDIX 1. WHO CLINICAL STAGING OF HIV DISEASE IN ADULTS AND ADOLESCENTS (2007)

Clinical Stage 1

- Asymptomatic
- Persistent generalized lymphadenopathy

Clinical Stage 2

- Unexplained[1] moderate weight loss (under 10% of presumed or measured body weight)[2]
- Recurrent upper respiratory tract infections (sinusitis, tonsillitis, otitis media, pharyngitis)
- Herpes zoster
- Angular cheilitis
- Recurrent pruritic ulcerations
- Seborrhoeic dermatitis
- Fungal nail infection

Clinical Stage 3

- Unexplained[1] severe weight loss (over 10% of presumed or measured body weight)2
- Unexplained[1] chronic diarrhoea for longer than one month
- Unexplained[1] persistent fever above 37.6°C (intermittent or constant, for longer than one month
- Persistent oral candidiasis
- Oral hairy leukoplakia
- Pulmonary tuberculosis (current)
- Severe bacterial infections (e.g. pneumonia, empyema, pyomysitis, bone or joint infection, meningitis, bacteraemia)
- Acute necrotizing ulcerative stomatitis, gingivitis or periodontitis
- Unexplained[1] anaemia (below 8 g/dl), neutropenia (below 0.5 x 109/L) or chronic thrombocytopenia (below 50 x 109/L

Clinical Stage 4[3]

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

[1] *Unexplained refers to where the condition is not explained by other conditions.*

[2] *Assessment of body weight among pregnant woman needs to take into consideration the expected weight gain of pregnancy.*

[3] *Some additional specific conditions can also be included in regional classifications, such as the reactivation of American trypanosomiasis (meningoencephalitis and/or myocarditis) in the WHO Region of the Americas, and penicilliosis in Asia*

APPENDIX 2. WHO CLINICAL STAGING OF HIV IN INFANTS AND CHILDREN (2007)

Stage 1 (Asymptomatic)

- Asymptomatic
- Persistent generalised lymphadenopathy

Clinical Stage 2 (Mild)

- Unexplained persistent hepatosplenomegaly
- Papular pruritic eruptions
- Angular cheilitis
- Extensive wart virus infection
- Extensive molluscum contagiosum
- Recurrent oral ulcerations
- Unexplained persistent parotid enlargement
- Lineal gingival erythema
- Herpes zoster
- Recurrent or chronic upper respiratory tract infections (otitis media, otorrhoea, sinusitis, tonsillitis)
- Fungal nail infections

Clinical Stage 3 (Advanced)

- Unexplained moderate malnutrition or wasting not adequately responding to standard therapy
- Unexplained persistent diarrhoea (14 days or more)
- Unexplained persistent fever (above 37.5 ºC, intermittent or constant, for longer than one month)
- Persistent oral candidiasis (after first 6-8 weeks of life)
- Oral hairy leukoplakia
- Acute necrotizing ulcerative gingivitis/periodontitis
- Lymph node TB
- Pulmonary TB
- Severe recurrent bacterial pneumonia
- Symptomatic lymphoid interstitial pneumonitis
- Chronic HIV-associated lung disease including bronchiectasis
- Unexplained anaemia (< 8.0 g/dl), neutropaenia (< 0.5 x 109/L) or chronic thrombocytopaenia (< 50 x 109/L)

Clinical Stage 4 (Severe)

- Unexplained severe wasting, stunting or severe malnutrition not responding to standard therapy
- Pneumocystis pneumonia
- Recurrent severe bacterial infections (e.g. empyema, pyomyositis, bone or joint infection, meningitis, but excluding pneumonia)
- Chronic herpes simplex infection (orolabial or cutaneous of more than one month's duration, or visceral at any site)
- Extrapulmonary TB
- Kaposi sarcoma
- Oesophageal candidiasis (or candida of trachea, bronchi or lungs)
- Central nervous system toxoplasmosis (after one month of life)
- HIV encephalopathy
- Cytomegalovirus (CMV) infection; retinitis or CMV infection affecting another organ, with onset at age over 1 month
- Extrapulmonary cryptococcosis (including meningitis)
- Disseminated endemic mycosis (histoplasmosis, coccidiomycosis)
- Chronic cryptosporidiosis (with diarrhoea)
- Chronic isosporiasis
- Disseminated non-tuberculous mycobacteria infection
- Cerebral or B cell non-Hodgkin lymphoma
- Progressive multifocal leukoencephalopathy
- Symptomatic HIV-associated cardiomyopathy or nephropathy

APPENDIX 3. ROUTINE LABORATORY MONITORING BY REGIMEN

Regimen	W 2	M1	W 6	M3	M6	M9	M12	M15 & every 3 months thereafter	M18 & Every 6 months thereafter	M24 & Every 12 months thereafter
TDF/[FTC or 3TC]/NVP			***CrCl***		***CrCl*** ***VL***		***CrCl*** ***VL***		***VL if<19y***[1]	***CrCl*** ***VL***
TDF/[FTC or 3TC]/EFV			***CrCl***		***CrCl*** ***VL***		***CrCl*** ***VL***		***VL if<19y***[1]	***CrCl*** ***VL***
AZT/3TC/NVP	***Hb***		***Hb***	***Hb***	***VL***		***VL***		***VL if<19y***[1]	***VL***
AZT/3TC/EFV	***Hb***		***Hb***	***Hb***	***VL***		***VL***		***VL if<19y***[1]	***VL***
TDF/[FTC or 3TC]/AZT/ LPV/r	***Hb***[2]	***CrCl***	***Hb***[2]	***Hb***[2] ***CrCl***	***CrCl*** ***VL***		***CrCl*** ***VL***		***VL if<19y***[1]	***VL***
ABC/3TC/EFV					***VL***		***VL***		***VL if<19y***[1]	***VL***
ABC/3TC/LPV/r					***VL***		***VL***		***VL if<19y***[1]	***VL***
ABC/AZT/3TC/LPV/r	***Hb***[2]		***Hb***[2]	***Hb***[2]	***VL***		***VL***		***VL if<19y***[1]	***VL***
ABC/AZT/3TC/EFV	***Hb***[2]		***Hb***[2]	***Hb***[2]	***VL***		***VL***		***VL if<19y***[1]	***VL***
Special situations										
HBsAg positive at diagnosis	***ALT***		***ALT***	***ALT***	***Repeat HBsAg***	***ALT***[3]			***ALT***[3]	

Notes: [1]Viral Load testing at 6 months and 6 monthly thereafter only for children <19 years old
[2]Only do Hb if patient has NOT had AZT in first line
[3]Continue to monitor ALT only if repeat HBsAg is positive
Any other Lab test can be requested as clinically deemed necessary

APPENDIX 4. SUMMARY INFORMATION ON ANTIRETROVIRAL FORMULATIONS FOR ADULTS

ARV	Formulation /Strength	Dose for adults*	Special Considerations	Adverse effects
Nucleoside Reverse Transcriptase Inhibitors (NRTIs)				
Zidovudine (AZT)	Tablet : 300mg, 250mg, 100mg	300 mg bd	With or without food	Anaemia, neutropenia, Gastrointestinal intolerance, Headache, insomnia, myopathy Lactic acidosis with hepatic steatosis (rare)
Abacavir (ABC)	Tablet: 300mg	600 mg od (or 300 mg bd if part of an FDC)	With or without food	Hypersensitivity reaction (can be fatal) Fever, rash, fatigue Nausea, vomiting, anorexia Respiratory symptoms(sore throat, cough) Lactic acidosis with hepatic steatosis (rare)
Lamivudine (3TC)	Tablet : 150mg	150 mg bd (or 300 mg od if given with TDF or ABC)	With or without food	Minimal toxicity Lactic acidosis with hepatic steatosis (rare)
Emtricitabine (FTC)	Tablet: 200mg (as part of FDC)	200 mg od	With or without food	Headache, nausea, skin rash and discoloration Lactic acidosis with hepatic steatosis(rare)
Stavudine (d4T)	Capsule: 30mg, 20mg, 15mg	30 mg bd	With or without food	Pancreatitis Peripheral neuropathy Lactic acidosis with hepatic steatosis (rare) Lipoatrophy
Didanosine (ddI)	Capsule (delayed release): 250mg, 400mg	<60 kg:125 mg bd or 250 mg od >60 kg: 200 mg bd or 400 mg od	Empty stomach (1/2h prior or 2 h after meals) doses reduced by half with TDF	Pancreatitis Peripheral neuropathy Nausea, diarrhoea Lactic acidosis with hepatic steatosis (rare)

ARV	Formulation /Strength	Dose for adults*	Special Considerations	Adverse effects
Nucleotide Reverse Transcriptase Inhibitor (NtRTIs)				
Tenofovir (TDF)	Tablet: 300 mg (tenofovir disoproxil fumarate equivalent to 245 mg tenofovir disoproxil)	300 mg od	Take with food	Abdominal pain, anorexia, asthenia, diarrhoea, dizziness, dyspnoea, flatulence, headache, hypophosphatemia, lactic acidosis, nausea, pancreatitis, renal impairment, rash, vomiting, lactic acidosis with hepatic steatosis (rare)
Non-Nucleoside Reverse Transcriptase Inhibitors (NNRTIs)				
Efavirenz (EFV)	Tablet: 600mg	600 mg od	With or without food; Bed time administration to avoid CNS symptoms	CNS Symptoms: dizziness, somnolence, insomnia, confusion, hallucinations, agitation Elevated transaminase levels Skin rash
Nevirapine (NVP)	Tablet 200 mg	200 mg od x 14 days, then 200 mg bd	With or without food	Skin rash, Stevens-Johnson Syndrome Elevated serum aminotransferase levels Hepatitis, life-threatening Hepatic toxicity
Etravirine (ETV)	Tablet: 200mg, 100mg	200 mg bd	Take with food	Skin rash, nausea, and diarrhoea, elevation in serum cholesterol, triglyceride, glucose, and hepatic transaminase levels.
Protease Inhibitors (PIs)				
Lopinavir + ritonavir (LPV/r)	Tablet (heat-stable): 200mg/50 mg	400 mg/100 mg bd	With food	GI intolerance, nausea, vomiting, elevated transaminase enzymes, hyperglycaemia, fat redistribution and lipid abnormalities
Ritonavir (RTV)	Capsule: 100 mg	Use only as booster PI	Take with food. High-fat snacks may reduce side effect	Gastrointestinal intolerance, nausea, vomiting, paraesthesia, hepatitis and pancreatitis, hyperglycaemia, fat redistribution and lipid abnormalities

ARV	Formulation /Strength	Dose for adults*	Special Considerations	Adverse effects
Atazanavir (ATV)	Tablet: 300mg, 150mg	300mg od (must be used in combination with ritonavir 100mg)	Take with a light meal	Benign increase in bilirubin, prolonged QT (caution with conduction defects or drugs that do this), increased glucose, lipodystrophy, and increased haemorrhage in patients with haemophilia.
Darunavir (DRV)	Tablet: 600mg, 300mg,	600mg bd (must be used in combination with ritonavir 100mg)	Take with food	Nausea, diarrhoea, GI discomfort, headache, hypercholesterolemia, hypertriglyceridemia, lipodystrophy, increased glucose, transaminitis, inflammation of the nose and throat, and increased haemorrhage in patients with haemophilia. Rash, SJS, Erythema multiforme, Hepatotoxicity, crystaluria
Integrase Inhibitor				
Raltegravir (RAL)	Tablet: 400mg	400 mg bd	Take with or without food	Diarrhoea, nausea, and headache. Use with caution in patients who are at increased risk for myopathy and rhabdomyolysis, which includes patients using other medications known to cause these conditions. rash, SJS, TEN, hypersensitivity reaction, depression, suicidal ideation
Dolutegravir (DTG)	Tablet: 50mg	50mg od	Take with or without food	Increase chlestrol, fat maldistributionNot recommended for patient with severe hepatic impairment **New Medicine: subject for additional monitoring **
Fixed-Dose Combinations (FDC)				
Tenofovir + Lamivudine	FDC Tablet: TDF 300mg + 3TC 300mg	One tablet once daily	Refer to the corresponding single formulations above	
Tenofovir + Lamivudine + Efavirenz	FDC Tablet: TDF 300mg + 3TC 300mg + EFV 600mg	One tablet once daily		

ARV	Formulation /Strength	Dose for adults*	Special Considerations	Adverse effects
Tenofovir + Emtricitabine	FDC Tablet: TDF 300mg + FTC 200mg	One tablet once daily		
Tenofovir + Emtricitabine + Efavirenz	FDC Tablet: TDF 300mg + FTC 200mg + EFV 600mg	One tablet once daily		
Zidovudine + Lamivudine	FDC Tablet: AZT 300mg + 3TC 150mg	One tablet twice daily		
Zidovudine + Lamivudine + Nevirapine	FDC Tablet: AZT 300mg + 3TC 150mg + NVP 200mg	One tablet twice daily		
Abacavir + Lamivudine + Zidovudine	FDC Tablet: ABC 300mg + 3TC 150mg + AZT 300mg	One tablet twice daily		
Stavudine + Lamivudine	FDC Tablet: d4T 30mg + 3TC 150mg	One tablet twice daily		
Stavudine + Lamivudine + Nevirapine	FDC Tablet: d4T 30mg + 3TC 150mg + NVP 200mg	One tablet twice daily		

**For appropriate paediatric formulations and dosage, please see table 3.5 in section 3.5.1*

APPENDIX 5: ANTIRETROVIRAL MEDICATION DOSAGE ADJUSTMENT FOR RENAL AND HEPATIC FAILURE

Medicine Name	Form	Usual adult dose	Renal failure dosing				Liver failure dosing
			CrCl 30-50 ml/ min	CrCl 10-29 ml/ min	CrCl <10 ml//min	Dialysis	
Abacavir (ABC)	300mg tablets	300mg BD	Dosing adjustment not necessary				Usual dose Avoid in severe cases
Didonasine (ddI)	125, 250, 400mg tablets	<60kg: 250mg od	125mg od	125mg od	125mg od	125mg od	Usual dose Monitor for toxicity
	250mg, 400mg tablets	>60kg: 400mg od	200mg od	125mg od	125mg od	125mg od	
Lamivudine (3TC)	150mg tablet	150 mg BD	150mg od	150mg 1st dose, then 100mg od	150mg 1st dose, then 50mg od	150mg 1st dose, then 50mg od	Usual dose
Stavudine (d4T)	15, 20, 30mg tablets	30mg BD	15mg BD	15mg od	15mg od	15mg od	Usual dose
Zidovudine (AZT)	100mg capsule, 300mg tablets	300mg BD	Usual dose	Usual dose	(<15 ml/min) 100mg tds	100mg tds	Reduction in daily dose or extension of dosing interval may be needed; 50% decrease in dose or doubling of the dosage interval has been recommended (limited data)
Tenofovir (TDF)	300mg tablets	300mg od	300mg q48h	300 mg twice per week	300mg weekly	300mg weekly	Usual dose

APPENDIX 6. DIETARY MANAGEMENT OF COMMON HIV-RELATED SYMPTOMS

Illness	Diet	Care and nutrition practices
Anorexia (appetite loss)	• Stimulate appetite by eating favourite foods. • Eat small amounts of food more often. • Eat more energy-dense foods. • Avoid strong-smelling foods.	If appetite loss is a result of illness, seek medical treatment.
Diarrhoea	• Drink a lot of fluids (soups, diluted fruit juices, boiled water and light herbal teas) to avoid dehydration. • Avoid strong citrus fruits (orange, lemon) because they irritate the stomach. • Eat foods rich in soluble fibre (millet, banana, peas, and lentils) to help retain fluids. • Eat fermented foods such as porridges and yoghurt. • Eat easily digestible foods such as rice, bread, millet, maize porridge, potato, sweet potato, and crackers. • Eat small amounts of food frequently. • Continue to eat after illness to recover weight and nutrient loss. • Eat soft fruits and vegetables such as bananas, mashed sweet potato, and mashed carrots. • Drink non-fat milk if there is no problem with lactose. • Boil or steam foods if diarrhoea is associated with fat mal-absorption. • Avoid or reduce intake of some dairy products such as milk, caffeine (coffee and teas) and alcohol, fatty foods, fried foods and extra oil, lard or butter, and gas-forming foods such as cabbage, onions, and carbonated soft drinks.	**Prevention** • Drink clean boiled water. • Wash hands with water and soap before handling, preparing, serving, or storing food. • Wash hands with water and soap after using a toilet or latrine or cleaning a child after defecation. **Treatment** • Drink more fluids to prevent dehydration. Prepare rehydration solutions using oral rehydration salt sachets or a homemade solution from cereals. • Go to a health facility if symptoms such as severe dehydration, fainting, dizziness, shortness of breath, bloody stools, high fever, vomiting, severe abdominal pain, or diarrhoea persist for more than 3 days.
Fever	• Eat soups rich in foods that give energy and nutrients, such as maize, potatoes, and carrots. • Drink plenty of fluids. • Drink teas from lemon, guava, and gum tree. • Continue to eat small, frequent meals as tolerated.	• Drink fluids to prevent dehydration, particularly clean boiled water. • Bathe in cool water. • Take two paracetamol tablets if available, with a meal three times a day (morning, afternoon, and evening). • Go to the health facility if you have fever that lasts several days and is not relieved with aspirin, loss of consciousness, severe body pain, yellow eyes, severe diarrhoea, or convulsions and seizures.

Illness	Diet	Care and nutrition practices
Nausea and vomiting	• Eat small frequent meals. • Eat soups, unsweetened porridge, and fruits such as bananas. • Eat lightly salty and dry foods such as crackers to calm the stomach. • Drink herbal teas and lemon juice in hot water. • Avoid spicy and fatty foods. • Avoid caffeine (coffee and tea) and alcohol. • Drink liquids such as clean boiled water.	• Avoid an empty stomach; nausea is worse if nothing is in the stomach. • Avoid lying down immediately after eating—wait at least 20 minutes. • Avoid vomiting. • Rest between meals.
Thrush	• Eat soft, mashed foods such as carrots, scrambled eggs, mashed potatoes, bananas, soups, and porridge. • Eat cold or room-temperature foods. • Avoid spicy, salty, or sticky foods that may irritate mouth sores. • Avoid sugary foods that cause yeast to grow. • Avoid strong citrus fruits and juices that may irritate mouth sores. • Avoid alcohol and drink plenty of fluids.	• Seek medical treatment. • Use a spoon or cup to eat small amounts of foods. • Tilt your head back when eating to help with swallowing. • Rinse your mouth with boiled warm, salty water after eating to reduce irritation and keep infected areas clean so yeast cannot grow.
Constipation	• Eat more high-fibre foods such as maize, whole wheat bread, green vegetables, and washed fruits with the peel. • Drink plenty of liquids. • Avoid processed or refined foods.	• Avoid cleansing practices such as enemas and medications. • Drink plenty of fluids, including boiled water.
Loss of taste or abnormal taste	• Use flavour enhancers such as salt, spices, herbs, and lemon.	• Eat small frequent meals • Chew food well and move it around the mouth to stimulate receptors

APPENDIX 7. ALGORITHM FOR CLASSIFICATION OF MALNUTRITION IN ADULTS

ASSESS				
HISTORY	**LOOK FEEL AND MEASURE**	**CRITERIA**	**CLASSIFICATION**	**TREATMENT/CARE**
Ask the client or refer to records: 1. Has the client lost weight in the past month/since the last visit? 2. Has the client had: ○ Active TB (on treatment)? ○ Another chronic opportunistic infection (OI) or malignancy (e.g., oesophageal infections)? ○ Mouth sores/oral thrush? 3. Has the client's body composition/fat distribution changed noticeably? ▪ Thinning of limbs and face? ▪ Fat distribution on limbs, breasts, stomach, back? 4. Has the client had: ✓ Nausea and vomiting? ✓ Persistent fatigue? ✓ Poor appetite?	**Prevention** • Drink clean boiled water. • Wash hands with water and soap before handling, preparing, serving, or storing food. • Wash hands with water and soap after using a toilet or latrine or cleaning a child after defecation. **Treatment** ○ Drink more fluids to prevent dehydration. Prepare rehydration solutions using oral rehydration salt sachets or a homemade solution from cereals. 1. Go to a health facility if symptoms such as severe dehydration, fainting, dizziness, shortness of breath, bloody stools, high fever, vomiting, severe If the client has oedema on both legs or base of the spine: ○ Rule out pre-eclampsia, kidney problems, elephantiasis, heart failure, and wet beriberi (vitamin B1 deficiency with oedema). 2. Measure the client's weight (kg) and height (cm). 3. Compute body mass index (BMI). 4. Measure mid-upper arm circumference	**Adults (non-pregnant and non-post-partum)** BMI < 16 kg/m^2 (If can't measure BMI, MUAC < 19 cm) **OR** Bilateral pitting oedema (both feet or legs are swollen, and the skin remains indented when pressed with a finger) **Pregnant women and women up to 6 months post-partum** MUAC < 19 cm	**Severe acute malnutrition (SAM) with complication** (fever, hypothermia, severe anaemia or dehydration, vomiting, bilateral oedema +++) **or no appetite**	**Inpatient treatment** **Refer to therapeutic feeding programmes**
			SAM with appetite and no complication	**Outpatient treatment** **Refer to therapeutic feeding programmes**
		Adults (non-pregnant and non-post-partum) BMI ≥ 16.0–< 18.5 kg/m^2 (If can't measure BMI, MUAC ≥ 19–< 22 cm) **Pregnant women and women up to 6 months post-partum** Weight loss or no weight	**Moderate/mild malnutrition** **Significant weight loss**	**Refer to supplementary feeding programmes**

	(MUAC) for all pregnant women, all women up to 6 months post-partum, and adults who cannot stand straight. 5. Examine the client for conditions that cause secondary malnutrition (e.g., injuries, burns, surgical procedures, pregnancy, diarrhoea, or disease of the gastrointestinal tract, thyroid, kidney, liver, or pancreas). 6. Look for medical complications and danger signs (e.g., anaemia, severe dehydration, active TB, severe bilateral oedema). 7. If the client has no medical complications, give an appetite test using ready-to-use therapeutic food (RUTF).	gain MUAC ≥ 19–< 22 cm		
		Severe lung disease Active TB (first 3 months of treatment) Chronic diarrhoea Difficulty swallowing	**Signs of symptomatic disease**	
		Adults (non-pregnant and non-post-partum) BMI ≥ 18.5 kg/m^2 (If can't measure BMI, MUAC ≥ 22 cm) **Pregnant and post-partum women** MUAC ≥ 23 cm	**Normal**	**Nutrition counselling**

APPENDIX 8. ALGORITHM FOR CLASSIFICATION OF MALNUTRITION IN CHILDREN 6 MONTHS–14 YEARS OLD

<table>
<tr><th>ASK</th><th>LOOK,FEEL and MEASURE</th><th>CRITERIA</th><th>CLASSIFICATION</th><th>TREATMENT/CARE</th></tr>
<tr>
<td rowspan="3">Ask mother or caregiver or refer to records:
1. Has the child lost weight in the past month/since the last visit?
2. Has the child had:
○ A cough for more than 21 days? (This may be a result of HIV-related chronic lung disease such as lymphocytic interstitial pneumonia [LIP] or bronchiectasis.)
○ Active tuberculosis (TB) (on treatment)?
○ Diarrhoea for more than 14 days?
○ Another chronic opportunistic infection (OI) or malignancy?</td>
<td rowspan="3">1. Look for severe visible wasting:
○ Loss of muscle bulk on arms, shoulders, buttocks, and thighs, with visible rib outlines
○ Sagging skin on buttocks
2. Check for oedema (swelling) in both feet or base of spine.
3. Measure child’s weight (kg) and height (cm) and find weight for height (WFH) using 2006 WHO child growth standards.
4. Measure mid-upper arm circumference (MUAC).
5. Look at the shape of the curve on the growth chart.
• Has the child lost weight since the last visit? (Measure again to confirm current weight.)
• Is the growth curve flattening?
• Is the child gaining weight?

Weight loss 
Growth curve flattening 
Weight gain  </td>
<td>Bilateral pitting oedema +++ (both feet and/or legs are swollen, and the skin remains indented when pressed with the thumb)
OR
WFH < –3 z-scores (WHO 2006)
OR
BMI for age
10–14 years: ≤ –3 z-score
OR
MUAC
6–59 months: < 11.5 cm
5–9 years: < 13.5 cm
10–14 years: < 16.0 cm
AND
Does not pass an appetite test</td>
<td>Severe acute malnutrition (SAM)</td>
<td></td>
</tr>
<tr>
<td>With medical complication (WFH <–4 z-scores, shock, anorexia, intractable vomiting, convulsions, lethargy, lower respiratory tract infection, high fever, severe anaemia or dehydration, hypoglycaemia, hypothermia, pneumonia, TB)or no appetite</td>
<td><u>Inpatient treatment</u>
Refer to therapeutic feeding programmes</td>
</tr>
<tr>
<td>Without medical complication and with appetite
Clinical wellness
Alertness
Caregiver able/willing to manage SAM at home and return to clinic every 14 days</td>
<td><u>Outpatient treatment</u>
Refer to therapeutic feeding programmes</td>
</tr>
<tr>
<td></td>
<td>6–59 months: WFH or BMI for age between –3 and –2 z-scores</td>
<td>Moderate/mild malnutrition (MAM)</td>
<td>Refer to supplementary feeding</td>
</tr>
</table>

		OR MUAC 6–59 months: ≥ 11.5–< 12.5 cm 5–9 years: ≥ 13.5–< 14.5 cm 10–14 years: ≥ 16.0–< 18.5 cm	**Poor weight gain**	**programmes**
		Weight gain parallel to or higher than median growth curve WFH ≥ –2 z-score **OR** MUAC ≥ 12.5 cm	**Normal** **Growing appropriately**	**Nutrition counselling**
		Chronic lung disease, TB, persistent diarrhoea, or other chronic opportunistic infection or malignancy	**Condition with increased nutritional needs**	**Refer to supplementary feeding programmes**

APPENDIX 9. SAFETY YELLO FORM

Republic of Namibia

Ministry of Health and Social Services

Adverse Medicine Reaction Reporting Form

A) PATIENT INFORMATION

Safety Yellow Form
Confidential

Patient initials or Hospital Reg. No.		DOB DD/MM/YYYY Age	Gender: ☐ Male ☐ Female	Weight (Kg):

B) ADVERSE EVENT INFORMATION

Type of report: **Initial:** ☐ **Follow up:** ☐ Write AMR ID number

DESCRIPTION OF ADVERSE EVENTS: Indicate provisional/final diagnosis of the adverse event	**Date event started**	**Date event stopped**	**Action taken:** (E.g. Medicine withdrawn/ substituted/Dose reduced /medical treatment etc...)

Serious-ness	☐ Hospitalization	☐ Disability or permanent damage	☐ Congenital anomaly/ birth defect
	☐ Life-threatening	☐ Other serious medical event	☐ Non serious adverse event

Relevant Laboratory tests	**Test date**	**Result**
	DD /MM./ YYYY	

Patient Outcome	☐Recovered ☐ Recovered with sequela ☐Recovering ☐ Not recovered ☐Unknown	**Died**	☐Due to reaction ☐ unrelated to reaction	☐ Reaction maybe contributory Date of death DD /MM./ YYYY

RELEVANT MEDICAL HISTORY: including pre-existing medical conditions (allergies, pregnancy, alcohol use, liver problems...)

C) INFORMATION ON MEDICINES: ***For vaccines please indicate the batch number***

List Medicines Used in the Last 3 Months Tick Suspected Medicines Enter FDC as One Medicine		**Strength**	**Frequency**	**Route of Admin**	**Start date**	**Stop date or ongoing**	**Indication**
	☐						
	☐						
	☐						
	☐						
	☐						

D) REPORTER INFORMATION

Name (last, first)		Region		Email	
Profession		Telephone		Date	DD /MM./ YYYY
Health Facility Name		Fax			

Please tick if you need ☐ *AMR forms* ☐ *Additional information*

Please note that submission of a report does not constitute an admission that medical personnel or the medicine caused or contributed to the event

Send/ Fax/Email to TIPC: Therapeutics Information and Pharmacovigilance Centre
Room 21, Basement Area, Windhoek Central Hospital. Windhoek.
Tel: 061 203 2312 Fax: 061 22 66 31/ 088 618 776. Email: info@tipc.com.na

APPENDIX 10. INTERACTIONS BETWEEN ARVS AND SOME COMMONLY USED MEDICINES

Note: All the drug interaction tables are derived from the University of Liverpool's drug interaction website: http://www. hiv-druginteractionslite.org

Antiepileptics	Antiretrovirals				Comments and/ recommendations
	EFV	NVP	DTG	LPV/r	
Carbamazepine	↓	↓	DTG↓	↑	Carbamazepine effect not achieved (with NNRTIs) or side effects occur (with PIs). Use alternative that is sodium valproate or newer antiepileptics if available, which include lamotrigine, topiramate and gabapentin.
Phenytoin	↓	↓	DTG ↓	↓	Reduction in phenytoin plasma concentration. Coadministration not recommended. Use alternative that is sodium valproate or newer antiepileptics if available, The new one include lamotrigine, topiramate and gabapentin.
Phenobarbital	↓	↓	DTG ↓	↓	Reduction in phenobarbital concentration (with NNRTIs); reduction in LPV/r concentration. Use alternative. Use alternative that is sodium valproate or newer antiepileptics if available, The new one include lamotrigine, topiramate and gabapentin.
Valproate	↔	↔	↔	↓ or ↔	Concentration of valproate not changed with NNRTI and INSTI, but with PI valproate plasma concentration may reduce.
Lamotrigine	↔	↔	↔	↓ or ↔	
Topiramate	↔	↔	↔	↔	
Gabapentin	↔	↔	↔	↔	

Antidepressants	Antiretrovirals				Comments and/or recommendations
	EFV	NVP	DTG	LPV/r	
Amitryptyline	↔	↔	↔	↑	Monitor for amitriptyline side effects if given with LPV/r.
Imipramine and Trimipramine	↓	↓	↔	↑	Monitor clinical effect of Imipramine with EFV and NVP, and side effects with LPV/r.
Fluoxetine	↔	↔	↔	↔ or ↑	Monitor for fluoxetine clinical and side effects if given with LPV/r.
Citalopram	↓	↓	↔	↓ or ↑	Monitor for clinical effect of citalopram if given with NNRTIs and both clinical and side effects if given with PIs.
Paroxetine	↔	↔	↔	↔ or ↑	Monitor for paroxetine clinical and side effects if given with LPV/r.
Sertaline	↓	↓	↔	↓	Increase dose of sertaline based on clinical effect.
Fluvoxamine	↔	↔	↔	↔	No clinically important interactions occur.

Anticoagulants	Antiretrovirals				Comments and/or recommendations
	EFV	NVP	DTG	LPV/r	
Warfarin	↑ or ↓	↑ or ↓	↔	↓	With NNRTIs warfarin effect may increase or decrease. Close monitoring of INR is advised and warfarin dose adjusted appropriately. If given with PIs, effect of warfarin may decrease. Monitor INR closely and increase the dose of warfarin appropriately.

Calcium channel blockers	Antiretrovirals				Comment and/or recommendation
	EFV	NVP	DTG	LPV/r	
Nifedipine	↓	↓	↔	↑	When CCB are co-administered with NNRTIs, their concentration of CCBs in plasma may be reduced. Monitor clinical effect of CCBs and adjust the dose. When CCB are co-administered with LPV/r their concentration in plasma may be increased. Since CCBs and LPV/r both increase the PR interval, co-administration of these medicines must be done with caution.
Verapamil	↓	↓	↔	↑	
Diltiazem	↓	↓	↔	↑	
Amlodipine	↓	↓	↔	↑	
Felodipine	↓	↓	↔	↑	

Rifamycins	Antiretrovirals				Comments and/or recommendations
	EFV	NVP	DTG	LPV/r	
Rifampicin	↔	↓	DTG↓	↓	Rifampicin should not be coadministered with NVP. When given with LPV/r the dose of the PI should be adjusted by one of the following options: • Double the dose of LPV/r: 800/200mg twice daily or • Increase the dose of ritonavir: 400/400mg of LPV/r twice daily.
Rifabutin	↓	↑	↔	↑	When rifabutin is given with EFV its plasma concentration is reduced. Increase rifabutin dose by 50%. When given with NVP, rifabutin's concentration in plasma increases. Monitor the patient for rifabutin's adverse effects. When given with LPV/r rifabutin's plasma concentration is increased 3fold. The dose should be reduced by 75%.

Statins	Antiretrovirals				Comments and/or recommendations
	EFV	NVP	DTG	LPV/r	
Artovastatin	↓	↓	↔	↑	When given with NNRTIs plasma concentration of artovastatin in plasma is reduced. Monitor clinical effect and adjust dose accordingly. When co-administered with LPV/r plasma concentration is increased five fold. Use alternative statin e.g. pravastatin or fluvastatin.
Lovastatin and Simvastatin	↓	↓	↔	↑	When given with NNRTIs the plasma concentration of these statins in plasma is reduced. Monitor clinical effect and adjust dose if necessary. Co-administration of these statins with LPV/r is contraindicated. If co-administered, the concentration of lovastatin and simvastatin in plasma may increase significantly leading to myopathy including rhabdomyolysis.
Pravastatin	↓	↔	↔	↔	Co-administration with EFV would reduce plasma concentration of pravastatin. Adjust dose based on clinical effect.
Fluvastatin	↑	↔	↔	↔	Co-administration with EFV could result in an increase in plasma concentration of fluvastatin. Monitor toxicity of fluvastatin.

Symbols explained:

- ↓= plasma concentration of other medicine decreases: this means that the therapeutic effect may be lost;
- ↑ = plasma concentration of other medicine increases: this means that toxicity (side effect) may occur;
- ↔ = plasma concentration of other medicine not affected: this means that the clinical effect is not affected.

APPENDIX 11 PAEDIATRIC DOSAGE CHART FOR NRTIS

Weight	Abacavir* (ABC)		Lamivudine (3TC)		ABC/3TC		AZT/3TC /ABC	Zidovudine (AZT)		AZT/3TC		Stavudine (d4T/3TC)		Stavudine (d4T)	Tenofovir (TDF)			
	Once daily (od) Max 600mg daily		Twice daily Max 150 mg bd		Once daily (od) Max 600mg/300 mg daily		Twice daily (bd) Max 600mg/ 300mg/ 600mg	Twice daily Max 300mg bd		Twice daily Max 300/150mg bd		Twice daily Max 30mg/150mg bd		Twice daily Max 30mg bd	Once daily Max 300mg			
Kg	Dispers tablet 60mg	Tablet 300mg	Oral solution 10mg/ ml	Tablet 150 mg	Dispersible tablet 60mg/30mg	Tablet 300mg/ 150mg	Tablets 300mg/150 mg/ 300mg	Dispers. tablet 60mg	Tablet 300mg	Dispers. tablet 60mg/30 mg	Tablet 300mg/ 150mg	Dispersible tablet 6mg/30mg	Tablet 30mg d4T/ 150mg 3TC	Syrup 1mg/ml	Tablet 150mg	Tablet 200mg	Tablet 250mg	Tablet 300mg
3-5.9	2 tabs od		3ml bd		2 tabs od			1 tab bd		1 tab bd		1 tab bd		5mls bd				
6-9.9	3 tabs od		4ml bd		3 tabs od			1.5 tabs bd		1.5 tabs bd		1.5 tabs bd		10mls bd				
10-13.9	4 tabs od		5ml bd		4 tabs od			2 tabs bd		2 tabs bd		2 tabs bd		15mls bd				
14-19.9		1 tab od		0.5 tab bd		1 tab od	0.5 tab bd	2.5 tabs bd	0.5 tab bd		0.5 tab bd	2.5 tabs bd						
17-21.9															1 tab od			
22-27.9		1.5 tabs od		1 tab am 0.5 tab pm		1.5 tabs od	1 tab am 0.5 tab pm	3 tabs bd	1 tab am 0.5 tab pm		1 tab am 0.5 tab pm	3 tabs bd	1 tab am 0.5 tab pm			1 tab od		
28-34.5		2 tabs od		1 tab bd		2 tabs od	1 tab bd		1 tab bd		1 tab bd	4 tabs bd	1 tab bd				1 tab od	
≥35																		1 tab od

APPENDIX 12 PAEDIATRIC DOSAGE CHART FOR NNRTIS, NNRTI-CONTAINING FDCS

Weight	Efavirenz (EFV)	Nevirapine (NVP)						Etravirine (ETR) (for use in 3rd line regimens)			D4T/3TC/NVP		AZT/3TC/NVP	
	Once daily at night (nocte) Ma: 600mg od	Twice daily* Max 200 mg bd						Twice daily* Max 200 mg bd			Twice daily* Max 30/150/200mg bd		Twice daily* Max 300/150/200mg bd	
		Induction dose* once daily (od) for first 14 days			Maintenance dose* twice daily						Dispersible tablet 6mg d4T/ 30mg 3TC/ 50mg NVP	Tablet 30mg/ 150mg/ 200mg	Dispersible tablet	
Kg	200mg 600mg	Oral susp. 10mg/ml	Dispers. tablet 50 mg	Tablet 200mg	Oral susp. 10mg/ml	Dispersible tablet 50mg	Tablet 200mg	Tablet 25mg	Tablet 100mg	Tablet 200mg	Maintenance dose*	Maintenance dose*	60mg AZT/ 30mg 3TC/ 50mg NVP	Tablet 300/150/ 200mg
3-5.9		5ml od	1 tab od		5ml bd	1 tab bd					1 tab bd		1 tab bd	
6-9.9		8ml od	1.5 tabs od		8ml bd	1.5 tabs bd		1 tab bd			1.5 tabs bd		1.5 tabs bd	
10-13.9	200mg nocte	10ml od	2 tabs od	0.5 tab od	10ml bd	2 tabs bd	0.5 tab bd				2 tabs bd		2 tabs bd	
14-16.9	300mg nocte			0.5 tab od			1 tab am 0.5 tab pm		1 tab bd		2.5 tabs bd		2.5 tabs bd	
17-19.9				1 tab od										
20-24.9											3 tabs bd	1 tab am 0.5 tab pm	3 tabs bd	1 tab am 0.5 tabs pm
25-29.9	400mg nocte						1 tab bd		1.5 bd		4 tabs bd	1 tab bd		1 tab bd
30 – 34.9										1 bd	4 tabs bd			
35-39.9														
≥40 kg	600mg nocte			1 tab od			1 tab bd					1 tab bd		1 tab bd

**any child or adolescent initiating nevirapine instead of efavirenz should start with an "induction" dose which is generally half of the daily maintenance dose for 2 weeks.*
If there is no rash or other sign of hypersensitivity, the patient can be given the bd maintenance dose.This means that if a child is initiating ART with an FDC that contains nevirapine, the child should take the triple FDC in the morning and the dual FDC (e.g. ABC/3TC or AZT/3TC) in the evening for the first 2 weeks.

APPENDIX 13 PAEDIATRIC DOSAGE CHART FOR PIS AND ISTIS

Weight	Lopinavir/ritonavir (LPVr)				Atazanavir (ATVr) *ALWAYS GIVE RITONAVIR BOOST*					Darunavir* (DRVr) (for use in 3rd line regimens) *ALWAYS GIVE RITONAVIR BOOST*					Raltegravir** (RAL)	
	Twice daily Max 400mg/100mg bd				Once daily (od) Max 300mg					Twice daily Max 600 mg bd					Twice daily Max 600mg bd	
Kg	Pellets (Capsule) 40mg LPV/ 10mg RTV	Liquid 80mg LPV/ 20mgRTV per ml	Heat stable tablet ***Must swallow whole*** 100mg LPV/ 25mg RTV	Tablet 200mgLPV / 50mg TV 1 tab bd	Powder (Satchet) 50mg	Capsule 200mg	Syrup 80mg/5 ml **Ritonavir** for Boosting ATV	Tablets 100mg **Ritonavir** for Boosting ATV	Tablet Boosted Atazanavir (ATV 300 /RTV100)	Tablet s 75mg	Tablets 150mg	Tablets 600mg	Syrup 80mg/5 ml **Ritonavir** for Boosting DRV	Tablets 100mg **Ritonavir** for Boosting DRV	Chewabl e tablets 25mg	Chewable tablets 100mg
3-4.9	2 caps bd	1 ml bd														
5-5.9					4 sachet s od		**5 ml od**									
6-9.9	3 caps bd	1.5 ml bd														
10-13.9	4 caps bd	2 ml bd	2 tabs am 1 tab pm Pm												3 tabs bd	
14-14.9		2.5 ml bd	2 tabs bd	1 tab bd												1 tab bd
15-19.9					5 sachet s od					1 tab bd	2 tabs bd		**0.6ml bd**			
20-24.9		3 ml bd				1 od		**1 tab od**			3 tabs bd			**1 tab bd**		1.5 tabs bd
25-34.9			3 tabs bd	2 tabs am 1 tab pm												2 tabs bd
35-39.9				2 tabs bd												
≥40 kg									1 tab od			1 tab bd				3 tabs bd

**These medicines will be used in the management of pediatrics on 3rd line regimens*

*** In special circumstances, raltegravir may be used in 1st or 2nd line, otherwise it will be reserved for 3rd line treatment*

APPENDIX 14: SUPER BOOSTING LPV/R IN CHILDREN ON TB TREATMENT.

Weight	Lopinavir/ritonavir (LPVr) Twice daily Max 400mg/100mg bd							
Kg	Pellets (Capsule) 40mg LPV/ 10mg RTV	Super Boosting RTV	Tablet 200mgLPV/ 50mg RTV 1 tab bd	Super Boosting RTV	Liquid 80mg LPV/ 20mgRTV per ml	Super Boosting RTV	Heat stable tablet ***Must swallow whole*** 100mg LPV/ 25mg RTV	Super Boosting RTV
3-4.9	2 caps bd				1 ml bd			
5-5.9								
6-9.9	3 caps bd				1.5 ml bd			
10-13.9	4 caps bd				2 ml bd		2 tabs am 1 tab pm pm	
14-14.9			1 tab bd		2.5 ml bd		2 tabs bd	
15-19.9								
20-24.9					3 ml bd			
25-34.9			2 tabs am 1 tab pm				3 tabs bd	
35-39.9			2 tabs bd					

APPENDIX 15 STANDARD OPERATING PROCEDURES: COMMUNITY ART GROUPS (CARGS)

Description	• Self-formed groups of clients on ART comprised of 6-12 members. They are usually from the same geographic area and usually in hard-to reach communities with limited access to a health facility. Members should be willing to disclose their status to each other. They rely on pre-existing social networks, such as support groups, workmates and family relations. Each member should attend the clinic and seen by doctor or nurse for their clinical visits and monitoring blood visits every 6 months. However, group members take turns to collect each other's medicines. • Group members must meet at least 24 hours prior to the members' scheduled refill date. During this initial meeting, the booklets for group members are handed over to the group representative. The representative, with the support of the group leader, will also ask general screening questions as elaborated in the standard operating procedures. Unwell group members should accompany the representative to the clinic so that their conditions are reviewed. The ARV refills will be for a period of 1-3 months depending on the available stock of ARV medicines. • After the visit to the facility, the group representative should meet with the group members within 24 hours preferably on the same day of collection, to distribute and return the members' medicines and booklets
Eligibility Criteria	• Virally suppressed (two previous consecutive tests should be < 50) • In the absence of VL, rising CD4 cell counts or CD4 counts above 350 cells/mm3 • No OIs (eg TB) • Patients who stayed > 12 months on ART • Patients with challenges related to access to health facilities • Non-pregnant, non-breast-feeding women • Adults >18 years of age
Setting up CARGs	**At facility level**: • A multidisciplinary team (MDT) should meet to discuss client flow, roles and responsibilities and identify focal persons. Facilities should also work together with community partners and community support groups to facilitate demand creation in the community. • Each group's files should be stored at the same place, facilitating recording of information, finding test results and identifying which member has come to represent the group. Group folders containing all members' files can be used to improve filing efficiency.
	Recruitment of clients: • The health care worker should screen clients to assess them based on eligibility criteria for the groups during a clinical visit. • Once assessed as stable by the HCW, the client can choose to join a CARG and be referred to the HCW focal point coordinating CARG formation. • If the clients wish to form a group; they should visit a clinic as a group for screening • All clients joining a CARG group should undergo an orientation session • Each group should identify a group leader who will ensure that group ethics are adhered to • The newly formed group is trained on: (a) the approaches, roles and responsibilities of members; (b) how to monitor the adherence of members and (c) how to provide group counselling and education sessions.
Group meeting in the community prior to clinic visit	• CARG members meet in the community at a convenient venue and time • Each member of the group reports on his/her adherence. The representative or focal person (if other group members are illiterate) will collect the information of each member's adherence assessment result. • Clients must be empowered to self-screen for TB and report symptoms of TB or any other condition. Group members who are unwell or have TB symptoms must join the

	group representative to attend a consultation at the health facility. • Unwell group members will be identified and must join the group representative to attend a consultation at the health facility. • The group representative attending the facility for consultation and on behalf of the other members must collect all ART booklets and other group monitoring tools for the group members and bring them to the clinic for refill. • Members of the group may opt to all contribute financially for transport fare. • Members discuss the venue for meeting when the representative is back from the facility to distribute the drugs.
Procedures during visit at health facility	• During consultation, the group representative will report back on the adherence and general health of other group members. • ART booklets are updated (visit date, comment on refill, i.e., group representative refilled, and next visit date to be written). • Chronic care files must also be updated with this information for each group member file. • The visiting group representative has the opportunity to have a clinical review, as well as adherence counselling. • All routine and other required laboratory investigations must be done on this visit day. • Pending results for any member who might have been consulted prior to this must only be communicated as "normal" if there are no abnormalities. Otherwise, individual clients with abnormal results are supposed to be called at the time of receipt of their results by healthcare workers. • Any member requiring additional clinical follow up should be identified and asked to attend the clinic. • Prescription sheets should be written for all group members. • The community ART group tools including registers should be updated by the nurse whenever there are any changes in CARG composition or an outcome occurs.
CARG group meeting after clinic visit	• The group must meet within 24 hours at a convenient place for drug distribution. • When necessary and as advised by the staff at the health facility, the group representative may request a group member to go to the clinic for a special consultation.

APPENDIX 16 STANDARD OPERATING PROCEDURES FOR ART ADHERENCE CLUBS

Description	• To maximize efficiencies in the delivery of ART care, a group of stable clients is enrolled into a treatment adherence group/club where they receive their ART refills, quick symptom screening and counselling support. Adherence groups/treatment clubs meets four times per year as a group and receive their treatment refill within the group. Following every other group visit, i.e., every six months, each member of the group will have a clinical consultation following their meeting. Clients will be enrolled to an adherence group by an expert client (EC) or nurse. • Services are provided at group level, resulting in shared general review time, as well as shared dispensing time although medicines are distributed to individuals. Clinically significant matters (e.g., an illness) should, however, be addressed at individual level through referral back to the mainstream care. • An adherence group will consist of a group of stable clients (maximum 20) that meet at the facility. HCWs, including facility counsellors and expert clients, facilitate the assessment of TB screening and distribution of ARVs. Nurses and doctors should write the prescription forms for the group members in advance so that medicines are prepared at least a day prior to the visit. Nurses and doctors must also update client ART booklets and Adherence Group register. Members will receive three months' supply of ARVs at every club visit. Members' files are to be kept in an Adherence Group folder. • Members are free to consultant at any time they feel unwell, and they have access to all other services, including laboratory monitoring and referrals to other facilities or other services.
Eligibility Criteria	• Virally suppressed (two previous consecutive tests should be < 50) • In the absence of VL, rising CD4 cell counts or CD4 counts above 350 cells/mm3 • No OIs (eg TB) • Patients who stayed > 12 months on ART • Patients with challenges related to access to health facilities • Non-pregnant, non-breast-feeding women • Adults >18 years of age
Prior to adherence group visit	The group facilitator will: • Prepare a the registration book • Retrieve folders/files for all new adherence group members and make sure they are all labelled appropriately • Deliver folders/files to focal nurse to prescribe drugs to be prepared for the adherence group visit • Deliver request or prescriptions to the pharmacy for medicines for members • Help with preparing medication for group visit • Prepare adherence session/talks for group members
Day of Group Visit	Group facilitator will give welcome talk • Weight taken and recorded into AGRregister and patient ART booklets • TB symptom screen, individually/in group/both, recorded into AGRs and patient ART booklets • Referral for clinical consultation if indicated • Distribution of medicines • Next visit date is entered on client ART appointment booklet and AGR • Facilitator should note members who missed their appointment and trigger a follow up mechanism. Group members can also conduct defaulter tracing.

APPENDIX 17 STANDARD OPERATING PROCEDURES FOR FAST-TRACK ART REFILL MODEL

Description	• This model is offered to stable ART clients who wish to refill at the facility **individually**. The minimum standard is that **clinical reviews must be conducted every six months coupled with laboratory tests as appropriate. In between the clinical visits (i.e., at every three months), refills should be fast-tracked.** Stable ART clients eligible for fast-track should be educated on basic self-care management and empowered to conduct self-assessments to decide whether they can directly pick up their ARVs from the pharmacy or return to mainstream care for unscheduled visits if unwell. Adequate client empowerment is critical to limit loss to follow up, non-adherence to their ARVs, disease progression and treatment failure.
Eligibility Criteria	• Virally suppressed (two previous consecutive tests should be < 50) • In the absence of VL, rising CD4 cell counts or CD4 counts above 350 cells/mm3 • No OIs (eg TB) • Patients who stayed > 12 months on ART • Patients with challenges related to access to health facilities • Non-pregnant, non-breast-feeding women • Adults >18 years of age
Recruitments of clients into Fast Track model	• Facility nurse should identify clients that meet the eligibility criteria and wish to be fast-tracked for their ARV refill • Patient should be booked for the next refill and clinical visits
During the clinic visit	• The client should go straight to the pharmacy to collect their medication • If unwell, the client can visit nurse/doctor for a clinical consultation • The pharmacist will update the client's care booklet
After the visit	• The patient monitoring books are taken for data entry into ART register or the ePMS

APPENDIX 18. ARV RESISTANCE TEST REQUEST FORM

NAMIBIA INSTITUTE OF PATHOLOGY LIMITED
P.O. Box 277 Windhoek, Namibia
Practice No.: 052/000/5201438
Practice No.: 075/005/0148377
Tel: +264-61-2954200
Fax: +264-61-233285

ARV RESISTANCE TEST REQUEST FORM

REFERRING DOCTOR		PRACTICE No.	
COPIES TO DR/s	HOSPITAL	WARD	
PATIENT'S SURNAME		PATIENT'S FIRST NAME	URGENT
ID No.	SEX M F	DATE OF BIRTH DD MM YY	*Contact Person*
ACCOUNT TO (Mr. / Ms)	Tick for **STATE**		*Tel No.* _____
ADDRESS			*Fax No.* _____
TEL No. (Home)	TEL (Work)	EMPLOYER	Collection Date / Time
MEDICAL AID	MEDICAL AID No.		Collected By

INSTRUCTIONS ON SPECIMEN COLLECTION

PLEASE NOTE:
BLOOD MUST BE COLLECTED IN 2 X PPT TUBES AND MUST REACH THE NIP WINDHOEK CENTRAL REFERENCE LABORATORY WITHIN 48 HOURS AFTER COLLECTION. NO SPECIMENS WILL BE REFERRED TO THE REFERENCE LABORATORY IN SOUTH AFRICA WITHOUT HIV SPECIALIST/CONSULTANT AUTHORIZATION.

PATIENT CLINICAL INFORMATION

REASON FOR RESISTANCE TESTING:

.....
.....
.....
.....
.....

MOST RECENT VIRAL LOAD & LAB NO IF AVAILABLE:

.....

CURRENT ARV REGIMEN OF THIS PATIENT:

.....
.....

INITIATION DATE OF FIRST ARV TREATMENT:

.....

PREVIOUS ARV REGIMEN OF THIS PATIENT:

.....
.....
.....
.....
.....

AUTHORIZATION REQUIRED FOR STATE PATIENTS

NAME OF SPECIALIST/CONSULTANT WITH WHOM CASE WAS DISCUSSED AND AUTHORIZED ARV RESISTANCE TESTING:

.....
.....

PHONE NUMBER OF REQUESTING DOCTOR:

.....

PHONE NUMBER OF AUTHORISING SPECIALIST/CONSULTANT:

.....

Rec 001/03 Version 1

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