GUIDELINES FOR HIV CARE AND TREATMENT IN PAPUA NEW GUINEA

June, 2009
FOREWORD

Over two decades have passed since the HIV epidemic was first recognized in Papua New Guinea. 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.

Despite the earlier efforts, the epidemic has grown and established itself into a generalized epidemic in both rural and urban communities. The epidemic has been more severe in certain vulnerable groups including sex workers, women, children, youth and migrant populations. As a result of this, more than 46,000 people are currently estimated to be living with HIV in the country. 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 scale up plan, which includes prevention, care and treatment, is a culmination of different initiatives including the Global Fund for AIDS, Tuberculosis and Malaria (GFATM). The GFATM is providing a framework for the establishment of a five-year program that will enrol about 7,000 patients on anti retroviral treatment. This program will result in the need to train more healthcare workers as well as the need to develop tools to guide the safe and effective implementation of care and treatment.

The National Guidelines for HIV Care and Treatment in PNG are one of the many tools that have been developed to provide healthcare workers guidance on various aspects of care and treatment. In this the third edition of the Guidelines, there is much wider coverage of such areas as; Adult and Paediatric HIV management including adherence issues and nutrition; treatment of opportunistic infections; PPTCT, and infant feeding options. The guidelines can also serve as reading and reference material for a wide range of healthcare professionals.

HIV and AIDS 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 process.

Dr Clement Malau
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 must 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 healthcare workers who are at the forefront of this epidemic. The National Department of Health also appreciates and acknowledges the valuable support given by various partners including WHO, UNICEF and the Clinton Foundation.
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ABBREVIATIONS

3TC  Lamivudine
AFB  Acid fast bacteria (Mycobacteria)
ABC  Abacavir
AIDS Acquired immunodeficiency syndrome
ART  Antiretroviral therapy
ARV  Antiretroviral
BBA  Born Before Arrival
CD4  Cluster Differentiation 4 cells
CSF  Cerebral Spinal Fluid
CT   Computerised Tomography
CXR  Chest X-ray
d4T  Stavudine
ddi  Didanosine
ECG  Electrocardiogram
EFZ  Efavirenz also known as EFV
ESR  Erythrocyte Sedimentation Rate
FBC  Full Blood Count
HAART Highly active antiretroviral therapy
HCMV Human Cytomegalo Virus
HIV  Human immunodeficiency virus
HSV  Herpes Simplex Virus
INH  Isoniazid
LFT  Liver Function Test
LPV  Lopinavir
MAC  Mycobacterium Avium Complex
MTCT Mother to child transmission
NAC  National AIDS Council
NDoH National Department of Health
NNRTI Non-nucleoside reverse transcriptase inhibitor
NsRTI Nucleoside analogue reverse transcriptase inhibitor
NtRTI Nucleotide analogue reverse transcriptase inhibitor
NVP  Nevirapine
OI   HIV-related opportunistic infection
ORT  Oral Rehydration Therapy
PCP  Pneumocystis carinii pneumonia (also known as PJP or Pneumocystis Jirovecii Pneumonia)
PI   Protease inhibitor
PEP  Post Exposure Prophylaxis
PGL  Persistent Generalised Lympadenopathy
PJP  Pneumocystis Jirovecii Pneumonia
PNG  Papua New Guinea
PPE  Pruritic Pupura Eruption
r    Ritonavir boosted
ROM Rupture of Membrane
sAg  Surface antigen
<table>
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<th>Abbreviation</th>
<th>Description</th>
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<tr>
<td>SQV</td>
<td>Saquinavir</td>
</tr>
<tr>
<td>TB</td>
<td>Tuberculosis</td>
</tr>
<tr>
<td>TDF</td>
<td>Tenofovir</td>
</tr>
<tr>
<td>TLC</td>
<td>Total lymphocyte count</td>
</tr>
<tr>
<td>UPNG</td>
<td>University of Papua New Guinea</td>
</tr>
<tr>
<td>VCT</td>
<td>Voluntary counselling and testing</td>
</tr>
<tr>
<td>WHO</td>
<td>World Health Organisation</td>
</tr>
<tr>
<td>ZDV</td>
<td>Zidovudine (also known as AZT)</td>
</tr>
<tr>
<td>VZV</td>
<td>Varicella Zoster Virus</td>
</tr>
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CHAPTER ONE

THE USE OF ANTIRETROVIRAL DRUGS IN ADULTS AND ADOLESCENTS
1.1. PURPOSE

The following guidelines have been prepared to guide healthcare workers in their choice of antiretroviral treatment for HIV infected individuals and to assist them in the management of associated issues such as Prevention of Parent to Child Transmission and infant feeding. It is also 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 distributed to healthcare workers and other partners involved in the HIV/AIDS National Response.

1.2. WHO CAN PRESCRIBE ART DRUGS

Initiation of antiretroviral therapy (ART) is a complex undertaking, and 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. For this reason the prescribing of antiretroviral medication will be restricted to registered medical practitioners who have completed training 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 or HEOs who have support and mentoring will occur to enable timely access to treatment throughout PNG (see 1.3). 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.

1.3. WHO CAN INITIATE, MONITOR AND SUPPLY TREATMENT

Uncomplicated patients 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.
1.4. WHEN TO START TREATMENT

1. The patient has written confirmation of HIV positive status.

2. They are medically eligible.

A patient is medically eligible for ART if they have one of the following:

- WHO stage IV of HIV disease (clinical AIDS), regardless of the CD4 Count

- Advanced WHO stage III disease (Characterized by HIV wasting, chronic diarrhoea, prolonged fever, atypical pulmonary tuberculosis, recurrent invasive bacterial infections, or recurrent/persistent mucosal candidiasis), regardless of the CD4/TLC;

- WHO stages I, II or III of HIV disease with CD4 below 350 or Stage II with TLC equal or below 1200/mm³

<table>
<thead>
<tr>
<th>WHO Clinical Staging</th>
<th>CD4 Available</th>
<th>CD4 not Available</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>Treat if &lt;350</td>
<td>No treatment</td>
</tr>
<tr>
<td>II</td>
<td>Treat if &lt;350</td>
<td>Treat if TLC &lt;1200</td>
</tr>
<tr>
<td>III</td>
<td>Treat irrespective of CD4 but consider CD4 values for better management and decision making in some situations (eg. TB)</td>
<td>Treat irrespective of TLC</td>
</tr>
<tr>
<td>IV</td>
<td>Treat irrespective of CD4 count</td>
<td>Treat irrespective of TLC count</td>
</tr>
</tbody>
</table>

* WHO clinical staging is attached as appendix 1

3. The patient has a treatment supporter (ie a responsible adult who has been fully informed about the condition of the patient and who comes with the patient to confirm that they are prepared to assist the patient) Refer 1.12

4. Any opportunistic infection has been or is being treated/stabilized

5. The patient understands their diagnosis and need for lifelong treatment have been thoroughly discussed with the patient and the patient is prepared and willing to undertake a commitment to life-long treatment. They also understand the dangers and risks of non-adherence to treatment.

6. There is a reliable drug supply

7. Favorable social criteria should be considered. This includes social support and the ability to attend for appointments and drug collection.
1.5. BASELINE TESTS

The absolute minimum laboratory tests before initiating antiretroviral therapy are:

- An HIV antibody test (in persons over 18 months of age); and,
- Haemoglobin or haematocrit measurement
- CD4 (if available) or total lymphocyte count (TLC).
- Liver functions test, especially serum alanine (ALT) or aspartase aminotransferase (AST)

Additional basic testing should include:

- A baseline haemoglobin, white blood cell count and differential cell count (to identify anaemia or a decline in neutrophils and the possibility of the occurrence of neutropenia during ART);
- Hepatitis B virus (HBV) surface antigen
- Serum creatinine and/or blood urea nitrogen to assess baseline renal function;
- Serum glucose;
- Pregnancy tests for women.
- Pap Smear (if available)
- Syphilis serology
- Sputum for AFB and/or CXR

As an example some routine tests to be performed during the course of the treatment

### Table 1 Schedule of Essential Laboratory Monitoring of ART

<table>
<thead>
<tr>
<th>Laboratory test</th>
<th>Three months</th>
<th>Six months</th>
<th>Nine months</th>
<th>Every six months thereafter if stable</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hb</td>
<td>√</td>
<td>√</td>
<td>√</td>
<td>√</td>
</tr>
<tr>
<td>ALT</td>
<td>√</td>
<td>√</td>
<td>√</td>
<td>√</td>
</tr>
<tr>
<td>WBC with diff</td>
<td>√</td>
<td>√</td>
<td>√</td>
<td>√</td>
</tr>
<tr>
<td>CD4 (if available)</td>
<td>√</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cholesterol (Lipids)</td>
<td>√</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Blood Glucose</td>
<td>√</td>
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</tbody>
</table>

HIV positive patients who are not on ART should have the same baseline testing as described above and then monitored in accordance with the following chart. Other testing may be added according to the patients clinical condition.
Table 2 Schedule of Essential Laboratory Monitoring of HIV Positive Patients NOT on ART

<table>
<thead>
<tr>
<th>Laboratory test</th>
<th>Six months</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hb</td>
<td>√</td>
</tr>
<tr>
<td>WBC with diff</td>
<td>√</td>
</tr>
<tr>
<td>CD4 (if available)</td>
<td>√</td>
</tr>
</tbody>
</table>

1.6. WHAT DRUGS TO USE

The use of fixed drug combinations is recommended wherever possible to facilitate compliance and minimize the potential for the development of viral resistance.

First line therapy

Zidovudine (ZDV 300mg BD)       Nevirapine (NVP 200mg daily for 14 days and then 200mg BD)
Lamivudine (3TC 150mg BD)       Efavirenz (EFV 600mg nocte)
Stavudine (d4T 30mg BD*)

The combination of ZDV/3TC/NVP is generally preferred. d4T may be associated with more mitochondrial toxicity and a greater frequency of lipodystrophy. ZDV, on the other hand, is associated with anaemia due to bone marrow toxicity in 5-10% of patients. If measurement of Haemoglobin is not routinely available, or if the Haemoglobin prior to initiation of therapy is less than or equal to 8 g/dL (without a correctable cause), the combination of d4T/3TC/NVP would be preferred. Both combinations have equivalent potency. Nevirapine is given as a single daily dose for the first 14 days to reduce possible side effects. This can be achieved using a Nevirapine containing triple combination tablet in the morning and a dual combination tablet without the Nevirapine at night, for the first 14 days.

*Note: Dose of Stavudine (d4T) only 30mg BD regardless of weight.

DRUG SUBSTITUTION

1.7 For 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. For example,
the ZDV containing regimen can be changed to D4T if significant unresponsive anaemia occurs. EFV may be substituted for NVP if a patient develops a moderately florid rash, but should not be given if there is mucosal ulceration, severe liver disease or systemic effects associated with the rash. Do not restart NVP in a patient who has experienced a severe reaction to the drug as this may be fatal. If the patient is unable to tolerate either EFV or NVP, ABC may be used as the third drug in a triple NRTI regimen although it should be noted that there is a higher rate of virological failure with the regimen ZDV/3TC/ABC.

Table 3: Drug toxicity and Substitution

<table>
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<th>If toxicity...</th>
<th>Due to ...</th>
<th>Then switch to ...</th>
</tr>
</thead>
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<tr>
<td>d4T/3TC/NVP</td>
<td>d4T – neurological or pancreatitis, d4T – lipodystrophy, NVP – hepatotoxicity, NVP – Steven Johnson Syndrome</td>
<td>ZDV, ZDV, EFZ (except in pregnancy) alternatively ABC</td>
</tr>
<tr>
<td>ZDV/3TC/NVP</td>
<td>ZDV – Bone Marrow Suppression, NVP – see above</td>
<td>D4T</td>
</tr>
<tr>
<td>d4T/3TC/EFV</td>
<td>EFV – Unremitting CNS toxicity, d4T – see above</td>
<td>NVP.</td>
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1.8 For Treatment Failure

WHO recommends that the entire regime 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, one of these 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.
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<th>Then switch to ...</th>
<th>NOTES</th>
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<tbody>
<tr>
<td>ZDV or d4T</td>
<td>TDF or ddI</td>
<td>As there is cross resistance between ZDV and D4T, second line regimes do not contain either. Individual mutations associated with resistance to ZDV/3TC can occasionally confer resistance to ABC. If this occurs, change to TDF.</td>
</tr>
<tr>
<td>+</td>
<td>+</td>
<td></td>
</tr>
<tr>
<td>3TC</td>
<td>ABC</td>
<td></td>
</tr>
<tr>
<td>+</td>
<td>+</td>
<td></td>
</tr>
<tr>
<td>NVP or EFZ</td>
<td>LPV/r or SQV/r</td>
<td></td>
</tr>
</tbody>
</table>

Patient on d4T/3TC/NVP change to TDF/ABC/LPV/r

Patient on ZDV/3TC/EFV change to ddI/ABC/SQV/r

Patient on d4T/3TC/EFV – change to TDF/ABC/SQV/r

Patient on ZDV/3TC/NVP Change to ddI/ABC/LPV/r

**3TC can be considered for maintenance in second-line regimens to potentially reduce viral fitness, confer residual activity and to improve viral sensitivity to ZDV or TDF. 3TC should not be stopped if an individual has hepatitis B co-infection. ZDV may prevent or delay the emergence of the K65R mutation (a mutation which shows broad cross-resistance to nucleos(t)ide reverse transcriptase inhibitors).**

**NB:**

(1) Both tenofovir and ddI are adenosine analogs and therefore block the same sub-step on the HIV replication cycle and in an identical manner. One possibility is that the combination of tenofovir and ddI will work as if there were only one and not two drugs in the regimen scheme, thereby resulting in duo therapy and not triple therapy. Tenofovir and ddI generally share the same antiretroviral resistance profile, and sometimes these two drugs are the only nucleoside/nucleotides analogs left to be used in more experienced patients. Given these observations, plus unclear pharmacokinetic interactions and a possible lymphotoxic effect of these drugs, it is recommended that the combination of tenofovir and ddI be avoided.

(2) If failure of therapy is due to non-adherence consider continuation of therapy until causes of non-adherence can be addressed. 2nd line therapies are far more complex and likely to fail with poor adherence. Drug costs and pill burden are also considerably higher.
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 dis-continuation of therapy until adherence can be improved.

Table 5: Clinical and Immunological indications of Treatment Failure

<table>
<thead>
<tr>
<th>CD4 Cell Criteria for Treatment Failure</th>
</tr>
</thead>
<tbody>
<tr>
<td>- Fall of CD4 cell to pre-therapy baseline or below without other concomitant infection to explain transient CD4 cell decrease(^1); or</td>
</tr>
<tr>
<td>- &gt;50% fall from on therapy CD4 peak level without other concomitant infection to explain transient CD4 cell decrease(^1); or</td>
</tr>
<tr>
<td>- persistent CD4 levels below 100 cells/mm(^3)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Clinical Failure</th>
</tr>
</thead>
<tbody>
<tr>
<td>- New or recurrent WHO stage 4 condition. The new or recurrent condition must be distinguished from immune reconstitution syndrome(^2) (^3) (^4).</td>
</tr>
</tbody>
</table>

\(^1\)If patient is asymptomatic and treatment failure is being defined by CD4 cell criteria alone, a confirmatory CD4 cell count should be performed. One off CD4 counts are difficult to interpret and longitudinal measurements are more meaningful.

\(^2\)Recurrence of tuberculosis may not represent HIV disease progression as re-infection may occur. Clinical evaluation necessary.

\(^3\)Immune reconstitution syndrome is characterized by the appearance of signs and symptoms of an opportunistic disease a few weeks to a few months after the start of potent antiretroviral therapy in the setting of advanced immuno-deficiency.

\(^4\)Certain WHO clinical stage 3 conditions (eg. pulmonary TB, severe bacterial infections) may be an indication of treatment failure and thus require consideration of second-line therapy.
Table 6: Clinical Staging events to guide decision-making on switching

<table>
<thead>
<tr>
<th>NEW OR RECURRENT EVENT ON ART$^1$</th>
<th>RECOMMENDATIONS</th>
<th>ADDITIONAL MANAGEMENT OPTIONS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Asymptomatic (T1)</td>
<td>Do not switch regimen</td>
<td>• Maintain scheduled follow-up visit including CD4 monitoring (if available)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Continue to offer adherence support.</td>
</tr>
<tr>
<td>Stage 2 Event (T2)</td>
<td>Do not switch regimen$^2$</td>
<td>• Treat and manage staging event.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Assess and offer adherence support.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Check if on treatment for at least six months.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Assess continuation or reintroduction of OI prophylaxis.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Schedule earlier visit for clinical review and consider CD4 (if available)$^3$.</td>
</tr>
<tr>
<td>Stage 3 Event (T3)</td>
<td>Consider switching regimen$^2$  $^4$</td>
<td>• Treat and manage staging event and monitor response.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Assess and offer adherence support.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Check if on treatment for at least six months.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Check CD4 count (if available)$^3$  $^4$.</td>
</tr>
<tr>
<td>Stage 4 Event (T4)</td>
<td>Switch regimen$^2$  $^5$</td>
<td>• Treat and manage staging event and monitor response.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Check if on treatment for at least six months.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Assess continuation or reintroduction of OI prophylaxis.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Check CD4 cell count (if available)$^3$.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Assess and offer adherence support.</td>
</tr>
</tbody>
</table>

1. Refers to clinical stages while on ART for at least six months (termed T1, T2, T3 and T4)
2. Differentiation of OIs from immune reconstitution syndrome is necessary.
3. Treat and manage the staging event before measuring the CD4 cell count.
4. Certain WHO clinical stage 3 conditions (eg. pulmonary TB, severe bacterial infections) may be indicators of treatment failure and thus require consideration of second line therapy. Response to appropriate antimicrobial therapy should be used to evaluate the need to switch therapy.
5. Some WHO clinical stage 4 conditions (lymph node TB, uncomplicated TB pleural disease, oesophageal candidiasis, recurrent bacterial pneumonia) may not be indicators of treatment failure and thus do not require consideration of second line therapy. Response to appropriate antimicrobial therapy should be used to evaluate the need to switch therapy.
1.9. PREVENTION OF OPPORTUNISTIC INFECTIONS

1. Cotrimoxazole PCP prophylaxis (two single strength tablets or one double strength tablet daily) should be given to all patients meeting the clinical criteria for WHO Clinical Stage II or greater (or whose CD4, <350/mm$^3$). Prophylaxis can be ceased in patients who have had a sustained clinical response (CD4>200/mm$^3$ for >12 months).

2. INH – 5mg/kg/day or maximum dose of 300mg daily for 6 months, after exclusion of active TB. Vitamin B6 or Pyridoxine 25mg daily should also be co-administered. TB preventive therapy is safe and effective in HIV positive individuals and can reduce the risk of TB by 33-67% for up to 48 months.

1.10. PEOPLE WITH TUBERCULOSIS AND HIV COINFECTION

It is recommended that people with TB/HIV Co infection complete TB therapy before beginning ART treatment unless there is a high risk of HIV disease progression and death during the period of TB treatment. If a person needs TB and HIV treatment concurrently, first-line treatment options include ZDV/3TC or d4T/3TC plus either a NNRTI or a triple NRTI regimen (ABC or TDF). 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. Current WHO recommendations are that the daily dose of EFV should remain unchanged (600mg/day) if Rifampicin is used to treat the TB. Unboosted Protease inhibitors are not recommended during TB treatment with Rifampicin because PI levels are subtherapeutic. If a PI based regime needs to be administered concurrently with Rifampicin LPV 400mg/RTV 400mg twice daily or SQV 400mg/ RTV 400mg twice daily can be considered. Patient education to present with early symptoms (e.g. nausea) and close clinical and laboratory monitoring (ALT) for hepatotoxicity is required when boosted PIs are administered concurrently with Rifampicin.

Table 7: Initiating first-line ART in relationship to TB Therapy

<table>
<thead>
<tr>
<th>CD4 Cell Count</th>
<th>ART Recommendations</th>
<th>Timing of ART in relation to start of TB Therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>CD4 &lt;200 cells/mm$^3$ (or if TLC = or &gt; 1200 or disseminated TB)</td>
<td>Recommend ART$^a$</td>
<td>Between 2 and 8 weeks$^b$</td>
</tr>
<tr>
<td>CD4 between 200 and 350 cells mm$^3$</td>
<td>Recommend ART</td>
<td>After 8 weeks</td>
</tr>
<tr>
<td>CD4 &gt;350 cells/mm$^3$</td>
<td>Defer ART$^c$</td>
<td>Re-evaluate patient at 8 weeks and at the end of TB treatment</td>
</tr>
<tr>
<td>CD4 not available</td>
<td>Recommend ART$^d$</td>
<td>Between 2 and 8 weeks</td>
</tr>
</tbody>
</table>
a. An EFV containing regimen is the preferred first line regime. ALT should be checked at 4, 8 and 12 weeks.
b. ART should start as soon as TB treatment is tolerated, particularly in patients with severe immunosuppression.
c. ART should be started if other non-TB stage 3 or 4 events are present.
d. For some TB diagnoses that generally respond well to TB therapy (ie. Lymph node TB, uncomplicated pleural effusion) deferral of ART should be considered.

1.11. WHO MAY INITIATE OI PROPHYLAXIS

Any healthcare worker who has completed training and demonstrated clinical competence through a training program approved by the National Department of Health (NDoH).

1.12. 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 medicines can stop working. 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.

1.13. NUTRITION AND HIV

Adequate nutrition is necessary to ensure optimal benefits from antiretroviral treatment, which is essential to prolong the lives of HIV-infected people. Although adequate nutrition cannot cure HIV infection, it is essential to maintain a person’s immune system, to sustain healthy levels of physical activity, and for optimal quality of life.

Malnutrition can exacerbate the effects of HIV and hasten AIDS-related illnesses in people living with HIV. A stronger, healthier body can better resist the opportunistic infections that affect people living with HIV, especially in remote and resource-poor settings where preventive health care is not often available.
**Women, food security and HIV**

Women are responsible for producing, purchasing and preparing food. When a woman is HIV-positive, household food security is impacted, as younger, more inexperienced women take on the responsibilities. Women are also primary caregivers. Caring for ill family members means less time is available for food production and preparation.

**Treatment**

Food security and nutrition are fundamental to HIV treatment. There is emerging evidence that patients who begin antiretroviral therapy without adequate nutrition have lower survival rates. Adequate dietary intake and absorption are essential for achieving the full benefits of the treatment. Antiretroviral therapy itself may increase appetite and it is possible to reduce some side-effects and promote adherence to the therapy if some of the medicines are taken with food. Given the importance of adherence in delaying viral resistance to first-line drugs, nutritional support becomes even more important in the longer run for sustaining antiretroviral treatment.

**General principles**

1. During a post-test counseling session, feeding counseling must not be offered, unless requested. A client who is HIV positive may be overwhelmed at that time. First the client has to think about it and how to cope with life as a HIV positive person.
2. All HIV positive clients should receive information on nutrition, health and hygiene to support themselves, whilst living with HIV infection and MUST BE offered family planning advice.
3. In determining the advice on feeding, the health care worker needs to take into account the client's personal circumstances, feeding choices must be acceptable, feasible, affordable, sustainable and safe.

**Feeding Advice**

1. Clients should be advised to eat a normal healthy diet, but increase their intake of staple foods like kaukau, taro, rice or bread. If possible they should add some type of grease (e.g. coconut cream, vegetable oil, margarine) to the food.
2. Because of the need for more energy, clients should eat 3 main meals with snacks in between.
3. There is no need to eat more than usual protein or body building foods.
4. Clients should eat lots of fresh fruits and vegetables, particular dark green leafy vegetables. Clients should aim to eat at least 5 serves of fruit and vegetables.
**Macronutrients**
Adults living with HIV have 10−30% higher energy requirements than a healthy adult without HIV, and children living with HIV 50–100% higher than normal requirements. Food availability and good nutrition are thus essential for keeping people living with HIV healthy for longer.

There is no evidence to support a need for increased protein intake by people infected by HIV over and above that required in a balanced diet to satisfy energy needs (12% to 15% of total energy intake).

Loss of appetite and poor dietary intake are important causes of weight loss associated with HIV infection in clients not on antiretroviral drugs.

**Micronutrients**
Micronutrient deficiencies are frequently present in HIV-infected adults and children. Check for anemia.

Daily adequate intake of micronutrients is important for HIV-infected adults and children and they should consume foods and drinks rich in vitamins and minerals, fortified foods, and micronutrient supplements as needed.

WHO’s recommendations on vitamin A, zinc, iron, folate and multiple micronutrient supplements remain the same. High dosage micronutrient supplements are not an alternative to comprehensive HIV treatment including therapy with antiretroviral agents.

**Interaction between nutrition and antiretroviral treatment**
Long-term use of antiretroviral agents can be associated with metabolic complications (e.g., cardiovascular disease, diabetes and bone related problems). Although, the value of antiretroviral therapy far outweighs the risks, the metabolic complications need to be adequately managed.

1.14. **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, 2008). The SOPs includes the following components:

- How to fill out ART Monthly Data Collection Sheet (Form SURV2)
- How, where, and when to report Form SURV2
- How to store, manage and secure the SURV2 data and forms
- How to request Form SURV2, ARVs, and other supplies
1.15. DRUG 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 8: Drug Interactions**

<table>
<thead>
<tr>
<th>Drug</th>
<th>ART Agent</th>
<th>Interaction</th>
<th>Suggested Action</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alpha blockers, beta blockers and calcium channel blockers</td>
<td>All PI’s and Efavirenz</td>
<td>Hypotension and syncope due to decreased drug clearance, at times potentially life threatening.</td>
<td>Monitor closely and adjust dose if signs of toxicity</td>
</tr>
<tr>
<td>Amitriptyline</td>
<td>RTV</td>
<td>Over sedation</td>
<td>Reduce dose</td>
</tr>
<tr>
<td>Anti-psychotic drugs</td>
<td>RTV</td>
<td>Increased potential for side effects due to decreased drug clearance.</td>
<td>Monitor closely and adjust dose if indicated, particularly with Haloperidol.</td>
</tr>
<tr>
<td>Benzodiazepines especially Midazolam</td>
<td>All PI’s</td>
<td>Over sedation and risk of respiratory depression</td>
<td>Avoid the use of these drugs unless clinically indicated i.e. Status epilepticus.</td>
</tr>
<tr>
<td>Cimetidine</td>
<td>RTV</td>
<td>Increased potential for side effects due to decreased drug clearance.</td>
<td>Monitor closely and adjust dose if indicated.</td>
</tr>
<tr>
<td>Ergometrine</td>
<td>All PI’s and EFV</td>
<td>Ergotism due to decreased clearance of ergot alkaloids</td>
<td>Use Syntocinon, and/or Misoprostol as clinically indicated.</td>
</tr>
<tr>
<td>Ketonconazole</td>
<td>NVP, SQV, RTV and EFV</td>
<td>Potential for toxicity due to decreased drug clearance.</td>
<td>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.</td>
</tr>
</tbody>
</table>

22
<table>
<thead>
<tr>
<th>Drug Class</th>
<th>PI(s)</th>
<th>Interactions</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nonsteroidal anti-inflammatory drugs</td>
<td>RTV</td>
<td>Increased potential for side effects due to decreased drug clearance.</td>
<td>Avoid the use of these drugs unless clinically indicated and no alternative available.</td>
</tr>
<tr>
<td>Oral Contraceptives (OCP)</td>
<td>EFV, NVP, LPV, and RTV</td>
<td>Failure of OCP due to increased clearance</td>
<td>Alternate or additional form of contraception</td>
</tr>
<tr>
<td>Oral hypoglycaemics</td>
<td>All PI’s</td>
<td>Risk of hypoglycaemia due to decreased drug clearance</td>
<td>Close monitoring of BSL</td>
</tr>
<tr>
<td>Pethidine</td>
<td>RTV</td>
<td>Increased potential for side effects due to decreased drug clearance especially seizures</td>
<td>Avoid the use of this drug unless clinically indicated and no alternative available.</td>
</tr>
<tr>
<td>Phenytoin and Carbamazepine</td>
<td>LPV, RTV, EFV and possibly other ART agents</td>
<td>Two-way interaction- LPV, EFV and Phenytoin have increased clearance. RTV may reduce Carbamazepine clearance.</td>
<td>Monitor clinically for toxicity or reduced levels. Monitor serum anticonvulsant drug levels if able.</td>
</tr>
<tr>
<td>Prednisone and Dexamethasone</td>
<td>RTV and SQV</td>
<td>Increased potential for side effects due to decreased drug clearance.</td>
<td>Monitor closely and adjust dose if indicated.</td>
</tr>
<tr>
<td>Rifampicin</td>
<td>PI</td>
<td>Increased PI levels due to decreased drug clearance.</td>
<td>Avoid combining Rifampicin and PI’s. EFV preferred drug for co-administration.</td>
</tr>
<tr>
<td>Thyroid Replacement Therapy</td>
<td>PI</td>
<td>Increased potential for side effects due to decreased drug clearance.</td>
<td>Monitor closely and adjust dose if indicated.</td>
</tr>
<tr>
<td>Warfarin</td>
<td>RTV</td>
<td>Unpredictable levels</td>
<td>Monitor closely</td>
</tr>
</tbody>
</table>
CHAPTER TWO

PREVENTION OF PARENT TO CHILD TRANSMISSION OF HIV (PPTCT)
2.1. PREVENTION OF PARENT TO CHILD TRANSMISSION

The best way to avoid mother to child transmission of HIV is to prevent women of reproductive age from becoming HIV–infected. However, for those women who are pregnant and are already infected, there is sufficient evidence that there are effective ARV regimes which can significantly reduce transmission of HIV from the mother to her child during pregnancy and childbirth.

The selection and use of ARVs in PNG will depend on the availability of the drugs, the knowledge and experience of the trained healthcare workers at the health facility. Most health care facilities do not have healthcare workers trained in the prevention of mother to child transmission (PPTCT), and where they are available, their background knowledge about PPTCT (specifically the use of ART) will have an impact on the drug regime used.

PPTCT entails more than just ART. A comprehensive approach to the prevention of HIV infection in infants should consist of:

- Primary prevention of HIV infection by women;
- Prevention of unintended pregnancies among women living with HIV;
- Prevention of transmission from mothers living with HIV to their infants; and
- Care, treatment and support for mothers living with HIV, their children and their families.

Mothers in PNG usually book late for antenatal care and less than 40% of mothers are delivered by skilled health professionals. The low incidence of supervised deliveries poses an additional challenge to the provision of PPTCT in PNG.

Triple therapy regimes are the most efficacious and should be the gold standard of treatment that is delivered to all HIV positive mothers. In settings with limited capacity for delivering health services, it may be necessary – as an absolute minimum – to implement the single dose (mother and infant) NVP regimen although this should not be the preferred regimen. Triple therapy initiated during pregnancy should be continued postnatally to optimize the mother's health and to minimize the risk of HIV transmission with breastfeeding. The mother should attend an adult and paediatric ART program prior to delivery so that ongoing care for her and her infant can be arranged.
2.2. WHEN TO INITIATE ARV TREATMENT IN PREGNANT WOMEN

Table 9: When to initiate ARV Treatment in Pregnant Women

<table>
<thead>
<tr>
<th>WHO Clinical Stage</th>
<th>CD4 Testing not available</th>
<th>CD4 Testing available</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Do not treat</td>
<td>Treat if CD4 cell count &lt;350 cells/mm³</td>
</tr>
<tr>
<td>2</td>
<td>Do not treat</td>
<td>Treat if CD4 cell count &lt;350 cells/mm³</td>
</tr>
<tr>
<td>3</td>
<td>Treat</td>
<td>Treat irrespective of CD4 count but consider CD4 values for better management</td>
</tr>
<tr>
<td>4</td>
<td>Treat</td>
<td>Treat irrespective of CD4 count</td>
</tr>
</tbody>
</table>


The recommended first line regimen for pregnant women who require ARV treatment is ZDV/3TC/NVP.

Table 10: Recommended first line regimen for Pregnant Women who Require ARV Treatment

<table>
<thead>
<tr>
<th>Mother</th>
<th>Regime</th>
</tr>
</thead>
<tbody>
<tr>
<td>Antepartum</td>
<td>ZDV + 3TC + NVP twice dailyᵃ,ᵇ</td>
</tr>
<tr>
<td>Intrapartum</td>
<td>ZDV + 3TC + NVP twice dailyᵇ</td>
</tr>
<tr>
<td>Postpartum</td>
<td>ZDV + 3TC + NVP twice daily</td>
</tr>
<tr>
<td>Infant</td>
<td>ZDV for 4 weekᶜ</td>
</tr>
</tbody>
</table>

ᵃ d4T may be substituted for ZDV in cases of anemia.
ᵇ When commencing NVP, ensure escalating dose (200mg OD for 14 days then 200mgs BD if no problems) is used. It should also be noted that there is an increased risk of liver toxicity and severe skin reactions when NVP is given to women with a CD4 count >250 cells/mm³. Monitor ALT levels and if ALT level >5 times the upper limit of normal cease NVP permanently.
ᶜ If the mother received less than 4 weeks of ART during pregnancy, infant should have four weeks of ZDV
ᵈ. In women with CD4 count >250 cells/mm³, it is recommended to use a ritonavir boosted protease inhibitor or EFV if past first trimester due to the increased risk of hepatitis associated with NVP rash.

2.3. GUIDELINES FOR USE OF ART DRUGS FOR PPTCT

Women living with HIV who do not yet need ART must still receive highly effective ARV prophylaxis. While in settings with limited capacity for delivering health services, it may be necessary – as an absolute minimum – to implement the single dose (mother and infant) NVP regimen. Single dose NVP is also an important option when HIV infection is identified late in pregnancy or during labour. However, where feasible, services should plan to
introduce more complex and efficacious regimes to maximize protection for
the baby and reduce the risk of NVP resistance.

### Table 11: PPTCT ART Guidelines

<table>
<thead>
<tr>
<th>Mother</th>
<th>Regime</th>
</tr>
</thead>
<tbody>
<tr>
<td>Antepartum</td>
<td>ZDV + 3TC + NVP twice daily&lt;sup&gt;a&lt;/sup&gt;,&lt;sup&gt;e&lt;/sup&gt; starting at 28 weeks of pregnancy or as soon as feasible thereafter&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>Intrapartum&lt;sup&gt;b&lt;/sup&gt;</td>
<td>Single dose NVP (200mg) plus ZDV (600mg) and 3TC (300mg) at the onset of labour</td>
</tr>
<tr>
<td>Postpartum</td>
<td>Continue antepartum regime of ZDV + 3TC + NVP twice daily&lt;sup&gt;a&lt;/sup&gt;,&lt;sup&gt;c&lt;/sup&gt;</td>
</tr>
<tr>
<td>Infant</td>
<td>Single dose NVP&lt;sup&gt;d&lt;/sup&gt; (2mg/kg) plus ZDV (4mg/kg) for 4 weeks</td>
</tr>
</tbody>
</table>

<sup>a</sup> Alternative regimens for programmes with limited capacity is detailed in Section 2.4. d4T may be substituted for ZDV in cases of anemia

<sup>b</sup> Mothers who arrive in labour and have not had any antepartum ARV prophylaxis, she should receive NVP/ZDV/3TC intrapartum and postpartum as detailed.

<sup>c</sup> Mothers who have commenced on ARV’s need to be continued on these for both their benefit and the benefit of the infant they are feeding and caring for.

<sup>d</sup> Single dose NVP is associated with the development of NVP resistance in both the mother and infant. Single dose NVP should only be used when the preferred regimen is not available.

<sup>e</sup> In women with CD4 count >250 cells/mm<sup>3</sup>, it is recommended to use a ritonavir boosted protease inhibitor or EFV if past first trimester due to the increased risk of hepatitis associated with NVP rash.

### 2.4 BASIC NEVIRAPINE ART REGIMEN FOR PPTCT

In limited capacity settings, a minimum ARV prophylaxis regimen will include NVP (200mg) to the mother at onset of established labour and NVP syrup 2mg/kg to the infant after delivery. Babies should be given the syrup as soon as possible after delivery but no later than 72 hours. In addition to the NVP syrup given after delivery, Zidovudine (ZDV) syrup (4mg/kg) twice a day for 28 days. In situations where the additional ZDV treatment is unable to be given, the single dose of NVP syrup should still be given.
2.5 GUIDELINES ON HIV AND INFANT FEEDING

Evidence from recent research\textsuperscript{12} in resource limited countries has demonstrated the superiority of breast feeding over formula feeding in terms of survival of infants born of HIV infected mothers. This is so whether or not the mother is on HAART. Parents must be advised of this. Whatever feeding option is chosen, it must be acceptable, feasible, affordable, sustainable and safe. Any mother who has medical eligibility for HAART should be maintained/initiated on HAART.

Studies have shown that HIV can be transmitted from a mother to her baby through breastfeeding. By 1998, it was known that the use of antiretroviral drugs could substantially reduce the risk of mother-to-child transmission before and during delivery. It then became more urgent to find ways to reduce the risk of postnatal transmission through breastfeeding.

In recent years great efforts have been made to promote breastfeeding by all mothers. There are considerable risks associated with not breastfeeding, particularly in resource poor settings. This has resulted in both policy makers and health workers being reluctant to suggest that a woman feed her infant in any other way. Accordingly, it has been difficult for health workers to advise a HIV-positive woman how best to feed their infant. It is perhaps even more difficult for a mother and her family to decide what is best.

In 1997, WHO, UNICEF and UNAIDS issued a joint policy statement, indicating that HIV-positive women should be enabled to make a fully informed decision about feeding their infants, and supported in whatever method of feeding they choose. Over the last 10 years research has shown clearly that the infant feeding option that gives the great majority of infants of HIV positive mothers the best chance of survival in resource poor settings like PNG is for the mother to exclusively breast feed the baby for at least the first 6 months of life. ‘Mixed Feeding’ (where the mother gives a mix of breast and other feeding to the infant) has been shown to be associated with a significantly higher risk of HIV transmission to the infant.

The following guidelines have been developed for the ‘Prevention of Parent-to-Child Transmission’ program in PNG to give the babies of HIV positive mothers the best chance of survival. The Guidelines also attempt to set out feeding options for women with atypical or particular circumstances and hope to protect, promote and support breastfeeding for those who are both HIV positive and negative. The recent research from resource limited countries

demonstrates the superiority of breast feeding over artificial feeding in terms of survival of infants born of HIV infected mothers.

**General Principles**

1. All women attending antenatal clinic should receive general antenatal education including information on HIV, Family Planning and the fact that exclusive breastfeeding for the first six months of life and continued breast feeding for 2 years gives the baby the best chance of survival whether a mother is HIV positive or negative.

2. For all women, pretest counseling must be offered. This should be followed by HIV testing. The result must then be disclosed to individual women during a post-test counseling session.

3. Infant feeding counseling must not be offered during a post-test counseling session.

4. In determining the advice to give to a woman regarding infant feeding, the health care worker needs to take into account the woman's personal circumstances. In virtually all situations in PNG, artificial feeding is not safe or sustainable and therefore is not an option. Exclusive breast feeding for the first six (6) months and continued breast feeding to two (2) years has been demonstrated to give infants in countries such as PNG the best possible option for survival. Infant feeding counseling should be followed up in subsequent antenatal and post-natal (including paediatric follow-up) visits.

5. All HIV positive women should also receive additional information on nutrition, health and hygiene to support them selves whilst living with HIV infection and **MUST BE** offered reliable family planning and dual protection beginning in the antenatal period and followed up again after birth.

**Feeding Options**

**The standard protocol for most PNG mothers should be exclusive and continued breastfeeding as this will provide the baby with the best chance of survival**  

- Exclusive Breastfeeding means that nothing other than breast milk is given to the baby for the first six (6) months. Exclusive breastfeeding minimizes the risk of HIV transmission associated with breastfeeding.

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3 Kuhn, ibid  
4 Shapiro, ibid
• Continued Breastfeeding means continuing to breastfeed after the introduction of other fluids and solid food at six (6) months. This option maximizes the advantages of breastfeeding. While continued breastfeeding is associated with an increased HIV transmission risk, studies have demonstrated that no differences were detected in breast milk immunologic profiles of HIV-infected women whose infants were either ill or well. Discontinuation of breast-feeding was the strongest predictor of morbidity in infants and the primary risk for infant morbidity\textsuperscript{5}.

• Women must be taught proper breast attachment to reduce the risk of subsequent breast problems, such as mastitis, breast abscess, engorgement etc must be treated accordingly.

• Continuation of maternal combined ARV therapy may reduce the risk of transmission of HIV through the breast milk and therefore should be continued. Any mother who did not commence/continue combined ARV therapy during her pregnancy and is medically eligible should be commenced on therapy.

• If PCR/DNA testing is performed on the baby and the result is that the baby is HIV Positive, then breast feeding should be continued and the baby referred to a paediatric HIV clinics for further management. If the PCR/DNA testing reveals that the baby is HIV –ve, then the mother should be congratulated that all the efforts so far have resulted in keeping the baby virus free and well, and that the best chance of survival for the baby is for her to continue to exclusively breast feed as above. Continuing to exclusively breast feed a baby after 2 months of age is associated with very small risk of HIV getting to the baby (especially if the mother is on ART), while evidence shows that complete weaning of a baby in PNG at 6-8 weeks of age is very dangerous indeed and often associated with life-threatening diseases and malnutrition.

• This option therefore should be promoted as the standard protocol in PNG as it gives the infant the best chance of overall survival.

**Express and Heat-Treat Breast milk**

• While this option offers an ideal nutrition for the baby, has some protection against infections and has a low risk of HIV transmission, in nearly all circumstances in PNG it will be impractical.

\textsuperscript{5} ibid
Breastfeeding by Another Woman

- This method is also called ‘Wet Nursing’. The chosen woman who has agreed to wet nurse should be counseled, tested and shown to be HIV-negative.

- If the wet nurse is sexually active she will also require counseling on safe sex practices so that she does not acquire the virus during the breastfeeding period.

- A wet nurse should have access to breastfeeding support and assistance to establish effective breastfeeding. This is to prevent and treat conditions such as nipple fissure and mastitis which may hinder breastfeeding.

Artificial or Replacement feeding from Birth

- Artificial or replacement feeding is the process of feeding a child who is not receiving any breast-milk with a diet that provides all the nutrients the child needs until the child is fully fed on family foods. With rare exceptions such as in situations where the mother has died or is incapable or breast feeding, this is not an option in the PNG context as replacement feeding in resource limited settings results in significantly higher infant mortality from gastro-enteritis and other illnesses.\(^6\)

**REMEMBER**: Whatever feeding option is chosen, it must be **acceptable**, **feasible**, **affordable**, **sustainable** and **safe**.

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\(^6\) Shapiro, ibid
CHAPTER THREE

THE USE OF ANTIRETROVIRAL DRUGS IN CHILDREN
3.1. BACKGROUND OF ART IN CHILDREN

The underlying principles of ART in children are similar to those of adults. However there are specific physiological, clinical, practical and social issues to consider when treating HIV-infected children with ART.

The following are some of these specific issues.

a. Data on efficacy of ART agents in adults can be extrapolated to children but issues on pharmacokinetics, formulation and ease of administration require special consideration. Young children metabolize drugs differently from adults and there is a particular need for data on pharmacokinetics in children under 3 years.

b. There are laboratory limitations to diagnosing HIV infection in children under 18 months old in resource limited settings. Detection of HIV DNA by PCR is the gold standard diagnostic test however it lacks sensitivity in the first weeks of life (as does plasma RNA and P24) and is not usually available in resource poor settings. Test sensitivity is close to 100% at 6 weeks of age.

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. (see Appendix 4)

d. Predictive values of surrogate markers to start and switch therapy is different from adults.

The CD4 count and percentage are less sensitive in identifying infants at risk for disease progression compared to older children and adults.

Plasma HIV-1 RNA (VL) levels are very high in infected infants (several million copies/ml) and persist at high levels for much longer (years rather than months) than in infected adults following primary infection. In developed countries there is no agreed cut-off for starting ART in children.

e. CD4 cell counts are higher and more variable in young children than in adults. They decline with age and reach adult values at 5-8 years. CD4 cell percentage is less variable although it also decreases with age. It is therefore preferable to use the CD4 cell percentage instead of the absolute cell count for decision-making on ART for infected children under 8 years.

f. Younger children have difficulties swallowing tablets and may require different formulations compared to adults. This may also lead to
adherence issues hence adherence counselors working with children should receive training specific for this population.

g. 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 regime that the parents or guardians are, or will be taking, should also be taken into consideration when deciding on the most appropriate regime 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.

3.2. CRITERIA TO INITIATE 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 regimes 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.

BOX 1: Summary of WHO recommendations for initiation of ART in infants and children.

<table>
<thead>
<tr>
<th>Infants and children with established HIV infection should be started on ART if they have:</th>
</tr>
</thead>
<tbody>
<tr>
<td>• WHO paediatric clinical stage 4 disease (irrespective of CD4);</td>
</tr>
<tr>
<td>• WHO paediatric clinical stage 3 disease (irrespective of CD4, although it may add guidance); children aged over 12 months with pulmonary or lymph node TB, LIP, OHL and or thrombocytopenia, may be delayed if CD4 markers are above thresholds in table 12</td>
</tr>
<tr>
<td>• WHO clinical stage 2 disease and CD4 or TLC value at or below threshold</td>
</tr>
<tr>
<td>• WHO paediatric clinical stage 1 disease and CD4 value at or below threshold</td>
</tr>
</tbody>
</table>
**BOX 2: 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 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

The infant is symptomatic with 2 or more of the following:

- oral thrush  
- severe pneumonia  
- severe sepsis

Other factors that support the diagnosis of severe HIV disease in an HIV-seropositive infant include:

- Advanced disease or recent AIDS-related death of the mother  
- CD4% <20***

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

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* DNA PCR methods using dried blood spots (DBS) are being implemented through a separate training program in Papua New Guinea, but may not be available at all sites.  
**AIDS indicator conditions include some but not all HIV paediatric clinical stage IV conditions, such as PCP, cryptococcal meningitis, HIV wasting, Kaposi sarcoma, extrapulmonary TB  
***It is unclear how often CD4 is lowered in the above conditions in HIV-uninfected children
Table 12: Immunologic Criteria for Initiation of ART in children

<table>
<thead>
<tr>
<th>Age</th>
<th>HIV status (determined by appropriate method)</th>
<th>TLC</th>
<th>CD4 count</th>
<th>CD4%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infants &lt; 12 months</td>
<td>Positive</td>
<td>Treat all</td>
<td>Treat all</td>
<td>Treat all</td>
</tr>
<tr>
<td>12 - 35 months</td>
<td>Positive &lt;3000 cells/mm³</td>
<td></td>
<td>&lt;750 cells/mm³</td>
<td>&lt;20%</td>
</tr>
<tr>
<td>36 - 59 months</td>
<td>Positive &lt;2500/mm³</td>
<td></td>
<td>&lt;350 cells/mm³</td>
<td>&lt;20%</td>
</tr>
<tr>
<td>5 years or over</td>
<td>Positive &lt;2000/mm³</td>
<td></td>
<td>&lt;350 cells/mm³</td>
<td>&lt;15%</td>
</tr>
</tbody>
</table>

REMEMBER

- ART is recommended in all HIV infected infants under 12 months of age irrespective of clinical or immunological stage.
- Associated clinical conditions need to be treated before ART initiation.
- Definitive diagnosis of HIV in infants should be made at 6 – 8 weeks of age or at the earliest opportunity using HIV DNA PCR. This can be done in the Central Public health Laboratory using Dried Blood Spots (DBS).

3.3. Social Criteria for Initiation of ART in children

i. Children considered for treatment should live within 2 hours 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 >3 visits) counseling in the antenatal period followed by more than three sessions of follow-up counseling after birth. Information given should include details of 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 also have a minimum of three counseling sessions before a decision of ART 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 organisation within the area in which they live. The organisation must be credible and acceptable to the family and be able to provide continued support outside of the hospital.

Four out of the six (4/6) criteria need to be fulfilled prior to initiating ART

3.4. BASELINE TESTS IN CHILDREN

- Full blood count (HB, TLC, WBC and Differential)
- CD4 if available
- Electrolytes, Hepatic transaminases and Blood Glucose
- Sputum for AFB and/or CXR
- Hepatitis B surface antigen

3.5. WHAT DRUGS TO USE IN CHILDREN

Table 13: First-line antiretroviral regimes for children

<table>
<thead>
<tr>
<th>Paediatric First Line ART Regimen</th>
</tr>
</thead>
<tbody>
<tr>
<td>4 possible regimes for first line</td>
</tr>
<tr>
<td>➢ ZDV+3TC+NVP</td>
</tr>
<tr>
<td>➢ ZDV+3TC+EFV</td>
</tr>
<tr>
<td>➢ d4T+3TC+NVP (FDC 6 and FDC 10)</td>
</tr>
<tr>
<td>➢ d4T+3TC+EFV</td>
</tr>
</tbody>
</table>

NB: If <3 years or <10kg, NVP is preferred and EFV should not be used
If ≥/=3 years or ≥/=10kg, NVP or EFV

Drugs for children are now available in a fixed dose combination (FDC) form that may be split or dissolved in water, and is in a more appropriate dose ratio for children. Because of the tremendous convenience, cost, and adherence advantage of these formulations, FDC are the preferred combinations for children. They are available as FDC 6 and FDC 10 (based on the dose of stavudine contained – either 6 or 10 mg). FDC containing zidovudine are expected to be made available very soon.

ZDV/3TC plus ABC may be used if concomitant anti-tuberculosis therapy is being received but caution should be exercised as the regimen has shown lower virological potency in adult studies and therefore its use should be restricted to special circumstances and in consultation with experts only.

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 cause 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. Children using FDC should take the triple FDC (containing NVP, d4T and 3TC) in the morning and the dual FDC (containing d4T and 3TC ONLY) in the evening for the first 14 days.

ZDV is associated with anaemia due to bone marrow toxicity in 5-10% of patients. If haemoglobin prior to initiation is less than 8g/dl (without a correctable cause) combination with d4T should be used. TDF is not recommended for children due to concerns about bone mineralization and renal toxicity and a lack of dosing information or appropriate formulations for children.

Children who have had previous exposure to ART through PPTCT and/or breastfeeding, should be considered eligible for the standard first line regimen using the same dose and criteria until other preferred regimens are more widely available.

**3.6. SWITCHING FOR SIDE EFFECTS AND TOXICITIES**

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. Children switching a drug for toxicity purposes should be assessed for evidence of treatment failure at the same time, which would require a more comprehensive change in regimen.
Table 14: Drug substitution for toxicity

<table>
<thead>
<tr>
<th>If toxicity…</th>
<th>Due to …</th>
<th>Then switch to …</th>
</tr>
</thead>
</table>
| d4T/3TC/NVP  | d4T – neurological or pancreatitis  
d4T – lipodystrophy or lactic acidosis  
NVP – hepatotoxicity  
NVP – Steven Johnson Syndrome | ZDV  
ABC, ZDV  
EFZ (except in children <3yrs) alternatively ABC or PI |
| ZDV/3TC/NVP  | ZDV – Bone Marrow Suppression  
NVP – see above | d4T or ABC |
| d4T/3TC/EFV  | EFV – CNS toxicity  
d4T – see above | NVP. |
| NVP or d4T/3TC/ABC | Hypersensitivity to ABC | NVP or EFV |

3.7. SWITCHING FOR TREATMENT FAILURE

WHO recommends that the entire regime 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, one 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 regime is the same as in adults.

Clinical failure: a lack of growth response to treatment or a decline in growth among those who show initial response to therapy (in the absence of another identifiable cause such as malnutrition or tuberculosis); a loss of neuro-developmental milestones or the development of encephalopathy and the recurrence of infections, such as oral candidiasis that is refractory to treatment.

Immunological failure: Continued decline of the CD4 cell count/CD4 % despite assured drug adherence. The definition of immunologic failure can follow 3 types: 1) by a drop in CD4 to values below their age-related CD4 threshold for initiation of treatment after an initial recovery, 2) a return to pre-treatment baseline levels following initial recovery, and 3) a 50% decline from peak values after initial recovery. These values must be confirmed on repeated measurement. Decisions regarding change in regimen should not be
made based on a single laboratory value. Correlation with clinical symptoms is advised.

**Virological failure:** Develops as a consequence of viral resistance and can only be confirmed by documentation of a rising viral load. In the absence of this measurement the important clinical signs of antiretroviral drug failure in an adherent patient include a lack of clinical response (such as persistent diarrhea, weight loss, appearance or a previous or new OI). If treatment failure is due to non-adherence, considerations should be given to discontinuation of therapy.

**Table 15: Drug substitution for Treatment Failure**

<table>
<thead>
<tr>
<th>First-line regimen</th>
<th>Second-line regime</th>
</tr>
</thead>
<tbody>
<tr>
<td>ZDV or d4T/3TC/NVP or EFV</td>
<td>ddI/ABC/LPV/r or ddI/ABC/SQVr</td>
</tr>
<tr>
<td>ZDV or d4T/3TC/ABC</td>
<td>ddI/EFV or NVP plus LPV/r</td>
</tr>
</tbody>
</table>

**3.8. MONITORING AND WHEN TO CHANGE**

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.

**NB:** It is recommended that all children on ART have their WEIGHT and (if possible) HEIGHT measured on each visit to the clinic.

**3.9. PREVENTION OF OPPORTUNISTIC INFECTIONS**

**Cotrimoxazole Prophylaxis**

Cotrimoxazole prophylaxis should be given to all babies with the following conditions

- All HIV exposed infants from 6 weeks to 18 months of age (until confirmed negative) to prevent PCP and other bacterial infections when born to an HIV infected mother (irrespective of whether the woman received ART prophylaxis during pregnancy).
- All HIV positive infants from 6 weeks to 5 years regardless of clinical stage or CD4 percentage. Reassess after 5 years of age.
- A CD4 cell percentage of <15% in children older than 5 years.
- All children who have had an episode of PCP or another AIDS defining illness.
- All children who have had an episode of PCP or another AIDS defining illness.
- Symptomatic HIV disease or Clinical stage II, III or IV.
- A CD4 cell percentage of <25% if >12 months old.

Table 16: Dosage of cotrimoxazole in children

<table>
<thead>
<tr>
<th>Age</th>
<th>Dosage</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 Less than 6 months</td>
<td>100mg SMX/20 mg TMP (2.5 mls of syrup)</td>
</tr>
<tr>
<td>2 6 months to 5 years</td>
<td>200 mg SMX/40 mg TMP (5 mls of syrup or half single strength adult tablet)</td>
</tr>
<tr>
<td>3 6 – 14 years</td>
<td>400mg SMX/80mg TMP (10 mls of syrup of one single strength adult tablet)</td>
</tr>
<tr>
<td>4 &gt;14 years</td>
<td>800mg SMX/160mg TMP (2 adult single strength tablets)</td>
</tr>
</tbody>
</table>

- INH prophylaxis (5-10mg/kg orally once daily for 6 months) should be given to children whose mothers have TB.

It is important that all children whether HIV infected or not should receive immunizations according to the normal schedule except BCG and OPV which is not given to children with WHO stage III or IV disease. IPV may be used in place of OPV.

Children with symptomatic HIV infection and meeting established criteria should receive antiretroviral therapy and once immune reconstituted should then receive appropriate vaccinations.

3.10. CHILDREN WITH TUBERCULOSIS AND HIV COINFECTION

It is recommended that children with TB/HIV co-infection complete TB treatment before ART.

However children with very low CD4 cell counts/% should begin ART as soon as their TB treatment is tolerated to avoid acquiring a new opportunistic infection during the course of TB therapy. Since children without HIV may also get TB, the urgency of ART may be driven by CD4 cell count measurement and clinical condition. If CD4 cells can not be measured, children with TB should be offered ART.
CD4 >200 (>15%), begin ART at the end of the intensive phase (2 months).

CD4<200 (<15%), begin ART as soon as TB therapy is tolerated, usually at 2 weeks.

If a child needs treatment of both infections concurrently then use the regimen for children with co-infection - d4T or ZDV/3TC/ABC. If the child is more than 3 years and heavier than 10 kg then d4T or ZDV/3TC/EFV is recommended.

3.11. NON OCCUPATIONAL EXPOSURE

In cases of significant or potential exposure of a child to HIV either through percutaneous injury or mucosal (sexual) exposure, consideration may be given to the use of antiretroviral drugs for the prevention of infection. Whether to give prophylaxis and which drugs to use depends on the nature and risk of the exposure. In any case, even following significant non-occupational exposures the risk of transmission with no intervention may be estimated at approximately 0.5-1%. This risk needs to be balanced against the potential risk of toxicity from the medications and the associated inconvenience and side effects.

The benefits of non-occupational post exposure prophylaxis (nPEP) diminish with time. Children suffering sexual and percutaneous exposures to a person of unknown HIV status that occur less than 72 hours prior to evaluation may be offered a 2 drug prophylaxis combination of either AZT/3TC or d4T/3TC (for doses see appendix 2) beginning as soon as possible and continuing for 28 days. Children exposed to a person known or likely to have HIV infection may be offered an expanded regimen that includes the above drugs with the addition of either efavirenz (if greater than 3 yrs) or a protease inhibitor if available. Because of reported severe reactions to nevirapine when used for this indication, it is not recommended to use this drug for prophylaxis. Children evaluated more than 72 hours after the exposure occurred are generally not offered prophylaxis but still require care and follow-up. If possible the source case should be tested and if HIV negative, nPEP may be stopped.

Baseline evaluations following exposure should include a rapid HIV antibody test. This helps to avoid treating patients already infected with HIV using sub-optimal regimens. 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 older children. Prior to giving a female of reproductive potential efavirenz a pregnancy test should be performed since efavirenz is associated with birth defects if given in the first trimester.
Other baseline laboratory tests should include a full blood count, liver enzymes, and a creatinine. After 2 weeks or if the child experiences symptoms a full blood count and liver enzymes may be repeated to monitor for toxicity.

Finally, HIV testing should be repeated at 1 month, 3 months, and 6 months following the exposure, with additional STI and hepatitis virus testing as clinically indicated. Negative results at 6 months effectively exclude infection and routine follow-up may continue. Children who are victims of sexual assault must have appropriate evaluation and referral for psychological support.

**Table 17: Antibiotic Drug Regimen for Sexual Assault**

<table>
<thead>
<tr>
<th>Weight</th>
<th>Azithromycin</th>
<th>Amoxicillin</th>
<th>Augmentin</th>
<th>Probenecid</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;10 kg</td>
<td>250 mg (1/2 tab)</td>
<td>1 G (4x250mg)</td>
<td>½ tab</td>
<td>½ tab</td>
</tr>
<tr>
<td>&gt;10 kg</td>
<td>500 mg (1 tab)</td>
<td>1 ½ G (6x250)</td>
<td>1 tab</td>
<td>1 tab</td>
</tr>
</tbody>
</table>
CHAPTER FOUR

PROTECTIVE MEASURES AGAINST HIV TRANSMISSION IN HEALTH CARE SETTINGS AND POST EXPOSURE PROPHYLAXIS
4.1. INTRODUCTION

HIV and other blood borne diseases such as Hepatitis B may be transmitted in health care settings from a patient to a health care worker, patient to patient or from health care worker to patient. HIV is likely to be present in body fluids from infected person. The occupational risk of becoming HIV infected from patients in health care settings although minimal, is mostly associated with needle stick injuries from a patient infected with HIV. Patient to patient transmission usually results from contaminated equipment, which has been incorrectly or inadequately disinfected. Infection control practices should therefore be in accordance with the PNG Infection Prevention Policy Guidelines for Health Facilities.7

Most patient care settings should not pose any significant risk of HIV transmission. At the same time, minimal infection control measures such as washing hands with soap and water can prevent transmission during care. Nevertheless, all healthcare workers must adopt appropriate infection risk assessment and apply accident prevention procedures. The context and environment in which health care is provided must offer safety to the health care provider.

Prevention of the transmission of HIV through applying Standard Precautions (previously known as Universal Precautions) is very important. Standard Precautions are simple standards of infection control practices to be used in the care of all patients, at all times, to reduce the risk of transmission of infections.8 These include:

Hands should be washed with soap and water;
- Before and after contact with each patient.
- Before and after each procedure
- Before wearing and after removal of gloves
- When hands are visibly soiled
- Before preparing, handling, serving or eating food and before feeding a patient
- Before leaving the area of work

Adequate supply of disposable towels (paper towels) is encouraged in order to avoid reusable towels. (If disposable towels are not available, reusable towels should only be used once then washed and dried in the sun.)

4.2. USE OF PROTECTIVE BARRIERS

Gloves should be worn in all procedures involving contact with blood or other body fluids. Gloves must be discarded after each patient (Hazardous waste

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management Guidelines). Gloves are not required for routine care activities in which contact is limited to a patient’s intact skin.

**Clean non-sterile gloves will be worn:**

- For invasive examination and non surgical procedures;
- Contact with blood, body fluids, secretions, excretions, mucous membranes, draining wounds, or non-intact skin; and
- For handling items visibly soiled with blood, body fluids or, secretions.

Protective clothing such as waterproof gowns, aprons, eye protection and or masks should be worn where there is likelihood of exposure to large amounts of blood or body fluids such as in theatre, labour room or in the laboratory.

**4.3 CAREFUL HANDLING AND DISPOSAL OF SHARP INSTRUMENTS**

- All sharps should be handled extremely carefully to avoid needle stick or other sharp injuries.
- Needles should not be recapped, bent, broken or removed from syringes. If they must be removed from syringes, then use forceps.
- Remove vacutainers with forceps.
- Holders must be used for all blades.

All needles and other sharp instruments should be deposited in puncture resistant sharps containers that must be placed near the working place. The containers (safety boxes) should be clearly labelled, easily accessible and incinerated when three quarters full.

**4.4 SAFE DISPOSAL OF WASTE CONTAMINATED WITH BODY FLUIDS**

Soiled waste that is contaminated with blood, body fluids, laboratory specimen or other tissues, should be placed in leak proof containers with special labels and incinerated, or buried in a 7 feet deep pit at least 30 feet away from any water source or in a pit latrine. Liquid waste such as blood or body fluids should be poured down a drain connected to a septic tank or an adequately treated sewer or pit latrine.

**4.5 DISINFECTION OF CONTAMINATED EQUIPMENT**

All material including linen used repeatedly must be properly disinfected and or sterilized. Disinfections should be by immersing in 1.0% hypochlorite solutions, using bleach powered or liquid bleach as described in the PNG Infection Prevention Policy Guidelines. Thorough cleaning with soap and hot water removes a high proportion of micro-organisms. All equipment should be dismantled before cleaning. Gloves must be worn during cleaning of equipment and if splashing with body fluids is likely, additional protective
clothing such as water proof aprons, gowns, boots, protective eye wear or masks should be worn. The method of decontamination can be decided based on the following table.

**Table 18: Criteria for selecting decontamination method**

<table>
<thead>
<tr>
<th>Level of risk</th>
<th>Items</th>
<th>Decontamination method</th>
</tr>
</thead>
<tbody>
<tr>
<td>High risk</td>
<td>Instruments which penetrate the skin/body</td>
<td>Single use of disposables and sterilization of re-usable equipment</td>
</tr>
<tr>
<td>Moderate risk</td>
<td>Instruments which come in contact with non-intact skin or mucous membrane</td>
<td>Sterilization, boiling or chemical disinfection</td>
</tr>
<tr>
<td>Low risk</td>
<td>Equipment which comes in contact with intact skin</td>
<td>Thorough washing with soap and water</td>
</tr>
</tbody>
</table>

### 4.6 PROPER HANDLING OF SOILED LINEN

Soiled linen should be touched as little as possible, they should be collected in bags and not rinsed or sorted out at the patient care area. If possible linen with large amounts of blood should be transported in leak proof containers, and if not available they should be folded with the soiled parts inside, and handled carefully with gloves. Soiled linen should be soaked in 0.5% bleach solutions as per PNG Infection Prevention Policy Guidelines for not less than thirty (30) minutes, then washed separately in hot soapy water and then air dried in direct sun light.

### 4.7 STERILIZATION AND DISINFECTION

The Human Immunodeficiency Virus does not survive well outside the human body. Nevertheless, it is mandatory that healthcare workers and other care providers caring for HIV infected persons take precautions in order to prevent accidental spread of the virus.

All forms of sterilization will destroy HIV. Recommended methods of sterilization include steam under pressure e.g. autoclave or pressure cooker, or dry heat such as oven. Disinfection will usually inactivate HIV. Recommended disinfectants are Bleach (corresponding to a 1.0% sodium hypochlorite solution) and 1% Lysol. Commonly methods used are boiling and chemical disinfection with hypochlorite solution. If there is a need for boiling equipment, then the equipment must be cleaned and then boiled for at least 20 minutes at sea level and longer at higher altitudes.

### 4.8 SPILLAGE MANAGEMENT

Detergents and hot water are adequate for routine cleaning of floors, beds and toilets. In case of spillage of blood or body fluids, the area should be cleaned with chlorine based disinfectant which is left for 20
minutes and followed by thorough cleaning with soap and hot water. Alternatively, pour hypochlorite solution 0.5% on the site and leave it for 20 minutes. Then clean with a mop or disposable rag. Then pour hypochlorite solution again and clean. All healthcare workers and other care givers must be made conversant with Standard Precautions

4.9 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.

Occupational exposure

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 (EHCW)

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 24 – 72 hours of the exposure. The exposed healthcare worker should be counseled and tested for HIV before PEP is given (i.e., to establish infection status at the time of exposure). In case of refusal to test, PEP should not be started.
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 (i.e., pregnancy, breast feeding, or renal or hepatic disease).

Hepatitis B vaccination should also be considered.

**4.10 PEP DRUG REGIMES**

For most HIV exposures, a combination of ZDV and 3TC should be used. For exposures that pose an substantially increased risk for transmission (e.g. hollow needle, fresh blood and advanced HIV illness in source patient):

Zidovudine 300 mg orally 12 hourly  
Plus Lamivudine 150 mg orally 12 hourly  
Plus Efavirenz 600 mg once daily

**NOTE**

*Nevirapine should not be used for post exposure prophylaxis*

Stavudine 30 mg orally 12 hourly may be used in place of Zidovudine for patients with anaemia.  
Ensure negative pregnancy test and adequate contraception for women being administered Efavirenz.  
Lopinavir/r may be considered after consultation with a HIV trained physician.  
**Dual drug therapy should only be considered in the absence of other alternatives if the risk is high.**

**4.11 TIMING OF POST EXPOSURE PROPHYLAXIS (PEP)**

PEP should be initiated within 12 hours but up to 72 hours maximum

**4.12 DURATION OF POST EXPOSURE PROPHYLAXIS (PEP)**

The optimal duration of PEP is 28 days. This is based on evidence from occupational and animal studies where AZT, administered for 4 weeks if tolerated, appeared protective.

**4.13 FOLLOW-UP OF OCCUPATION EXPOSURE TO HIV**

Healthcare workers with occupational exposure should be tested at baseline, 4 weeks, 12 weeks and 6 months post exposure to HIV.
4.14 MONITORING AND MANAGEMENT OF PEP TOXICITY

If PEP is used, the Health care provider should be monitored for drug toxicity. The scope of testing should be based on medical conditions in the exposed person and the toxicity of drugs included in the PEP regimen. Minimally, laboratory monitoring for toxicity should include a complete blood count and renal and hepatic function tests.

4.15 PEP FOR VICTIMS OF SEXUAL ASSAULT

Counselling

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 managed at Hospitals.

When to start PEP

All persons presenting to a health facility within 72 hours of being allegedly raped should be offered PEP if it is available. Before starting PEP and following counseling and the obtaining of informed consent, HIV testing must be offered. 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. IF THE VICTIM DOES NOT WISH TO UNDERGO HIV TESTING AT THIS TIME THEY CAN STILL HAVE PEP ARV. HIV testing should be offered again at a later time.

Drug Regimen

The recommended treatment regimen is Triple therapy (first line regimen) daily for 4 weeks. The noted contraindications for each of these drugs must be considered as detailed in these guidelines. In addition, women should be offered:

Treatment for gonorrhoea and Chlamydia:

Amoxicillin 2g plus
Augmentin 2 tabs plus
Probenecid 1g plus
Azithromycin 1g
(all above orally, stat, supervised)

Emergency oral contraception:
If there is a possibility that the assault may cause pregnancy and the assault occurred in the past 72 hours, then after counselling and consent:
3 combined contraceptive pills and another 3 after 12 hours. (The woman should be told to expect some nausea after this high dose). **NB** Make sure that she takes the actual hormone pills not the 7 iron/fefol pills that are on the card.

**OR**

20 Microlut tabs stat and another 20 tabs after 12 hours. (This dose of Microlut does not cause nausea). (This regime 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.)

**OR**

Postinor2 (levonorgestrel) is an alternative that, if available, can also be used for emergency contraception. Both tablets must be taken with 72 hours of the assault.

**Patient monitoring**

Routine testing with a full blood count and liver enzymes for patients on ZDV and 3TC is not recommended for such a short duration of therapy. Blood tests should be performed according to patient’s condition. Three (3) months after the PEP period, the individual should return for a confirmatory set of HIV tests to determine that the treatment was effective. If it was not effective and they have sero-converted, they should be enrolled in a HIV Care and Treatment program and monitored appropriately as all HIV positive individuals.
Table 19: Algorithm for assessment before PEP initiation in Occupational Exposure

1. Perform medical examination and key tests (STI, Pregnancy, HIV)
   Determine time when the event occurred

2. Determine if consent is provided.
   - Less than 72 hours:
     - Consent Denied, NO test done
     - Consent Provided, Test is done
       - HIV negative
         - Give PEP
         - Do follow up HIV test after 3 months
         - HIV negative—Counsel to stay negative
       - HIV positive
         - NO PEP
         - HIV/AIDS Care and Treatment program
   - More than 72 hours:
     - Counselling No PEP

3. If HIV is negative:
   - Give PEP
   - Do follow up HIV test after 3 months
   - HIV negative—Counsel to stay negative

4. If HIV is positive:
   - NO PEP
   - HIV/AIDS Care and Treatment program
Table 20: Algorithm for assessment before PEP initiation in Sexual Assault

<table>
<thead>
<tr>
<th>Step</th>
<th>Action</th>
</tr>
</thead>
<tbody>
<tr>
<td>Perform medical examination and key tests (STI, Pregnancy, HIV)</td>
<td>Determine time when the event occurred</td>
</tr>
<tr>
<td>Less than 72 hours</td>
<td>Consent Denied, NO test done</td>
</tr>
<tr>
<td>Consent Denied, NO test done</td>
<td>Offer PEP, STI treatment and, if appropriate, the morning after pill</td>
</tr>
<tr>
<td>Consent Provided, Test is done</td>
<td>HIV negative</td>
</tr>
<tr>
<td>HIV negative</td>
<td>Offer PEP, STI treatment and, if appropriate, the morning after pill</td>
</tr>
<tr>
<td>HIV Positive</td>
<td>NO PEP</td>
</tr>
<tr>
<td>More than 72 hours</td>
<td>Counselling No PEP</td>
</tr>
<tr>
<td>Consent Denied, NO test done</td>
<td>Offer HIV testing at a later date</td>
</tr>
<tr>
<td>Consent Provided, Test is done</td>
<td>Do follow up HIV test after 3 months</td>
</tr>
<tr>
<td>HIV negative</td>
<td>HIV positive</td>
</tr>
<tr>
<td>HIV Positive</td>
<td>HIV/AIDS Care and Treatment program</td>
</tr>
</tbody>
</table>
CHAPTER FIVE

OPPORTUNISTIC INFECTIONS (OIs)
5.1. INTRODUCTION

Currently there is no cure for HIV infection. There is however prophylaxis and treatment for some opportunistic infections resulting from HIV induced immune deterioration. It should always be recognized that we only treat and cure the associated diseases and symptoms and not HIV itself. Patients don’t die from HIV-infection, but succumb to the complications that the HIV induced immune deterioration cannot handle. With this approach the length and quality of life of the HIV infected patient can be substantially improved.

The purpose of the investigations recommended in these guidelines is to identify and manage treatable causes of morbidity in HIV infected individuals. Treatment is available for most of the opportunistic infections, and all efforts should be made to deal with all treatable conditions in people with HIV and AIDS. Cancer conditions in HIV positive patients should be managed as in sero-negative individuals.

In the following section, the guidelines also recommend how to identify and manage treatable causes of morbidity in HIV infected individuals. All efforts should be made to deal with all treatable conditions in people with HIV and AIDS. These conditions will be managed at various levels of care from aid posts to national level health care facilities, and as such, require all health care workers to be able to detect, treat and undertake appropriate referral for these conditions.

5.2. PROPHYLAXIS

Many opportunistic infections can be prevented by the use of Co-trimoxazole prophylaxis. The diseases include; Bacterial pneumonias, Pneumocystis Jiroveci Pneumonia, and Toxoplasmosis.

**Prophylactic treatment using Cotrimoxazole**

Indications:

- In all HIV positive adults and adolescents in stage II, III, or IV regardless of CD4.
- Asymptomatic HIV infected individuals with CD4+ counts <350 cells/ml.*

NB: Baseline Liver Function Tests (LFT) and Renal Function Tests (RFT) are recommended before long term administration of Cotrimoxazole.
* For children, see appropriate section of the guidelines.
Dose

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

Duration

- It is recommended that HIV positive adults remain on Cotrimazole prophylaxis for life. For those on ART, cotrimoxazole prophylaxis can be stopped if CD4+ is >200 for 6 months or if ART commenced when CD4 >200, 6 months after ART commenced if CD4 count is increasing.
- If cessation of treatment is based on CD4 count, Cotrimazole prophylaxis should be recommenced if the CD4 count falls below the initiation threshold or a new or recurrent WHO clinical stage II, III or IV condition occurs.

Criteria for stopping

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

Follow up

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.

Preventive therapy against TB in PLWHA

The dramatic spread of the HIV epidemic throughout PNG has been accompanied by up to a fivefold increase in the number of TB cases registered.

There is thus a need for strong collaboration between HIV and AIDS and TB programs. Therefore strategies to control HIV must also include interventions to control TB. TB preventive therapy is the use of one or more antituberculosis drugs given to individuals with latent infection with *M. tuberculosis* in order to prevent progression to active TB disease. Trials have shown that maximum benefits from TB preventive therapy are achieved in HIV infected patients with evidence of latent tuberculosis infection. Development of clinical Tuberculosis is reduced by about 60% and survival is also prolonged. However, some benefit is also shown in HIV positive groups in general, regardless of the tuberculin test result.
TB preventive therapy 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

INH will be provided to eligible clients through collaboration between HIV/AIDS and TB Control Programs. It is also essential that HIV inpatients in health care facilities are isolated from those patients with active TB.

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

**Symptoms and signs to be noted**

Patients for TB preventive therapy should be specifically asked about signs and symptoms of tuberculosis:

- Cough > 2 weeks
- Fever > 2 weeks
- Night sweats
- Weight loss of > 1.5 kg in the past 4 weeks. Weight should be measured at each clinic visit to allow documented evidence of weight loss. A weight loss of >1.5 kg should be considered a positive screen indicator.
- Pleuritic chest pains and haemoptysis
- Other symptoms suggesting extrapulmonary TB

**Investigations to be done**

All patients with 1 or more signs and symptoms must be investigated further for TB and are not immediately eligible for TB preventive therapy. Sputum specimens must be collected for AFB. Chest x-ray is also recommended in the screening for TB Preventive therapy, and has an important role in those who are TB suspects with negative sputum smears as per the national TB guidelines.

**Eligibility for TB Preventive Therapy**

All HIV positive people who have no signs and symptoms suggestive of active TB are eligible for TB preventive therapy. For patients with history of TB treatment:
• Patients who had active tuberculosis in the past 2 years should not be considered for preventive therapy.
• Patients who were treated for tuberculosis more than 2 years earlier may be considered because they may have already been re-infected with TB.

Patients who receive TB preventive therapy and who are required to start antiretroviral therapy can complete their TB preventive therapy even if the ART is started as there is no interaction between isoniazid and the current ART regimen used. Whenever INH is used, pyrodoxine (B6), 25mg daily is recommended to be given concurrently with the INH.

**Recommended Regimen**

The standard regimen for TB preventive therapy is Isoniazid (INH) daily 5 mg/kg/day (maximum 300 mg per day) and Vitamin B6 (Pyridoxine) 25mg daily. The recommended duration is 6 months.

**5.3. 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
• Sputum for AFB x 3
• Sputum for pyogenic culture and sensitivity
• Chest x-ray
• FBC
• 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

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

NB: 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 cryptoccccal meningitis
- Blood cultures and sensitivity studies.
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

5.4 CLINICAL STAGE I - DISEASE STATES AND TREATMENT

PERSISTENT GENERALIZED LYMPHADENOPATHY (PGL)

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

- HIV itself. (It is however not a bad prognostic sign.)
- Mycobacterium tuberculosis infection.
- Kaposis’ 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

5.5 CLINICAL STAGE II - DISEASE 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 consist 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 will 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 will 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.

If infection severe:

- Amoxycillin 500mg TDS PO for 5 days.

If no response try:

- Flucloxacillin 250mg QID PO for 10 days OR
- Erythromycin 500mg QID PO for 7 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; Cotrimazole 1% with Hydrocortisone 1% topically OR azole drugs (such as Fluconazole) for unresponsive or extensive diseases) to decrease colonization by yeast. If topically Cotrimazole 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. 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/CURRIS/PEDIS**

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

**Treatment**

Fluconazole 150 mg/day PO for 2 – 4 weeks, 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**

Hyperpigmented papules and nodules (up to 1 cm) with severe itching. Often ulcerations and scars because of scratching. Most frequently on 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

Herpese 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 characterised by localised 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 alldynia (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

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 aciclovir 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 opthalmic 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 for 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 (eg. bacterial sinusitis)

Bacterial sinustitis usually caused by Streptococcus Pneumoniae or H. Influenzae. 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

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

5.6 CLINICAL STAGE III - DISEASE 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
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:

- Nystatin oral suspension (100,000 u/ML) 1 ml QID for 10 – 14 days, OR
- Miconazole Gel 2% 2.5ml PO QID for 10 – 14 days OR
- Fluconazole 50mg/day PO 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 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 immunocompromised. Whether OHL develops after superinfection with EBV or activation of a latent infection due to reduced immune surveillance is not known. OHL Is more common in immunocompromised patients who smoke.

Treatment

OHL is rarely treated. Painful superinfection 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:

- Clotrimazole pessaries
- Nystatin Pessaries

If unresponsive or pessaries unavailable; give:

- Fluconazole 150mg PO Stat; OR
- *Itraconazole 400mg PO TDS for 2 doses only (total of 800mg).

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

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.

*NB: Due to resistant of Shigella and Campylobacteria to cotrimoxazole, Ciprofloxacin is the drug of choice
PULMONARY TUBERCULOSIS

Please see national treatment guidelines for Tuberculosis

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 noninfected 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-seronegative 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*.

Treatment

As for HIV negative patients:

- Amoxycillin 500mg TDS PO for 5 – 7 days if mild; OR
- Benzyl Penicillin 1,000,000 units QID parenterally then change to oral Amoxycillin when improved; OR
• If no response or deteriorating, Chloramphenicol 1gram QID parentrally 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

*NB: Remember that in immunocompromised patients pneumonia can be caused by fungal infection such as Aspergiullus and Cryptococcus.

If suspected, treat patient with Amphotericin B parentrally (0.7 mg/kg for Cyprotococcus and 1.0/mg/kg for Aspergillus). 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).

5.7 CLINICAL STAGE IV - DISEASE 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.
HERPES SIMPLEX VIRUS INFECTION (HSV)

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 or immunoassay are 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 - 14 days

HUMAN CYTOMEGALOVIRUS (HCMV)

Clinical features

HCMV is a common human pathogen, infecting approximately 50% of adult populations in developed countries. HCMV 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 HCMV 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 HCMV disease. In acute HCMV 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**

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.

**Treatment**

The preferred regimen is Amphotericin B 0.7mg/kg/day IV and 5 Fluorocytosine 100mg/kg/day orally for 14 days (induction phase) then:

- Fluconazole IV 400mg/day for 3 days (consolidation phase) then
- Fluconozole 400mg per day orally for 10 weeks (maintenance phase) then
- Fluconazole 150mg daily as secondary prophylaxis until CD4 >200 for 6 months of indefinitely if no CD4 count available.
- Child: 6-12mg/kg daily (every 72 hours in neonate up to 2 weeks old, every 48 hours in neonate 2-4 weeks old); maximum, 400mg daily.
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.

NB. 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 oesophageal 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 oesophageal 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)

- Co-trimoxazole (Trimethroprim 15-20 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)

- Co-trimoxazole 1920 mg 3 times /day for 21 days (4tabs 8 hourly for 7 days, Then 4 Tablets 12 hourly for 7 days, then 4 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 concomitant 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 corticosteroid 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 parental 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.

**TOXOPLASMA ENCEPHALITIS**

**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 regime

**Alternative Treatment Regime (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 Regime**

- 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 Co-trimoxazole 2 SS or 1 DS (SMX 800/TMP 160mg) twice daily.

**5.8 OTHER**

**HUMAN PAPILLOMA VIRUS (HPV)**

**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 traumatised 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 anogenital 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:

- Podophyllin resin 10% to 25% solution in ethanol or tinc benz co – applied to warts by health worker once to twice a week (for up to 6 weeks) and washed off 1 to 4 hours after application. This is not to be used in pregnancy. Extended use may lead to bone marrow depression so it is not appropriate to use for large masses of warts. Podophyllin is no longer available through the public health system in PNG.
- 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**

For intestinal protozoa which is a common cause of diarrhoea and difficult to diagnose, the recommended treatment: Tabs Albendazole 800mg BD for one week. Other alternatives are Metronidazole Tabs or Thiabendazole
### APPENDIX 1

**LIST OF RECOMMENDED DRUGS FOR ADULTS AND ADOLESCENTS**

<table>
<thead>
<tr>
<th>Drug class/drug</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Nucleoside RTIs</strong></td>
<td></td>
</tr>
<tr>
<td>Zidovudine (ZDV)</td>
<td>300 mg twice daily</td>
</tr>
<tr>
<td>Stavudine (d4T)</td>
<td>40 mg twice daily if &gt;60 kg</td>
</tr>
<tr>
<td></td>
<td>(30 mg twice daily if &lt;60 kg)</td>
</tr>
<tr>
<td>Lamivudine (3TC)</td>
<td>150 mg twice daily</td>
</tr>
<tr>
<td>Didanosine (ddl)</td>
<td>400 mg once daily if &gt;60 kg</td>
</tr>
<tr>
<td></td>
<td>(250 mg once daily if &lt;60 kg)</td>
</tr>
<tr>
<td>Abacavir (ABC)</td>
<td>300 mg twice daily or 600 mg once daily</td>
</tr>
<tr>
<td>Tenofovir (TDF)</td>
<td>300 mg once daily</td>
</tr>
<tr>
<td><strong>Non-nucleoside RTIs</strong></td>
<td></td>
</tr>
<tr>
<td>Efavirenz (EFZ)</td>
<td>600 mg once daily</td>
</tr>
<tr>
<td>Nevirapine (NVP)</td>
<td>200 mg once daily for 14 days, then 200 mg twice daily</td>
</tr>
<tr>
<td><strong>Protease inhibitors</strong></td>
<td></td>
</tr>
<tr>
<td>Saquinavir/ritonavir (SQV/r)</td>
<td>1000 mg/100 mg twice daily</td>
</tr>
<tr>
<td>Lopinavir/ritonavir (LPV/r) (Kaletra)</td>
<td>400/100 twice daily or 800/200 once daily*</td>
</tr>
</tbody>
</table>

ZDV/3TC/NVP (300mg/150 mg /200 mg), combination tablets  
D4T/3TC/NVP (30 mg /150 mg /200 mg and 40 mg /150 mg /200 mg),  
combination tablets  
ZDV/3TC (300 mg /150 mg), combination tablets  
D4T/3TC (30 mg /150 mg and 40 mg /150 mg), combination tablets  
NVP syrup (50mg/5ml)  
ABC (300 mg)  
ZDV (300 mg)  
D4T (30 mg and 40 mg)  
DDI (EC 250 mg and EC 400 mg)  
EFZ (200 mg and 600 mg)  
TDF (300mg)  
SQV (200 mg)  
RTV (100 mg)  
LPV/r (133/33; 200/50)

*Once daily dosing is only recommended for treatment naive adults. If Lopinavir/Ritonavir is used with Efavirenz or Nevirapine, the dose should be increased to 533/133 twice daily.
## APPENDIX 2: DRUGS FORMULATIONS AND DOSES FOR CHILDREN

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dose and method of Administration</th>
<th>Absorption and meal</th>
</tr>
</thead>
<tbody>
<tr>
<td>ZDV</td>
<td>Oral: 180mg-240/m² 12 hourly</td>
<td>Can be administered with food</td>
</tr>
<tr>
<td>(Syrup 10mg/ml) (Capsule:100mg &amp; 300mg)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>d4T</td>
<td>1mg/kg 12 hourly (up to 30kgs)  &gt;30kgs see adult dose</td>
<td>Can be administered with food</td>
</tr>
<tr>
<td>(Solution 1mg/ml) Capsules: 15, 20, 30 and 40mg</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ddl (powder)</td>
<td>90 – 120mg/m² 12 hourly</td>
<td>Administer on an empty stomach</td>
</tr>
<tr>
<td>(solution 10mg/ml) Chewable tablets With buffers 25, 50, 100 &amp; 150mg</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3TC</td>
<td>4mg/kg 12 hourly</td>
<td>Can be administered with food</td>
</tr>
<tr>
<td>(Solution 10mg/ml) Capsule 100mg</td>
<td></td>
<td></td>
</tr>
<tr>
<td>EFV</td>
<td>15/mg/kg/day 10-14kg 200mg 15-19kg 250mg 20-24kg 300mg 25-32.5kg 350mg 32.5-40kg 400mg &gt;40kg 600mg Not before 3 years of age</td>
<td>Not with high fat meal</td>
</tr>
<tr>
<td>Capsule 50, 100, And 200mg</td>
<td></td>
<td></td>
</tr>
<tr>
<td>NVP</td>
<td>200mg/m² 12 Hourly</td>
<td>During first two week once a day</td>
</tr>
<tr>
<td>(50mg/ml) Tab 200mg</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ABC</td>
<td>8mg/kg/dose 12 Hourly Use in children &gt;3/12</td>
<td></td>
</tr>
<tr>
<td>20mg/ml Tab. 300mg</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
### APPENDIX 3. WHO HIV/AIDS 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
- 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

**And/or performance scale 4: bedridden >50% of the day during the last month**
Note: 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.
<table>
<thead>
<tr>
<th>Clinical stage I</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Asymptomatic</td>
<td></td>
</tr>
<tr>
<td>Persistent generalized lymphadenopathy</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Clinical stage II (1)</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Unexplained persistent hepatosplenomegaly</td>
<td></td>
</tr>
<tr>
<td>Papular pruritic eruptions</td>
<td></td>
</tr>
<tr>
<td>Extensive wart virus infection</td>
<td></td>
</tr>
<tr>
<td>Extensive molluscum contagiosum</td>
<td></td>
</tr>
<tr>
<td>Recurrent oral ulcerations</td>
<td></td>
</tr>
<tr>
<td>Unexplained persistent parotid enlargement</td>
<td></td>
</tr>
<tr>
<td>Lineal gingival erythema</td>
<td></td>
</tr>
<tr>
<td>Herpes Zoster</td>
<td></td>
</tr>
<tr>
<td>Recurrent or chronic upper respiratory tract infections (otitis media, otorrhoea, sinusitis, tonsillitis)</td>
<td></td>
</tr>
<tr>
<td>Fungal nail infections</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Clinical stage III (1)</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Unexplained moderate malnutrition not adequately responding to standard therapy</td>
<td></td>
</tr>
<tr>
<td>Unexplained persistent diarrhea (14 days or more)</td>
<td></td>
</tr>
<tr>
<td>Unexplained persistent fever (above 37.5° C, intermittent or constant, for longer than one month)</td>
<td></td>
</tr>
<tr>
<td>Persistent oral candidiasis (after first 6 weeks of life)</td>
<td></td>
</tr>
<tr>
<td>Oral hairy leukoplakia</td>
<td></td>
</tr>
<tr>
<td>Acute necrotizing ulcerative gingivitis/periodontitis</td>
<td></td>
</tr>
<tr>
<td>Lymph node TB</td>
<td></td>
</tr>
<tr>
<td>Pulmonary TB</td>
<td></td>
</tr>
<tr>
<td>Severe recurrent bacterial pneumonia</td>
<td></td>
</tr>
<tr>
<td>Symptomatic lymphoid interstitial pneumonitis</td>
<td></td>
</tr>
<tr>
<td>Chronic HIV associated lung disease including bronchiectasis</td>
<td></td>
</tr>
<tr>
<td>Unexplained anemia (&lt;8), neutropenia (&lt;0.5 x 10⁹), or chronic thrombocytopenia (&lt;50 x 10⁹)</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Clinical stage IV (1)</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Unexplained severe wasting, stunting or severe malnutrition not responding to standard therapy</td>
<td></td>
</tr>
<tr>
<td>Norwegian Scabies &gt; 1 month</td>
<td></td>
</tr>
<tr>
<td>Pneumocystis pneumonia</td>
<td></td>
</tr>
<tr>
<td>Recurrent bacterial infections (e.g. empyema, pyomyositis, bone or joint infection, meningitis, but excluding pneumonia)</td>
<td></td>
</tr>
<tr>
<td>Chronic herpes simplex infection (orolabial or cutaneous of more than one month’s duration or visceral at any site)</td>
<td></td>
</tr>
<tr>
<td>Extrapulmonary TB</td>
<td></td>
</tr>
</tbody>
</table>
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
# APPENDIX 5: ART ADHERENCE PREPARATION, SUPPORT AND MONITORING

| Assess | Person’s goals for today’s visit  
Understanding of ART therapy  
Interest in receiving therapy |
| --- | --- |
| Advise | HIV illness, expected progression  
ART therapy  
- Benefits—lifesaving drugs. Your life depends on taking them every day at the right time  
- Very strong medicines  
- The pills do not cure HIV  
- The pills do not prevent HIV transmission to others – you must still use condoms and practice safer sex  
- Need for complete adherence to daily treatment (more than other drugs you may be familiar with – essential to maintain drugs levels in the blood for ART therapy to work). Must be taken twice daily without interruption  
If you forget a dose, do not take a double dose  
Must be taken at right time, every 12 hours (adjust this if on different regime)  
If you stop, you will become ill (not immediately – after weeks, months or years)  
Possibility of side effects and drug interactions  
Importance of disclosure of HIV+ status (partner, family etc)  
Importance of testing partner and children  
Drugs must not be shared with family or friends |
| Agree | Establish that the person is willing and motivated and agrees to treatment, before initiating ART therapy  
- Has the person demonstrated ability to keep appointments, to adhere to other medications?  
- Has the person disclosed his or her HIV status? If not, encourage him / her to do so. Disclosure to at least one person who can be the supporter is important  
- Does the person want treatment and understand what treatment is?  
- Is the person willing to come for the required clinic follow-up? |
| Assist | Help the person develop the resources / support / arrangements needed for adherence:  
- Ability to come for required schedule of follow-up. Discuss how the person will do this  
- Home and work situation that permits taking medications every 12 hours without stigma  
- Regular supply of free or affordable medication  
- Supportive family or friends  
- ART adherence support group  
- Treatment supported |
| Arrange | When the person is ready for ART therapy, discuss at the clinical team meeting then make a plan |
## APPENDIX 6: Guide for Supporting ART initiation

| **Assess** | Person’s goals for today’s visit  
Check understanding of the information given before – make sure the person understands the illness, treatment and possible side effects |
| **Advise** | Reinforce the information given before  
Advise on the details of first line regimen  
- Explain the purpose of and how to take each pill. Provide and explain card summarising treatment (with drawing of each pill and common side effects)  
- Make sure person understands the importance of adherence  
Advise on diet  
- Explain limits on alcohol and drug use. These are important for adherence.  
**Explain side effects**  
- Prepare person and treatment supporter to handle common side effects. Most side effects can be treated symptomatically.  
- Explain which side effects are likely to be transitory (related to the initiation of treatment) and their likely duration.  
- Explain which are more serious and require return to clinic.  
Explain that person can still transmit HIV infection when on ART therapy.  
It is very important to still practice safer sex and other practices to prevent transmission. |
| **Agree** | Make sure the person agrees to the regimen and is a true partner in the treatment plan  
Make sure the person understands that his / her life depends on taking the medicine every day  
Agree on plan for support by treatment buddy and support groups. |
| **Assist** | Develop (then reinforce on each visit) a concrete plan for the specific ART regimen  
- When to take / times for every 12 hour dosing / how to make it a habit  
- Explain escalating dose of niverapine  
- How to remember – provide and explain written schedule, pillbox, pill chart, other aids  
Prepare person and treatment supporter for adherence, possible common side effects, what to do if they occur, and when to seek care.  
Provide psychosocial support.  
Encourage person to join ART adherence support group.  
Arrange home visit. |
| **Arrange** | Next follow-up in clinic, home visit.  
Agree on best way to access help between visits.  
Make sure the person understands where / when s/he will see health worker. |
### APPENDIX 7:
Guide for Monitoring and supporting adherence

| Assess | Do clinical review and respond to any problems or changes in status. To assess adherence:  
Review the medications with the person and their treatment supporter. Determine whether there is an adherence problem.  
Ask questions in a respectful and non-judgmental way:  
o “Many people have trouble taking their medications, what troubles are you having?”  
o “Can you tell me when and how you take each pill?”  
o “When is it most difficult for you to take the pills?”  
Ask about the common and locally important factors that may interfere with adherence.  
Ask about stigma related to taking the pills.  
Count pills.  
How many pills forgotten yesterday, last 3 days, last month?  
**If poor adherence: Determine what the problem is:**  
Side effect? Simply forgot?; Ran out of pills?; Which dose missed morning or evening? Why?; Cost?; Reminds you of HIV?; Misunderstood?; Changed work situation?; Not comfortable taking medications around others?; Stigma?; Different timing when away from home or holiday, travel, weekend?; Seldom at home and disorganised?; Problems with diet?; Another medical problem?; Screen for excess alcohol use and depression and treat, if present.  
**Advise**  
Reinforce the information given before.  
Give additional information that may help with adherence problem.  
Advice on any suggested changes in the regimen.  
| Advise | Agree | Agree on any changes in Treatment Plan and solutions to adherence problems (if present).  
Discuss the agreements you have reached and check for their commitment.  
| Agree | Provide adherence support.  
Reinforce interventions which match the person’s needs and adherence problems, if present.  
Make sure that the person has:  
o Plan to link taking medications with daily events such as meals  
o Any device or skills that he or she needs (e.g. how to use a diary)  
Make sure person has the support he or she needs  
o Get help from supporter, other family and friends or peers  
o Help person and supporter to find solutions  
If adherence problem:  
o Get help – call for advice  
o Link with home based care or home visits  
| Assist | Arrange | Record adherence estimate on persons card.  
Arrange for refills  
Arrange for next follow-up visits:  
o In clinic  
o Home visits  
Make sure that the person and supporter understand the follow-up plan and how to contact the clinic team if there is a problem.  
|
## APPENDIX 8: PAEDIATRIC ARV DOSING SCHEDULE

<table>
<thead>
<tr>
<th>Drug</th>
<th>Strength of child tab (mg)</th>
<th>Number of tablets by weight band (twice daily)</th>
<th>Strength of adult tab (mg)</th>
<th>Number of tablets by weight band (twice daily)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>3-3.9 kg</td>
<td>4-4.9 kg</td>
<td>5-5.9 kg</td>
<td>6-9.9 kg</td>
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<tr>
<td>EFV</td>
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<td>n/r</td>
<td>n/r</td>
<td>n/r</td>
</tr>
<tr>
<td>FTC</td>
<td>35</td>
<td>0.5</td>
<td>0.5</td>
<td>1</td>
</tr>
<tr>
<td>EFV/FTC</td>
<td>100/35</td>
<td>n/r</td>
<td>n/r</td>
<td>n/r</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Drug</th>
<th>Strength of child tab (mg)</th>
<th>Number of tablets by weight band (once daily)</th>
<th>Strength of adult tab (mg)</th>
<th>Number of tablets by weight band</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>3-3.9 kg</td>
<td>4-4.9 kg</td>
<td>5-5.9 kg</td>
<td>6-9.9 kg</td>
</tr>
<tr>
<td>EFV</td>
<td>100</td>
<td>n/r</td>
<td>n/r</td>
<td>n/r</td>
</tr>
<tr>
<td>FTC</td>
<td>35</td>
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<td>0.5</td>
<td>1</td>
</tr>
<tr>
<td>EFV/FTC</td>
<td>100/35</td>
<td>n/r</td>
<td>n/r</td>
<td>n/r</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Drug</th>
<th>Strength of child tab (mg)</th>
<th>Number of tablets by weight band (twice daily)*</th>
<th>Strength of adult tab (mg)</th>
<th>Number of tablets by weight band</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>3-3.9 kg</td>
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<td>5-6.9 kg</td>
<td>7-11.9 kg</td>
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<tr>
<td>Lop/Rit</td>
<td>100/25</td>
<td>n/r</td>
<td>1</td>
<td>1.5</td>
</tr>
</tbody>
</table>

*Note different weight bands

* Except in the infant less than 6 months of age where 3-3.9 kg 0.5/0.5 and 4-4.9 kg 1/0.5 is recommended.

*Note different weight bands
Currently manufactured paediatric d4T containing FDC products

<table>
<thead>
<tr>
<th>Fixed dose combination(^{10})</th>
<th>Active Components</th>
<th>Strength in mg</th>
</tr>
</thead>
<tbody>
<tr>
<td>FDC 5</td>
<td>d4T/3TC/NVP</td>
<td>5:20:35</td>
</tr>
<tr>
<td>FDC 6</td>
<td>d4T/3TC/NVP</td>
<td>6:30:50</td>
</tr>
<tr>
<td>FDC 7</td>
<td>d4T/3TC/NVP</td>
<td>7:30:50</td>
</tr>
<tr>
<td>FDC 10</td>
<td>d4T/3TC/NVP</td>
<td>10:40:70</td>
</tr>
<tr>
<td>FDC 10s</td>
<td>d4T/3TC/NVP</td>
<td>10:40:70 per 5 ml reconstituted suspension</td>
</tr>
<tr>
<td>FDC 12</td>
<td>d4T/3TC/NVP</td>
<td>12:60:100</td>
</tr>
</tbody>
</table>


\(^{10}\) These are simple numerical names given to FDC products given by the working group members, and the number denotes the milligrams of d4T contained, the s denotes solution. A range on manufacturers produce these products.