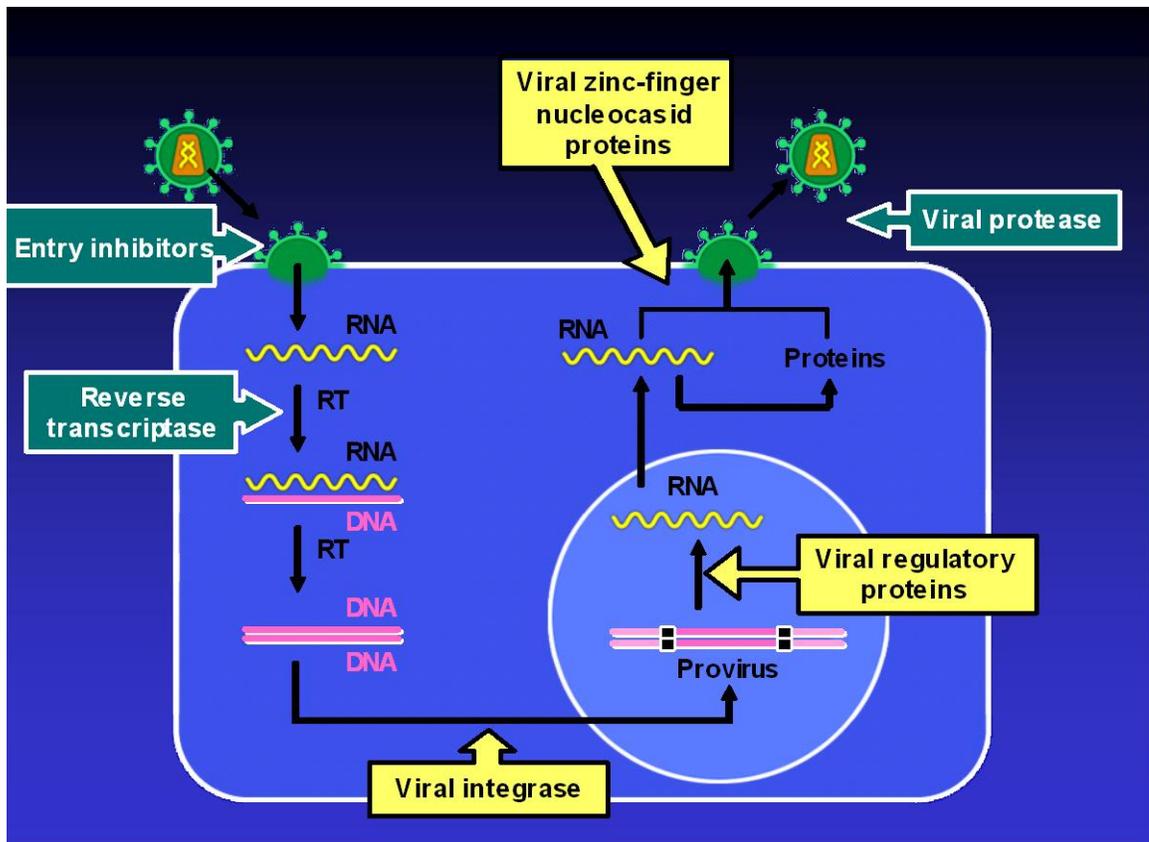


NATIONAL ANTIRETROVIRAL THERAPY GUIDELINES



1st EDITION

JULY 2004



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JULY 2004

**MINISTRY OF HEALTH
GOVERNMENT OF FIJI**

PREPARED BY

NATIONAL DRUGS & THERAPEUTICS COMMITTEE 2004

DISCLAIMER

The authors do not warrant the accuracy of the information contained in the ARV Guidelines and do not take responsibility for any death, loss, damage or injury caused by using the information in the ARV Guidelines.

While every effort has been made to ensure that the ARV Guidelines is correct and in accordance with current evidence based and clinical practice, the dynamic nature of drug information requires that users exercise in all cases independent professional judgement and understand the individual clinical scenario when referring, prescribing or providing information from the ARV guidelines.

PREFACE

The Fiji Ministry of Health has adopted a HIV/AIDS policy and a Strategic Plan that covers Care and Support of people living with HIV/AIDS (PLHA) and their families. The development and implementation of an expanded antiretroviral treatment (ART) program has been included within this Strategic Plan. Standard treatment guidelines are considered to be of crucial importance for the optimal and cost-effective use of antiretroviral agents on a national level. The guidelines as presented here do not make final choices from the preferred regimens as such choices heavily depend on the prices that can be negotiated.

It is recognised that antiretroviral drugs, although they can temporarily suppress viral replication and improve symptoms, do not cure human immunodeficiency virus infection (HIV). Promotion of all possible measures to prevent new infections remains essential and its need is not diminished by the availability of antiretroviral drugs.

This guideline is designed to provide a technical basis for the planning of national ART program, in terms of selection of drugs, monitoring and content of training. This should be considered as the introduction and basic manual of ART and not the comprehensive details of the complex treatment.

This is a simplified and standardized guideline for reference and not a substitution for appropriate training. This manual is primarily for physicians and nurses who do not have much experience in ART at primary and secondary level. As such, it takes into consideration the limited resources available at these levels and is based on the WHO's guideline "Scaling up antiretroviral therapy in resource-limited settings".

SINCE THIS IS A RATHER NEW AND RAPIDLY EVOLVING TREATMENT, THE CONTENT OF THIS GUIDELINE SHOULD BE REVISED AND UPDATED EVERY YEAR OR TWO IN ORDER TO CATCH UP AS WELL AS ADAPT TO CHANGES IN THE LOCAL SITUATION.

.....
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2004

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CONTENTS

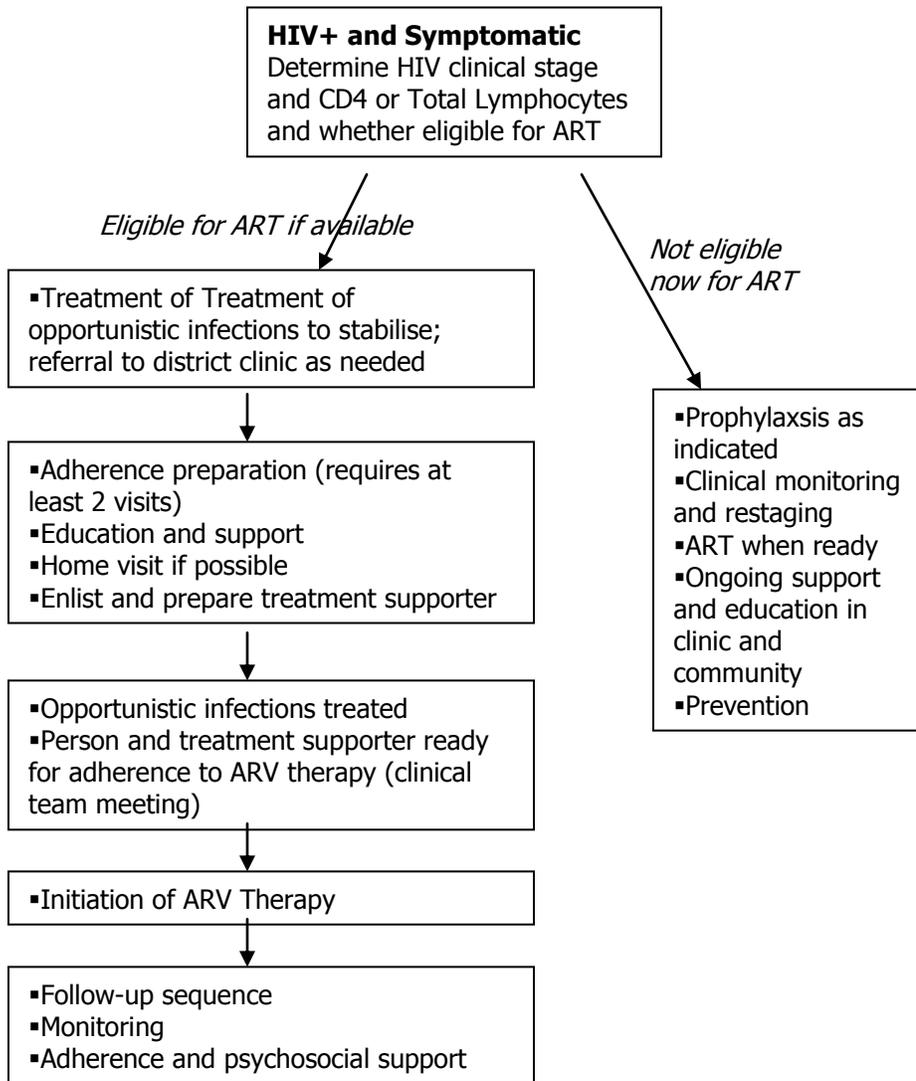
Abbreviations	7
Summary of flow to initiating ART	8
1. Who should provide treatment	9
2. When to start treatment	9
3. Minimum and baseline tests	10
4. What drugs to use	10
5. Management of Opportunistic Infections and other conditions before commencing ART	14
6. People with tuberculosis and HIV co-infection	15
7. Women of childbearing	16
8. Guidelines for children	17
9. What to monitor	18
10. Adherence	20
11. Post-exposure prophylaxis	20
12. Data collection	20
13. Management of Opportunistic Infections (OIs)	21
Sources used	34
ANNEXE 1: Flow chart for voluntary counseling and testing (VCT)	35
ANNEXE 2: Sequence of care after positive HIV test	36
ANNEXE 3: WHO HIV clinical staging	37
ANNEXE 4: Drugs used to treat HIV infection	38
ANNEXE 5: Fixed dose combinations of ARVs available as at 1 December 2003	39
ANNEXE 6: WHO staging system for HIV infection and disease in children	40
ANNEXE 7: ARV therapy: adherence, preparation, support and monitoring	41
Index	44

ABBREVIATIONS

3TC	Lamivudine*
ABC	Abacavir*
APV	Amprenavir
ART	Anti-retroviral treatment
ARV	Anti-retroviral
d4T	Stavudine*
ddC	Zalcitabine
ddI	Didanosine*
DLV	Delavirdine
EFZ	Efavirenz, also abbreviated as EFV*
HIV	Human immunodeficiency virus
IDV	Indinavir*
LPV	Lopinavir*
NACA	National Advisory Committee on AIDS
NFV	Nelfinavir*
NNRTI	Non-nucleoside reverse transcriptase inhibitor
NsRTI	Nucleoside analogue reverse transcriptase inhibitor
NVP	Nevirapine*
PCP	pneumocystis carinii pneumonia
PI	Protease inhibitor
PLHA	People living with HIV / AIDS
RTV, r	Ritonavir*
RTV-PI	Ritonavir boosted protease inhibitor
SQV	Saquinavir*
ZDV	Zidovudine, also abbreviated as AZT*

* Included in the WHO model list of Essential Medicines, although lopinavir only in the combination with low dose ritonavir.

Summary of flow to initiating ART



For additional information about the sequences of voluntary counselling and testing as well as care after positive HIV test, refer to annexes 1 and 2 respectively.

1. WHO SHOULD PROVIDE TREATMENT

Prescription of anti retroviral therapy is complex and requires a complete understanding of the rationale, pharmacology, and adverse effects of medication. In addition, the practitioner needs to be knowledgeable about the treatment of coexisting conditions and the treatment of HIV in special groups such as children and pregnant women. For this reason, the prescription of antiretroviral medication will be restricted to registered medical practitioners who have undertaken a National Advisory Committee on AIDS (NACA) recognised prescriber's course.

2. WHEN TO START TREATMENT

NACA has adopted the WHO recommendation that infected adolescents and adults should start ARV therapy when they have:

<p><u>If CD4 Testing Unavailable</u></p> <ul style="list-style-type: none">▪ WHO Stage IV disease, irrespective of total lymphocyte count▪ WHO Stage III disease (Characterised by HIV wasting, chronic diarrhoea, prolonged fever, atypical pulmonary TB, recurrent invasive bacterial infections or recurrent / persistent mucosal candidiasis), irrespective of total lymphocyte count▪ WHO Stage I or II disease with a total lymphocyte count = 1200/mm³
<p><u>If CD4 Testing Available</u></p> <ul style="list-style-type: none">▪ WHO Stage IV disease, irrespective of CD4 cell count▪ WHO Stage III disease (Characterised by HIV wasting, chronic diarrhoea, prolonged fever, atypical pulmonary TB, recurrent invasive bacterial infections or recurrent / persistent mucosal candidiasis), with consideration of using CD4 cell counts below 350/mm³ to assist decision-making▪ WHO Stage I or II disease with CD4 cell counts below 200/mm³

For full details of the WHO HIV Clinical Staging see Annexe 3.

Before any person is started on ART, they should undergo a baseline assessment that examines the following questions:

- What is the clinical status?
- What is the laboratory status?
- What is the socio-economic status?

Having fully explored these questions then decide:

- Should OI treatment and/or prophylaxis be provided?
- Should ARV be considered? (determine other medical conditions e.g. TB, pregnancy, major psychiatric illness and other medications being taken including traditional therapies)

- Is the person interested in and motivated to take ART? (assessing person’s readiness, *see section 7 and annexe 5 on adherence*)
- Should other support services be provided? (e.g. counselling, self help groups)

The following table¹ provides a framework for a clinical review of symptoms and signs, medication use, side effects and complications.

Framework for a clinical review

ASK	LOOK
<p><u>If this is the first visit:</u></p> <p>Review history. Check record for TB, other opportunistic infections, chronic problems</p> <p><u>For all visits:</u></p> <ul style="list-style-type: none"> ▪ How have you been? ▪ What problems have you developed? ▪ Have you had any of the following? <i>If yes</i>, ask for how long: <ul style="list-style-type: none"> ○ Cough? ○ Night Sweats? ○ Fever? ○ STI signs? (use locally adapted screening question) ○ Diarrhoea? ○ Mouth sores? ○ New skin rash? ○ Headache? ○ Fatigue? ○ Nausea or vomiting? ○ Poor appetite? ○ Tingling, numb or painful feet/legs? ○ Any other pain? <i>If yes</i>, where? ○ Sexual problems? ▪ Have you needed urgent medical care? <i>If yes</i>, ask for record/diagnosis ▪ Which medications are you taking and how often? ▪ Assess adherence ▪ What problems have you had taking the medicines, how are they taken? ▪ Taking any other drugs (traditional remedies, TB, ARV, illicit drugs, etc.)? ▪ How are things at home? ▪ Is there any thing else you would like to talk about? 	<p><u>In all persons:</u></p> <ul style="list-style-type: none"> ▪ Look for pallor. <i>If pallor</i>, check haemoglobin ▪ Look at whites of the eye-yellow? ▪ Look for thrush ▪ Weigh, calculate weight gain or loss. Record. If weight loss, ask about food intake ▪ Count pills to estimate adherence ▪ <i><u>If person is sad or has lost interest, assess for depression.</u></i> <p><u>If any new symptoms:</u></p> <ul style="list-style-type: none"> ▪ Measure temperature ▪ Check for nodes. ▪ Look for rash ▪ Look for evidence of violence ▪ Do further assessment of symptoms. <p><u>If first visit (also check every 6 months; skip if known problem)</u></p> <p>Tell the person you want to check his memory:</p> <ul style="list-style-type: none"> ○ Name 3 unrelated objects clearly and slowly. Ask person to repeat them: ○ Can he/she repeat them? (registration problem?) <p><i>If yes:</i> wait 5 minutes and ask again: “Can you recall the 3 objects? (recall problem?)”</p>

¹ WHO (2004). Chronic HIV Care with ARV Therapy. Integrated Management of Adolescent and Adult Illness: Interim guidelines for first level facility health workers.

3. MINIMUM AND BASELINE TESTS

The absolute minimum laboratory tests before initiating antiretroviral therapy are:

- an HIV antibody test (in persons over 18 months of age); and,
- a haemoglobin or haematocrit measurement.

Additional basic testing should include:

- a baseline white blood cell count and differential cell count (to identify a decline in neutrophils and the possibility of the occurrence neutropenia during ART);
- total lymphocyte count;
- serum alanine or aspartate aminotransferase concentration to assess the possibility of hepatitis co-infection;
- serum creatinine and/or blood urea nitrogen to assess baseline renal function;
- serum glucose;
- pregnancy tests for women.

If available, a CD4 count can assist treatment decisions.

4. WHAT DRUGS TO USE

The use of fixed drug combinations is recommended wherever possible to facilitate compliance and minimise potential for the development of viral resistance. In addition to the recommended first and second line therapies as outlined, refer to annexe 4 for normal drug doses and annexe 5 for available fixed dose combinations.

Recommended First Line Therapy

Regimen	Pregnancy and TB considerations
Zidovudine (ZDV) / Lamivudine (3TC) / Nevirapine (NVP)	Give NVP in pregnant women or women for whom effective contraception cannot be assured
Stavudine (d4T) / Lamivudine (3TC) / Nevirapine (NVP)	
Zidovudine (ZDV) / Lamivudine (3TC) / Efavirenz (EFZ)	Give EFZ for patients requiring simultaneous ARV treatment and TB therapy containing Rifampicin
Stavudine (d4T) / Lamivudine (3TC) / Efavirenz (EFZ)	

- Zidovudine (ZDV) / lamivudine (3TC) are recommended for the initial dual nucleoside component based on efficacy, toxicity and clinical experience.
- Other dual nucleoside combinations can be substituted for ZDV / 3TC, including stavudine (d4T) / 3TC, which is available at the country level.
- ZDV / d4T should never be used together because of proven antagonism between the two drugs.

Recommended Second Line Therapy

Intolerance to adverse effects and drug-induced organ dysfunction usually require a change in therapy. The choice of an alternative regimen depends on factors such as the response to previous treatment, tolerance and the possibility of cross-resistance.

Drug Substitution for Toxicity

If toxicity is the reason for changing the regimen and the offending drug is known this agent can be replaced with another drug that does not have the same adverse effects. For example:

First Line Therapy	Toxicity	Single Substitution for Toxicity
ZDV + 3TC + NVP	ZDV - persistent GI intolerance or severe haematological toxicity	d4t + 3TC + NVP
	NVP - severe hepatotoxicity, or NVP - severe rash (not life threatening)	ZDV + 3TC + EFZ (in pregnancy, use ABC or NVF or LPV/r)
	NVP - life-threatening rash	ZDV + 3TC + (LPV/r or SQV/r or IDV/r or NFV)
d4T + 3TC + NVP	d4T - neuropathy or pancreatitis	ZDV + 3TC + EFZ
	d4T - lipoatrophy	(TDF or ABC) + 3TC + NVP
	NVP - hepatotoxicity, or NVP - severe rash (not life threatening)	d4T + 3TC + EFV (in pregnancy, use ABC or NVF or LPV/r)
	NVP - life-threatening rash	d4T + 3TC + (LPV/r or SQV/r or IDV/r or NFV)
ZDV + 3TC + EFZ	ZDV - persistent GI intolerance or severe haematological toxicity	d4t + 3TC + NVP
	EFZ – persistent CNS toxicity	ZDV + 3TC + NVP
d4T + 3TC + EFZ	d4T - neuropathy or pancreatitis	ZDV + 3TC + EFZ
	d4T - lipoatrophy	(TDF or ABC) + 3TC + NVP
	EFZ – persistent CNS toxicity	ZDV + 3TC + NVP

Drug Substitution for Regime Failure

It is recommended that the entire regimen is changed in the case of treatment failure. Primarily clinical and where possible CD4 count criteria are used to define treatment failure.

When failure is established the new second-line combination regimen will ideally include at least three new drugs with one from at least one new class, in order to increase the likelihood of treatment success and minimise the risk of cross resistance.

The table below shows the clinical and CD4+ cell count definitions of treatment failure in HIV+ adolescents and adult.

Clinical Signs of Treatment Failure	CD4 Cell Criteria for Treatment Failure
<ul style="list-style-type: none"> ▪ Occurrence of new opportunistic infection or malignancy signifying clinical disease progression. This must be differentiated from the immune reconstitution syndrome which can occur in the first three months following the initiation of ART¹. The latter does not mean treatment failure and the opportunistic infection should be treated as usual, without changes in the antiretroviral regimen. ▪ Reoccurrence of prior opportunistic infection². ▪ Onset or reoccurrence of WHO stage III conditions (included but not restricted to HIV wasting, chronic diarrhoea of unknown aetiology, prolonged fever of unknown aetiology, recurrent invasive bacterial infections, or recurrent / persistent mucosal candidiasis) 	<ul style="list-style-type: none"> ▪ Return of CD4 cell to pre-therapy baseline or below without other concomitant infection to explain transient CD4 cell decrease³ ▪ >50% fall from on therapy CD4 peak level without other concomitant infection to explain transient CD4 cell decrease³
<p>¹. Immune reconstitution syndrome is characterized by the appearance of signs and symptoms of an opportunistic disease a few weeks after the start of potent antiretroviral therapy in the setting of advanced immuno-deficiency.</p> <p>². Recurrence of tuberculosis may not represent HIV disease progression as re-infection may occur. Clinical evaluation necessary.</p> <p>³. If patient is asymptomatic and treatment failure is being defined by CD4 cell criteria alone, consideration should be given to performing a confirmatory CD4 cell count if resources permit</p>	

The table below shows first the combination of failing first line regimens, the possible second line regimens and the considerations when making the change.

For failing 1st line regimens ..	Switch to ..
ZDV + 3TC + NVP Or D4t + 3TC + NVP Or ZDV + 3TC + EFZ Or D4T + 3TC + EFZ	ABC + ddI + LPV/r Or TDF + ddl + LPV/r Or ABC + ddI + SQV/r Or TDF + ddl + SQV/r
<p>Considerations</p> <ul style="list-style-type: none"> ▪ Dose of ddl should be reduced from 400 mg to 250 mg when co-administered with TDF ▪ LPV/r and SQV/r require a secure cold chain. NFV can be considered as an alternation in resource limited settings without a cold chain ▪ If failure due to non-adherence consider cessation of therapy (2nd line therapies are far more complex and likely to fail with poor adherence. Drug costs are considerably higher). 	

5. MANAGEMENT OF OPPORTUNISTIC INFECTIONS AND OTHER CONDITIONS BEFORE COMMENCING ART

Prevention

Every person who has symptomatic disease (oral candida, fevers, weight loss etc.) or another AIDS-defining illness such as Kaposi's sarcoma, or has been successfully treated for pneumonia due to *Pneumocystis carinii*, or who has a CD4+ lymphocyte count of less than 200/mm³, where test available, should receive continuous prophylaxis.

	Drug	Dose
1st choice	Trimethoprim-sulfamethoxazole (TMP-SMX, Bactrim, Septra, Cotrimoxazole)	One double-strength tablet per day 160 mg trimethoprim/800 mg sulfamethoxazole
2nd choice	Dapsone oral or Dapsone oral and Pyrimethamine oral	50-100 mg Daily 100 mg 3 x week and 25 mg 3 x week

Approximately 25 – 50% people with HIV infection have toxicity to TMP-SMX. The most common side effects include fever, rash, and leukopenia. Strategies for managing mild reactions include discontinuation of the drug and resuming it at same or lower dose or use of a desensitization protocol (gradually increasing doses administered over several days). Many patients can be treated through mild drug reactions using acetaminophen and/or antihistamine for symptom management.

Dapsone is recommended as the alternative agent in patients who cannot tolerate TMP-SMX. Side effects of dapsone include fever, rash, and hemolytic anemia. G6PD qualitative assay should be performed before starting dapsone therapy. For dapsone to be effective as prophylaxis against toxoplasmosis, it should be given in conjunction with pyrimethamine. Folic acid is recommended to prevent bone marrow suppression.

Treatment

HIV infected persons presenting with opportunistic infections should have these treated prior to commencement of ART.

<u>If patient has this condition</u>	<u>Do this</u>
Tuberculosis (TB)	Treat TB first Start ART according to the next table
Pneumocystis pneumonia (PCP) Bacterial pneumonia Cryptococcal meningitis, Toxoplasmosis, Penicilliosis, Invasive fungal diseases, Significant diarrhoea which may reduce absorption of ART (e.g. more than 5	Treat these illnesses first Start ART when treatment is completed

loose stools per day) Malaria	
Oesophageal candida,	Treat esophageal candida first. Start ART as soon as the patient can swallow comfortably
Any undiagnosed active infection with fever and patient is unwell	Diagnose and treat first Start ART when stable
Drug reaction	Do not start ART during an acute reaction
Elevated ALT 3-5 times higher than normal limit	Look for cause and treat if possible (Hepatitis B and C)
Anaemia: Hemoglobin (Hgb) < 8 g/dl	Look for treatable cause (blood loss, MAC). If no treatable cause, commence ART with no-AZT containing regimen (HIV is often the cause of the anaemia)
Pregnancy	Initiate ART after the first trimester. If severely ill and early therapy clearly outweighs any potential fetal risk, commence ART. EFV should be avoided for pregnant women or women with the potential

<u>Conditions which may be improved or resolved with ART</u>
MAC CMV Diarrhea due to Cryptosporidiosis and Microsporidiosis Skin conditions such as PPE, seborrheic dermatitis

Further detail and standard operating procedures for treatment and prophylaxis of opportunistic infections is contained in Section 13.

6. PEOPLE WITH TUBERCULOSIS AND HIV CO-INFECTION

Prevention

Isoniazid preventive treatment reduces the risk of PLHA with latent TB infection developing active TB. All PLHA should be asked about any symptoms of TB (i.e. cough > 2 weeks). Those with TB symptoms should be examined and have the following investigations sputum smear, chest X-ray and Mantoux test to exclude active TB. Active TB cases are referred to Twomey Hospital or Lautoka Hospital. After active TB is excluded, Mantoux test should be done. When result is positive (i.e. induration size > 10 mm), self-administered Isoniazid 5mg / kg (to a maximum 300 mg) once daily for at least 9 months is given with monthly follow up.

Treatment

It is recommended that people with TB/HIV co-infection complete their TB therapy prior to beginning ARV treatment unless there is a high risk of HIV disease progression and death during the period of TB treatment (i.e., a CD4 count $< 200/\text{mm}^3$ or if disseminated TB is present). If a person needs TB and HIV treatment concurrently, first line treatment options include ZDV/3TC or d4T/3TC plus either a NNRTI or ABC. If a NNRTI regimen were used, EFZ would be the preferred drug as its potential to aggravate the hepatotoxicity of TB treatment appears less than that of NVP. However, its dosage may need to be increased to 800 mg/day. Except for SQV/r, protease inhibitors are not recommended during TB treatment with rifampicin due to their interactions with this drug.

Recommended ART for individuals with tuberculosis co-infection

Situation	Recommendations
Pulmonary TB; and CD4 count if available $< 200/\text{mm}^3$ Or CD4 count unavailable but meets clinical criteria for commencement	Start TB therapy PLUS one of these regimes as soon as TB therapy is tolerated: ZDV / 3TC / EFZ D4t / 3TC / EFZ ZDV / 3TC / NVP
Pulmonary TB; and CD4 if available 200 - $300/\text{mm}^3$	Start TB therapy for 2 months THEN start one of these regimens: ZDV / 3TC / EFZ D4t / 3TC / EFZ ZDV / 3TC / NVP
Pulmonary TB and CD4 $> 350/\text{mm}^3$ or total lymphocyte count $> 1200/\text{mm}^3$	Treat TB. Monitor CD4 counts if available or total lymphocyte count. Start ART according the recommendations for adults or children after completion of TB treatment.

7. WOMEN OF CHILDBEARING POTENTIAL OR WHO ARE PREGNANT

Women who are receiving ART should have available to them effective and appropriate contraceptive methods to reduce the likelihood of unintended pregnancy. It is important to note that some antiretroviral drugs (the NNRTIs NVP and EFZ and all the RTV boosted PIs) can lower blood concentrations of oral contraceptives and additional or alternative contraception needs to be used to avoid pregnancy in women receiving these drugs.

A distinction must be made whether:

- the mother requires ART for maternal health (meets the criteria for initiation of ART as outlined in section 3), or,
- ART prophylaxis is required for mother and child (PMTCT)

The mother requires ART for maternal health.

HIV infected pregnant women who meet the criteria for initiation of ART (outlined in section 3 – when to start treatment) should be offered treatment. Treatment should be delayed until after the first trimester, if this can be done safely. It is recommended that pregnant women use one of the following regimens:

Zidovudine (ZDV) / Lamivudine (3TC) / Nevirapine (NVP)
Stavudine (d4T) / Lamivudine (3TC) / Nevirapine (NVP)

EFZ and the combination of D4t / ddl are contraindicated in pregnancy.

ART prophylaxis is required for mother and child

Current estimates suggest that *of those infected through MTCT*, about 2/3 are infected during pregnancy and around the time of delivery and about 1/3 are infected through breast milk. Most of the HIV transmission in pregnancy occurs at the time of labour and delivery (more than 60%). In February 2004 WHO recommended the following regimen as the most effective in PMTCT:

Mother: Zidovudine (ZDV) from 28 weeks gestation with single dose Nevirapine (NVP) at onset of labour
Child: A single dose Nevirapine (NVP) immediately following delivery plus one week Zidovudine (ZDV)

8. GUIDELINES FOR CHILDREN

Recommended First Line Therapy

The preferred first line and alternate treatment for children includes the following regimens:

Zidovudine (ZDV) / Lamivudine (3TC) / Nevirapine (NVP)
Stavudine (d4T) / Lamivudine (3TC) / Nevirapine (NVP)
Zidovudine (ZDV) / Lamivudine (3TC) / Efavirenz (EFZ)
Stavudine (d4T) / Lamivudine (3TC) / Efavirenz (EFZ)

Appropriate formulations for infants and children may not be readily available. Until ARV formulations can be made more widely available, the splitting of adult dose solid formulations may be the only way a severely ill child can currently receive therapy. EFV cannot be used in children under age 3 years or weighing <10 kg. See Annexe 4 for Paediatric doses.

There is still a great deal that is unknown about ART for infants and children therefore expert advice should be sought where ever possible. However, the principles on which to base changes in therapy for children are similar to those applied to adults and management of toxicity is the same. When toxicity is related to an identifiable drug in the regimen, the offending drug can be

replaced with another drug that does not have the same side effects (see adult regimens for drug substitution in toxicity – section 5).

When to start ART in infants and children

Clinical staging for HIV infection in children is different from adults and normal ranges for CD4 cells are higher, therefore a decision to initiate ART will be based on different criteria to adults. In children, ARV initiation be divided into categories related to age. Where CD4 cell assays are available, the use of CD4 cell percentage is recommended for decision making on ART rather than absolute CD4 cell count because it varies less with age. See Annexe 6 for WHO paediatric staging:

For HIV-seropositive infants aged <18 months, WHO recommends starting ART if the infant has virologically-proven infection (unlikely in resource limited settings) and has:

- WHO Paediatric stage III eg. clinical AIDS, irrespective of CD4%, or
- WHO Paediatric stage II with CD4% <20%

For HIV-seropositive children aged >18 months, WHO recommends initiation of ARV therapy if:

- WHO Paediatric Stage III disease eg. clinical AIDS irrespective of CD4%, or
- WHO Paediatric Stage II disease, with consideration using CD4% <15%, or
- WHO Paediatric Stage 1 (eg. asymptomatic) and CD4% ,15%

Clinical assessment of infants and children receiving ARV therapy

- Nutrition and nutritional status
- Weight and height growth
- Developmental milestones
- Neurological signs

Important clinical signs of response to ART in infants and children include

- Improvement in growth in children who are failing to grow
- Improvement in neurological symptoms and development in children who are demonstrating delay in development milestones or encephalopathy
- Decreased frequency in infections (bacterial, oral thrush, and other opportunistic infections)

Laboratory assessment: Same as adults.

9. WHAT TO MONITOR

Clinical monitoring is essential for the provision of safe and effective ARV therapy. People on ARV therapy require close and regular (1- to 3-monthly) follow-up. The follow up laboratory testing will include:

- white blood cell count and differential to permit assessment of neutropenic side effects
- total lymphocyte count as a measure of efficacy

- Serum alanine or aspartate aminotransferase level determinations to monitor for hepatotoxicity.
- Haemoglobin and haematocrit measurements to assess the occurrence of anaemia.

Desirable supplemental tests include:

- measurement of bilirubin, amylase and serum lipids
- Regular serum glucose measurements are desirable when PI is used.

WHO recommends that where ever possible ART should be based on CD4 cell determinations. CD4 should be measured every six months. The CD4 cell count generally increases when viral replication is suppressed.

In addition to laboratory monitoring, follow up of physical, mental and social situation as well as adherence to the medication is necessary. A sample follow up treatment schedule is provided below.

	CD4 count <200 Absolute lymphocyte count < 1200 Symptomatic HIV disease	CD4 count >200 Absolute lymphocyte count > 1200 Asymptomatic disease
First visit	Medical history Symptom checklist Physical examination Chest X-ray if chest symptoms present Behavioural/psychosocial assessment: Education level, employment history, financial resources Social support, family/household structure Disclosure status, readiness to disclose Understanding of HIV/AIDS, transmission, risk reduction, treatment options Nutritional assessment Family/household assessment for other HIV-infected family members who may need care.	
Month 1	History (new problems) Symptom checklist Examination Cotrimoxazole prophylaxis Isoniazid prophylaxis for 9 months Psychosocial support Adherence counselling Medication prescription for 1 month	History (new problems) Symptom checklist Examination INH prophylaxis for 9 months Psychosocial support
Month 2	History (new problems) Symptom checklist Examination Adherence assessment/support Psychosocial support Repeat medication prescription for 1 month	
Month 3	History (new problems) Symptom checklist Examination Adherence assessment/support Psychosocial support Repeat medication prescription for 3 months Cotrimoxazole INH	History (new problems) Symptom checklist Examination Adherence assessment/support if taking INH Psychosocial support
Month 6	History (new problems)	History (new problems)

	Symptom checklist Examination Adherence assessment/support Psychosocial support Repeat medication prescription for 3 months Cotrimoxazole INH	Symptom checklist Examination Adherence assessment/support if taking INH Psychosocial support
Follow-up	VISITS EVERY 3 MONTHS and more often as needed	VISITS EVERY 3-6 MONTHS and more often as needed

10. ADHERENCE

For people on ARV therapy, medication adherence is critically important to treatment success. If there is a concern about a person's adherence ART should not be commenced.

Counselling for adherence preparation, support and monitoring is essential for addressing the needs and problems that PHA is facing. Refer to annexe 7 checklists / guides for:

- Preparing for ARV therapy
- Supporting ARV initiation (as the person first starts on medication)
- Monitoring and supporting adherence

11. POST-EXPOSURE PROPHYLAXIS

Treatment with antiretroviral drugs may be appropriate following occupational exposure to potentially HIV contaminated material. If the source of the inoculated blood or body fluids is HIV antibody positive, post exposure prophylaxis with an antiretroviral regimen should be started as soon as possible, generally within 72 hours and continued for 28 days.

12. DATA COLLECTION

It is very important that ART is monitored within Fiji to determine how improvements can be made in managing the epidemic. Prescribers are required to maintain a database of persons on treatment and forward specified data to NACA / MoH when required.

13. MANAGEMENT OF OPPORTUNISTIC INFECTIONS (OIs)

13.1 OPPORTUNISTIC INFECTIONS FREQUENTLY CAUSING RESPIRATORY SYMPTOMS

13.1.1. PNEUMOCYSTIS CARINII PNEUMONIA (PCP)

Symptoms

Fever, dry cough (no sputum) difficulty in breathing, weight loss, night sweats and fatigue. PCP and Tuberculosis are the MOST COMMON infections in patients with HIV and the most common reasons why patients die.

100% PCP prophylaxis for all patients with HIV-related symptoms is essential.

Diagnosis

- **District level providers:**
PCP can be diagnosed by the clinical symptoms.
- **"Hub" and Tertiary level providers:**
Chest X-ray and induced sputum examination should be done at district or tertiary hospital.

Preventative Therapy (Primary Prophylaxis)

- **District level providers:**
WHO Stage II, III and IV condition regardless of CD4 count, Stage I with CD4 < 200 (if available)
Trimethoprim-sulfamethoxazole (TMP-SMX, Bactrim, Septrin, Cotrimoxazole two single strength tablets per day.
Dapsone 100mg once a day if intolerant to Trimethoprim-sulfamethoxazole.

Treatment

- **District level providers:**
Cotrimoxazole (2 double-strength tablets or 4 single strength tablets every 8 hours for two weeks.
Cotrimoxazole can be given IV if available.
Dose is based on trimethoprim (15mg/kg/day in four divided doses)
- **"Hub" and Tertiary level providers:**
Prednisone (orally or IV) should be considered for people with acute illness (40mg every 12 hours for 5 days, then 40mg once a day for 5 days, then 20mg once a day for 11 days)

Secondary Prophylaxis

Everyone who has had PCP must continue with maintenance therapy two tablets per day for life (unless ARV is available and then can only be discontinued when the CD4 count is >200 for 3-6 months)

Referral to tertiary level hospital

Patients who do not respond to Cotrimoxazole (2 double-strength tablets or 4 single strength tablets every 8 hours). There should be improvement in 3 days.

Refer patients who do not improve within three days and patients who develop rash from cotrimoxazole to tertiary level

Refer patients with severe shortness of breath, high fever (>39 deg) and those who are very sick.

13.1.2. TUBERCULOSIS (TB): SYSTEMATIC COLLABORATION WITH TB PROGRAMME IS CRUCIAL

Symptoms

Night sweats, cough, fever, shortness of breath and weight loss.

TB in patients with HIV is often extra-pulmonary and can present with enlarged lymph glands especially in the neck, diarrhoea, headache.

Diagnosis

- **District level providers:**
Sputum examination for AFBs, chest X-ray, stool examination for AFBs if diarrhoea, lymph node biopsy for AFB stain
- **"Hub" and Tertiary level providers:**
CT scan, lumbar puncture for suspected CNS TB.

Primary Prophylaxis (In collaboration with TB/HIV program)

- **District level providers:**
EXCLUDE ACTIVE TUBERCULOSIS by history (cough, fever, weight loss) examination and chest X-ray if any lung symptoms are present. Look for large painful lymph nodes.
- **"Hub" and Tertiary level providers:**
Isoniazid (300mg once a day) for 6 months plus pyridoxine 50 mg/day.

Treatment in collaboration with TB program

Follow protocol of National TB Program (NTP). An example for smear positive pulmonary TB includes: Isoniazid (300mg once a day) + rifampicin (600mg once a day) + pyrazinamide (1500mg once a day) + ethambutol (1200 mg once a day) all for 2 months followed by isoniazid (300mg once a day) + rifampicin (600mg once a day) for 4 months.

Treat at district level

Prevention and treatment in collaboration with TB program.

13.1.3. BACTERIAL PNEUMONIA

Symptoms

Productive cough, purulent sputum and fever for 1-2 weeks. PCP presents more slowly and there is normally no sputum. Typical CXR finding is lobar consolidation. Gram-positive pyogenic bacteria will be the most probable cause of bacterial pneumonia

Diagnosis

- **District level providers:**
Chest X-ray (lobar consolidation), sputum examination including:
Gram stain- Streptococcus pneumoniae, Haemophilus influenzae, Staphylococcus aureus
Acid Fast stain -Tuberculosis
Wright stain -Histoplasmosis, Cryptococcus, Penicillium marnefei
- **"Hub" and Tertiary level providers:**

Sputum culture and sensitivity

Primary Prophylaxis

Cotrimoxazole 2 single-strength tablets once a day. Cotrimoxazole (given for PCP prophylaxis) may reduce the incidence of bacterial pneumonia

Treatment

Selection of antibiotics should be based on sputum examination

Refer to tertiary hospital

Patients who do not respond to initial therapy IV antibiotics according to identified pathogens and antibiotic sensitivities

13.2 OPPORTUNISTIC INFECTIONS FREQUENTLY CAUSING HEADACHE/NEUROLOGICAL SYMPTOMS

13.2.1. CRYPTOCOCCAL INFECTION

Symptoms

Cryptococcal meningitis presents with headaches, nausea, fever, fatigue, altered mental status and irritability. Can also cause seizures, coughing, sweats and difficulty in breathing.

Diagnosis

Lumbar puncture, India Ink stain of CSF and light microscopy, CT scan (if available)

Primary Prophylaxis

Not recommended (except in some countries with high prevalence)

Treatment

Preferred: IV amphotericin B (0.7mg/kg daily) + flucytosine (25mg/kg 4 times a day) for 2 weeks then fluconazole (400mg daily) for 8 weeks.

Alternatives: IV amphotericin B (0.7mg/kg daily) for 2 weeks then fluconazole (400mg daily) for 8 weeks

Notes on the use of amphotericin B

Amphotericin B is given by slow IV infusion over 45 minutes 4 times per day. Patient needs careful observation, especially with initial doses as fever and chills can occur. The other main side effects of Amphotericin B are electrolyte disturbances (especially hypokalaemia) and hypoglycaemia. Frequent monitoring of electrolytes and blood sugar are required, with 5% dextrose co- infusion and potassium supplements to maintain normal levels

Secondary Prophylaxis

Everyone who has had cryptococcal disease should be on maintenance therapy for life.

Preferred: Fluconazole (200mg daily).

Pregnant women should not take fluconazole.

Refer to tertiary hospital

If hospital has the required treatment and staff have necessary training. Maintenance therapy (Fluconazole)

Many district hospitals will refer to higher level health facilities for diagnosis complex treatments

13.2.2. TOXOPLASMOSIS (TOXO)

Symptoms

Altered mental state (confusion, delusional behavior), severe headaches, focal signs such as hemi-paresis, fever, seizures and coma. Can also affect the eye causing eye pain and reduced vision.

Diagnosis

- **District level providers:**
Clinical diagnosis based on the symptoms
- **“Hub” and Tertiary level providers:**
Cerebral CT scan

Primary Prophylaxis

Cotrimoxazole 2 single-strength tablets once a day.

Treatment

Pyrimethamine (200mg loading dose then 50-75mg once a day) + sulfadiazine (1g every 6 hours) for 3-6 weeks depending on response to treatment followed by long-term secondary prophylaxis.

Sulphadiazine may cause anaemia, thrombocytopenia, and leucopenia. Careful hematological monitoring with complete blood count is recommended. Rash can be associated with the use of pyrimethamine and sulphadiazine. Patients who do not show response to therapy within 1-2 weeks or who develop complications of therapy should be referred to specialist facility.

- **In addition, “Hub” and Tertiary level providers:**
Clindamycin (600mg every 6 hours).

Secondary Prophylaxis

Pyrimethamine (50 mg once a day)+Sulfadiazine (500 mg four times per day)

Refer to tertiary hospital

In most cases, all patients with suspected toxoplasmosis.

13.3 Opportunistic Infections frequently causing skin and mucosal symptoms

13.3.1 ORAL AND OESOPHAGEAL CANDIDIASIS

Symptoms

White patches on gums, tongue or lining of mouth, pain, difficulty in swallowing (esophageal candida) and loss of appetite. Can also cause vaginal irritation, itching, burning and thick white discharge

Diagnosis

Visual examination, white plaques which can be easily removed with swab or gloved finger. Swab and microscopic examination if available
Oesophageal candida can be diagnosed clinically by the presence of pain on swallowing and typical oral lesions. Endoscopy is not normally required unless unresponsive to fluconazole treatment

Primary Prophylaxis

Not recommended

Treatment

Mild: topical therapy like gentian violet applied 3 times per day or nystatin or clotrimazole lozenges dissolved in mouth 3 times per day.
For vaginal candidiasis, clotrimazole or nystatin pessaries (which can also be used in the mouth) inserted 3 times per day for 7 days.
Moderate: Systemic therapy with fluconazole 200mg per day or ketoconazole 200mg per day for 14-21 days
Start ART as soon as patient can swallow pills comfortably

Refer to tertiary hospital

Severe mouth, vaginal infection and severe pain on swallowing or if patient cannot swallow fluconazole. Refer for endoscopy if no response to fluconazole within 3 days

13.3.2 PENICILLIOSIS

Symptoms

Caused by the fungus, penicillium marnefei, this disease presents as typical papulo-necrotic skin lesions and often as systemic disease with fever, lung involvement and cough, weight loss, anaemia, lymphadenopathy.

Diagnosis

- **District level providers:**
Presumptive: Smear, Wright stain and microscopy from skin lesions
- **"Hub" and Tertiary level providers:**
Definitive: Culture

Primary Prophylaxis

Not recommended

Treatment

- **District level providers, "Hub" and Tertiary level providers:**
IV amphotericin B (0.7mg/kg daily) for 2 weeks then itraconazole 400 mg orally daily for 10 weeks. In mild cases: Itraconazole 400 mg orally daily for 8 weeks.
EPSA=
- **District level providers:**
Maintenance therapy (Fluconazole)

Secondary Prophylaxis

Itraconazole 200mg per day for life

Refer to tertiary hospital

- **District level providers:**
If hospital has the required drugs and staff have necessary training
- **"Hub" and Tertiary level providers:**
For many cases, refer to tertiary hospitals for complex treatments

13.3.3. HERPES SIMPLEX

Symptoms

Typical blisters usually in genital area or face

Diagnosis

Clinical diagnosis based on history and examination
No laboratory tests required

Primary Prophylaxis

Not recommended

Treatment

Usually self-limiting and may not require treatment. Local lesion care, such as with acyclovir topical and chlorhexidine. If indicated, aciclovir 200-400 mg 5 times daily for 7 days. In immunosuppressed herpes simplex can be chronic and invasive (e.g. esophagitis, encephalitis)

Secondary Prophylaxis

In cases of frequent recurrences, long-term suppressive therapy with acyclovir 400 mg twice daily may be necessary

Refer to tertiary hospital

Patient with suspected systemic infection, such as H. simplex encephalitis or oesophagitis

13.3.4.HERPES ZOSTER

Symptoms

Typical painful blisters in clusters along dermatomes. Can involve the eye

Diagnosis

Clinical diagnosis based on history and examination
No laboratory tests required

Primary Prophylaxis

Not recommended

Treatment

Local lesion care, such as with aciclovir topical and chlorhexidine. Aciclovir 800 mg 5 times daily orally for 7 days, commenced within 72 hours of onset of blisters. Famciclovir and valaciclovir are alternatives. Acyclovir eye ointment applied into eye every 4 hours for ophthalmic H. zoster. Pain relief may be required such as aspirin or paracetamol. If a secondary infection is present treat with a suitable antibiotic.

Secondary Prophylaxis

Not recommended

Refer to tertiary hospital

Patient who do not respond to initial oral acyclovir therapy and patients with severe, extensive or necrotizing lesions.

13.4 OPPORTUNISTIC INFECTIONS FREQUENTLY CAUSING DIARRHOEA

13.4.1.DIARRHOEA

(Diarrhoea may be caused by organisms which effect any person or by organisms specific to HIV related immunosuppression)

Common causes

Salmonellosis and shigellosis, Campylobacter spp, Giardia, Entamoeba histolytica, Isospora belli, Strongyloidiasis, Cryptosporidiosis, Mycobacterium tuberculosis, Mycobacterium Avium Complex (MAC) infection, Cytomegalovirus (CMV),
HIV (no other pathogens)

Diagnosis

- **“Hub” and Tertiary level providers:**
Identification of the organism by multiple stool examinations
Stain for AFBs (TB and MAC) & modified AFB stain (cryptosporidium, isospora)
Culture for bacterial pathogens (salmonella, shigella, campylobacter)

Preventive Therapy

Cotrimoxazole (given for PCP prophylaxis) may reduce the incidence of some bacterial diarrheas

Treatment

- **District level providers:**

Initial treatment should be with rehydration fluids (oral and/or IV fluids and electrolytes). Anti-motility agents like loperamide 10-20mg 3times per day unless blood in stool or fever

Empirical therapy

Cotrimoxazole 2 tablets BID P0 5 days plus metronidazole: 400 mg TID P0 7 days. If no response and/or fever and bloody stools: ciprofloxacin: 500 mg BID P0 5 days. If no response, mebendazole 100 mg TID P0 3 days.

- **"Hub" and Tertiary level providers:**

Specific therapy

Salmonellosis and shigellosis: Ciprofloxacin 500 mg, 1 tablet bid for 7 days or Ofloxacin or Ceftriaxone 1g, IM or IV, 1 injection each day, for 5 days.

Campylobacter spp: Erythromycin (tablet 500mg) 3 tablets daily for 5 days.

Giardiasis: Metronidazole tablet 250 mg, 2 tablets tid for 5 days.

Entamoeba histolytica: Metronidazole tablet 250mg, 2 tablets tid for 7-10 days.

Isospora belli: TMP-SMX tablet 480 mg, 2 tablets 4 times daily for 7 days.

Helminth infection: Mebendazole 100 mg TID P0 3 days

Strongyloidiasis: Thiabendazole 25 mg/kg, 3 times daily for 3 days.

Cryptosporidiosis: No proven effective treatment. Maintenance of fluid and electrolyte balance is of greatest importance, and constipating agents may also be useful.

Cryptosporidiosis may resolve with immune reconstitution on ART. Commence ART if available

Micobacterium tuberculosis (TB): Treat as extra-pulmonary TB according to national TB guidelines

Mycobacterium avium complex (MAC) infection: drugs to be given are Ethambutol, Clarithromycin, Rifampicin or/and Azithromycin.

Salmonellosis, shigellosis, campylobacteriosis and isosporiasis in HIV-infected patients often relapse. If relapse occurs after an initial course of antimicrobial therapy, a 6-12 weeks course therapy should be administered. These conditions (especially if recurrent) may respond to immune reconstitution on ART. Commence ART if available.

Refer to tertiary hospital

Patients not responding to symptomatic and initial antibiotic therapy and those who are severely dehydrated

13.5. OTHER OPPORTUNISTIC INFECTIONS AND HIV-RELATED ILLNESSES

13.5.1 CYTOMEGALOVIRUS (CMV) (Cytomegalovirus is a virus that infects the entire body)

Symptoms (CMV related)

Retinitis (in eye, retina): blurry vision or loss of central vision that can lead to blindness.

Colitis (colon): fevers, diarrhea and stomach pain.

Esophagitis (throat): ulcerations, pain and difficulty in swallowing.

Pneumonitis (lungs): pneumonia-like symptoms.
Encephalitis (brain): confusion, fever and tiredness.

Diagnosis

▪ **“Hub” and Tertiary level providers:**

Retinitis: eye doctor (ophthalmology) exam.

Esophagitis and colitis: endoscopy and/or biopsy.

Pneumonitis: Check for PCP and tuberculosis first (**EPSA**). Diagnosis of CMV needs referral to specialized hospital

Encephalitis: CT scan, etc.

Treatment

By specialized hospital refer all patients with suspected CMV

If specific therapy is unavailable, commence ART

13.5.2. MYCOBACTERIUM AVIUM COMPLEX (MAC)

(MAC is a bacterial infection found in water, dust, soil and bird droppings)

Symptoms

Persistent fever, night sweats, fatigue, weight loss, anemia, abdominal pain, dizziness, diarrhea and weakness

Diagnosis

Culture from a sterile site such as blood, bone marrow or cerebral spinal fluid by specialized laboratory

Primary Prophylaxis

Azithromycin 250 mg 4 or 5 tablets once weekly (if available) for patients with CD4<50 (if known). With increasing availability of ART, the preferred option is to start ART and not give azithromycin

Treatment

Azithromycin (500-600mg once a day); or clarithromycin (500mg twice a day) + ethambutol (15mg/kg/day) + rifabutin (300mg once a day).

Persistent fever and anemia after ruling out common active OIs including TB may suggest MAC.
ART may resolve the condition

Secondary Prophylaxis

Everyone who has had MAC should be on maintenance therapy with either clarithromycin (500mg twice a day) or azithromycin (500mg once a day) if it has been proven there is no resistance to either drug + ethambutol (15mg/kg once a day) +/- rifabutin (300mg once a day).

Refer to tertiary hospital

All patients with suspected MAC

13.5.3. CERVICAL CANCER

Symptoms

Often asymptomatic. Can cause vaginal discharge, vaginal bleeding and pelvic pain

Diagnosis

- **District level providers:**

Annual PAP smear is recommended for all HIV positive women as they are at increased risk of cervical dysplasia and cancer

PAP smear will detect human papilloma virus (HPV), the cause of most cervical cancers, cervical dysplasia and cancer

- **"Hub" and Tertiary level providers:**

Colposcopy and cone biopsy

Treatment

Patients with Pap smear reports of dysplasia or intraepithelial neoplasia require colposcopy and may require cone biopsy or surgery. Adjuvant therapy (chemotherapy/radiotherapy) may be required

Refer to tertiary hospital

If colposcopy and surgical facilities not available or if further investigations are indicated such as ultrasound (hepatic metastases) or CT scan (lymph node or bone metastases).

13.6 MANAGEMENT OF SYMPTOMS RELATED TO OPPORTUNISTIC INFECTIONS, OPPORTUNISTIC INFECTION PROPHYLAXIS, ART AND IRS

<u>Symptom</u>	<u>Managing symptoms of OIs and HIV-related illness</u>	<u>Side effects of ARV and OI prophylaxis and their management</u>	<u>Immune reconstitution syndrome (IRS) (Consider during first 3 months on ART)</u>
<u>Nausea, Vomiting</u>	Metoclopramide 10mg TID Prochlorperazine 5-10 mg TID Chlorpromazine 25-50mg every 6-12 hours	ART: Take ART with food (except ddI and indinavir). If on AZT, usually self-limiting after 2 weeks. Treat symptomatically. Stop ART if lactic acidosis suspected Cotrimoxazole: Take with food INH: Take at bedtime, if vomiting, stop INH	Hepatitis B and C can occur with IRS. Suspect if nausea, vomiting plus jaundice
<u>Diarrhoea</u>	Drink extra fluid. At least 200-300 ml in addition to usual fluid intake after each loose stool. Oral rehydration solution (ORS) 2-4 litres per day If persists or worsens, investigate and treat cause or give empirical therapy	ART: NFV commonly causes diarrhoea (less common with saquinavir) Loperamide 10-20 mg BID if no fever/no blood in stool If no response after 2-4 weeks, change ART	Temporary flare ups of MAC or CMV may cause diarrhoea. Continue ART and treat symptomatically
<u>Indigestion</u>	Aluminium or magnesium sulphate tablets 1-2 tabs every 6 hours If persists or worsens, treat for esophageal candidiasis. If no response, refer to next level	ART: Take ART with food except ddI and IDV	Oesophageal candida may require treatment
<u>Anxiety, bizarre dream, psychosis, depression</u>	Care counselling and referral to specialist as needed.	ART: This may be due to EFV. Give at night; counsel and support (usually lasts < 3 weeks). Amitriptyline 25 mg (increasing to 100mg) once daily before bed. Call for advice or refer if severe depression or suicidal or psychosis	These CNS effects are not associated with IRS

<u>Symptom</u>	<u>Managing symptoms of OIs and HIV-related illness</u>	<u>Side effects of ARV and OI prophylaxis and their management</u>	<u>Immune reconstitution syndrome (IRS)</u>
<u>Headache</u>	Paracetamol 1 gm 4-6 hourly Ibuprofen 400 mg 4-6 hourly Aspirin 600mg 4-6 hourly If persists or worsens, the most common causes are cryptococcal meningitis and toxoplasmosis	ART: If on AZT or EFV, reassure that this is common and usually self-limiting but can last 4-8 weeks. If persists more than 2 weeks or worsens, call for advice or refer	Assess for toxoplasmosis and cryptococcal meningitis
<u>Neuropathy</u>	Amitriptyline 25 mg (increasing to 100mg) once daily before bed. Plus analgesics as above (It takes 3 weeks before amitriptyline takes effect) If persists or worsens, commencing ART may help	ART: Commonly caused by d4T, ddI and ddC Reduce dosage of d4T if possible Add amitriptyline 25 mg (increasing to 100 mg) once daily before bed. Change ART if possible INH: Give pyridoxine 100 mg daily	Not an IRS symptom
<u>Abdominal or flank pain, and/or Jaundice (yellow eyes)</u>	(Pancreatitis due to CMV Intestinal perforation due to CMV Hepatobiliary disease due to MAC and Cryptosporidiosis)	ART: d4T or ddI may cause pancreatitis which requires stopping these drugs NVP (and EFV less commonly) may cause liver dysfunctions which require stopping these drugs Stop ART if lactic acidosis suspected Cotrimoxazole: if jaundice, stop cotrimoxazole INH: if jaundice, stop INH	Hepatitis B and C can occur with IRS. Suspect if nausea, vomiting plus jaundice

<u>Symptom</u>	<u>Managing symptoms of OIs and HIV-related illness</u>	<u>Side effects of ARV and OI prophylaxis and their management</u>	<u>Immune reconstitution syndrome (IRS)</u>
<u>Skin rash, itch</u>	Emollient lotion Calamine lotion Mild steroid creams (1% hydrocortisone, 0,01% triamcinolone) Oral antihistamines If persists or worsens, investigate cause and treat or refer to next level	ART: If on EFV, give oral antihistamines and review daily. Rash is often self limiting If on NVP or ABC, assess carefully. Stop drug if rash is moderate or severe (generalized, peeling, mucosal involvement). NFV and IDV also can cause rash Cotrimoxazole: Stop if rash is moderate or severe INH: Stop if rash is moderate or severe	Skin conditions which can flare up due to IRS in the first 3 months of ART: - Herpes simplex and zoster - Papilloma virus (warts) - Fungal infections - Atopic dermatitis Treat as necessary
<u>Fever</u>	Paracetamol 1 gm 4-6 hourly Ibuprofen 400 mg 4-6 hourly Aspirin 600mg 4-6 hourly If persists or worsens, investigate cause and treat or refer to next level	ART: Stop all drugs when hypersensitive reaction of ABC is suspected	Fever soon after commencing ART could be IRS (MAC, TB, CMV HCV, HBV, cryptococcus, herpes zoster)
<u>Cough, difficulty breathing</u>	For wheezing: Salbutamol 2 puff s every 20 minutes x 3 times, then 2 puff s every 3 to 6 hours. If persists or worsens, common causes are PCP, TB, Bacterial or fungal pneumonia	ART: Stop ART if lactic acidosis suspected	IRS can be associated with PCP, TB, fungal or bacterial pneumonia
<u>Fatigue, pallor</u>	If persists or worsens, check Hemoglobin for anemia caused by HIV or by MAC Transfuse as necessary (Hb<8)	ART: Common for 4 to 6 weeks after starting AZT Stop AZT if severe pallor or symptoms of anaemia or low haemoglobin (<8). Cotrimoxazole: Stop the drug if Hb<8	Suspect MAC if fever, fatigue and anemia. Continue ART Once CD4 >50, should resolve without treatment

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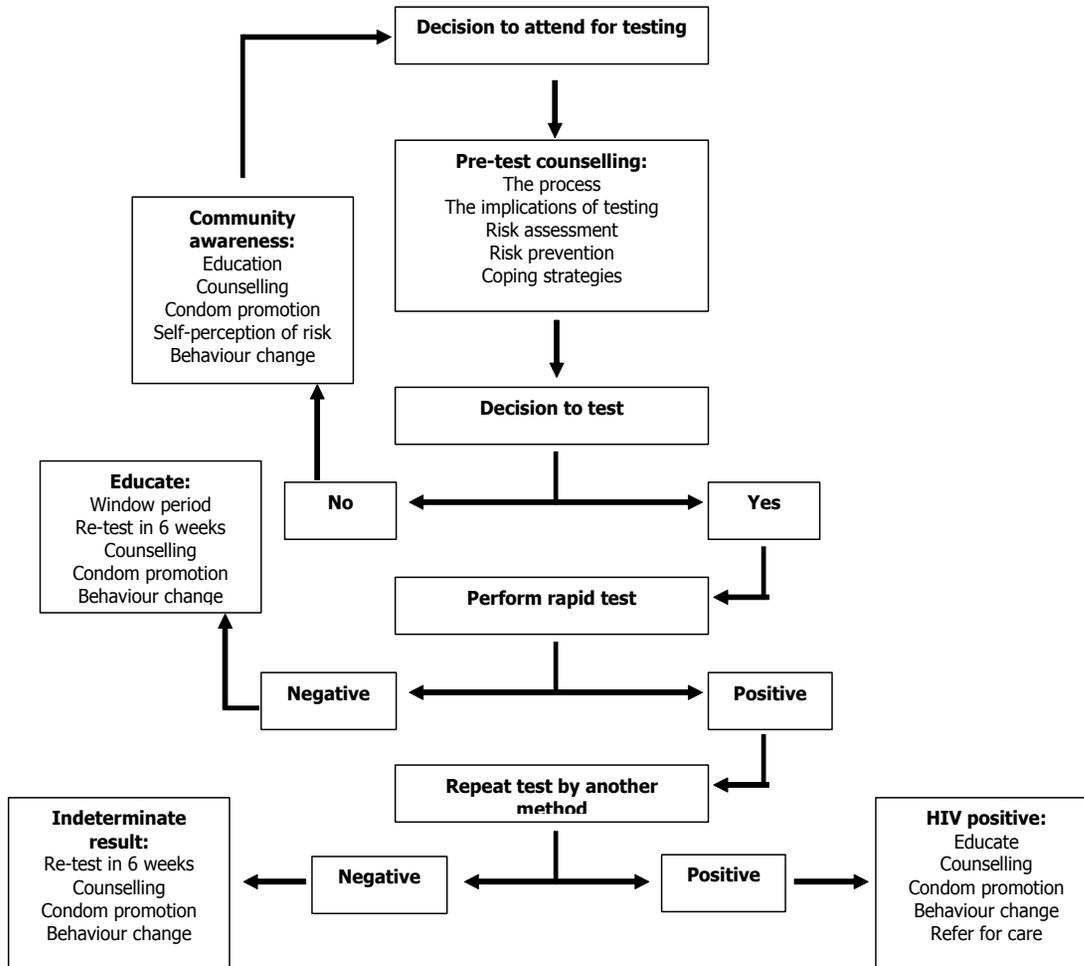
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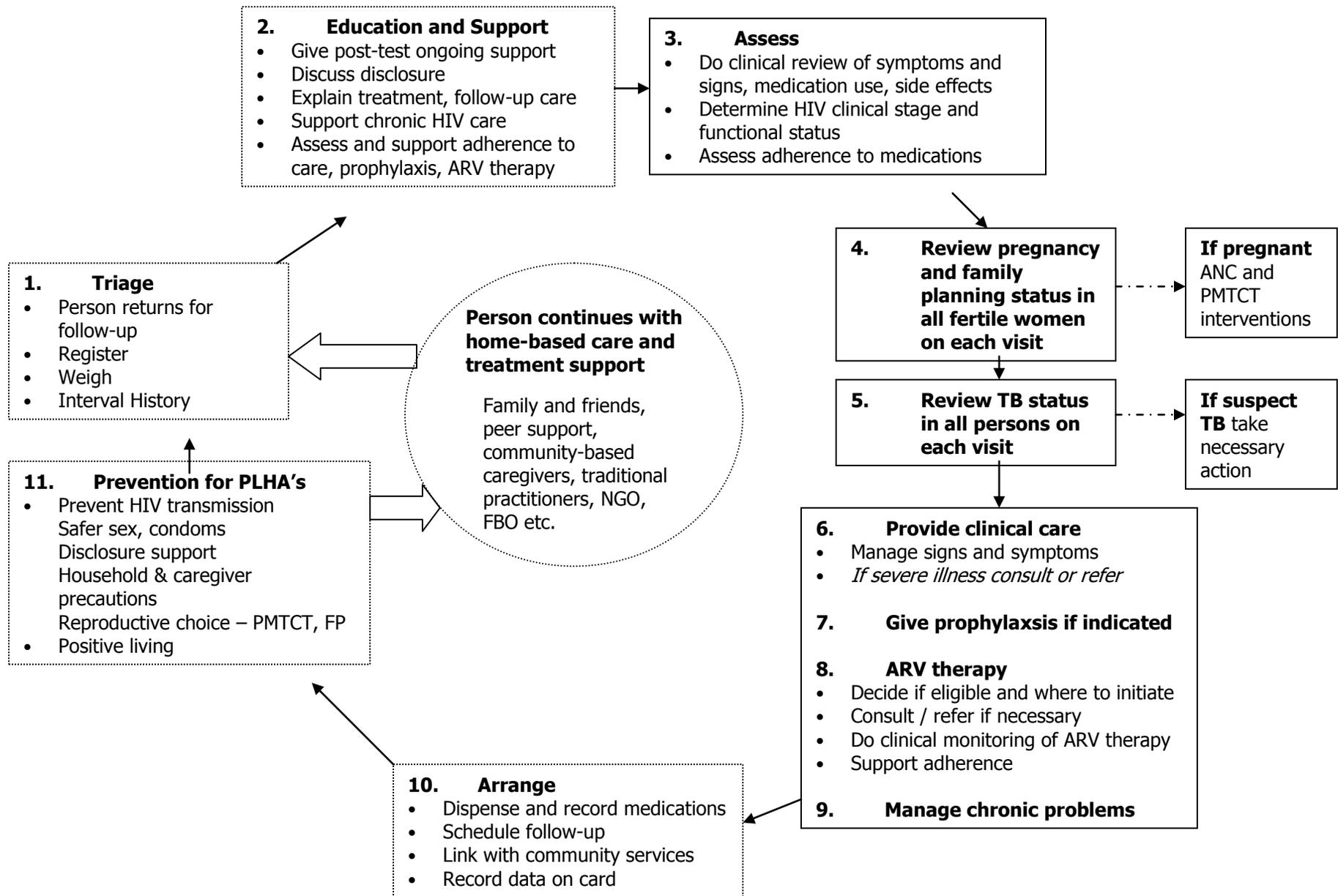
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ANNEXE 1: FLOW CHART FOR VOLUNTARY COUNSELING AND TESTING (VCT)



ANNEXE 2: SEQUENCE OF CARE AFTER POSITIVE HIV TEST



ANNEXE 3: WHO HIV CLINICAL STAGING

	WHO Clinical Stage I Asymptomatic	WHO Clinical Stage II Mild Disease	WHO Clinical Stage III Moderate Disease	WHO Clinical Stage IV Severe Disease (AIDS)
Weight	No weight loss	Weight loss 5-10%	Weight loss >10%	HIV wasting syndrome
Symptoms: Treat common and opportunistic infections in Part 4. Follow the treatment plan at district DCC or OPD	No symptoms or only: <ul style="list-style-type: none"> ○ Persistent generalized lymphadenopathy 	<ul style="list-style-type: none"> ○ Sores or cracks around lips (angular cheilitis) ○ Itching rash (seborrhea or prurigo) ○ Recurrent upper respiratory infections such as sinusitis or otitis ○ Recurrent mouth ulcers 	<ul style="list-style-type: none"> ○ Oral thrush (or hairy leukoplakia) ○ More than 1 month: <ul style="list-style-type: none"> - Diarrhoea - Vaginal candidiasis or - Unexplained fever ○ Pulmonary TB with last year 	<ul style="list-style-type: none"> ○ Oesophageal thrush ○ More than 1 month: <ul style="list-style-type: none"> - Herpes simplex ulcerations ○ Lymphoma* ○ Kaposi sarcoma ○ Invasive cervical cancer* ○ Pneumocystis pneumonia* ○ Extrapulmonary TB* ○ Cryptococcal meningitis ○ HIV encephalopathy <p>(significant neurological impairment interfering with independent functioning and not due to other cause, will often improve with ART)</p>
Prophylaxis (according to national policy)	<ul style="list-style-type: none"> ○ INH prophylaxis if eligible 	<ul style="list-style-type: none"> ○ INH prophylaxis if eligible ○ Cotrimoxazole prophylaxis 	<ul style="list-style-type: none"> ○ INH prophylaxis if eligible and able to exclude TB ○ Cotrimoxazole prophylaxis ○ Other prophylaxis on treatment plan 	<ul style="list-style-type: none"> ○ INH prophylaxis if eligible and able to exclude TB ○ Cotrimoxazole prophylaxis ○ Other prophylaxis on treatment plan
ARV therapy	<ul style="list-style-type: none"> ○ Only if CD4<200 	Only if CD4<200 or total lymphocyte <1200/mm3	<ul style="list-style-type: none"> ○ If CD4 not available, treat in all stage 3 ○ If CD4 available, take into consideration CD4<350 when deciding to treat ○ Evaluate for ART (see ART Part 4) ○ Prepare for adherence 	<ul style="list-style-type: none"> ○ All in stage 4 are medically eligible ○ Evaluate for ART (see ART Part 4) ○ Prepare for adherence (this requires several visits and home visit if possible)

* Require a clinical diagnosis - this can be from records of a previous hospitalization. Muscle infection, pneumocystis or any other severe pneumonia, toxoplasmosis, cryptococcal meningitis, and extrapulmonary TB are all infections which should be referred for hospital diagnosis and treatment.

ANNEXE 4: DRUGS USED TO TREAT HIV INFECTION

	Adult dose	Paediatric dose
Nucleoside reverse transcriptase inhibitors (NRTI's)		
Zidovudine (AZT)	300 mg twice daily	<4weeks: 2mg/kg twice daily 4 w-13 yrs: 10mg/kg twice daily
Stavudine (d4T)	<60kg: 30mg twice daily	< 30kg: 1mg/kg twice daily
	>60kg: 40mg twice daily	<60kg: 30mg twice daily
Lamivudine (3TC)	150mg twice daily	4mg/kg twice daily
Didanosine (ddI)	<60kg: 125mg twice daily	<3 months: 90mg/m ² ** twice daily
	>60kg: 200mg twice daily	>3 months: 90mg/m ² twice daily
Abacavir (ABC)	300 mg twice daily	>3 months: 8mg/kg twice daily
Non-nucleoside reverse transcriptase inhibitors (NNRTI's)		
Efavirenz (EFV)	600mg daily once daily	13 to <15kg: 200mg once daily
		15 to <20kg: 250mg once daily
		20 to <25kg: 300mg once daily
		25 to <32.5kg: 350mg once daily
		32.5 to <15kg: 400mg once daily
Nevirapine (NEV)	200mg daily for 2 weeks, then 200mg twice daily	15 to 30 days 5mg/kg once daily for 2 weeks
		>30days to 13yrs: 120mg/m ² daily for 2 weeks, then 200mg/m ² twice daily
Protease inhibitors (PI)		
Nelfinavir (NFV)	1.25g twice daily	<1yr 65-75mg/kg twice daily***
		>1yr to <13yrs 55-65mg/kg twice daily
Indinavir/ritonavir (IDV/r)	800mg/100mg twice daily	
Lopinavir/ritonavir (LPV/r)****	400mg/100mg twice daily (533/133mg twice daily when combined with EFZ or NVP)	7-15 kg: 12mg/kg LPV/3mg/Kg ritonavir twice daily
		15-14 kg: 10mg/kg LPV/5mg/kg ritonavir twice daily
Saquinavir/ritonavir (SQV/r)	1000mg/100mg twice daily	

* With renal or hepatic dysfunction dose adjustments may be indicated.

** Body surface area calculation: square root (height in cm x body weight in kg divided by 3600)

*** High doses required in infants <1yr because of kinetic variability

**** It should be noted that LPV/r is included in the WHO model list of Essential Medicines.

ANNEXE 5: FIXED DOSE COMBINATIONS OF ARVs AVAILABLE AS AT 1 DECEMBER 2003

Three drug fixed dose combinations	d4T (40 mg) + 3TC (150 mg) + NVP (200 mg)
	d4T (30 mg) + 3TC (150 mg) + NVP (200 mg)
	ZDV (300 mg) + 3TC (150 mg) + ABC (150 mg)
	ZDV (300 mg) + 3TC (150 mg) + NVP (200 mg)
Two drug fixed dose combinations	d4T (30 mg) + 3TC (150 mg)
	d4T (40 mg) + 3TC (150 mg)
	ZDV (40 mg) + 3TC (150 mg)

ANNEXE 6: WHO STAGING SYSTEM FOR HIV INFECTION AND DISEASE IN CHILDREN²

Clinical Stage I:

1. Asymptomatic
2. Generalized lymphadenopathy

Clinical Stage II:

3. chronic diarrhea >30 days duration in absence of known etiology
4. Severe persistent or recurrent candidiasis outside the neonatal period
5. Weight loss or failure to thrive in the absence of known etiology
6. Persistent fever >30 days duration in the absence of known etiology
7. Recurrent severe bacterial infections other than septicemia or meningitis (eg. osteomyelitis, bacterial (non-TB) pneumonia, abscesses)

Clinical Stage III:

8. AIDS defining opportunistic infections
9. Severe failure to thrive ("wasting") in the absence of known etiology*
10. Progressive encephalopathy
11. Malignancy
12. Recurrent septicemia or meningitis

- * Persistent weight loss >10% of baseline or less than 5th percentile on weight for height chart on 2 consecutive measurements more than 1 month apart in the absence of another etiology or concurrent illness

² WHO (December 2003). Scaling up antiretroviral therapy in resource-limited settings: Treatment guidelines for a public health approach.

ANNEXE 7: ARV THERAPY: ADHERENCE PREPARATION, SUPPORT AND MONITORING

Guide for preparing for ARV therapy

Assess	<ul style="list-style-type: none"> ▪ Person's goals for today's visit ▪ Understanding of ARV therapy ▪ Interest in receiving therapy
Advise on	<ul style="list-style-type: none"> ▪ HIV illness, expected progression ▪ ARV therapy <ul style="list-style-type: none"> ○ 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 ARV 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	<ul style="list-style-type: none"> ▪ Establish that the person is willing and motivated and agrees to treatment, before initiating ARV therapy <ul style="list-style-type: none"> ○ 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	<ul style="list-style-type: none"> ▪ Help the person develop the resources / support / arrangements needed for adherence: <ul style="list-style-type: none"> ○ 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 ○ ARV adherence support group ○ Treatment supporter
Arrange	<ul style="list-style-type: none"> ▪ When the person is ready for ARV therapy, discuss at the clinical team meeting then make a plan

Guide for Supporting ARV initiation (as the person first starts on medication)

Assess	<ul style="list-style-type: none"> ▪ 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 on	<ul style="list-style-type: none"> ▪ Reinforce the information given before ▪ Advise on the details of first line regimen <ul style="list-style-type: none"> ○ 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 <ul style="list-style-type: none"> ○ 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 ARV therapy. It is very important to still practice safer sex and other practices to prevent transmission.
Agree	<ul style="list-style-type: none"> ▪ 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	<ul style="list-style-type: none"> ▪ Develop (then reinforce on each visit) a concrete plan for the specific ARV regimen <ul style="list-style-type: none"> ○ 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 ARV adherence support group. ▪ Arrange home visit.
Arrange	<ul style="list-style-type: none"> ▪ 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.

Guide for Monitoring and supporting adherence

<p>Assess</p>	<p>Do clinical review and respond to any problems or changes in status. To assess adherence:</p> <ul style="list-style-type: none"> ▪ 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: <ul style="list-style-type: none"> ○ “Many people have trouble taking their medications, what troubles are you having?” ○ “Can you tell me when and how you take each pill?” ○ “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? <p>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.</p>
<p>Advise on</p>	<ul style="list-style-type: none"> ▪ Reinforce the information given before ▪ Give additional information that may help with adherence problem ▪ Advise on any suggested changes in the regimen.
<p>Agree</p>	<ul style="list-style-type: none"> ▪ 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.
<p>Assist</p>	<ul style="list-style-type: none"> ▪ Provide adherence support ▪ Reinforce interventions which match the person’s needs and adherence problems, if present. ▪ Make sure that the person has: <ul style="list-style-type: none"> ○ Plan to link taking medications with daily events such as meals ○ 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 <ul style="list-style-type: none"> ○ Get help from supporter, other family and friends or peers ○ Help person and supporter to find solutions ▪ If adherence problem: <ul style="list-style-type: none"> ○ Get help – call for advice ○ Link with home based care or home visits
<p>Arrange</p>	<ul style="list-style-type: none"> ▪ Record adherence estimate on persons card. ▪ Arrange for refills ▪ Arrange for next follow-up visits: <ul style="list-style-type: none"> ○ In clinic ○ 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.

INDEX

A

Adherence	19
ART Prophylaxis for mother and child	16
ART Regime for pregnant women	16

B

Bacterial Pneumonia	21
- Primary Prophylaxis	21
- Treatment	21

C

Cervical Cancer	29
- Treatment	29
Cryptococcal Infection	22
- Treatment	22
- Primary Prophylaxis	22
- Secondary Prophylaxis	22
Cytomegalovirus (CMV)	27
- Treatment	28

D

Data Collection	19
Diarrhoea	26
- Preventative Therapy	26
- Treatment	27
Drug substitution for regime failure	12
Drug substitution for toxicity	12

F

First line therapy	11
Framework for a clinical review	10

G

Guidelines for children	16
- First Line therapy	16
- When to start ART in infants and children	17

H

Herpes simplex	25
- Primary Prophylaxis	25
- Treatment	25
- Secondary Prophylaxis	25

Herpes zoster	26
- Primary Prophylaxis	26
- Treatment	26
- Secondary Prophylaxis	26

M

Management of Opportunistic Infections (OIs)	20
Management of symptoms related to OI, OIP, ART and IRs	30-31
Mycobacterium Avium Complex (MAC)	28
- Primary Prophylaxis	28
- Treatment	28
- Secondary Prophylaxis	28

N

NACA	9
------	---

O

Opportunistic Infections (OIs)	14
- Prevention	14
- Treatment	20
Oral and oesophageal Candidiasis	24
- Primary Prophylaxis	24
- Treatment	24

P

Penicilliosis	24
- Primary Prophylaxis	24
- Treatment	24
- Secondary Prophylaxis	24
People with TB and HIV Co-infection	14
- Prevention	14
- Treatment	15
- ART for individuals with TB co-infections	15

S

Second Line Therapy	11
---------------------	----

T

Toxoplasmosis (Toxo)	23
- Primary Prophylaxis	23
- Treatment	23
- Secondary Prophylaxis	23

W

What to monitor	17
-----------------	----