National Department of Health

PAPUA NEW GUINEA NATIONAL GUIDELINES FOR HIV CARE AND TREATMENT

February 2017

Foreword

The first case of HIV was detected in Papua New Guinea three decades ago and the epidemic has been labeled both concentrated and generalized. During this period, the country has responded in several ways, including formulating and implementing a series of strategic plans. Many of the initial interventions were geared towards preventing further spread of HIV.

With improved surveillance and monitoring system the epidemic has now been found to be severe in the key population and certain vulnerable groups including women, children, youth and migrant populations. This calls for a broadening of our approach to the epidemic through the strengthening and expansion of the care and treatment component of our response.

The National HIV Program scale up plan, which includes prevention, care and treatment, is a culmination of multiple initiatives. Now we are moving forward to achieve UNAIDS 90-90-90 targets of 90% of people living with HIV knowing their HIV status, 90% of people who know their HIV-positive status accessing treatment and 90% of people on treatment having suppressed viral load, by 2020.

HIV testing and Treatment have been expanded to all the 22 provinces of the country. Over 40,000 people have been estimated as people living with HIV (PLHIV) in PNG since 1987 when the first case of HIV was detected. Twenty thousand (20,000) people including children are taking HIV antiretroviral treatment (ART).

The National Guidelines for HIV Care and Treatment in PNG are one of the many tools that have been developed to provide healthcare worker with guidance on various aspects of care and treatment. In this the fifth edition of the Guidelines, there is much wider coverage of such areas as; Adult and Paediatric HIV management including adherence issues; PPTCT; Prophylaxis and Treatment of opportunistic infections; and management of co-morbidities.

For last 5 years PNG has been implementing test and treat for all pregnant women and key populations diagnosed with HIV. These guidelines have been aligned with the WHO HIV standard guidelines and will introduce "Test and Treat" and viral load testing for all people diagnosed with HIV. With the maturing ART program HIV resistance has been detected and routine viral load testing will be strategically scaled up to all provinces while CD4 count testing is gradually phased out.

HIV is a rapidly changing and growing field and therefore frequent revision of the material contained within these Guidelines will be required. I look forward to receiving feedback from the users of the document to assist in this continual process.

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Mr. Pascoe Kase
Secretary for Health

Acknowledgement

These guidelines were prepared by the Papua New Guinea National Department of Health (NDoH). The guidelines are based on best international evidence in practice in resource limited settings and are designed to ensure that HIV Care and Treatment in Papua New Guinea is implemented in a way that will benefit both individuals and the country overall. In particular, the use of antiretroviral medications needs to be regulated to ensure that the public benefit is not eroded by the development of viral resistance.

This document would not have been possible without the contribution and commitment of the many national healthcare workers who have been at the forefront of this epidemic. In particular, acknowledgement is given to all HIV Medical Doctors, all Physicians, Pediatricians and Obstetrics and Gynecology, Sexual Health societies and NDOH HIV Care and Treatment team. The National Department of Health also appreciates and acknowledges the valuable support for developing the new guidelines by various partners including WHO, USAID, CDC, FHI360, CHAI, and Oil Search Health Foundation.

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ABBREVIATIONS

3TC	Lamivudine
ABC	Abacavir
AFB	Acid fast Bacilli
AIDS	Acquired immunodeficiency syndrome
ALT	Alanine aminotransferase
ANC	Antenatal care
ART	Antiretroviral therapy
ARV	Antiretroviral
AST	Aspartase Aminotransferase
BSL	Baseline sugar level
CD4	Cluster Differentiation 4 cells
CHW	Community Health Worker
CMV	Cytomegalovirus
CNS	Central Nervous System
COPD	Chronic obstructive pulmonary disease
CPT	Cotrimoxazole preventive therapy
CSF	Cerebral Spinal Fluid
CT	Computerized Tomography
CVD	Cardiovascular disease
CXR	Chest X-ray
DBS	Dry Blood Spot
EAC	Enhanced adherence counselling
EBV	Epstein-Barr virus
ECG	Electrocardiogram
EFV	Efavirenz
EID	Early infant diagnosis
ESR	Erythrocyte Sedimentation Rate
FBC	Full Blood Count
HBsAg	Hepatitis B Surface Antigen
HBV	Hepatitis B virus
HEO	Health Extension Officer
HIV	Human immunodeficiency virus
HIV-DR	Human immunodeficiency virus drug resistance
HPV	Human papilloma virus
HSV	Herpes Simplex Virus
HTC	HIV testing and counselling
IMAI	Integrated management of adult and adolescent illness
INSTI	Integrase strand transfer inhibitor
INH	Isoniazid
IPT	Isoniazid Prophylaxis treatment
LFT	Liver Function Test
LTFU	Lost-to-follow-up
LPV	Lopinavir

MAC	Mycobacterium Avium Complex
MNCH	Maternal, neonatal, and child health
MTCT	Mother to child transmission of HIV
MTB	Mycobacterium Tuberculosis
NAC	National AIDS Council
NCD	Non-communicable disease
NDoH	National Department of Health
NGO	Non-government organization
NNRTI	Non-nucleoside reverse transcriptase inhibitor
NRTI	Nucleoside analogue reverse transcriptase inhibitor
NVP	Nevirapine
OCP	Oral Contraceptive
OHL	Oral Hairy Leukoplakia
OI	Opportunistic infection
ORT	Oral rehydration therapy
PCP	Pneumocystis Jirovecii Pneumonia
PCR	Polymerase chain reaction
PEP	Post Exposure Prophylaxis
PGL	Persistent Generalized Lymphadenopathy
PI	Protease inhibitor
PITC	Provider initiated testing and counselling
PLHIV	People living with HIV
PMTCT	Prevention of mother-to-child transmission
PNG	Papua New Guinea
PPE	Pruritic Purpura Eruption
PPTCT	Prevention of parent-to-child transmission
r	Ritonavir boosted
RTV	Ritonavir
RFP	Rifampicin
RFT	Renal Function Test
SOP	Standard Operating Procedure
SRH	Sexual reproductive health
STI	Sexual transmitted diseases
TB	Tuberculosis
TDF	Tenofovir
UEC	Urea Electrolytes Creatinine
TLC	Total lymphocyte count
WHO	World Health Organization
VCT	Voluntary counselling and testing
VZV	Varicella Zoster Virus
VL	Viral Load

QUICK GUIDE FOR THE NATIONAL HIV CARE AND TREATMENT GUIDELINES 2017

1. Criteria for ART initiation

"Test and treat all"

ART should be initiated in all people living with HIV, regardless of WHO clinical stage and at any CD4 cell count.

2. First-line ART regimen

	Preferred first-line regimens	Alternative first-line regimens
Adults Adolescent Pregnant or breastfeeding women	TDF + 3TC + EFV	AZT + 3TC + EFV or NVP TDF + 3TC + NVP
Children 3 years to less than 10 years	ABC + 3TC + EFV	ABC + 3TC + NVP AZT + 3TC + EFV or NVP TDF + 3TC + EFV or NVP
Children less than 3 years	ABC + 3TC + LPV/r AZT + 3TC + LPV/r	ABC +3TC + NVP AZT +3TC + NVP

3. Second-line ART regimen

Note: Assess the patient carefully for clinical, immunological or virological failure. Consult ARV physician or RMO before switching to second line ARVs.

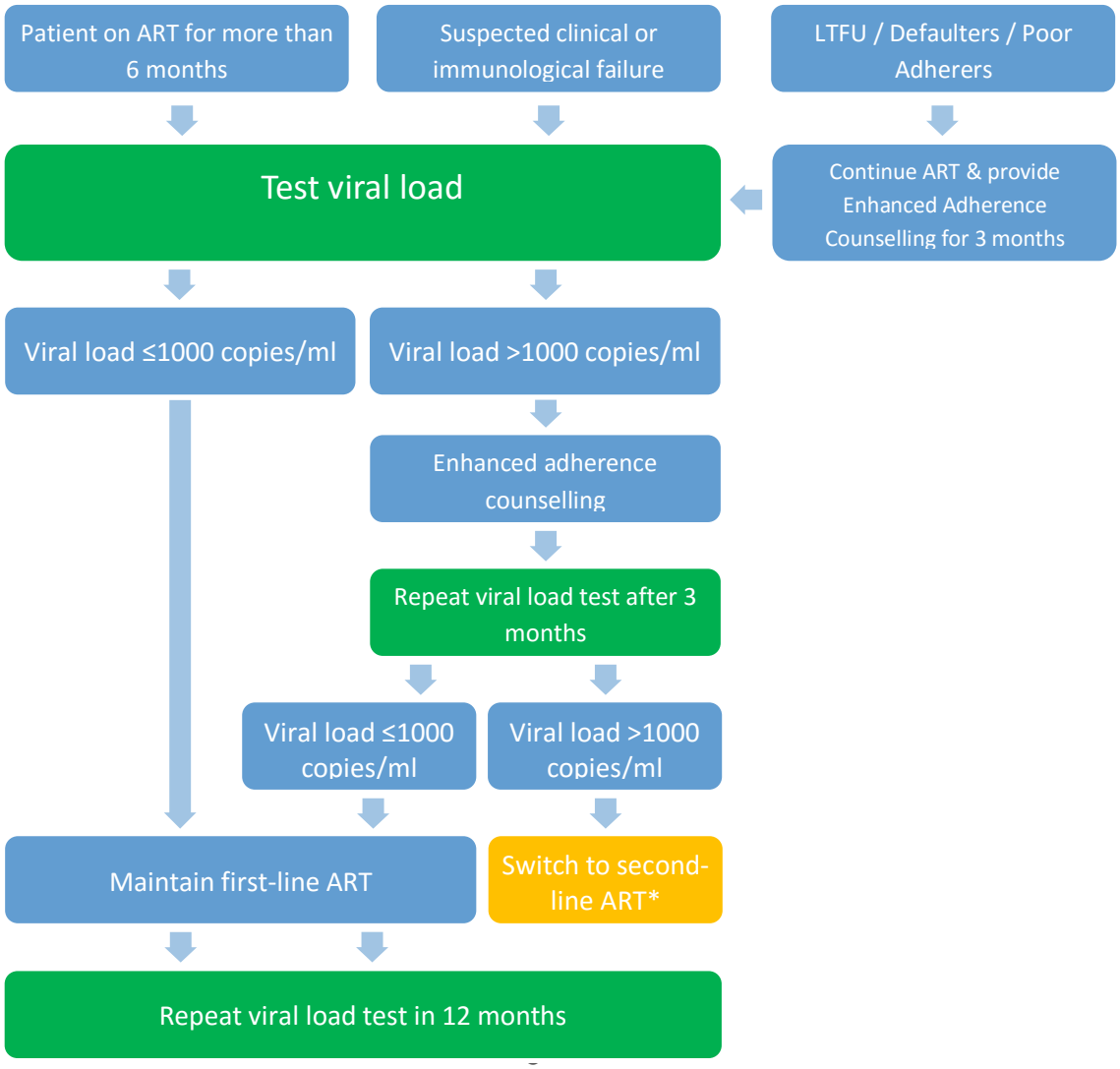
	If patient is failing first-line ART regimen below;	➡ Switch to second-line ART regimen below;
Adults Adolescent Pregnant or breastfeeding women	TDF + 3TC + EFV or NVP	AZT + 3TC + LPV/r
	AZT + 3TC + EFV or NVP	TDF + 3TC + LPV/r
Children 3 years to less than 10 years	ABC + 3TC + EFV or NVP	AZT + 3TC + LPV/r
	TDF + 3TC + EFV or NVP	AZT + 3TC + LPV/r
	AZT + 3TC + EFV or NVP	ABC + 3TC + LPV/r TDF + 3TC + LPV/r

Children less than 3 years	ABC + 3TC + LPV/r AZT + 3TC + LPV/r	If the patient has not been exposed to NVP : switch LPV/r to NVP If the patient has been exposed to NVP : maintain the failing regimen and switch LPV/r to EFV at 3 years of age
	ABC + 3TC + NVP AZT + 3TC + NVP	AZT + 3TC + LPV/r ABC + 3TC + LPV/r

4. Monitoring treatment failure with HIV viral load testing

At the sites where HIV viral load (HIV-VL) testing is available, HIV viral load testing should be used for monitoring/diagnosing treatment failure. HIV-VL testing should be done by following the national HIV-VL algorithm shown below.

At the site where HIV-VL is NOT available, CD4 cell count (every 6 months) can assist with treatment failure decisions.



*Repeat HIV-VL testing at 6 months after switching to 2nd line ART if patient is not responding, and refer the patient to medical officer for review

5. Prevention of Parent-To-Child Transmission of HIV (PPTCT)

Pregnant and breastfeeding mothers

Effective PPTCT is dependent on HIV-positive pregnant and breastfeeding women being retained on ART and virally suppressed during the critical time-limited period of pregnancy and breastfeeding. ART should be initiated urgently in all pregnant and breastfeeding women, even if they are identified late in pregnancy or in the postpartum.

Exposed infants

Infant prophylaxis regimen should be chosen based on the assessment of mother-to-child transmission (MTCT) risk as below;

Women at high-risk of MTCT	Women at low-risk of MTCT
Has received less than four weeks of ART at the time of delivery Or Has viral load >1000 copies/ml in the four weeks before delivery Or Diagnosed as HIV positive during labor or breastfeeding period following a negative prenatal HIV test result Or HIV positive mother identified for the first time during post-partum period with or without negative HIV test prenatally	Has received at least four weeks of ART before delivery Or Has viral load of less than 1000 copies/ml within four weeks prior to delivery
ARV prophylaxis for Infants at high-risk of MTCT	**ARV prophylaxis for Infants at low-risk of MTCT**
AZT and NVP for the **first 6 weeks** of life + **NVP only** for an **additional 6 weeks** **Total 12 weeks**	**NVP only** for the **first 6 weeks** of life **Total 6 weeks**

6. Prophylaxis for common coinfections

1) Cotrimoxazole preventive therapy (CPT)

Initiation of CPT

All patients are eligible for CPT initiation as soon as they have a diagnosis of HIV

Duration of CPT

CPT should not be discontinued; it should be continued throughout the persons' lifetime

2) Isoniazid prophylaxis treatment (IPT)

Eligibility for IPT

All the people living with HIV, including pregnant and breastfeeding women, who have **no** sign and symptoms suggestive of active TB are eligible for IPT
Children living with HIV who are 12 months and older should also receive IPT, and HIV-positive infants younger than 12 months should receive IPT only if they have a known TB contact.

Duration of IPT

For 6 months
Isoniazid (INH) (10mg/kg/day, maximum 300mg/day) plus Vitamin B6 or Pyridoxine (25mg daily) should be co-administered

Drug	Strength of tablet or oral liquid (mg or mg/5ml)	Number of tablets or millilitres by weight band once daily					Strength of adult tablet (mg)	Number of tablets by weight band once daily	
		3.0–5.9 kg	6.0–9.9 kg	10.0–13.9 kg	14.0–19.9 kg	20.0–24.9 kg		25.0–34.9 kg	Adolescent and Adults
Isoniazid	Tablet 100 mg	0.5	1	1.5	2	2.5	300 mg	1	1
Pyridoxine	25mg	0.25	0.25	0.25	0.5	0.5	25 mg	1	1
Co-trimoxazole	Suspension 200/40 per 5 ml	2.5 ml	5 ml	5 ml	10 ml	10 ml	–	–	–
	Tablets (scored) 800/160 mg	–	–	–	0.5	0.5	800 mg/ 160 mg	1	1

7. Post-exposure prophylaxis (PEP)

Adults and adolescents
First Choice: TDF + 3TC + EFV
Alternative Choice: AZT + 3TC + EFV

Children < 10 years
First Choice: AZT + 3TC + LPV/r*
Alternative Choice: ABC + 3TC + LPV/r or TDF** + 3TC + LPV/r

*LPV/r should not be used for premature babies and babies less than 2 weeks of age

**TDF is not recommended in children less than 3 years of age

Note: For non-occupational PEP, in addition to ARVs, PEP should includes presumptive treatment for Gonococci and Chlamydia, emergency contraceptives and trauma counseling if available.

CHAPTER ONE

ANTIRETROVIRAL DRUGS FOR HIV PREVENTION

1.1 Antiretroviral drugs for HIV prevention and treatment in PNG

The following guidelines have been prepared to guide healthcare workers in their choice of antiretroviral treatment for HIV infected individuals. The guidelines should be read in conjunction with the WHO document "Consolidated Guidelines on the use of Antiretroviral Drugs for treating and preventing HIV infection. Recommendations for a public health approach. June 2016"

This document also provides guidance on using antiretroviral drugs for treating pregnant women and preventing HIV infections in infants, feeding HIV exposed children as well as treatment of HIV infected children. It is envisaged that public, private, and NGO sectors will use these guidelines to assist them in their planning for the use of ART within the country.

Knowledge about efficacy of various antiretroviral combinations and their adverse effects is rapidly evolving, as is the price structure for individual drugs and drug combinations. These guidelines will therefore be subject to regular review by a panel of experts nominated by the National Department of Health. The guidelines will be disseminated to healthcare workers and other partners involved in the HIV/AIDS National Response.

WHO CAN PRESCRIBE ART DRUGS

Initiation of antiretroviral therapy (ART) requires a complete understanding of the rationale, pharmacology and adverse effects of medication. In addition the healthcare worker needs to be knowledgeable about the treatment of coexisting conditions and the treatment of HIV in special patient groups. The prescribers will be required to be:

1) Certified by NDOH and recognized to prescribe ART in PNG
2) Trained in HIV/AIDS care and treatment
3) Have access to sustainable drug supply and to health facilities to monitor therapy
4) Participate in the continuous medical education in the use of ARVs and monitoring of patients on HIV treatment

For this reason prescribing antiretroviral medication will be restricted to registered medical practitioners (i.e. Medical Doctors, Nurses, Health Extension Officers (HEOs), and community health worker trained in IMAI and demonstrated clinical competence through a training program approved by the National Department of Health (NDoH). A list of accredited medical practitioners will be distributed from time to time by the NDoH to pharmacies dispensing Antiretroviral (ARV) drugs. Delegation by these practitioners to appropriately trained Nurses, HEOs, and Community Health Workers (CHWs) who have support and mentoring will occur to enable timely access to treatment throughout PNG. Recognition of courses attended elsewhere will be at the discretion of the Secretary (or delegate)

of the NDoH. Applications for recognition must be made in writing to the Secretary.

WHO CAN INITIATE, MONITOR AND SUPPLY TREATMENT

Uncomplicated patients (i.e. those without OIs or those without advanced diseases [CD4<200, WHO State 3 or 4]) can have ART initiated by HEOs and Nursing Officers who have completed training and demonstrated clinical competence through a training program approved by the National Department of Health (NDoH). This initiation of ART treatment can ONLY occur after consultation with, and authorization (verbal or written) by an accredited medical practitioner. These healthcare workers may also monitor patients on ART and re-supply ART to patients they are monitoring.

1.2 Prevention of Parent-to-Child Transmission (PPTCT)

1.2.1 Four Prongs for PPTCT

Provision of antiretroviral drugs to pregnant and breast feeding mothers is effective in Preventing Parent-to-Child transmission of HIV (PPTCT). Elimination of parent-to-child transmission of HIV involves a spectrum of activities popularly summarized as the four prongs:

Prong 1: Primary prevention of HIV infection among women and men of reproductive age

This involves providing HIV prevention interventions with a focus on people in the reproductive age group.

Prong 2: Prevention of unintended pregnancies among women living with HIV

Increasing access to family planning and integration of family planning in ART programs to prevent unintended pregnancies among PLHIV.

Prong 3: Prevention of HIV transmission from mothers living with HIV to their infants

This involves provision of HIV testing early in pregnancy or breast feeding period for women who miss out on HIV testing during ANC, to identify PLHIV: Lifelong antiretroviral therapy and support should be provided to pregnant women to support adherence to treatment and retention in care during pregnancy, breastfeeding period and for life. Furthermore, mothers should receive the recommended antenatal care and the full package of safe motherhood. During labour and delivery precautions should be taken to avoid prolonged labour and and limit contact of the baby with maternal blood. Infection control procedures should be observed for all mothers in labour regardless of HIV sero-status.

Prong 4: Care, treatment and support for mothers living with HIV, their children and their families

Pregnant and breast feeding mothers living with HIV should receive the full package of HIV care and treatment as required including screening for TB, prevention and treatment of opportunistic infections (OIs), laboratory monitoring, follow up and support on adherence and retention on treatment.

Couples counselling should be provided to pregnant women and their partners. HIV positive partners should be started on ART.

Sero-discordant couples should be provided special attention to start the HIV positive individual on treatment as soon as possible to reduce the risk of transmission to the HIV negative partner.

HIV-infected infants, especially those infected *in utero*, have high mortality rates. It is important to provide HIV testing to children born to HIV positive mothers and provide them care and treatment appropriately and as early as possible. See Figure 1 for the infant HIV testing algorithm.

1.2.2 ARVs for Pregnant and breastfeeding women

When to start ART

Start lifelong ART in all HIV positive pregnant and breast feeding women as soon as possible regardless of CD4 count, WHO clinical stage or gestation age. Whenever possible, ART should be started on the same day as HIV diagnosis to provide rapid protection against maternal-to-child HIV transmission.

Efforts should be made to reduce the time between HIV diagnosis and ART initiation, because the most effective way to prevent vertical transmission of HIV is to reduce maternal viral load.

What ARV to start

Start one of the ART regimens recommended for adults/adolescent including pregnant women as soon as possible (see Chapter Two).

The preferred first-line regimen is TDF + 3TC + EFV (fixed-dose combination).

1.2.3 ARV prophylaxis for infants born to HIV positive mothers

What ARV prophylaxis should be given to HIV exposed infants

All infants born to HIV positive mothers should receive daily antiretroviral prophylaxis. However, the regimen and duration of prophylaxis depends on the infant's risk of vertical HIV transmission.

Table 1: Criteria for determining MTCT risk and prophylaxis regimens for exposed infants

Women at high-risk of MTCT	Women with low-risk of MTCT
Has received less than four weeks of ART at the time of delivery Or Has viral load >1000 copies/ml in the four weeks before delivery Or Diagnosed as HIV positive during labor or breastfeeding period following a negative prenatal HIV test result Or HIV positive mother identified for the first time during post-partum period with or without negative HIV test prenatally	Has received at least four weeks of ART before delivery Or Has viral load of less than 1000 copies/ml within four weeks prior to delivery
ARV prophylaxis for Infants with a High Risk of MTCT	**ARV prophylaxis for Infants with low risk of MTCT**
AZT and NVP for **the first 6 weeks** of life **+** **NVP only for an additional** 6 weeks **Total 12 weeks**	**NVP only** for the first **6 weeks** of life **Total 6 weeks**

Table 2: Simplified infant prophylaxis dosing

Infant age	NVP	AZT
Birth to 6 weeks		
Birth weight 2000 – 2499 g*	10mg once daily or 1ml of syrup once daily	10mg twice daily or 1ml of syrup twice daily
Birth weight ≥ 2500 g	15mg once daily or 1.5ml of syrup once daily	15mg twice daily or 1.5ml of syrup twice daily
>6 weeks to 12 weeks (for high-risk MTCT)		
	20mg once daily or 2mls of syrup once daily or half a 50mg tablet once daily	

*For infants weighting less that 2000g and older than 35 weeks of gestational age, the suggested dosage are: NVP is 2mg/kg per dose once daily and AZT 4mg/kg per dose twice daily. Consults a pediatrician or medical officer to review and prescribe ARV prophylaxis for premature infants.

Infant feeding

In Papua New Guinea, breast feeding is essential for infant survival including among infants born to HIV infected mothers.

Therefore, NDoH decided that in principle all health facilities will promote and support breastfeeding among all women irrespective of HIV sero-status. Furthermore, HIV infected breastfeeding mothers should receive ART and support to adhere to treatment especially during the breastfeeding period.

Recommendation for breast feeding among HIV infected mothers

Mothers known to be HIV-infected should exclusively breastfeed their infants for the first 6 months of life, introducing appropriate complementary foods thereafter, and continue breastfeeding for at least 12 months of life. Breastfeeding should then stop only once a

nutritionally adequate and safe diet without breast milk can be provided.

They may continue breastfeeding for up to 24 months or longer while being fully supported for ART adherence. In settings where health services provide and support lifelong ART, including adherence counselling, and promote and support breastfeeding among women living with HIV, the duration of breastfeeding should not be restricted.

When a mothers known to be HIV-infected decides to stop breastfeeding at any time should stop gradually within one month. Stopping breastfeeding abruptly is not advisable. The infants should continue receiving ARV prophylaxis based on their risk of MTCT.

If infants and young children are known to be living with HIV, mothers are strongly encouraged to exclusively breastfeed for the first six months of life and continue breastfeeding in accordance with the recommendations for the general population: that is, up to two years or beyond.

Advising mothers who are HIV uninfected or whose HIV status is unknown

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

Mothers whose status is unknown should be offered HIV testing.

Mothers who are HIV uninfected should be counselled about ways to prevent HIV infection and about the services that are available, such as family planning, to help them to remain uninfected.

Establishing a diagnosis of HIV infection in infants and children

HIV virological testing should be used to diagnose HIV infection in infants and children less than 18 months of age

It is strongly recommended that all HIV-exposed infants have HIV virological testing at four to six weeks of age or at the earliest opportunity thereafter. The country will use HIV PCR testing laboratory method on Dry Blood Spot (DBS) specimens taken from the children.

In infants with an initial positive PCR test result, it is strongly recommended that ART be started without delay and, at the same time, a second specimen be collected to confirm the initial positive PRC test result. Do not delay ART. In HIV-infected infants immediate initiation of ART saves lives and commencement of ART should not be delayed while waiting for the results of the confirmatory test.

Testing laboratories should return the test results from PCR testing in

infants to the clinic and child/mother/career as soon as possible, but at the very latest within four weeks of specimen collection. Positive test results should be fast-tracked to the mother baby pair as soon as possible to enable prompt initiation of ART.

All infants with unknown or uncertain HIV exposure being seen in health-care facilities at the first postnatal visit (usually 6 weeks), or other child health visit, should have their HIV exposure status ascertained by rapid HIV testing of the mother if she is accompanying the infants.

It is strongly recommended that infants with signs or symptoms suggestive of HIV infection undergo HIV serological testing and, if positive (reactive), PCR testing should be done.

In sick infants in whom HIV infection is being considered as an underlying cause of symptoms and signs, and PCR testing is not available. HIV serological testing and use of the clinical algorithm for presumptive clinical diagnosis of HIV infection is strongly recommended.

In breastfeeding infants or children, it is strongly recommended that breastfeeding is not discontinued in order to perform any kind of diagnostic HIV test.

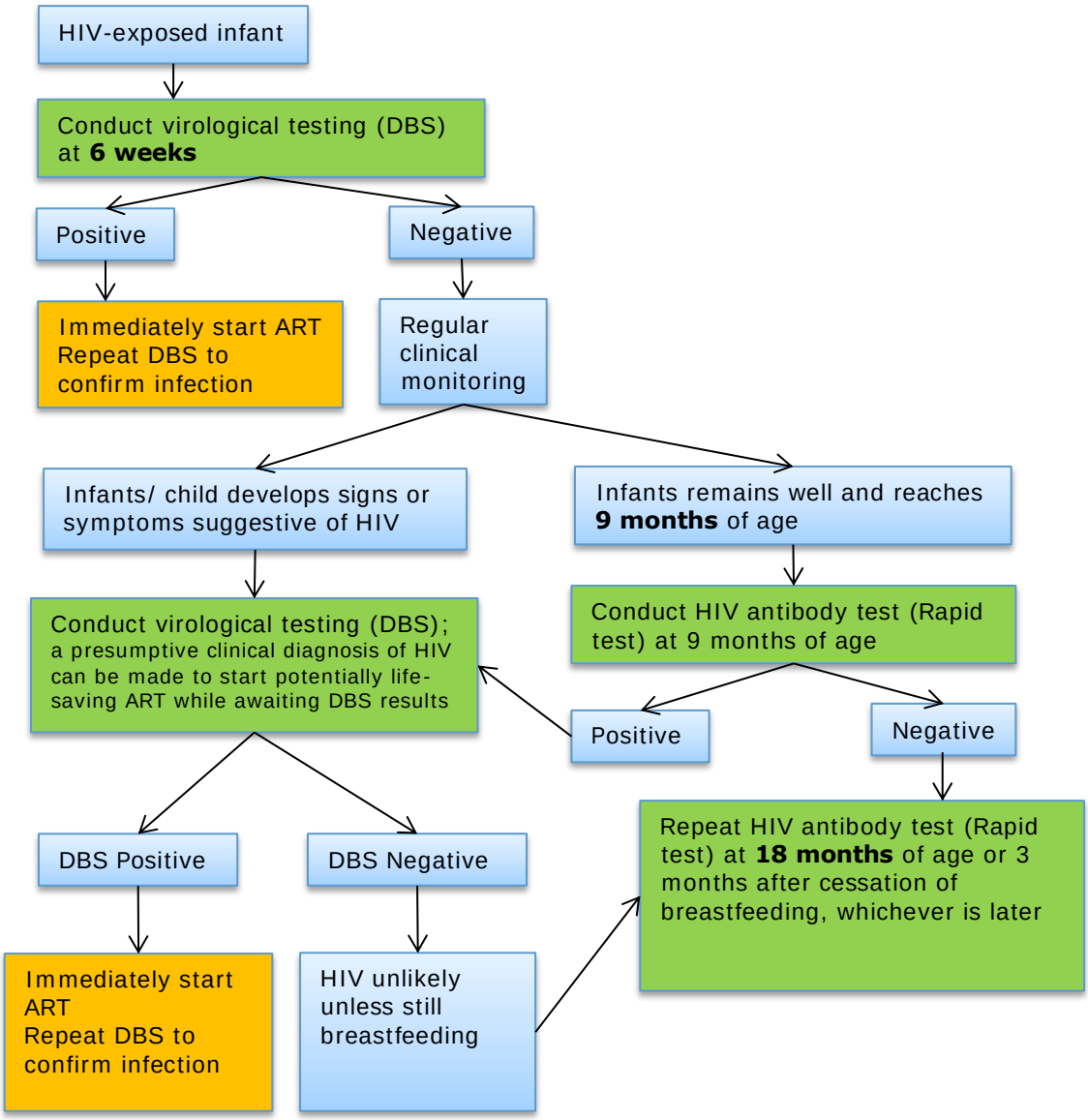
Children aged 18 months or older, with suspected HIV infection or HIV exposure, should have HIV serological testing performed according to the standard diagnostic HIV serological testing algorithm used in adults.

Table 3: Summary of HIV testing for children less than 18 months of age

Category	Test required	Purpose	Action
Infant <18 months with– unknown HIV exposure	Maternal HIV serological test (HIV Rapid Antibody test) or infant serological test, if mother is not available	To identify HIV exposure	Need virolgical test to confirm HIV diagnosis if exposed to HIV
Well, HIV-exposed infant at 4-6 weeks	Virological testing (Dried Blood Spot: DBS)	To diagnose HIV	Start ART if HIV-infected
Well, HIV exposed infant at 9 months	HIV serological test (HIV Rapid Antibody test)	To identify individuals who have persisting HIV antibodies or have sero-reverted or who have HIV infection.	If HIV seropositive, obtain virological test (DBS) and continue to follow up
Well or sick child sero-positive on rapid test between 9 and 18 months	Virological testing (Dried Blood Spot: DBS)	To diagnose HIV	Start HIV care and treatment if DBS is positive

Infant or child with signs /symptoms suggestive of HIV infection	HIV serological test (HIV Rapid Antibody test)	To confirm exposure	Perform virological tests if less than 18 months; a presumptive clinical diagnosis of HIV can be made to start potentially life-saving ART while awaiting for definitive diagnosis.
Infant or child who has completely discontinued breast feeding	Repeat testing three months or more after breast feeding cessation –usually initial HIV serological testing followed by virological testing for HIV positive child < 18 months of age	To exclude HIV after exposure ceases	Infected infants and children need to start HIV care , including ART. Children who are still breastfeeding at 18 months have ongoing HIV risk and and should be followed and tested three months after breastfeeding cessation.

Figure 1: Testing strategy for early infant diagnosis



1.3 Post-exposure prophylaxis (PEP)

The most common mode of exposure to occupationally acquired HIV is in health care and first aid settings where health care providers are at increased risk of HIV infection through exposure to infectious body fluids through accidents or when safety precautions are not followed. However the other most common method of exposure is through sexual assault.

1.3.1 Management of occupational exposure to HIV

Health care settings are the most common source of exposure to occupationally acquired HIV. Exposure prevention remains the primary strategy for reducing occupational HIV transmission. In the event that an occupational exposure occurs, the following should be done.

Treatment of an Exposure Site

Wounds and skin sites that have been in contact with blood or body fluids should be washed with soap and water; mucous membranes should be flushed with tap water. Little evidence exists that using antiseptics for wound care or expressing fluid by squeezing the wound further reduces the risk of blood borne pathogen transmission; however, the use of antiseptics is not contraindicated. The application of disinfectant agents (e.g. bleach) or the injection of antiseptics or disinfectants into the wound is not recommended.

Exposure Report

If an occupational exposure occurs, the circumstances and post exposure management should be recorded in the exposed person's confidential form for easy follow up and care. The exposure should also be documented in accordance with any institutional requirements and the appropriate authorities notified.

Evaluation of the Exposed Health Care Worker

Healthcare workers exposed to HIV should ideally be evaluated as soon as possible after their exposure in order to allow early initiation of PEP. At the latest, this must occur within 72 hours of the exposure. The exposed healthcare worker should be counseled and tested for HIV before PEP is given If the exposed health care worker were already infected at the time of exposure, he/she should commence ART (not PEP). In case of refusal to HIV test, PEP should not be started. In emergency situations where HIV testing and counselling is not readily available but the potential HIV risk is high or if the exposed person refuses initial testing, post exposure prophylaxis should be initiated and HIV testing and counselling undertaken as soon as possible. The provider should clearly document the reason why HCT was not done.

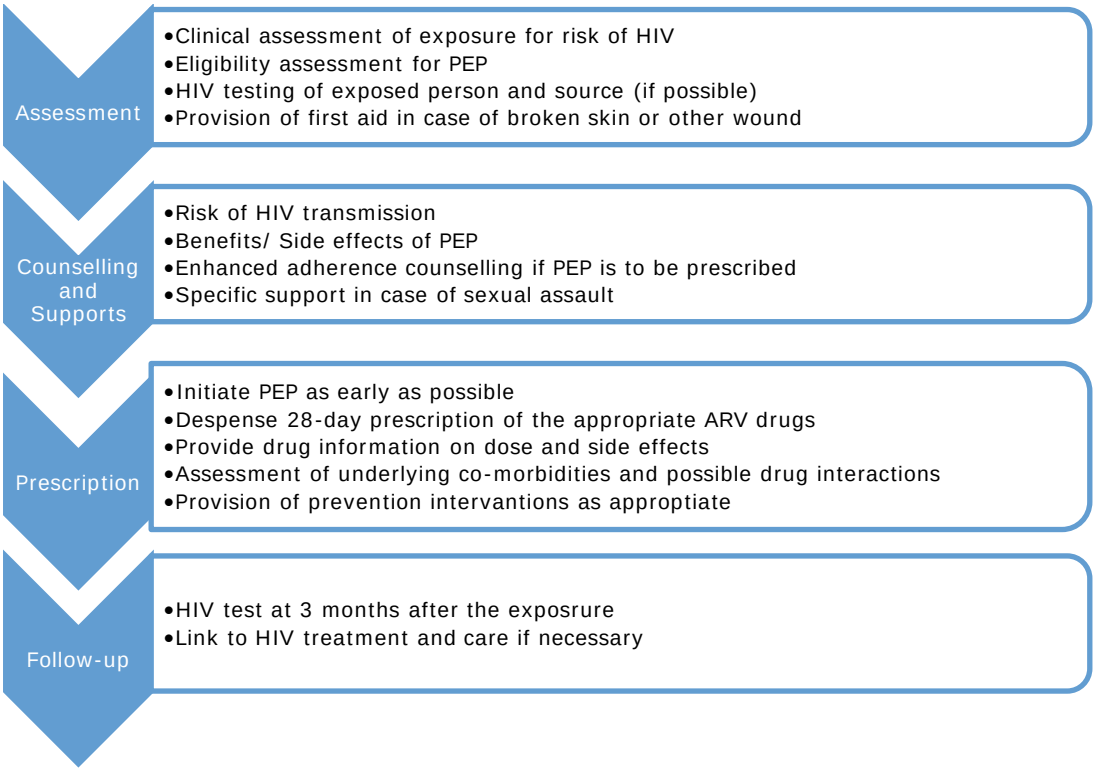
For purposes of considering HIV PEP, the evaluation also should include

the following information that might influence drug selection:

- Medications that the exposed person might be taking
- Any current or underlying medical conditions or circumstances (e.g. pregnancy, breast feeding, renal or hepatic disease)

For the healthcare setting, the risk of transmitting HBV and HCV is higher than the risk of transmitting HIV. Hepatitis B vaccination should also be considered to exposed healthcare workers not previously immunized.

Figure 2: Care Pathway for people exposed to HIV



1.3.2 PEP for victims of sexual assault

Counseling

All persons presenting to a health facility after allegedly being raped should be counseled by the examining healthcare worker about the potential risks of HIV transmission post rape. Children below 12 years of age need to be referred to the hospitals if possible.

The survivor should be provided HIV testing and counselling but lack of HTC should not cause delay in initiating PEP.

If the survivor presents shortly after the incident and is too traumatized for HTC, the survivor can decline the test. However, even though the survivor refuses HTC, they are still eligible for PEP within 72 hours of the sexual assault. Testing should be offered again at the one week follow-up

visit.

The provider should clearly document the reason why HTC was not done. Otherwise, persons who are previously known or found to be HIV positive should be referred to an appropriate health care clinic for long-term management of their HIV infection.

Since individuals with HIV are often co-infected with other pathogens, such as syphilis, gonorrhea and hepatitis B, baseline evaluation and treatment should include these pathogens. A pregnancy test, as well as prevention of unintended pregnancy should be offered to not only adults but also adolescents.

Additional Treatment and Care to PEP

In addition to PEP, women should be offered:

1) Presumptive treatment for Syphilis, Gonorrhea and Chlamydia:
   - Amoxicillin 2g plus
   - Augmentin 2 tabs plus
   - Probenecid 1g plus
   - Azithromycin 1g
     (all above orally, stat, supervised)
2) Emergency oral contraception:

   If there is a possibility that the assault may cause pregnancy and the assault occurred in the past 72 hours (as late as 5 days after sexual exposure), then after counseling and consent:

   Give Levonorgesterol tablets 3mg stat (if the person is on PEP-ARV) or 1.5mg stat (not on PEP-ARV) together with an enti-emetic as the high dose causes nausea

   The following alternatives can be used in the absence of emergency contraceptive pills.

   Combined oral contraceptives
   It may be used in the absence of emergency contraception. Give 3 hormone containing tablets stat and repeats 3 tablets after 12 hours. However, make sure that the survivor takes the actual hormone pills, not the 7 Iron/Fefol pills that are on the card.

   OR

   Progestogen only pills
   20 Microlut tabs stat and another 20 tabs after 12 hours. (This dose of Microlut does not cause nausea). (This regimen is obviously more cumbersome with the larger number of pills but is mentioned in case at a health centre there is only Microlut in stock or for any reason the woman cannot take the combined pill.)

Table 4: Antibiotic Drug Regimen for Sexual Assault by Weight

	Azithromycin	Amoxicillin	Augmentin	Probenecid
<10 kg	250 mg (1/2 tab)	1 G (4x250mg)	½ tab	½ tab
>10 kg	500 mg (1 tab)	1 ½ G (6x250mg)	1 tab	1 tab

For further details on managing sexual assault, refer to NDOH SGBV GUIDELINES

1.3.3 PEP Drug regimens

Table 5a: PEP for adults and adolescents

Triple PEP for **adults and adolescents**
First Choice: TDF + 3TC + EFV
Alternative Choice: AZT + 3TC + EFV

- Generally, the first choice (TDF+3TC+EFV) regimen should be selected.
- If second choice regimen is chosen (AZT+3TC+EFV) assess for anemia with hemocue if available. If hemocue not available, please use clinical assessment for anemia and avoid AZT only if anemia strongly suspected. If base line anaemia repeat the haemoglobin at 2 weeks for those patients on AZT as AZT can cause life-threatening anaemia if given for 4 weeks.

Table 5b: PEP for children < 10 years

Triple PEP for **children < 10 years**
First Choice: AZT + 3TC + LPV/r*
Alternative Choice: ABC + 3TC + LPV/r or TDF** + 3TC + LPV/r

*LPV/r should not be used for premature babies and babies less than 2 weeks of age
**TDF is not recommended in children less than 3 years of age

See Annex 4 (Paediatric dosing for PEP)

NVP should not be used for post exposure prophylaxis among children older than 2 years, adolescent and adults.

1.3.4 When to start PEP

PEP should be started as soon as possible after the incident (within 24 hours is ideal) but it can be given up to 72 hours.

PEP should not be given beyond 72 hours post-exposure, as there is no evidence of its effectiveness after this time.

However, for individuals who may not be able to access services

within 72 hours, providers should consider the range of essential interventions and referrals that should be offered to clients presenting after 72 hours.

1.3.5 Duration of PEP

A 28-day prescription of ARVs should be provided for HIV-PEP following initial risk assessment.

Enhanced adherence counselling should be provided to individuals initiating HIV PEP.
If possible the source case should be tested and if HIV negative, PEP can be stopped.

1.3.6 Follow-up of post exposure to HIV

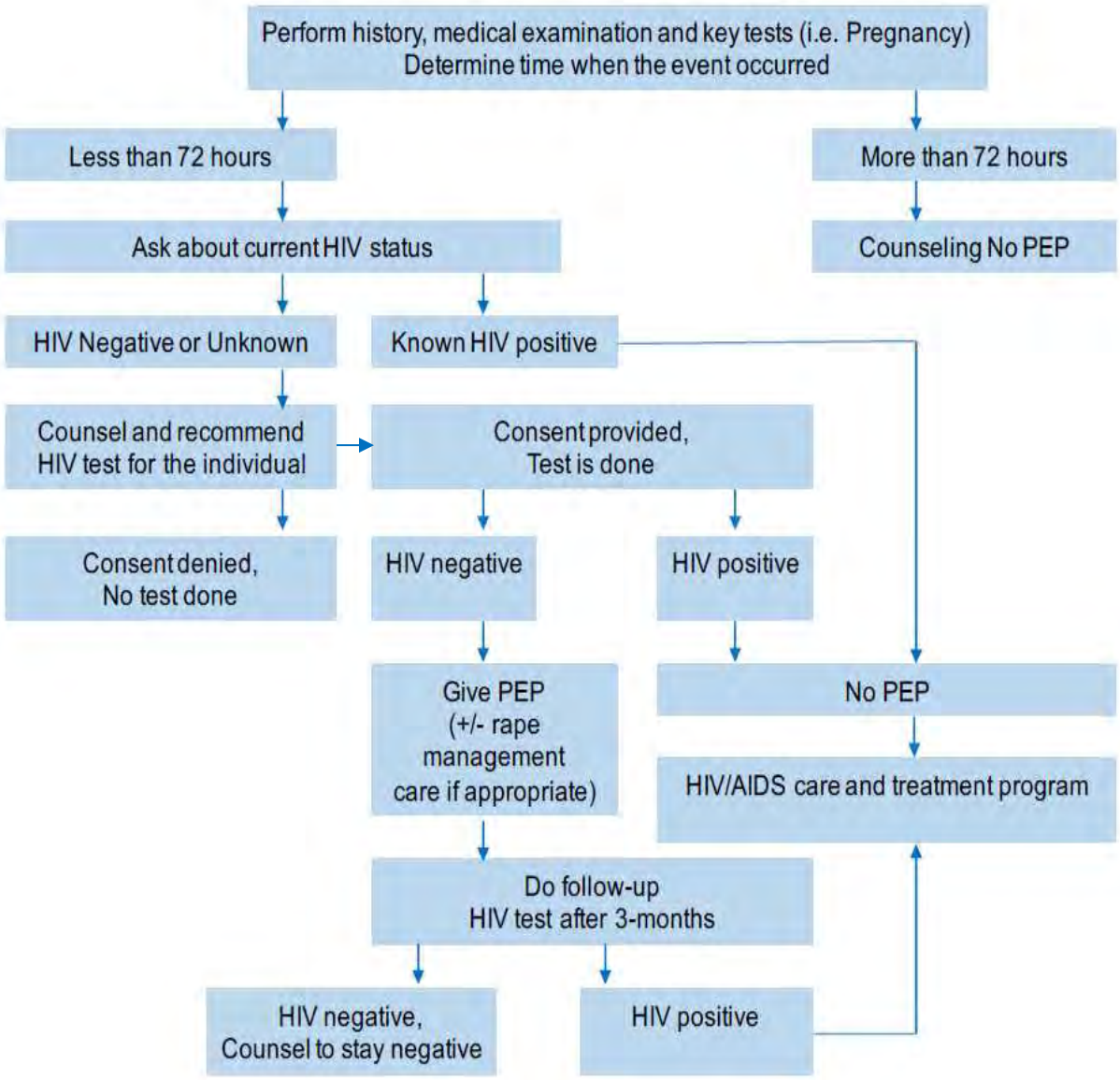
HIV testing should be provided 3 months after the exposure. Repeated testing of negative individuals is not necessary except if the individual has ongoing high risk HIV behavior or can identify a specific incident of HIV exposure in the past 3months.

Individuals diagnosed with HIV following a PEP should be started on HIV treatment.

Any source person confirmed to be HIV positive should also be started on treatment.

Counsel the client to reduce further exposure to HIV.

Figure 3: Algorithm for assessment before PEP initiation



CHAPTER TWO

ANTIRETROVIRAL DRUGS FOR HIV TREATMENT

2.1 ART in adults and adolescents including pregnant and breastfeeding women

2.1.1 WHEN TO START TREATMENT

ART should be initiated in all adults living with HIV, regardless of WHO clinical stage (Annex 1) and at any CD4 cell count.

In addition, when the patient initiates ART, those conditions below need to be assessed. However, the assessment should not delay the commencement of ART.

- **The patient has written confirmation of HIV positive status**
- Baselines tests must be done (refer 2.1.2)
- Any opportunistic infection has been or is being treated/stabilized
- The patient has been prepared and is ready for ART therapy by undergoing adequate counselling
- The patient has a treatment supporter
- There is a reliable drug supply

2.1.2 BASELINE TESTS (BEFORE ART INITIATION)

The minimum clinical and laboratory tests need to be done as a baseline data before initiating antiretroviral therapy.
However, lab tests should not be a pre-requisite to the initiation of ART.

- Baseline CD4 cell count

- Haemoglobin test for starting AZT
- Renal Function tests - creatinine clearance and electrolytes tests for TDF
- Liver function test - serum alanine (ALT) or aspartase aminotransferase (AST) for NVP

- Screening for TB
  - Symptom screening
  - Sputum smear for AFB and CXR if TB is suspected by symptom screening
  - GeneXpert MTB/RIF® examination needs to be done for suspected cases if available

- Screening for STIs
  - Syphilis serology (Rapid test, TPHA)
  - Syndrome-based diagnosis

- Pregnancy test for women

- Screening for non-communicable diseases
  - Blood pressure measurement
  - Blood glucose

Additional basic testing, where available, can include:

- Hepatitis B surface antigen (HBsAg)
- Pap Smear (if available)

2.1.3 WHAT DRUGS TO USE (FIRST LINE THERAPY)

Tenoforvir (TDF) + Lamivudine (3TC) + Efavirenz (EFV) as a fixed-dose combination is recommended as the preferred option for naïve adults and adolescent patients to initiate ART.

If TDF + 3TC + EFV is contraindicated or not available, one of the following alternative options is recommended:

- Zidovudine (AZT) + Lamivudine (3TC) + Nevirapine (NVP)
- Zidovudine (AZT) + Lamivudine (3TC) + Efavirenz (EFV)
- Tenofovir (TDF) + Lamivudine (3TC) + Nevirapine (NVP)

Stavudine (d4T) should no longer be used due to common metabolic toxicities.

See Annex 3 (Drugs formulations and doses for adults and adolescents)

ART for HIV/HBV co-infection

- Use TDF + 3TC + NVP or EFV antiretroviral regimen
- Evidence of severe chronic liver disease should be monitored, because these individuals are at greater risk of mortality from liver disease

ART for HIV/TB co-infection

- Use TDF + 3TC + EFV (preferred) or AZT + 3TC + EFV (alternative)
- If a NNRTI regimen is used, EFV is the preferred drug, as its potential for aggravating the hepatotoxicity of TB treatment appears smaller than that of NVP
- Start TB treatment first, followed by ART as soon as possible afterwards (and within the first 8 weeks). Those with profound immunosuppression (i.e. CD4 counts less than 50) should receive ART immediately within the first 2 weeks of initiating TB treatment
- If a PI based regimen needs to be administered concurrently with Rifampicin, an increased daily dose of LPV/r (800mg/200mg, twice daily) can be considered for the duration of Rifampicin treatment. Patients need close clinical and laboratory monitoring for hepatotoxicity when boosted PIs are administered concurrently with Rifampicin

2.2 ART IN CHILDREN

2.2.1 BACKGROUND ON ART IN CHILDREN

Children have specific physiological, clinical, practical and social issues to consider when treating HIV-infected children with ART. All children and infants diagnosed with HIV are eligible for ART, regardless of CD4 count or clinical staging (Annex 2).

The following are some of these specific issues.

a. Children metabolize drugs differently from adults.

b. For children under 18 months of age , detection of HIV DNA by PCR at 6 weeks of age is the gold standard diagnostic test for diagnosing HIV.

c. The natural history of the infection is different from adults. The disease progression in infants is more rapid and aggressive. Children are also more susceptible to neurologic complications and some WHO staging conditions are different.

d. This may also lead to adherence issues hence adherence counselors working with children should receive training specific for this population.

e. The absolute lymphocyte count is also higher and more variable in children than in adults. Age related thresholds have been developed to be used where CD4 counts are not available. These are less accurate and are not useful markers for longitudinal follow up.

As a general principle, the ART regimen that the parents or guardians are, or will be taking, should also be taken into consideration when deciding on the most appropriate regimen for the child. In determining the initial choice of ART the availability of a suitable formulation and the simplicity of the dosage schedule are also important and should be taken into consideration.

2.2.2 WHEN TO START ART IN CHILDREN

Initiating antiretroviral therapy in itself is a complex undertaking. To prescribe ART to the children of PNG whose compliance with routine drug regimens is in general, already a challenge will be a major task. Therefore in order to gain the benefits of being on ART and to minimize the risk of poor adherence and subsequent viral resistance, the use of both clinical and "social" selection criteria are recommended.

Initiation of ART in infants and children

ART should be initiated in all infants and children living with HIV, regardless of WHO clinical stage or at any CD4 count.

Initiation of ART in infants under 18 months of age

For infants and children aged under 18 months definitive diagnosis can be made at 6 weeks of age or at the earliest opportunity thereafter using HIV DNA PCR. However if there are symptoms suggestive of HIV infection a presumptive clinical diagnosis of severe HIV infection may be necessary in order to permit decision-making on the need for the initiation of potentially life-saving ART whilst arranging for a definitive diagnosis.

A presumptive diagnosis of HIV disease should be made if:

a) The infant is confirmed as being HIV antibody positive and
b) Diagnosis of any AIDS indicator condition can be made or
c) The infant is symptomatic with 2 or more of the following:

- oral thrush
- severe pneumonia
- severe sepsis/bacterial infection
- failure to thrive or wasting or AIDS indicator condition (See Annex 2 for AIDS indicator condition)

Confirmation of the diagnosis of HIV infection should be sought, either by DNA PCR as soon as possible or HIV antibody at 18 months of age

2.2.3 WHAT TO START ARV in Children

The following regimens should be given based on the age of the child.

ART regimens for children younger than 3 years old

Table 6a: Summary of ART regimen for children less than 3 years old

Preferred regimens	ABC[a] + 3TC + LPV/r[b] AZT + 3TC + LPV/r[b]
Alternative regimens	ABC[a] + 3TC + NVP AZT + 3TC + NVP
Special circumstances[c]	ABC + 3TC + AZT (only during TB Treatment)

[a] based on general principle of using non-thymidine analogues in second line regimens, ABC should be considered as the preferred NRTI whenever possible. The CHAIN group developed these recommendations. Availability and costs should be carefully considered

b LPV/r liquids should be avoided in premature babies (born one month or before the expected date of delivery)

c Special circumstances may include where preferred or alternative regimens are not available or suitable because of significant toxicities, anticipated drug interactions, drug procurement and supply management issues, or for other reasons.

ART regimens for children 3-10 years old

Table 6b: Summary of ART regimen for children 3-10 years old

Preferred regimens	ABC[a] + 3TC + EFV
Alternative regimens	AZT + 3TC + NVP or EFV ABC[a] + 3TC + NVP TDF + 3TC + EFV or NVP
a These recommendations apply to children and adolescents who are initiating first-line ART. Children and adolescents who are already taking ABC-containing regimens can safely substitute TDF for ABC, if this is needed.	

See Annex 4 (Drugs formulations and doses for children and Paediatric ARV dosing schedule)

Children with TB/HIV co-infection

It is recommended that any child with active TB disease should begin TB treatment immediately, and start ART as soon as tolerated after 2 weeks of starting TB therapy, irrespective of the CD4 count and clinical stage.

More than 3 years
The preferred ARV regimen for child older than 3 years of age with TB is 2NRTIs + EFV or Triple NRTIs.

- If the child is receiving EFV regimen, continue the same regimen (ABC+3TC+EFV, AZT+3TC+EFV or TDF+3TC+EFV)
- If the child is receiving NVP regimen, substitute with EFV
  Or
- Triple NRTI (AZT+3TC+ABC)

Younger than 3 years
The preferred ARV regimen for infants and children less than 3 years of age with TB is Triple NRTIs (AZT+3TC+ABC).

HIV-infected infants and children who develop TB while receiving ART should be started on TB treatment immediately upon the diagnosis of TB and ART should continue.

2.2.4 Assessment points for initiation of ART in children

i. Children considered for treatment should have easy access to or in walking distance from the ART distributing health facility.

ii. In the situation in which the child's parents were detected in the antenatal period, they should have had adequate (ideally 2-3 visits) counseling in the antenatal period followed by 2-3 sessions of follow-up counseling after birth. Information given should include details of ART, however do not delay commencing ART.

iii. Children born to parents detected to be HIV positive in the

antenatal period must have had regular monthly follow-up after birth.

iv. Parents (not on ART) of children whose diagnosis is made during an illness should have ongoing counseling sessions however ART must be commenced after HIV diagnosis is made. .

v. Parents are required to nominate a treatment support person who should also attend their counseling sessions. This is to ensure continuation of treatment in the event that the parents become ill.

vi. The family should be referred to a community-based organization within the area in which they live. The organization must be credible and acceptable to the family and be able to provide continued support outside of the hospital.

These assessment points are guides to consider for better treatment outcome. Each case should be assessed on individual bases. It should not be used to stop initiation of treatment

2.2.5 BASELINE TESTS IN CHILDREN (BEFORE STARTING ART)

- Full blood count (HB, TLC, WBC and Differential)
- CD4 if available with follow up every 6 to 12 months
- Electrolytes, Urea, Creatinine, LFT (every 6 months) and Blood Glucose
- Sputum for AFB and/or CXR and /or Gene-Xpert (if available)

In general children metabolize NNRTI and PI drugs faster than adults and require weight for kilogram higher doses than adults to achieve appropriate drug levels. ABC causes a potentially fatal hypersensitivity reaction in 5% of patients. This usually occurs in the first six weeks of treatment. Treatment should not be restarted if hypersensitivity has occurred.

NVP can be used for children of all ages while EFV should only be used in children over 3 years because of the lack of pharmacokinetic data for children under 3 years. NVP should be given as once per day for the first 14 days to reduce toxicity and then twice daily after 14 days.

Note: there is no need for 2-week NVP lead for those children less than 3 years old already on TB treatment containing Rifampicin as Rifampicin induces CYP450.

AZT is associated with anemia due to bone marrow toxicity in 5-10% of patients. If hemoglobin prior to initiation is less than 8g/dl (without a correctable cause) combination with ABC or TDF should be used.

TDF is not recommended for children under 3 years.

2.3 Drugs interactions

All antiretroviral medications have the potential to interfere with other medications. Particular drug interactions that more commonly will be encountered in PNG are listed in the following table.

Table 7: Drug Interactions

Drug	ART Agent	Interaction	Suggested Action
Alpha blockers, beta blockers and calcium channel blockers	All PIs and Efavirenz	Hypotension and syncope due to decreased drug clearance, at times potentially life threatening	Monitor closely and adjust dose if signs of toxicity
Amitriptyline	RTV	Over sedation	Reduce dose
Anti-psychotic drugs	RTV	Increased potential for side effects due to decreased drug clearance	Monitor closely and adjust dose if indicated, particularly with Haloperidol
Benzodiazepines especially Midazolam	All PIs	Over sedation and risk of respiratory depression	Avoid the use of these drugs unless clinically indicated i.e. Status epilepticus
Cimetidine	RTV	Increased potential for side effects due to decreased drug clearance	Monitor closely and adjust dose if indicated
Ergometrine	All PIs and EFV	Ergotism due to decreased clearance of ergot alkaloids	Use syntocin, and/or Misoprostol as clinically indicated
Ketonconazole	NVP, SQV, RTV and EFV	Potential for toxicity due to decreased drug clearance	Ketoconazole should not be used with NVP due to risk of hepatotoxicity Max. dose of 200mg/day if used with PI's. Fluconazole is recommended with PI's

Nonsteroidal anti-inflammatory drugs	RTV	Increased potential for side effects due to decreased drug clearance	Avoid the use of these drugs unless clinically indicated and no alternative available
Oral Contraceptives (OCP)	EFV, NVP, LPV, and RTV	Failure of OCP due to increased clearance	Alternate or additional form of contraception
Oral hypoglycaemics	All PIs	Risk of hypoglycaemia due to decreased drug clearance	Close monitoring of BSL
Pethidine	RTV	Increased potential for side effects due to decreased drug clearance especially seizures	Avoid the use of this drug unless clinically indicated and no alternative available
Phenytoin and Carbamazepine	LPV, RTV, EFV and possibly other ART agents	Two-way interaction- LPV, EFV and Phenytoin have increased Clearance RTV may reduce Carbamazepine clearance	Monitor clinically for toxicity or reduced levels Monitor serum anticonvulsant drug levels if able
Prednisone and Dexamethasone	RTV and SQV	Increased potential for side effects due to decreased drug clearance	Monitor closely and adjust dose if indicated
Rifampicin	PIs	Increased PI levels due to decreased drug clearance	Avoid combining Rifampicin and PI's. EFV preferred drug for co-administration
Thyroid Replacement Therapy	PIs	Increased potential for side effects due to decreased drug clearance	Monitor closely and adjust dose if indicated
Warfarin	RTV	Unpredictable levels	Monitor closely

2.4 Adherence

For patients on antiretroviral therapy (ART), medication adherence is critically important to treatment success. Patients for whom there is concern about adherence should not be commenced on ART. Near-perfect pill taking is required to achieve viral suppression and to avoid the emergence of viral resistance. When patients skip doses and do not take their ART medications regularly, viral resistance develops and the patient does not improve or condition may even deteriorate while on treatment. Missing doses is a common problem, and all patients need help to take 100 percent of their medicines as prescribed. The risks of non-adherence are so clear and so large that adherence assessment and support are integral parts of HIV care programs worldwide. Missing as little as 3 doses per month can trigger drug resistance. Antiretroviral therapy should not be prescribed in the absence of adherence support, including a treatment supporter. Ongoing counseling about the importance of adherence, the role of a treatment supporter in assisting with adherence, and the measurement of adherence are an essential component of HIV Care and Treatment.

2.5 Data collection

It is very important that ART use is monitored within PNG to define how improvements can be made in the management of the HIV/AIDS conditions. It will be a requirement for healthcare workers to maintain a database of patients on treatment and forward specified data to NACS/NDOH when and as required. For more detailed guidelines and procedures on ART (or HIV treatment) data collection, please refer to the Standard Operating Procedures (SOPs) for HIV Routine Data Reporting (NDoH, 2013). The SOPs includes the following components:

- How to fill out ART Monthly Data Collection Sheet (Form SURV1,2 and 4)
- How, where, and when to report Form SURV1,2 and 4
- How to store, manage and secure the SURV1, 2 and 4 data and forms
- How to request Form SURV1, 2 and 4, and ARVs and other supplies

Training of HCW at clinics will be important to be able to collect, enter quality data in ART site data bases. The staff at clinic should be able to conduct clinic monthly analysis of ART data in their specific clinics to improve the quality of services delivered. They should be able to conduct patients' retention rates analysis in their clinics to inform their quality of their programmes.

CHAPTER THREE

MONITORING DRUG TOXICITY AND TREATMENT FAILURE

3.1 Monitoring ART (After ART initiation)

Symptom directed lab monitoring for safety and toxicity is recommended for those on ART. Other testing may be added according to the patients' clinical condition.

Monitoring Drug Toxicity

- Haemoglobin test for starting AZT
- Renal Function tests - creatinine clearance and electrolytes tests for TDF
- Liver functions test - serum alanine (ALT) or aspartase aminotransferase (AST) for NVP

Monitoring Treatment Failure

- Clinical monitoring should be mandatory for all the health facility condition.

- CD4 cell count and/or HIV viral load (VL) testing should be alternated to monitor treatment failure based on the health facility condition.

- The site where HIV-VL testing is available
    - HIV-VL testing is used for monitoring treatment failure
    - CD4 cell count monitoring can be stopped where routine HIV-VL testing is available
    - HIV- VL testing should be done by following the national HIV-VL algorithm (see Figure 4)
    - HIV VL testing is not essential as a baseline
    - In the case of suspected treatment failure and at routine intervals (per the table), viral load testing is done to assess for treatment failure. If the VL is greater than 1,000 copies/mL, enhanced adherence counselling (EAC) must be done for adherence and VL testing is done after 3 months
    - If the VL is still greater than 1,000 copies/mL at this second test, this confirms treatment failure

- The site where HIV-VL is NOT available
    - CD4 cell count (every 6 months) can assist with treatment failure decisions
    - Targeted VL, however, can be done any time there is suspected treatment failure

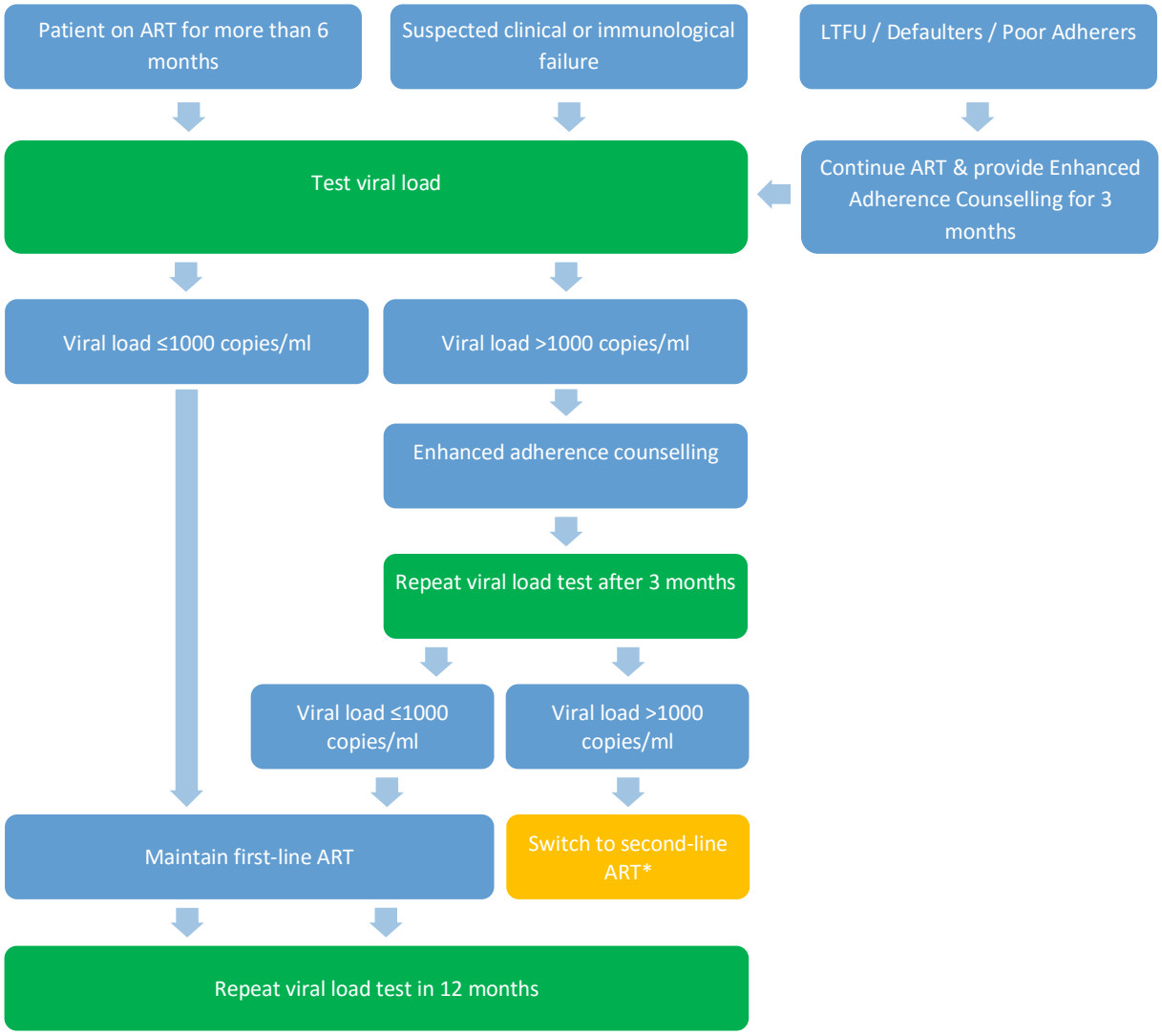
HIV positive patients who are not on ART should be monitored in accordance with the following chart. As an example, some routine tests to be performed during the course of the treatment are shown in Table 8.

Table 8: Schedule of Routine Laboratory Monitoring of ART

Laboratory test	*Baseline*	*At 3 months*	*At 6 months*	*At 9 months*	*At 12 months*	*Every 6 months thereafter if stable*	*Every 12 months thereafter if stabl*
CD4	✓		✓		✓	✓	
Viral Load			✓				✓
Hb	✓	✓	✓	✓	✓	✓	
Liver Function	✓	✓	✓	✓	✓	✓	
Renal Function Test	✓	✓	✓	✓	✓	✓	

Note: where HIV-VL is NOT available, CD4 cell count (baseline and every 6 month) can assist with treatment failure decisions; where routine HIV-VL is testing is available, follow-up CD4 cell count monitoring can be stopped (baseline CD4 cell count should be done).

Figure 4: HIV Viral Load Testing Algorithm



*Repeat HIV-VL testing at 6 months after switching to 2nd line ART if patient is not responding, and refer the patient to medical officer for review

3.2 Drug substitution

3.2.1 Drug Toxicity

Substitution of single agents can be made if drug toxicity occurs and can be ascribed to a component of the triple therapy given as first line.

Table 9a: Drug toxicity and substitution for adults and adolescent

If toxicity…	Due to …	Then switch to …
TDF/3TC/EFV	EFV – Unremitting CNS toxicity	NVP
	TDF – see above	AZT
TDF/3TC/NVP	TDF – Renal failure	AZT Do not initiate TDF at Creatinine clearance (CrCl) <50 mL/min, uncontrolled hypertension, untreated diabetes, proteinuria, or presence of renal failure
	NVP – hepatotoxicity NVP – Steven Johnson Syndrome	EFV If hepatotoxicity is mild, consider substitution with EFV, including in children 3 years and older LPV/r For severe hepatotoxicity and hypersensitivity, substitute with LPV/r
AZT/3TC/NVP	AZT – Bone Marrow Suppression	TDF
	NVP – see above	EFV or LPV/r

Table 9b: Drug toxicity and substitution for children

If toxicity…	Due to …	Then switch to …
TDF/3TC/NVP	TDF – Renal Failure	AZT or ABC Do not initiate TDF at CrCl <50 mL/min, uncontrolled hypertension, untreated diabetes, proteinuria, or presence of renal failure
	NVP – hepatotoxicity NVP – Steven Johnson Syndrome	EFV If hepatotoxicity is mild, including in children 3 years and older LPV/r Severe hepatotoxicity and hypersensitivity, and in children under the age of 3 years
AZT/3TC/NVP	AZT – Bone Marrow Suppression	ABC or TDF TDF not recommended for children < 3 years
	NVP – see above	See above
TDF/3TC/EFV	EFV – CNS toxicity →	NVP For CNS symptoms with EFZ, dose EFZ at night-time
ABC/3TC/EFV ABC/3TC/NVP	ABC - Hypersensitivity	AZT or TDF TDF not recommended for children < 3 years
	EFV – see above	see above
	NVP – see above	see above

3.2.2 Treatment Failure

Definition of treatment failure

Failure of a drug regimen is usually on the basis of viral resistance, and can only be confirmed by documentation of a rising viral load. In the absence of this measurement, a lack of clinical response (such as persistent diarrhoea, weight loss, appearance of a previous or new OI) after 6 months of treatment in a patient adherent to medication is likely to be due to viral resistance. If the treatment failure is due to non-adherence, consideration should be given to measures for adherence can be improved. Treatment failure using clinical and immunological criteria should not be used before six months as immunological reconstruction syndrome (IRIS) may be a confounding factor and responsible for the apparent treatment failure. In Papua New Guinea treatment failure will be recognized by using viral loads which will be at the regional laboratories in conjunction with CPHL.

Table 10: Clinical, Immunological and Virological Failure

Failure	Definition	Remarks
Clinical Failure	**Adults and adolescents** New or recurrent clinical event indicating severe immunodeficiency (WHO stage 3 and 4 condition) after 6 months of effective treatment **Children** New or recurrent clinical event indicating advanced or severe immunodeficiency (WHO clinical stage 3 and 4 clinical condition with the exception of TB) after 6 months of effective treatment	The new or recurrent condition must be distinguished from immune reconstitution syndrome For adults, certain WHO clinical stage 3 conditions (pulmonary TB and severe bacterial infections) may also indicate treatment failure*
Immunological Failure	**Adults and adolescents** CD4 cell count at or below 250 cells/mm^3 following clinical failure; or persistent CD4 levels below 100cells/mm^3 **Children** Younger than 5 years Persistent CD4 levels below 200 cells/mm^3 Older than 5 years Persistent CD4 levels below 100 cells/mm^3	Where viral load testing is not available, CD4 monitoring and clinical monitoring are recommended Without other concomitant or recent infection to explain transient CD4 cell decrease; previous guidelines defined immunological failure based on a fall from baseline, which is no longer applicable in the context of CD4-independent treatment initiation Current WHO clinical and immunological criteria have low sensitivity and positive predictive value for identifying individuals with virological failure. There is currently no proposed alternative definition of treatment failure and no validated alternative definition of immunological failure
Virological Failure	Viral load above 1000 copies/mL based on two consecutive viral load measurements in 3 months, with adherence support following the first viral load test	Where available, use viral load (VL) to confirm treatment failure An individual must be taking ART for at least 6 months before it can be determined that a regimen has failed

* See the list of clinical conditions associated with advanced or severe HIV disease associated with immunodeficiency in Annex 1

3.3 Second-line regimen for adults and adolescent

WHO recommends that the entire regimen be changed if treatment failure occurs. The new second-line regimen in adults and adolescent should consist of new 2 nucleoside reverse-transcriptase inhibitors (NRTIs) plus a ritonavir-boosted protease inhibitor (PI).

3.3.1 Choice of new 2 NRTIs

The following sequence of second-line NRTIs option is recommended:

- After failure on a TDF + 3TC –based first-line regimen, use AZT + 3TC as the new 2 NRTIs in second-line regimens
- After failure on an AZT + 3TC –based first-line regimen, use TDF + 3TC as the new 2 NRTIs in second-line regimens

3.3.2 Choice of PI

- Use a ritonavir-boosted protease inhibitor (PI/r)
- LPV/r is the preferred boosted PI for second-line ART

3.3.3 Second-line for co-infected patients

Second-line for HIV/TB Co-infection

- Choice of new 2 NRTIs is the same as mentioned above
- If rifampicin is used for TB treatment, the dose of LPV/r needs to be **doubled** (**LPV/r 800mg/200mg twice daily**)
- If rifabutin is available for TB treatment, standard second-line regimen is recommended

Second-line for HIV/HBV Co-infection

- **AZT + TDF + 3TC + LPV/r** is the second-line regimen for HIV/HBV co-infection
- TDF with 3TC are active against HBV. Treatment of HIV/HBV coinfection without the use of TDF in the regimen may lead to flares of hepatitis B due to ART-associated immune reconstitution. Similarly, treatment discontinuation, especially of 3TC, has been associated with HBV reactivation, ALT flares and, in rare cases, hepatic decompensation.
- If ARV drugs need to be changed because of treatment failure or toxicity, then TDF with 3TC should be continued together with the new ARV drugs.

Table 11: Preferred second-line ART regiments for adults and adolescent

Target population	Preferred second-line regimen	
Adults and adolescent	If AZT has been used in first-line ART - AZT + 3TC + EFV or NVP	TDF + 3TC + LPV/r
	If TDF has been used in first-line ART - TDF + 3TC + EFV or NVP	AZT + 3TC + LPV/r
Pregnant or breast feeding women	Same regimens as recommended for adults and adolescents	
HIV/TB co-infection	If rifampicin is used for TB treatment	Same 2 NRTIs as recommended for adults and adolescent plus double-dose LPV/r needs (LPV/r 800mg/200mg twice daily)
	If rifabutin is available for TB treatment	Same LPV/r containing regimen as recommended for adults and adolescents
HIV/HBV co-infection	AZT + TDF + 3TC + LPV/r	

3.4 Second-line regimen for children

WHO recommends that the entire regimen be changed if treatment failure occurs. The new second line regimen has to involve drugs that retain activity against the patient's virus strain and should ideally include a minimum of three active drugs, on of them drawn from a new class, in order to increase the likelihood of treatment success and minimize the risk of cross-resistance.

The Protease Inhibitor (PI) class is thus reserved for second line treatments, preferably supported by two new NRTIs. Definitive diagnosis of failure of a drug regimen is the same as in adults.

The important clinical signs of response to therapy include improvement in growth for those failing to thrive, improvement in neurological symptoms, development in those with delayed developmental milestones and decrease in the frequency of opportunistic infections.

Clinical monitoring should include weight and height growth, developmental milestones and neurological symptoms. Children with evidence of developmental delay should be referred to a paediatrician for more detailed evaluation. In the absence of CD4 cell assays charted height and weight growth may be the most important indicator of response to therapy. Monitoring height and weight for height can also provide additional information. It is recommended that all children on ART have their WEIGHT and (if possible) HEIGHT measured on each visit to the clinic.

Table 12a: Second-line ART regiments for children 3 years to less than 10 years

Failing first-line regimen	Second-line regimen
ABC + 3TC +EFV or NVP TDF + 3TC + EFV or NVP	AZT + 3TC + LPV/r
AZT + 3TC + EFV or NVP	ABC + 3TC + LPV/r TDF + 3TC + LPV/r

Table 12b: Second-line ART regiments for children less than 3 years

Failing first-line regimen	Second-line regimen
ABC + 3TC + NVP	AZT + 3TC + LPV/r
AZT + 3TC + NVP	ABC + 3TC + LPV/r
ABC + 3TC + LPV/r	If the patient has not been exposed to NVP : switch LPV/r to NVP If the patient has been exposed to NVP : maintain the failing regimen and switch LPV/r to EFV at 3 years of age
AZT + 3TC + LPV/r	

3.5 Third-line regimens

The Government has not provided recommendations for third-line ARV regimen given the costs and capacity to monitor patients. However, the National HIV programme should consider developing policies for third-line ART. If available, third-line regimens should include new drugs with minimal risk of cross-resistance to previously used regimens, such as integrase strand transfer inhibitors (INSTIs) and second-generation NNRTIs and PIs.

Patients failing a second-line regimen with no new ARV options should continue with a tolerated regimen.

CHAPTER FOUR

PROPHYLAXIS FOR COMMON COINFECTIONS

4.1 Cotrimoxazole Preventive Therapy (CPT)

Many opportunistic infections in HIV infected individuals can be prevented by the use of Cotrimoxazole prophylaxis. The diseases include; Bacterial pneumonias, Pneumocystis Jirovecii Pneumonia, Toxoplasmosis, Severe bacterial infections and Malaria.

4.1.1 CPT for Adults and adolescent

Initiation of CPT

All patients are eligible for CPT initiation as soon as they have a diagnosis of HIV.
The only exclusions are those who have allergy to Cotrimoxazole.
Baseline Liver Function Tests (LFT) and Renal Function Tests (RFT) are recommended before long term administration of Cotrimoxazole.

Dose of CPT

One double strength tablet (800/160mg) or two single strength tablets once a day on a daily basis.

4.1.2 CPT for Children

Cotrimoxazole prophylaxis should be given to all infants and children with HIV, irrespective of clinical and immune conditions.

Co-trimoxazole prophylaxis is recommended for HIV-exposed infants 4 to 6 weeks of age and should be continued until HIV infection has been excluded by an age-appropriate HIV test to establish final diagnosis after complete session of breastfeeding.

Table 13a: Simplified dosage of cotrimoxazole in children (by Age)

Age	Dosage
Less than 6 months	100mg SMX/20 mg TMP (2.5 mls of syrup)
6 months to 5 years	200 mg SMX/40 mg TMP (5 ml of syrup or half single strength adult tablet)
6 – 14 years	400mg SMX/80mg TMP (10 ml of syrup of one single strength adult tablet)
>14 years	800mg SMX/160mg TMP (2 adult single strength tablets)

Table 13b: Dosage of cotrimoxazole in children (by weight)

Drug	Strength of tablet or oral liquid (mg or mg/5ml)	Number of tablets or millilitres by weight band once daily					Strength of adult tablet (mg)	Number of tablets by weight band once daily	
		3.0–5.9 kg	6.0–9.9 kg	10.0–13.9 kg	14.0–19.9 kg	20.0–24.9 kg		25.0–34.9 kg	Adolescent and Adults
Co-trimoxazole	Suspension 200/40 per 5 ml	2.5 ml	5 ml	5 ml	10 ml	10 ml	–	–	–
	Tablets (scored) 800/160 mg	–	–	–	0.5	0.5	800 mg/ 160 mg	1	1

4.1.3 Duration of CPT

CPT should not be discontinued; it should be continued throughout the person's lifetime.

However, regular follow up initially every month for the first three months, then every three months if the medication is well tolerated. It is mandatory to monitor for side effects and adherence. It is recommended that monitoring includes assessment of skin reactions, measurements of haemoglobin, and white blood counts every six months and when clinically indicated.

Exceptions (Criteria for stopping) are:

- Occurrence of severe side effects such as cutaneous reactions, or fixed drug reactions.
- Renal and/or hepatic insufficiency or severe haematological toxicity

4.2 Isoniazid Preventive Therapy (IPT)

4.2.1 Background

TB is the most common cause of death in hospitalized adults and children living with HIV, accounting for about a third of all mortality. Development of clinical TB is reduced by about 60% and survival is also prolonged.

Isoniazid preventive therapy (IPT) is an intervention that should be part of the package of care for people living with HIV. However it should only be offered in the following situations (prerequisites):

- Effective screening for active TB before initiating TB preventive therapy
- Capacity for follow up and monitoring of patients to encourage
  adherence to preventive therapy in order to address eventual side effects and exclude active TB disease

Isoniazid (INH) will be provided to eligible clients through collaboration between HIV/AIDS and TB Control Programs. This information must be captured in the appropriate surveillance forms for

reporting purposes. It is also essential that HIV inpatients in health care facilities are isolated from those patients with active TB.

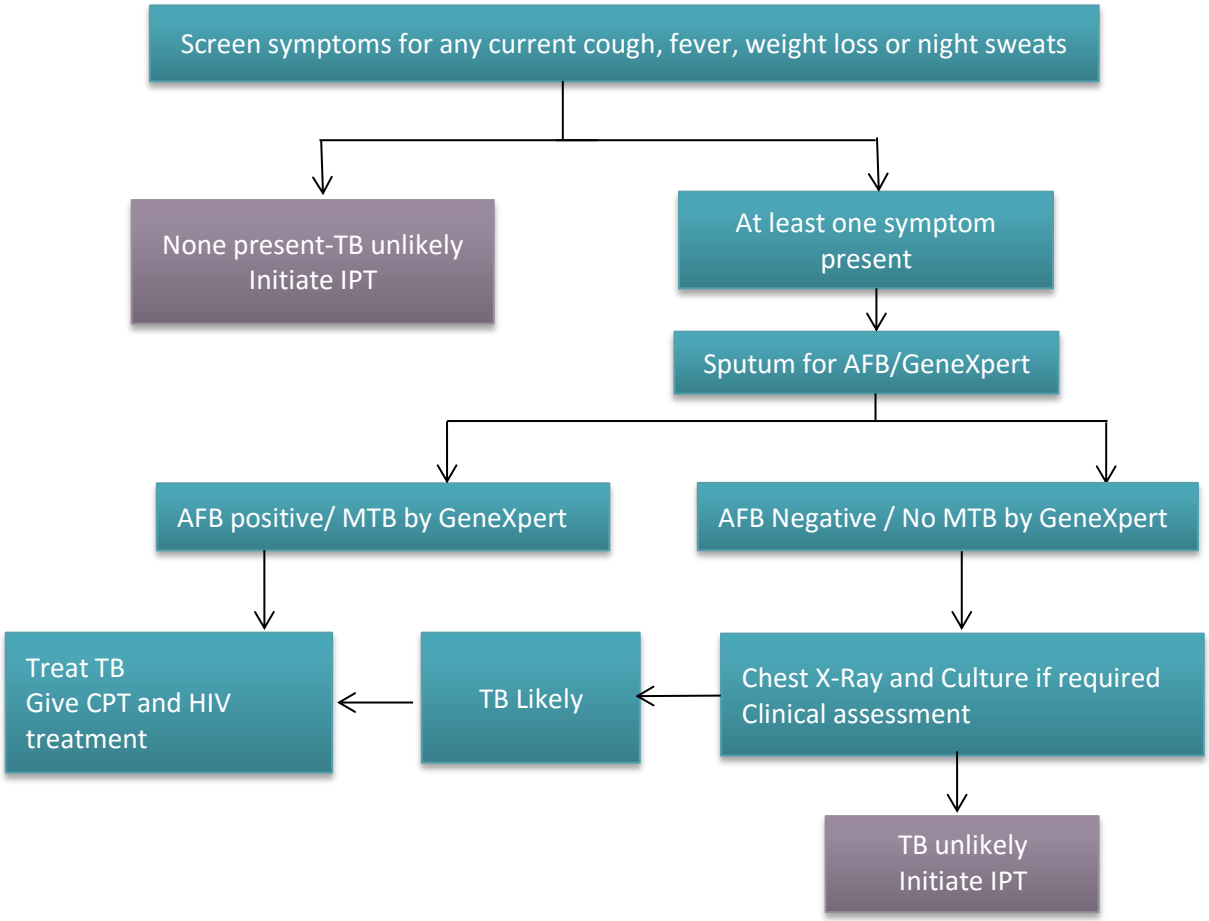
4.2.2 Eligibility for IPT in Adults and adolescent

All HIV positive people who have no signs and symptoms suggestive of active TB (cough, fever, body weight loss, or night sweat) are eligible for TB preventive therapy (Figure 5). Of note, pregnant and breastfeeding women with HIV can receive IPT.

It is essential to exclude active tuberculosis in every patient prior to starting preventive therapy by using TB screening algorithms. This is critical in order to avoid drug resistance when drugs are given to patients with TB disease who require the full regimen.

Patients who are eligible for IPT and who are required to start antiretroviral therapy need to complete their IPT even if the ART is started as there is no interaction between isoniazid and the current ART regimen used.

Figure 5: Algorithm for TB screening for ambulatory people infected with HIV



4.2.3 Eligibility for IPT in children

IPT for children with HIV should be given after ruling out TB. Antiretroviral therapy (ART) in children with HIV improves immune function and reduces the risk of TB infection. Always consult a paediatrician on the management of all children with suspected HIV and TB.

Eligibility for IPT in children is:

a. Any child, who is less than 5 years old, who has close contact to an adult with TB, such as a family or household member diagnosed with TB (bacteriologically confirmed or not), as long as the child is *not* symptomatic for TB (in which case they need full assessment and treatment) and if no active TB disease IPT six months should be given.

b. Children living with HIV who have poor weight gain, fever or current cough or contact history with a TB case may have TB and should be evaluated for TB and other conditions. If the evaluations show no TB, they should be offered IPT regardless of their age.

c. Children living with HIV who are more than 12 months of age and who are unlikely to have active TB on symptom based screening and have no contact with a TB case should receive IPT.

d. Children living with HIV who are less than 12 months of age, only those who have contact with TB case and who are evaluated for TB should receive IPT if the evaluation shows no TB disease.

If children are symptomatic for TB (i.e. have chronic cough, fever, weight loss, malnutrition, enlarged lymph nodes or prolonged pneumonia), a pediatrician should fully evaluate them to exclude active TB disease. If the child has TB, then s/he should receive full TB treatment. Never give IPT to children who are symptomatic for TB without a proper evaluation.

4.2.4 Recommended Regimen and Duration

The standard regimen for IPT is:

- Isoniazid (INH) daily 10 mg/kg/day (maximum 300 mg per day) and
- Vitamin B6 (Pyridoxine) 25mg daily.

INH should be always co-administered with Vitamin B6 or Pyridoxine to prevent neurologic side effect.

The recommended duration is 6 months.

The doses of Isoniazid for IPT in children, adolescent and adults are listed below:

Table 14: Simplified, weight- based dosing for Isoniazid and Vitamin B6 (Pyridoxine)

Drug	Strength of tablet or oral liquid (mg or mg/5ml)	Number of tablets or millilitres by weight band once daily*					Strength of adult tablet (mg)	Number of tablets by weight band once daily	
		3.0–5.9 kg	6.0–9.9 kg	10.0–13.9 kg	14.0–19.9 kg	20.0–24.9 kg		25.0–34.9 kg	Adolescent and Adults
Isoniazid	100 mg	0.5	1	1.5	2	2.5	300 mg	1	1
Pyridoxine	25 mg	0.25	0.25	0.25	0.5	0.5	25 mg	1	1

CHAPTER FIVE

MANAGING OPPOTUNISTIC INFECTIONS

5.1 Introduction

HIV infection destroys the CD4 cells in a person thereby causing immunosuppression.
Immune deterioration in an HIV positive individual makes way for opportunistic infections to occur.

Identifying and managing treatable opportunistic infection in HIV positive individuals is an important component of managing HIV infected individuals.

Note: In this chapter, showing only adult treatment doses. Please refer to PNG National Paediatric Guidelines for Paediatric doses

5.2 Clinical features

COUGH AND DYSPNOEA

Persistent cough and or dyspnoea can usually be attributed to one of the following:

- Bacterial pneumonia
- Viral pneumonia
- Pulmonary TB
- PCP
- Cardiac failure
- Allergic bronchitis
- Chronic bronchitis
- Bronchial asthma

It may not be possible to determine the underlying cause of cough and dyspnoea on clinical history and physical examination alone and hence laboratory tests may be of critical value.

Investigations:

- Full Blood Count
- Xpert MTB/RIF
- Sputum for AFB x 2 (if GeneXpert® is not available)
- Sputum for pyogenic culture and sensitivity
- Chest x-ray
- ECG (where available)

SKIN RASHES, SORES AND GENERALIZED PRURITIS

Causes include:

- Generalized pruritic papular eruption (PPE)
- External parasites e.g. scabies
- Generalized fungal skin infections
- Herpes zoster
- Herpes simplex
- Kaposi sarcoma

- Generalized bacterial skin infection e.g, Impetigo
- Drug reaction

Investigations

- Exclude scabies, bacterial, and fungal infections for which treatment are available
- Skin scraping for fungal element
- Pus swab for culture and sensitivity

Management

- Treat the underlying cause
- Refer for specialize management.
- Advise on skin care and refer to skin specialist

ALTERED MENTAL STATUS AND PERSISTENT SEVERE HEADACHE

Amongst the numerous causes of altered mental status and severe headache are:

- Malaria
- Typhoid
- Severe dehydration
- Hypoglycemia
- Bacterial and/or fungal meningitis
- Toxoplasma encephalitis
- HIV-dementia
- Depression
- Psychotic conditions

Note: In altered consciousness, cerebral malaria must always be excluded since this is a common and curable infection.

Investigations

- Blood slide for malarial parasites
- Lumbar puncture for CSF examination including Indian ink stain for Cryptococcal meningitis
- Blood cultures and sensitivity studies
- CT Scan (where available)

WEIGHT LOSS

Weight loss in persons with HIV disease including AIDS may be due to:

- Reduced food intake
- Difficulty/painful swallowing
- Diminished gastrointestinal uptake (malabsorption, diarrhoea),
- TB (a frequent cause of rapid weight loss)
- Intestinal worms
- Other debilitating diseases e.g, cancer
- Intractable vomiting

Treatment of weight loss

- Treat underlying cause
- High calorie and protein food intake

5.3 Clinical stage I – Diseases states and treatment

PERSISTENT GENERALIZED LYMPHADENOPATHY (PGL)

Lymphadenopathy may be due to a number of causes including those listed below:

- HIV itself
- Mycobacterium tuberculosis infection.
- Kaposi's Sarcoma or lymphomas
- Other causes e.g, pyogenic bacterial infection

Investigations

- Aspirate the node with a 21G needle and stain the aspirate for acid- fast bacilli (AFB)
- Lymph node biopsy for histological diagnosis
- Chest X-ray
- FBC and ESR

5.4 Clinical stage II – Diseases states and treatment

IMPETIGO

A highly contagious bacterial infection, impetigo often starts when a small cut or scratch becomes infected. This type of bacterial infection is usually more common in children but can affect HIV positive adults. The nose is most often the source of the infection.
The symptoms of impetigo are honey-colored, crusty sores that often appear on the face between the upper lip and nose. The rash consists of red spots or blisters that rupture, discharge, and become encrusted. People with impetigo should not scratch the sores because they may inadvertently spread the infection to other parts of their bodies.

This skin infection is caused by one of two bacteria; group A Streptococcus, which is the bacteria also responsible for "Strep throat," or Staphylococcus. If impetigo is caused by streptococcus it will begin with tiny blisters. These blisters can eventually erupt revealing small, wet patches of red skin. Gradually, a tan or yellowish brown crust will cover the affected area giving the appearance that it is coated with honey. If caused by staphylococcus, people can notice larger blisters that appear to contain a clear fluid. These blisters stay intact for a longer period of time compared to the smaller ones.

Treatment

Local antiseptics to clean lesions:

- Mucopurin 2% TDS topical application
- Fusidic Acid Cream 2% TDS topical application

If infection severe:

- Amoxicillin 500 mg TDS PO for 5 days

If no response try:

- Flucloxacillin 250mg QID PO for 10 days OR
- Erythromycin 500mg QID PO for 7 days
- Peadiatric Syrup Cephalixin 20mg/Kg/ Dose BD for 10 days

SEBORRHOEIC DERMATITIS

Seborrheic dermatitis is a disease that causes flaking of the skin. It usually affects the scalp. In adolescents and adults, it is commonly called "dandruff." In babies, it is known as "cradle cap." Seborrheic dermatitis can also affect the skin on other parts of the body, such as the face and chest, and the creases of the arms, legs and groin. Seborrheic dermatitis usually causes the skin to look a little greasy and scaly or flaky.

Treatment

Good general hygiene including washing with soap removes oils from affected areas and improves seborrhea. Pharmacologic treatment options for seborrheic dermatitis include antifungal preparations (selsun shampoo for the head; Clotrimazole 1% with Hydrocortisone 1% topically OR azole drugs (such as Fluconazole) for unresponsive or extensive diseases) to decrease colonization by yeast. If topical Clotrimazole is not used, apply Hydrocortisone 1% cream twice daily to the affected area until inflammation clears.

For severe disease, Keratolytics such as Salicylic acid or coal tar preparations may be used to remove dense scale; then topical steroids may be applied. Other options for removing adherent scale involve applying any of a variety of oils (peanut, olive or mineral) to soften the scale overnight, followed by use of a detergent or coal tar shampoo.

A severe, explosive onset of seborrheic dermatitis may be evident in HIV infection, regardless of age. It may appear as a butterfly rash, similar to the acute facial eruption associated with Systemic Lupus Erythematosus (SLE). The dermatitis may be treated with topical preparations, but if severe, treatment with Fluconazole 150mg/day PO for 5-10 days, OR Ketoconazole* 200 mg/day PO for 5-10 days OR Itraconazole* 200mg/day PO for 5-7 days may be necessary.

TINEA CAPITIS/CORPORIS/CRURIS/PEDIS

Use of topical treatments such as Benzoic Acid Compound Ointment (Whitfield's) or Clotrimazole 1% cream is often adequate. Where there is no response, or there is extensive spread, and/or involvement of two or more body areas, systemic azole therapy may be indicated.

Treatment

Fluconazole 100 mg/day PO for 7 days, OR Ketoconazole* 200mg/day PO for 2 - 4 weeks OR Itraconazole* 100mg/day PO for 2 – 4 weeks.

*Due to liver toxicity concerns, Ketoconazole and Itraconazole should not be given to patients taking Nevirapine (NVP)

PAPULAR PRURITIC ERUPTIONS

Hyper pigmented papules and nodules (up to 1 cm) with severe itching. Often ulcerations and scars because of scratching. Most frequently on the extensor side of arms and legs.

Treatment

- Antihistamines
  (Phenergan 10 mg TDS PO if bothersome during the day otherwise just Phenergan 25mg Nocte PO)
- Mild topical steroids
  (such as Hydrocortisone 1%) applied BID to QID as necessary
- Calamine lotion for comfort
- Commence ART ASAP

HERPES ZOSTER

Herpes Zoster (or Shingles as it is commonly known) is caused by a reactivation of the varicella-zoster virus (VZV). Chicken pox is the clinical manifestation of primary infection with VZV. After recovery from primary infection, VZV is not eliminated from the body but rather, the virus lies dormant in the sensory nervous system. When latent infection reactivates, the result is an episode of shingles, which is characterized by localized rash and pain along a dermatomal distribution. This can involve any dermatome, including the lower sacral dermatome. However, as lower sacral dermatomal zoster is much less common than genital herpes, so-called "recurrent zoster" is usually recurrent HSV infection.

The rash of zoster is often intensely pruritic and spreads throughout the dermatome, evolving through papular, vesicular and crusting stages. It usually lasts two to four weeks. The most troubling symptom is usually pain, which ranges from mild to severe, and from burning to lancinating

(piercing knifelike pain). Paraesthesiae, or anaesthesia and allodynia (pain induced by touch, often from trivial stimuli), can accompany severe pain. The pain may be self-limited or persist beyond the rash for up to a year ("post herpetic neuralgia").

It is important to note that primary VZV infection in immuno-compromised persons may be associated with the following:

- Numerous lesions
- Disseminated disease associated with pneumonitis, hepatitis and hemorrhagic skin lesions
- CNS manifestations including encephalitis and cerebellar ataxia
- Prolonged healing time
- Bacterial super-infection
- Herpes zoster in HIV infected individuals may be more severe, with more recurrences and may involve more than one dermatome

Treatment

Uncomplicated Zoster does not require indoor admissions. However, admissions should be considered if:

- There are severe symptoms in presence of immunosuppression
- Atypical presentations like Myelitis
- Involvement of more than two dermatomes
- Significant bacterial super-infections
- Disseminated Herpes Zoster
- Ophthalmic involvement
- Meningo-encephalic involvement

Antiviral therapy is appropriate for all patients presenting with shingles within 72 hours of rash onset. On current evidence, Valaciclovir is probably the most effective agent available, based on the knowledge that it speeds pain resolution faster than Acyclovir and offers more convenient dosing than Aciclovir but either can be used.

- Valciclovir 1 gram TDS PO for 7-14 days; OR
- Aciclovir 800mg PO 5 times/day for 7 – 14 days
- With disseminated VZV or ophthalmic nerve involvement give IV/Oral Acyclovir 10 mg/kg 8hourly for 7 - 14 days
- Strong analgesics are indicated (Codeine with Paracetamol or Codeine phosphate). The pain may be refractory even to potent analgesics.
- Erythromycin or Cloxacillin 500mg 6 hourly times daily for 7 days for bacterial super-infection if present
- Patients on NVP or LPV/r should not be provided with Cabamazapine or post-herpetic neuralgia however Amitriptyline may be used. The usual dose is 25mg orally nocte. The dose may be increased every 2 to 3 days but care should be taken to avoid excessive drowsiness. Most adults require less than 100mg daily
- Evidence has shown that the complications of steroid therapy (prednisolone) tends to outweigh the benefits in herpes zoster and is therefore not recommended

UPPER RESPIRATORY TRACT INFECTIONS (e.g. bacterial sinusitis)

Bacterial sinusitis usually caused by Streptococcus Pneunmoniae or H. Influenza. In health adults spontaneous resolution will occur in about 70% of people within about 2 weeks. HIV positive patients however should be treated with antibiotic therapy to avoid complications.

Treatment

- Amoxicillin 500 mg TDS PO for 5 – 7 days
- If no response use Amoxicillin + Clavulanate 875 + 125 mg (Augmentin) TDS PO for 7 – 14 days.
- If hypersensitive to Penicillin, use Doxycycline 100mg PO daily for 5 – 7 days.

5.5 Clinical stage III – Diseases states and treatment

FEVER

Fever may be due to a variety of causes and clinical features may suggest diagnosis. If no pointing features to a diagnosis are present, as a minimum the following should be done:

- Blood slide for malaria parasites,
- Blood and urine cultures if clinically indicated.
- Chest X-ray
- Blood for culture
- Urinalysis
- Full blood Count and ESR
- Sputum for AFB if indicated. Use Xpert if available

ORAL CANDIDIASIS

Patients with oral candidiasis will have white "curd like" lesions in the oral cavity. These are characteristically painful lesions and may be scrapped off with a spatula.

Treatment

For treatment any of the following may be used:

- Fluconazole 100/200mg/day PO for 5-7 days OR
- Nystatin oral suspension (100,000 u/ML) 4-6 ml QID for 10–14 days OR
- Miconazole Gel 2% 2.5ml PO QID for 10–14 days OR
- *Itraconazole 100mg/day PO for 10–14 days OR
- *Ketoconazole 200mg/day PO for 10–14 days

Where none of the above is available, 5mls of Gentian Violet 1% can be

used BD as a mouth gargle for 5−7 days.

*Due to liver toxicity concerns, Ketoconazole and Itraconazole should not be given to patients taking Nevirapine (NVP)

ORAL HAIRY LEUKOPLAKIA

Oral hairy leukoplakia (OHL) is a white thickening or coating of the lining of the mouth. It looks like white vertical folds or ridges. These ridges are almost always located on the sides of the tongue, although in unusual cases they can sometimes they can be found under the tongue or on the inside of the cheek. Oral hairy leukoplakia may look like oral candidiasis (thrush). Thrush can be scraped off. The white ridges of oral hairy leukoplakia do not scrape off nor is OHL painful. Oral hairy leukoplakia occurs in people who have HIV and who have moderate to severe immune system damage.

It is associated with Epstein-Barr virus (EBV) and occurs almost exclusively in patients who are immuno-compromised. Whether OHL develops after super infection with EBV or activation of a latent infection due to reduced immune surveillance is not known. OHL is more common in immuno- compromised patients who smoke.

Treatment

OHL is rarely treated. Painful super infection with *Candida* can be addressed with Nystatin and other antifungals. Patients with OHL are generally eligible for ART. Immune restoration with ART will eliminate the condition.

VAGINAL CANDIDIASIS

This is one of common illnesses presenting with itchy curd-like discharge. It can be managed with:

- Clotrimoxazole pessaries
- Nystatin Pessaries

If unresponsive or pessaries unavailable; give:

- Fluconazole 150mg PO Stat

DIARRHEOA

Diarrhoea in persons with HIV disease including AIDS can be due to a number of causes including:

- Common pathogens such as: Amoebiasis, Salmonella or Shigella
- Chronic malabsorption
- Cryptosporidiosis
- Mycobacterium Avium Complex (MAC) infection

- Isosporidiosis
- Clostridium Difficile infection

Investigations

Examine stools for treatable causes

Treatment

- Rehydration, Oral Rehydration Therapy (ORT)
- Treat underlying cause – give antibiotic therapy* and Albendazole 400mg stat
- Nutritional therapy
- In persistent diarrhoea among adults with no obvious treatable cause and no response to antibiotic therapy, give anti-diarrhoeal drugs such as Loperamide to minimize fluid loss and commence on ART. Cease Loperamide ASAP

***Note: Due to resistant of Shigella and Campylobacteria to Cotrimoxazole, Ciprofloxacin is the drug of choice**

PULMONARY TUBERCULOSIS

There is now only one category for treatment for TB patients. All TB patients whether bacteriologically confirmed or clinically diagnosed will receive Category 1. The following table indicates the drugs and different durations of treatment.

- All TB patients whether pulmonary or EPTB, new or previously treated and regardless of the results of their bacteriological investigations (bacteriologically confirmed or not) will receive Category 1 treatment.

- Category 1 treatment consists of only 2 months of intensive phase with 4 drugs (RHZE) and 4 months continuation phase with 2 drugs (RH) only. All health workers in PNG must strictly adhere to this.

- There is no separate treatment for previously treated TB patients. Category 2 treatment previously used for retreatment cases is not used anymore as is no longer recommended for PNG by NTP.

- All patients who are suspected of drug resistant TB including all previously treated TB patients and all patients who do not convert their smears to negative during treatment or do not improve on Category 1 treatment during any stage in the treatment must be screened for drug resistant TB by GeneXpert.

- All TB patients must be treated using Fixed Dose Combination (FDC) drugs and treatment must be given daily under observation.

- All treatment must be directly supervised or observed by a DOT provider.

Sputum smear must be examined to monitor progress of treatment for all pulmonary TB patients at the end of intensive phase (2 months), at the end of 5th month and at the end of treatment (6 months). Sputum should be collected and sent for GeneXpert testing for patients whose sputum smear examinations continuously shows positive during those follow-up examinations.

Please see the National Treatment Guidelines for Tuberculosis.

Table 15: Categories of Treatment and their Anti-TB Drug Regimens

Treatment category	Type of patient	Drug Regimen and duration			
		Intensive Phase		**Continuation Phase**	
		Drugs	Duration	Drugs	Duration
Category I	**All TB patients and EPTB except for severe forms of EPTB (TBM, Osteoarticular, etc)**	Rifampicin (R) Isoniazid (H) Pyrazinamide (Z) Ethambutol (E)	2 months	Rifampicin (R) Isoniazid(H)	4 months
	For severe forms of EPTB (eg: TBM, Osteoarticular, etc)	Rifampicin (R) Isoniazid (H) Pyrazinamide (Z) Ethambutol (E)	2 months	Rifampicin (R) Isoniazid(H)	7 months
		Drug Regimen code: ***2 (RHZE)/4 & 7 (RH)*** *- in FDC given daily*			
Category IV	**DR/MDR TB**	Second line drugs as per PMDT TB SOP			

SEVERE BACTERIAL INFECTION

Bacterial pneumonia is a common cause of HIV-1-related morbidity and mortality. Incidence of approximately 100 cases per 1,000 HIV-1–infected persons per year have been reported, a rate much higher than that in the non-infected population. In a study comparing rates among cohorts with similar other risk factors for bacterial pneumonia, those with HIV-1 infection were 7.8 times more likely than HIV-sero-negative persons to develop bacteria pneumonia. For certain persons, bacterial pneumonia is a symptom of HIV-1 disease. Patients can develop serious pneumococcal infections with relatively preserved CD4+ T lymphocyte counts. The high rates of bacterial pneumonia and other pyogenic respiratory tract infections probably result from multiple factors including qualitative B-cell defects that impair the ability to produce pathogen-specific antibody, impaired neutrophil function or numbers or both.

The etiology of bacterial pneumonia among patients with HIV-1 infection shows a relative prominence of *Streptococcus Pneumoniae*, followed by *Haemophilus Influenzae*, *Pseudomonas aeruginosa*, and *Staphylococcus Aureus*. In the majority of studies, the pathogens of atypical pneumonia (*Legionella Pneumophila, Mycoplasma Pneumoniae,* and *Chlamydia Pneumoniae*) are rarely encountered.

On the basis of data derived from studies of pneumococcal bacteremia, infection with *S Pneumoniae* is 150–300 times more common in patients with HIV-1 infection than in age-matched HIV-uninfected populations. Recurrent pneumococcal pneumonia, either with the same or unrelated serotype, is also more common among HIV infected patients, with a rate of 8%–25% within 6 months. Reinfection with a different strain is more common than relapse.

The presentation of bacterial pneumonia in HIV positive patients will be similar to that in HIV negative patients. Remember that in immuno-compromised patients pneumonia can be caused by fungal infection such as *Aspergillus* and *Cryptococcus*.

Treatment

Same as for HIV negative patients:

- Amoxicillin 500 mg TDS PO for 5 – 7 days if mild; OR
- Benzyl Penicillin 1,000,000 units QID parentally then change to oral Amoxicillin when improved; OR
- If no response or deteriorating, Chloramphenicol 1gram QID parentally then when improved and no fever, change Chloramphenicol 750mg TDS PO for a total period of at least 10 days.
- Adjunct treatment such as oxygen, pain relief etc. as required – see Standard Treatment Manual

If suspected, treat patient with Amphotericin B parentally (0.7 mg/kg for Cyprotococcosis and 1.0/mg/kg for Aspergillosis). Alternatively

Fluconazole can be used (20mg/kg daily for the first dose (PO or IV) then 10mg/kg daily for subsequent doses for at least 4 weeks).

5.6 Clinical stage IV – Diseases states and treatment

NORWEGIAN SCABIES

Clinical diagnosis is made by observing typical lesions on wrists, finger web spaces, axillae, penis or thighs or on eliciting the classic pattern of pruritus (at night, after a hot shower/bath). If associated with exposure to an infected person, the index of suspicion should be high even in the context of non-specific symptoms. Immunosuppressed patients may present with Norwegian scabies. Large numbers of mites are present and the condition may not be pruritic. Extensive crusting may be seen.

Treatment

Immunosuppressed/HIV patients are generally resistant to the topical therapy of Permethrin 5% applied topically. If used, Permethrin should be applied from the neck down. Pay particular attention to the areas between the fingers and toes, under fingernails and toenails, wrists, armpits, genitals, buttocks and perianal area. It is usually helpful for a second person to assist with the application of cream to areas that are not easily accessible. Permethrin should be kept on for at least 8 hours but no more than 24 hours. Reapply to hands if washed before 8 hours. This treatment needs to be given weekly for 6 weeks. Oral antihistamines can be given for pruritus.

If there is no response to Permethrin, if no Permethrin is available or if clinically indicated, Ivermectin is given at a dose of 200ucg/kg stat with a further 200ucg/kg dose repeated one week later. If clinically indicated, a third dose can be given after a further week but this is generally not needed. Washing in warm water, drying clothes/linens in the sun and observing personal hygiene is part of treatment.

HERPES SIMPLEX VIRUS (HSV) INFECTION

Clinical features:

Classical presentation of primary HSV infection includes:

- Lymph node enlargement
- Small painful vesicles
- Painful ulcers on the mucosa and skin
  Pain along gluteal and upper thigh muscles (Sacral radiculomyelitis) may occur with genital/rectal HSV
- Lymph node enlargement
- Headache

Lesions usually resolve within 10-21 days after primary infection. The

HSV then becomes latent in trigeminal and sacral nuclei and may reactivate. Clinical features common in those with HIV and AIDS include persistent/erosive genital/peri-rectal ulcerations. These are mainly associated with HSV-2 and more recurrent herpetic lesions.

Diagnosis

The diagnosis is usually based on clinical history and physical findings. Laboratory tests include serology, culture, immunoflorescence or immunoassay. Neither immunoflorescence nor immunoassay is available in the public health system in PNG.

Treatment

- Acyclovir 400mg PO TDS for 7−10 days; OR
- Valaciclovir 500mg PO TDS for 7−10 days.
- With severe HSV infections, give IV/Oral Acyclovir 10 mg/kg/day TDS, for 7-14days

CYTOMEGALOVIRUS (CMV) INFECTION

Clinical features

HCMV is a common human pathogen, infecting approximately 50% of adult populations in developed countries. CMV infections are typically sub-clinical but can become life threatening in immuno-compromised individuals. HCMV infection itself causes immunosuppression and has been linked with the progressive immunosuppression in persons infected with HIV. The most common manifestation is retinitis but colitis and pneumonitis are also frequently seen. HCMV may also present as encephalitis, hepatitis, adrenalitis, pancreatitis and/or epididymitis.

Diagnosis

The definitive diagnosis relies on clinical and laboratory findings:

- End organ disease such as retinitis with cotton wool and haemorrhage changes seen in retina, severe diarrhea and
- Microscopic finding of cytomegalic cell containing large central basophilic intranuclear inclusion (Papanicolaou or hematoxylin eosin stain)
- HCMV Antigen detection (monoclonal antibodies) of tissue, blood or bronchoalveolar lavage specimens
- Serology − seroconversion is a good marker for primary CMV infection but many individuals have past infection and are antibody positive at baseline

Treatment

- Ganciclovir − IV infusion over 1 hour at 5mg/kg given twice a day during initial induction (2 − 3 weeks) and then 5mg/kg IV

once daily for 7 days. (Decrease dose in renal impairment). Maintenance dose of 3 grams orally daily for 20 weeks.

- **It should be noted that oral Ganciclovir is not recommended for induction therapy of acute CMV disease. In acute CMV disease, IV Ganciclovir must be used for induction therapy**.

Valganciclovir is more effective and produces higher blood levels than ganciclovir but is not available in PNG.

CRYPTOCOCCUS NEOFORMANS INFECTION

A major cause of meningitis in HIV infected persons and disseminated disease. Contrary to bacterial meningitis, fever may be absent in these cases. Diagnosis depends on demonstration of positive CSF Indian Ink preparation. Prompt lumbar puncture with measurement of CSF opening pressure and rapid CSF cryptococcal antigen (CrAg) assay or rapid serum CrAg is the preferred diagnostic approach in case available.

Treatment

The routine use of antifungal primary prophylaxis for Cryptococcal disease is HIV infected adults, adolscents and children with a CD4 count of less than 100 cells/mm^3 and who are CrAg negative or where the CrAg is unknown is not recommended prior to ART initiation unless a prolonged delay in ART initiation is likely.

Induction, consolidation and maintenance antifungal treatment regimens:

- **For the induction phase** of treatment in HIV infected adults, adolescents and children with cryptococcal disease (meningeal and disseminated non-meningeal) the following two weeks of antifungal regimens are recommended in order of preference:

  Amphotericin B 0.7mg/kg/day IV and 5 Flucytosine 100mg/kg/day orally for 14 days (this is preferred regimen)

  Amphotericin B plus Fluconazole
  Amphtercin B short course (5-7 days) plus high doses of Fluconazole (to complete two weeks of induction) when a minimum package of pre-emptive hydration and electrolyte replacement and toxicity monitoring and management cannot be provided for the full two week induction period

  Fluconazole high dose plus Flucytosine when Amphotericin is not available

  Fluconazole high dose alone when others not available

- **For the consolidation phase** the following 8 weeks of antifungal treatment is recommended:

Fluconazole 400 to 800 mg/day after a two week induction with Amphotericin B regimen (6 to 12 mg/kg/day upto 400 to 800 mg/day if below 19 years)

Fluconazole 800mg/day after induction treatment with short course of Amphotericin B or fluconazole based induction regimen (fluconazole 12mg/kg/day up to 800mg/day if below 19 yrs)

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

Prevention, monitoring and management of amphotericin B toxicity

In HIV infected adults receiving amphtercin B – containing regimens for treatment of Cryptococcal disease, a minimum package of toxicity prevention, monitoring and management is recommended related to toxicities of hypokalemia and nephrotoxicity.

Timing of ART initiation:

Immediate ART initiation is not recommended in HIV patients with cryptococcol meningitis due to high risk of IRIS that maybe life threatening.

In HIV infected adults, adolescents and children with a recent diagnosis of cryptococcal meningitis, ART initiation should be deferred until there is evidence of sustained clinic response to anti- fungal therapy, and after 4 weeks of induction and consolidation with Amphotericin B – containing regimens combined with flucytosine or fluconazole, or after 4-6 wks of treatment with high doses of oral fluconazole induction and consolidation phase.

Discontinuation of azole maintenance treatment (secondary prophylaxis)

In HIV infected adults and adolescents with successfully treated cryptococcal disease (meningeal and non-meningeal), discontinuation of antifungal maintenance treatment is recommended based on the following criteria:

a) If HIV viral load monitoring is not available. When Patients are stable and adherence to ART and antifungal maintenance therapy for at least one year and have a CD4 count of greater than or equal to 200 cells/mm^3 (two measurements six months apart).

b) If HIV viral load is available, the patient is stable and adherence to ART and antifungal maintenance treatment for at least one year and with CD4 count greater than or equal to 100 cells/mm^3 (two measurement six months apart) and have a suppressed viral load.

In HIV infected children aged between 2 and 5 years with successful treated cryptococcal disease (meningeal and non-meningeal), discontinuation of antifungal treatment maintenance is recommended if child is stable and adherent to ART amd antifungal maintenance treatment for at least one year and with a CD4 count percentage greater than 25% or absolute count greater than 750 cells/mm^3(two measurements done six months apart).

Maintenance therapy for cryptococcal disease should NOT be discontinued in children less than two years.

Maintenance treatment for cryptococcal disease should be restarted if CD4 count drops to 100 cells/mm3 or below in HIV infected adults and adolescents (or CD4 count less than or equal to 25% or 750 cells/mm3 in children between two and five years, or if WHO clinical stage 4 event occurs, irrespective of patients age.

OESOPHAGEAL CANDIDIASIS

Candidiasis is the most common fungal infection in HIV and AIDS. Clinical manifestations depend on the site of disease, which can include mouth, pharynx, esophagus, and vagina.

Note: Candidiasis in the esophagus, trachea, bronchi or lungs is diagnostic of WHO Clinical Stage IV.

Diagnosis

The diagnosis is mainly based on clinical findings.

Treatment

For oesophageal candidiasis patients will usually complain of painful swallowing. If the patient has oral candidiasis or has a recent history of this, a presumptive diagnosis should be made of esophageal candidiasis. The following treatment options are available:

- Fluconazole 200mg PO Stat then 100mg daily for 14 days; OR
- Itraconazole 200mg PO daily for 14 days.

If unresponsive or unable to swallow:

- Amphotericin B 0.5mg/kg IV daily for 14 days.

Once oseophageal candidiasis is treated with Fluconazole, the dose should be reduced to 100 mg daily and then continued indefinitely or until immune recovery occurs on HAART.

PNEUMOCYSTIS JIROVECII PNEUMONIA (PCP)

Quite common in HIV infected individuals.

Clinical presentation:

- Non-productive cough, fever, chest tightness and shortness of breath that has evolved over 2-4 weeks
- Chest signs may be minimal despite severe shortness of breath
- CXR may show diffuse and symmetrical increased interstitial markings to diffuse alveolar pattern with infiltrations characterized by asymmetry, nodularity or cavitations. Chest radiograph may appear normal in 10% of patients. Pneumothorax is sometimes seen

Diagnosis

In our circumstances diagnosis is based on clinical presentation and exclusion of other common causes of severe dyspnoea.

Treatment of PCP

The management of PCP depends on the severity of the disease.

Severe Disease (Dyspnoea without exertion and severe hypoxia)

- Cotrimoxazole (Trimethroprim15-20 mg/kg/day + Sulphamethoxazole 75-80 mg/kg/day) IV or oral for 21 days in 3 divided daily doses plus corticosteroids (see below).

Mild and Moderate Disease PCP is normally considered moderate if there is dyspnoea on minimal exertion)

- Cotrimoxazole 1920 mg 3 times /day for 21 days (4 single strength tabs 8 hourly for 7 days, Then 4 single strength tablets 12 hourly for 7 days, then 4 single strength tablets daily for 7 days). With patients with moderate disease, consideration should be given to commencing initial therapy IV, particularly where treatment compliance may be an issue.
- Trimethoprim 12-15mg/kg/day + Dapsone 100mg/day for 21 days

For those allergic to Sulphur

Trimethoprim 12-15mg/kg/day + Dapsone 100mg/day for 21 days

Use of Corticosteroids in PCP

Research has demonstrated that there is reduced morbidity and mortality with PCP if corticosteroids are administered concomitantly with antimicrobial therapy. In moderate and severe disease, Prednisone 40mg PO BD for five days, then 40mg PO Daily for five days, then 20mg PO Daily until completion of therapy. If oral corticorsteroid therapy is not possible, then hydrocortisone (100mg IV q6h) may be used until oral therapy can be commenced (Methylprednisolone at 75% of the prednisone dose can be used if parental therapy is indicated and there is no parenteral prednisone). The
21 day course can then be completed orally in accordance with the above schedule. Corticosteroid therapy can be complicated by CNS toxicity and other opportunistic infections.

Prophylaxis (Primary and Secondary) therapy for PCP
Adults – One double strength tablet (160/800 mg) or two single strength tablets once a day on a daily basis
Children – check the dose

CEREBRAL TOXOPLASMOSIS

Clinical features

- Focal paralysis or motor weakness depending on area affected
- Neuro-psychiatric manifestation corresponding to the affected area in the brain
- Altered mental status (forgetfulness, etc.)

Treatment Acute infection

Tabs Sulphadiazine 1 g (<60kg) or 1.5 g (>60kg) 6hourly + Tabs Pyrimethamine 200mg loading dose then 50mg /day (<60kg) or 75mg (>60kg)+ Tabs Folinic acid 10 - 20mg /day for 6 weeks. After six weeks of treatment move to prophylaxis regimen

Alternative Treatment Regimen (less effective)

Cotrimoxazole (TMP 10mg/kg and SMX 50 mg/kg daily) given 12 hourly either IV or PO. Continue for 4 – 6 weeks after the resolution of signs/symptoms then on to secondary prophylaxis

Secondary Prophylaxis Regimen

- Tabs Sulphadiazine 500mg 6hourly + Tabs Pyrimethamine 25-50mg/day + Tabs Folinic acid 25mg /day
- For those allergic to sulphur:
  Replace Tab Sulphadiazine with capsule Clindamycin 450mg 6 hourly.
- Discontinue maintenance therapy when CD4 count>200 cells/ml for 6 months

Alternative Secondary Prophylaxis

Use Cotrimoxazole 2 SS (SMX 400/TMP 80mg X 2tabs) or 1 DS (SMX 800/TMP 160mg) twice daily.

5.7 Other diseases

HUMAN PAPILLOMA VIRUS (HPV) INFECTION

Clinical features

The virus may be present for years before symptoms develop. Genital warts develop following infection with some sub-types of HPV and usually progress rapidly whenever there is a decline in immune status (such as in pregnancy or in HIV infection). The warts are soft and fleshy and are easily traumatized during sexual activity. In pregnancy or in immuno-compromised individuals the warts may develop so greatly as to completely cover the vulva and occlude the introitus and urethral meatus.

Women who have ano-genital HPV infection (ano-genital warts) have an increased risk of developing cancer of the cervix and both men and women who have anal warts have an increased risk of later developing anal cancer.

Diagnosis

The diagnosis in PNG is based on clinical history and physical findings.

Treatment

The options in PNG are limited:

- Trichloroacetic acid in 80% to 90% solution may be used to treat small moist warts. It should be applied by the clinician to each wart (being careful not to burn surrounding tissue) weekly for up to 6 weeks. This is only appropriate for small numbers of discrete warts.
- Imiquimod 5% cream is applied to warts (with the fingers) 3 times a week (alternate nights) for up to 16 weeks. This medication stimulates the production of interferon and other cytokines. It is not available in the public health system but can be obtained by prescription from some private pharmacies. Safety in pregnancy has not yet been established.
- Electrocautery is probably the only real option available in PNG to treat the large mass genital warts that are becoming increasingly seen.
  Female patients are usually referred to the Gynaecology Clinic and
  males to the Surgical Clinic for booking. Cautery will usually need to be done under general (ketamine) anaesthesia.

INTESTINAL PROTOZOA INFECTION

For intestinal protozoa, which is a common cause of diarrhoea and difficult to diagnose, the recommended treatment:

Tabs Albendazole 400mg BD for one week

Other alternatives are Metronidazole Tabs or Thiabendazole.

5.8 Non-communicable diseases and HIV

People living with HIV are at risk of developing a range of chronic non-communicable disease (NCDs), including

- cardiovascular disease (CVD)
- hypertension
- diabetes
- chronic obstructive pulmonary disease (COPD)
- kidney disease
- cancers
- mental illness (e.g, depression)

It is recommended that all PLHIV should be assessed and have a cardiovascular risk assessment routinely and managed according to protocols recommended for the general population. All PLHIV must be offered advice on prevention and risk reduction of cardiovascular diseases by addressing modifiable factors such as high blood pressure, smoking, obesity, unhealthy diet and lack of physical activity.

Depression in People Living with HIV is also common. All PLHIV should be assessed for depression and linked to mental health services accordingly. People living with HIV are at risk of mental, neurological and substance –use disorders.

CHAPTER SIX

SERVICE DELIVERY

6.1 Service Delivery Approaches

Implementing "Test and Treat for all PLHIV" poses a higher demand to the health system particularly in the following areas.

- Exponential increase in demand for antiretroviral treatment puts a burden on the health system to provide chronic care/lifelong care to high number of clients with diverse needs.

- Most clients will be starting HIV treatment earlier, in the asymptomatic stage, a situation that has been found to be associated with low adherence to treatment. These people require support to commit to lifelong ART.

- Decline in levels of retention on treatment in the health care system. Adopting "Test and Treat for all" requires more effort to retain the increased number of PLHIV on treatment considering the fact that many of them will be asymptomatic with varied commitment to lifelong therapy.

- Although most people will present earlier programs must maintain or improve the capacity to respond to clients who present with advanced disease and are at high risk of mortality and morbidity.

Health facilities need to adapt service delivery models to address the above challenges by

- Differentiating HIV care to target the individual needs

- Strengthening continuum of HIV care from testing to initiation of treatment and retention in treatment

Differentiated HIV care

The differentiated HIV care framework, proposes that service delivery packages and models of care should be targeted to meet the specific needs of the respective category of clients.

The differentiated care framework (Table 16) is characterized by four delivery components:

- Types of services delivered
- Location of service delivery
- Provider of services
- Frequency of services

Table 16: Recommended Differentiated HIV care Model for PNG

Category of Client	Definition	Service package	Service Frequency	Service Location	Health Care carder
New Clients presenting with early HIV infection	Clients starting ART or are within six months of commencing ART with WHO stage 1 or 2	Early initiation of ART Baseline lab tests Adherence counselling Pharmaco-vigilance reviews OI prophylaxis Follow up services and tracking	2 weeks after initiation, 4 weeks after initiation, thereafter 4weekly for 6 months.	Health Facility initiating ART. After 6 months the client can start attending a satellite ART site for drug refills	ART prescriber trained on IMAI Link client to adherence or peer support groups.
People with Advanced Disease	Presenting with CD4 count below 200cells/mm3 or WHO disease stage 3 or 4	Rapid initiation of ART (once the risk of immune reconstitution inflammatory syndrome is ruled out); Screening and treatment for tuberculosis (TB) or isoniazid preventive treatment (IPT) as indicated; Co-trimoxazole (CTX) prophylaxis;	Client may require more frequent visits. Service frequency is guided by the mode of care for the predominant or life threatening medical condition.	Main ART site. i.e. Hospital or health center with human resource and laboratory capacity to provide the service package required	Doctor Or HEO

		Systematic screening for cryptococcus antigen; Screening for toxoplasmosis; Intensive follow-up.			
PLHIV stable on ART	Clients who have received ART for at least 12 months. Client has no adverse drug reactions that require regular monitoring, No current illnesses Not pregnant or currently breastfeeding Has good understanding of lifelong adherence There is evidence of treatment success (i.e. two	Drug refills Medication pick-ups. Laboratory monitoring 6 monthly Cessation of CD4 count monitoring if viral load testing is available.	Less frequent (every 2-3 months) clinic visits Children aged 0 –5 years old and adolescents need to be monitored more frequently for treatment dosing /weight changes and adherence support. less frequent (3 monthly) medication pick up	Health facility based care will continue Clients may use satellite ART site or other approach for drug refills but should visit the ART site at least once in 6 months for laboratory monitoring. Community ARV delivery may be used for stable patients in remote areas provided that sufficient support and resources can be provided.	Appointments for drug refills or adherence counselling can be attended by CHW or pharmacist/dispenser Client may see the clinician only when medical review is required or 6 monthly for laboratory monitoring Peer-led ART refills for programs with established trained peer educators provided regular mentoring and support can be provided to the peer educators.

	consecutive viral load measurements below 1000 copies /mL or rising CD4 cell counts, in the absence of viral load testing.				
PLHIV unstable on ART	PLHIV with treatment failure or Poor adherence Has OIs and adverse drug events High risk of LTFU or reconnected to care after LTFU Pregnant/breast feeding women, children and adolescents are included in this category because they require close monitoring.	Regular clinical and laboratory review depending on the condition until the client is no-longer at risk. Adherence support monthly for 3 months. Management of OIs. Re-assess viral load after 3months. Viral load literacy for client ARV regimen switch committee to assess if the client should be started on second line regimen.	Monthly until the client is no longer at risk	Facility based care reinforced with bi-weekly community level support where available through home visits, phone calls etc. The client should be managed in the hospital or major health center with capacity to manage the medical condition	Doctor or HEO Specialized clinics for PPTCT and pediatric HIV care to cater for needs for respective clients.

6.2 Strengthening the continuum of HIV care

6.2.1 Early Initiation of HIV treatment

NDoH recommends that all newly diagnosed HIV positive clients should be provided a package of services to ensure timely linkage to care and treatment.

Health workers should not unduly delay treatment especially for pregnant women, children or clients presenting with advanced disease.

Some of the approaches that can be used to improve linkage from HIV testing to treatment and accelerating ART initiation include;

- Providing integrated services, where HIV testing, HIV prevention, treatment and care, TB and sexually transmitted infection (STI) screening and other relevant services are provided together at a single facility or site
- Decentralized ART provision by using satellite ART sites to take the services nearer to the people. This reduces transport related barriers to initiation of treatment
- Promoting couple testing and male partner involvement in PPTCT may increase rates of HIV testing and linkage to care
- Support and involvement of trained peer educators and other lay providers to act as peer navigators, expert patients/clients and community outreach workers to provide support, identify and reach people lost to follow-up
- Providing on-site or immediate testing for CD4 cell count with same-day results using CD4 point of care machines
- Using communication technologies, such as mobile phones and text messaging, which may help with early initiation of ART among children receiving EID; disclosure, adherence and retention, particularly for adolescents and young people

6.2.2 Retention of PLHIV in HIV care and treatment

Health care workers and program managers should put concerted effort to maintain PLHIV on lifelong care. Some approaches that may be used to improve retention on treatment include;

- Using expert clients to provide education and counselling in the ART clinics
- Paying particular concern to pregnant and postpartum mothers to reduce LTFU which commonly occurs in the transition from MCH clinics to the ART clinic after the post-partum period
- Providing age-appropriate counselling on disclosure to children living with HIV

- Training care givers on the importance of disclosure and regular follow up for children on HIV treatment

- Peer psychosocial support through the use adherence clubs or mentor-mothers to provide counseling at the heath facility

- Providing adolescent friendly services that take into consideration their special needs

- Providing friendly services to key populations taking into consideration that they are often mobile. Eliminating stigma and discrimination in service delivery

6.2.3 Adherence Support

Adherence to ART is the primary determinant of viral suppression, risk of transmission, disease progression and death. Individual factors may include forgetting doses, being away from home, changes in daily routine, depression or other illness and substance or alcohol use.

Adherence to ART may be challenging in the absence of supportive environments for people living with HIV and in the presence of HIV-related stigma and discrimination.

Medication-related factors may include adverse events and the complexity of dosing regimens, such as those for children. Health system factors include distance to health services, long waiting times to receive care and obtain prescription refills, receiving only one month's supply of drugs, pharmacy stock-outs and the burden of direct and indirect costs of care.

The following specific population groups face challenges with adherence and need extra attention.

- Pregnant and postpartum women: Due to pregnancy-related conditions such as nausea and vomiting which negatively affect treatment adherence. Other individual factors e.g. lack of partner disclosure and support, and fear of stigma and discrimination

- Adolescents face specific challenges in adherence to treatment due to psychosocial issues such as peer pressure and the perceived need to conform, inconsistent daily schedules, transitioning from childhood to adult care and the assumption that the older adolescent has increased responsibility over their health

- Infants and young children require the commitment and involvement of a responsible caregivers to adhere to treatment. HIV care and treatment should be provided to parents and other family members of children living with HIV to support optimal care for the child living with HIV. Clinicians need to pay attention to other pediatric conditions like malnutrition. Choose appropriate ARV regimen and formulation to reduce pill or volume burden

- People with mental health conditions and substance use: Assessment and management of depression should be included in care services for all people living with HIV

- Use of alcohol and other substances (i.e. drug/substance abuse): Treatment of depression and substance use disorders should be provided regardless of HIV status

- Key populations face particular challenges. They are often mobile and have high risk of substance abuse and depression. Health workers should provide counselling, behavioral skills training and medication adherence training, treatment of depression and management of substance use where necessary. Provide supportive interventions and link key populations to peer psychosocial support groups, where available

6.2.4 Task shifting and task sharing

Task shifting and task sharing involves the redistribution of tasks within the health workforce teams so that specific tasks are reassigned to health workers with shorter training and fewer qualifications to make efficient use of the available human resources.

The following models of task shifting/task sharing have been used in PNG to support scale up of ART services and are therefore encouraged;

- Using IMAI Trained non-physician clinicians, midwives and nurses to initiate first-line ART

- Using trained non-physician clinicians, midwives and nurses to maintain clients on ART by providing refills at the satellite sites

- Trained and supervised community health workers to dispense ART

6.2.5 Decentralization of ART services

Decentralizing HIV treatment and care services reduces waiting times for people receiving care in facilities and brings HIV services closer to people's homes

NDoH recommends the following models of decentralized HIV care;

- Initiation of ART in hospitals with maintenance of ART in peripheral health facilities

- Initiation and maintenance of ART in peripheral health facilities

- Prescribing and dispensing AZT and NVP suspension for HIV exposed babies in MCH clinics with trained health workers

Community level approaches for example initiation of ART at peripheral health facilities with maintenance at the community level has not been used in PNG.
However, this approach could be tested to improve access to ART particularly for very remote areas where clients face high economic burden accessing ART sites.

6.2.6 Integrating and linking services

Providing integrated and linked services reduces missed opportunities for initiating ART, enhancing adherence support and retention of clients in care.

Maternal and Child health services

- NDoH recommends offering HIV testing and syphilis testing to pregnant women through provider-initiated approaches as an essential component of MNCH services
- ART should be provided in maternal and child health clinics, and clients linked to the ART site after the postpartum period.
- In the absence of a trained service provide clients should be linked to the most accessible ART site but continue to attend maternal and child health services.

Delivering ART in TB treatment settings and TB treatment in HIV care settings

- ART should be initiated for people living with HIV in TB treatment settings, with linkage to ongoing HIV care and ART
- Where possible, TB treatment may be provided for people living with HIV in HIV care settings where a TB diagnosis has also been made

ANNEX

Annex 1: WHO CLINICAL STAGING FOR ADULTS AND ADOLESCENTS

Clinical stage I

- Asymptomatic
- Persistent generalized lymphadenopathy

Performance scale 1: asymptomatic, normal activity

Clinical stage II

- Weight loss, <10% of body weight
- Minor mucocutaneous manifestations (seborrheic dermatitis, prurigo, fungal nail infections, recurrent oral ulcerations, angular cheilitis)
- Herpes zoster within the last five years
- Recurrent upper respiratory tract infections (i.e. bacterial sinusitis)

And/or performance scale 2: symptomatic, normal activity

Clinical stage III

- Weight loss, >10% of body weight
- Unexplained chronic diarrhoea, >1 month
- Unexplained prolonged fever (intermittent or constant, >1 month)
- Oral candidiasis (thrush)
- Oral hairy leukoplakia
- Pulmonary tuberculosis within the past year
- Severe bacterial infections (i.e. pneumonia, pyomyositis)

And/or performance scale 3: bedridden <50% of the day during the last month

Clinical stage IV

- HIV wasting syndrome[a]
- Norwegian Scabies > 1 month
- Pneumocystis carinii pneumonia
- Toxoplasmosis of the brain
- Cryptosporidiosis with diarrhoea >1 month
- Cryptococcosis, extrapulmonary
- Cytomegalovirus disease of an organ other than liver, spleen or lymph nodes
- Herpes simplex virus infection, mucocutaneous >1 month, or visceral any duration
- Progressive multifocal leukoencephalopathy
- Any disseminated endemic mycosis (i.e. histoplasmosis, coccidioidomycosis)
- Candidiasis of the oesophagus, trachea, bronchi or lungs
- Atypical mycobacteriosis, disseminated
- Non-typhoid Salmonella septicaemia
- Extrapulmonary tuberculosis
- Lymphoma
- Kaposi's sarcoma
- HIV encephalopathy, as defined by the Centers for Disease Control and Prevention[b]

And/or performance scale 4: bedridden >50% of the day during the last month

Notes
Both definitive and presumptive diagnoses are acceptable

[a] HIV wasting syndrome: weight loss of >10% of body weight, plus either unexplained chronic diarrhoea (>1 month) or chronic weakness and unexplained prolonged fever (>1 month).

[b] HIV encephalopathy: clinical findings of disabling cognitive and/or motor dysfunction interfering with activities of daily living, progressing over weeks to months, in the absence of a concurrent illness or condition other than HIV infection which could explain the findings.

- AIDS Indicator

Annex 2: WHO CLINICAL STAGING FOR CHILDREN

Clinical stage I

- Asymptomatic
- Persistent generalized lymphadenopathy

Clinical stage II ([1])

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

Clinical stage III ([1])

- Unexplained moderate malnutrition not adequately responding to standard therapy
- Unexplained persistent diarrheoa (14 days or more)
- Unexplained persistent fever (above 37.5 C, intermittent or constant, for longer than one month)
- Persistent oral candidiasis (after first 6 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 anemia (<8), neutropenia (<0.5 x 109), or chronic thrombocytopenia (<50 x 109)

Clinical stage IV ([1])

- Unexplained severe wasting, stunting or severe malnutrition not responding to standard therapy
  - Norwegian Scabies > 1 month
- Pneumocystis pneumonia
- Recurrent 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)
- Extra-pulmonary TB
- Kaposi sarcoma
- Oesophageal candidiasis (or Candida of trachea, bronchi or lungs)
- CNS Toxoplasmosis (after the neonatal period)
- 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 (extrapulmonary histoplasmosis, coccidiomycosis)
- Chronic cryptosporidiosis (with diarrhea) or chronic isosporiasis
- Disseminated non-tuberculous mycobacteria infection
- Cerebral or B cell non-Hodgkin lymphoma
- Progressive multifocal leukoencephalopathy
  - HIV associated cardiomyopathy or nephropathy

Note

Both definitive and presumptive diagnoses are acceptable

[1] Unexplained refers to where the condition is not explained by other causes

- AIDS Indicator conditions

Annex 3: DRUGS FORMULATIONS AND DOSES FOR ADULTS AND ADOLESCENTS (available in PNG)

Generic name	Dose
Nucleoside reverse-transcriptase inhibitors (NRTIs)	
Abacavir (ABC)	300 mg twice daily or 600 mg once daily
Lamivudine (3TC)	150 mg twice daily or 300 mg once daily
Zidovudine (AZT)	250–300 mg twice daily
Tenofovir (TDF)	300 mg once daily
Non-nucleoside reverse-transcriptase inhibitors (NNRTIs)	
Efavirenz (EFV)	400–600 mg once daily
Nevirapine (NVP)	200 mg once daily for 14 days, followed by 200 mg twice daily
Proteases inhibitors (PIs)	
Lopinavir/ritonavir (LPV/r)	400 mg/100 mg twice daily
	Considerations for individuals receiving TB therapy In the presence of rifabutin, no dose adjustment required. In the presence of rifampicin, adjusted dose of LPV/r: (LPV 800 mg + RTV 200 mg twice daily or LPV 400 mg + RTV 400 mg twice daily) with close monitoring.
Fix-dose combination tablets	
TDF/3TC/EFV	300mg/300mg/600mg once daily
AZT/3TC/NVP	300mg/150 mg /200 mg twice daily
AZT/3TC	300 mg/150 mg twice daily
ABC/3TC	600mg/300mg once daily

Annex 4: DRUGS FORMULATIONS, DOSES AND SCHEDULE FOR PAEDIATRIC CASES (available in PNG)

Fixed-dose solid formulations for twice-daily dosing for infants and children 4 weeks of age and older

Drug	Strength of tablets (mg)	Number of tablets by weight band morning and evening										Strength of adult tablet (mg)	Number of tablets by weight band	
		3.0–5.9 kg		6.0–9.9 kg		10.0–13.9 kg		14.0–19.9 Kg		20.0–24.9 kg			25.0–34.9 kg	
		AM	PM	AM	PM	AM	PM	AM	PM	AM	PM		AM	PM
AZT/3TC	Tablet (dispersible) 60 mg/30 mg	1	1	1.5	1.5	2	2	2.5	2.5	3	3	300 mg/ 150 mg	1	1
AZT/3TC/ NVP	Tablet (dispersible) 60 mg/30 mg/50 mg	1	1	1.5	1.5	2	2	2.5	2.5	3	3	300 mg/ 150 mg/200 mg	1	1
ABC/3TC	Tablet (dispersible) 60 mg/30 mg	1	1	1.5	1.5	2	2	2.5	2.5	3	3	600 mg/ 300 mg	0.5	0.5

Solid and oral liquid formulations for once- daily dosing for infants and children 4 weeks of age and older

Drug	Strength of tablet (mg)	Number of tablets or capsules by weight band once daily					Strength of adult tablet (mg)	Number of tablets or capsules by weight band once daily
		3.0–5.9 kg	6.0–9.9 kg	10.0–13.9 kg	14.0–19.9 kg	20.0–24.9 kg		25.0–34.9 kg
EFV [a]	Tablet (scored) 200 mg	–	–	1	1.5	1.5	200 mg	2
ABC/3TC	Tablet (dispersible) 60/30 mg	2	3	4	5	6	600 mg/ 300 mg	1
TDF [b]	Tablets 150 mg	–	–	–	1 (150 mg)	1 (200 mg)	300 mg	1

[a] EFV is not recommended for children younger than 3 years and weighing less than 10 kg.

[b] TDF is only approved for use for children 2 years and older. Target dose: 8 mg/kg or 200 mg/m^2 (maximum 300 mg).

Solid and oral liquid formulations for twice- daily dosing for infants and children 4 weeks of age and older

Drug	Strength of tablets (mg) or oral liquid (mg/ml)	Number of tablets or ml by weight-band morning (AM) and evening (PM)										Strength of adult tablet (mg)	Number of tablets by weight band	
		3.0–5.9 kg		6.0–9.9 kg		10.0–13.9 kg		14.0–19.9 kg		20.0–24.9 kg			25.0–34.9 kg	
		AM	PM	AM	PM	AM	PM	AM	PM	AM	PM		AM	PM
Solid formulations														
ABC	Tablet (dispersible) 60 mg	1	1	1.5	1.5	2	2	2.5	2.5	3	3	300 mg	1	1
NVP	Tablet (dispersible) 50 mg	1	1	1.5	1.5	2	2	2.5	2.5	3	3	200 mg	1	1
LPV/r[a]	Tablet[b] 100 mg/ 25 mg	–	–	–	–	2	1	2	2	2	2	100 mg/ 25 mg	3	3
	Pellets[c] 40 mg/ 10 mg	2	2	3	3	4	4	5	5	6	6	100 mg/ 25 mg	3	3
Liquid formulations														
AZT	10 mg/ml	6 ml	6 ml	9 ml	9 ml	12 ml	12 ml	–	–	–	–	–	–	–
ABC	20 mg/ml	3 ml	3 ml	4 ml	4 ml	6 ml	6 ml	–	–	–	–	–	–	–
3TC	10 mg/ml	3 ml	3 ml	4 ml	4 ml	6 ml	6 ml	–	–	–	–	–	–	–
NVP	10 mg/ml	5 ml	5 ml	8 ml	8 ml	10 ml	10 ml	–	–	–	–	–	–	–
LPV/r[a]	80/20 mg/ml	1 ml	1 ml	1.5 ml	1.5 ml	2 ml	2 ml	2.5 ml	2.5 ml	3 ml	3 ml	–	–	–

[a] LPV/r liquid requires a cold chain during transport and storage. The LPV/r heat-stable tablet formulation must be swallowed whole and should not be split, chewed, dissolved or crushed.

[b] The adult 200/50 ml tablet could be used for children 14.0–24.9 kg (1 tablet in the morning and 1 tablet in the evening) and for children 25.0–34.9 kg (2 tablets in the morning and 1 tablet in the evening)

[c] The LPV/r pellets formulation should not be used for infants younger than 3 months. More details on the administration of LPV/r pellets is available at http://www.emtct-iatt.org/wp-content/uploads/2015/09/IATT-LPVr-Factsheet-Final-30-September-2015.pdf.

Drug dosing of liquid formulations for twice-daily dosing for infants younger than 4 weeks of age[a]

Drug	Strength of oral liquid (mg/ml)	2–3 kg	3–4 kg	4–5 kg
AZT	10 mg/mL	1 mL	1.5 mL	2 mL
NVP	10 mg/mL	1.5 mL	2 mL	3 mL
3TC	10 mg/mL	0.5 mL	0.8 mL	1 mL
LPV/r[b]	80/20 mg/mL	0.6 mL	0.8 mL	1 mL

[a] There is limited experience with initiating treatment among newborns living with HIV <2 weeks of age, with few pharmacokinetic data to fully inform accurate dosing for drugs other than AZT during a time that renal and liver functioning is rapidly maturing, and LPV/r solution should not be given to infants aged <2 weeks, making management of HIV treatment in newborns challenging. In addition, reliable pharmacokinetic data for preterm infants are available only for AZT, with uncertainty of dosing for NVP and 3TC; LPV/r solution should not be given in preterm infants until they have reached 42 weeks of gestational age. This guidance will be updated when more evidence is available from ongoing trials.

[b] Do not use LPV/r solution for infants <2 weeks of age. LPV/r pellets should not be used for infants younger than 3 months. More details on the administration of LPVr pellets is available at http://www.emtct-iatt.org/wp-content/uploads/2015/09/IATT-LPVr-Factsheet-Final-30- September-2015.pdf.