NATIONAL HIV/AIDS SECRETARIAT
HEALTH SECTOR RESPONSE GROUP



National Antiretroviral Treatment Guidelines

Ministry of Health and Sanitation

Sierra Leone

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Abbreviations

3TC	Lamivudine
ABC	Abacavir
AIDS	Acquired Immune Deficiency Syndrome
ALT	Alanine amonitransferase also known as SGPT
APV	Amprenavir
ARV	Antiretroviral
ART	Antiretroviral Therapy
CBC	Complete Blood Count
CD	Cluster of Differentiation
CD4	T Lymphocyte Cells
CMV	Cytomegalovirus
d4T	Stavudine
ddC	Zalcitabine
ddI	Didanosine
DLV	Delavirdine
DOT	Directly Observed Treatment
EFV	Efavirenz also abbreviated as EFZ
ELISA	Enzyme Linked Immunosorbent Assay
HCW	Health Care Worker
HIV	Human Immunodeficiency Virus
IDV	Indinavir
IRS	Immune Reconstitution Syndrome
LPV	Lopinavir
MTCT	Mother-to-child transmission of HIV
NFV	Nelfinavir
NNRTI	Non-Nucleoside Reverse Transcriptase Inhibitor
NsRTI	Nucleoside Analog Reverse Transcriptase Inhibitor
NtRTI	Nucleotide analog Reverse Transcriptase Inhibitor
NVP	Nevirapine
OI	Opportunistic Infection
PEP	Post Exposure Prophylaxis
PCP	Pneumocystis Carinii Pneumonia
PCR	Polymerase Chain Reaction
PI	Protease Inhibitor
PO	Per OS
RTV,r	Ritonavir
RTV-PI	Ritonavir Boosted Protease Inhibitor
SGPT	Serum Glutamic pyruvic Transaminase, also known as ALT
SQV	Saquinavir
RNA	Ribo Neucleuic Acid
RPR	Rapid Plasma Reagent
RT	Reverse Transcriptase
STI	Sexually Transmitted Disease
TB	Tuberculosis
TLC	Total Leucocyte Count
VCCT	HIV Voluntary Confidential Counselling and Testing
VL	Viral Load
WHO	World Health organization
ZDV	Zidovudine, also known as AZT

FOREWORD

The need to revise the previous HIV/AIDS Treatment Guidelines is obvious. The epidemic is the greatest health challenge the World faces today. Since it was first identified, an estimated 40.3 million people are living with the virus globally; with 25.8 million living in Sub Saharan Africa. Women form 57 percent; that is, an estimated 13.5 million women infected with HIV. In Sierra Leone, 1.53 percent of the population are living with the virus. Dealing with HIV/AIDS issues is one of the priorities of the Health Sector and the Government of Sierra Leone.

The 3 by 5 initiative offers new opportunities as well as new imperatives for strengthening HIV prevention efforts and increasing access to Antiretroviral Treatment (ART) for people in need. This opportunity further offers and allows us to develop a comprehensive public health response to the epidemic that fully integrates prevention, care and treatment.

It has been proven that the triple-drug therapy (ART) reduces the level of HIV in the body to barely visible levels in many patients. Whilst the virus is never eliminated, the risk of a person on effective treatment transmitting HIV is also greatly reduced. Coupled with strategies to emphasize safer behaviours of those in treatment, there will be a considerable impact and acceleration of HIV prevention.

Also, there is evidence that the introduction of treatment in affected communities can reduce the fear, stigma and discrimination that surround HIV/AIDS, increase demand for and uptake of HIV testing and counselling, and reinforce prevention efforts.

Health Workers providing treatment are an integral part of the prevention of HIV and AIDS paradigm. It is hoped that these guidelines will be resourceful to them and complement their wealth of knowledge and experience in providing professional care and treatment to their clients.

I wish to recognize the role played by the leadership of the Health Sector Response at the National HIV/AIDS Secretariat in providing coordination for the development of these guidelines. It is hoped that this book will serve its purpose of contributing to the national effort of mitigating the suffering of PLWHA whilst at the same time creating hope for the wider populace.

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ACKNOWLEGEMENT

This revised Treatment Guidelines is a product of several years of work and experience by professional medical practitioners on treatment of HIV/AIDS cases in Sierra Leone.

Many people contributed to the development of the original and indeed the review of this book. The contribution of PLWHA was also of immense importance in arriving at national specific treatment guidelines.

On behalf of the National AIDS Secretariat, I wish to thank profusely the under mentioned people who represent a long but not exhaustive list of contributors whose direct involvement was extremely helpful in developing the final version that you are about to read:

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I thank also the Government of Sierra Leone, WHO, UNICEF, Global Fund and UNAIDS for generously providing both moral and financial assistance to the Secretariat for the production of the National Treatment Guidelines. It is my fervent hope that these guidelines would be useful and count upon as a major contribution to the overall goal of fighting HIV/AIDS in our country.

Dr Brima Kargbo
Acting Director
NATIONAL AIDS SECRETARIAT

Introduction

Human Immunodeficiency Virus (HIV) was first recognised in Sierra Leone in 1987, and since its recognition cases have been identified by finding severe opportunistic infections that indicate profound defects in cellular immunity in the absence of other causes of immunodeficiency.

Since then, the number of people living with HIV/AIDS has steadily increased with a seroprevelence rate of 4.9% in 2005. Like in most Sub-Saharan countries, urgent actions are needed in Sierra Leone to prevent an escalating epidemic. Hence, WHO and UNAIDS have begun extending Antiretroviral Therapy to most African populations although this attempt has remained dismal. Evidence suggest that Antiretroviral drugs do not cure HIV infection, but are known to significantly improve the quality of life of HIV infected persons, and at the same time dramatically reduce mortality associated with the infection.

Majority of people living with HIV/AIDS have no access to Antiretroviral drugs. Over the years, WHO and UNAIDS have shown increase commitment to making these drugs available to all HIV infected persons, which has indeed been effective in reducing HIV related morbidities and mortalities.

In Sierra Leone, the development of a National Guideline for Antiretroviral Therapy is part of the Government's commitment to making Antiretroviral drugs available to all HIV infected persons. These guidelines will also assist the Health Care provider in the management of persons living with HIV/AIDS.

This revised edition of the Treatment Guidelines consolidates treatment options into first-line and second-line regimens. It also outlines clinical and laboratory monitoring of patients, with guidelines on the recognition of drug side-effects. Paediatric Antiretroviral Therapy has been addressed separately as certain drug combinations are now advocated for this age group. Although it cannot be considered as an exhaustive document, this handbook can be used by all levels of Health Care Workers providing Antiretroviral Therapy for HIV/AIDS Patients.

1. Antiretroviral Therapy in Adults and Adolescents

1.1 Principles of Antiretroviral Therapy

The principal criteria for successful implementation of antiretroviral therapy should include improving the quality of life of the patients, restore and preserve immune function; reduction of HIV related morbidity and mortality, prevention of viral resistance and treatment failure. It should also ensure effective response by involving PLWHA, their families and community in care, strengthen HIV prevention by increasing awareness and creating a demand for testing and counselling as well as reducing stigma and discrimination.

1.2 Goals of Antiretroviral Therapy

The goal of antiretroviral therapy is to improve the quality of lives of individuals by:

- Restoration or preservation of immunological function
- Improvement in clinical symptoms
- Reduction in morbidity and mortality
- Maximal and durable suppression of viral load.

The secondary goal is to decrease the incidence through:

- The increased uptake in voluntary confidential counseling and testing with more people knowing their HIV status.
- Reducing the risks of HIV transmission from mother to child.

1.3 Strategy

The overall strategy is to:

- Choose a suitable regimen of ARV drugs that the patient has not either experienced or to which the virus has the minimum possibilities of cross-resistance.
- Choose an ARV regimen which can be well tolerated using combination formulation that are potent and have less adverse side effects.

1.4 Classes of Antiretrovirals and functions

Antiretrovirals generally target two key enzymes that the virus requires in order to replicate: protease and reverse transcriptase

There are currently 20 approved Antiretroviral Drugs for the treatment of HIV that includes **seven** Nucleoside Reverse Transcriptase Inhibitors, **one** Nucleotide Reverse Transcriptase Inhibitors, **three** Non-Nucleoside Reverse Transcriptase Inhibitors, **eight** Protease Inhibitors and one fusion inhibitor.

1.4.1 Nucleoside Reverse Transcriptase Inhibitors (NRTIs): These drugs inhibit the transcription of RNA into DNA, which is necessary for the reproduction of the virus. These include Zidovudine (**ZDV or AZT**), Lamivudine (**3TC**), Didadosine (**ddI**), Stavudine (**d4T**), Abacavir (**ABC**)Zalcitabine (ddC).

1.4.2 Non-Nucleoside Reverse Transcriptase Inhibitors (NNRTIs): these are chemically different from NRTIs but also inhibit transcription of viral RNA to DNA. These include Nevirapine (**NVP),** Efavirenz (**EFZ**) and Delavirdine (DLV).

1.4.3 Protease Inhibitors (PIs) - target the protease enzymes thus cutting the long chains of amino acids into smaller proteins. It includes Indinavir (**IDV)**, Nelfinavir (**NFV)**, Saquinavir (**SQV**), Amprenvir (APV), Ritonavir (**RTV**) Lopinavir-Ritonavir (LPV/r), Atazanavir (ATV) and Darunadir (TMC 114).

1.4.4 Nucleotide Reverse Transcriptase Inhibitors (NtRTI): These include Tenofovir **(TDF).**

1.4.5 Fusion inhibitors: these work by blocking HIV entry into cells. These include Enfuvirtide (T-20)

List of Antiretroviral Drugs and their Doses

Table 1: Nucleoside reverse transcriptase inhibitors (NRTI).

Generic Name	Trade Name	Presentation	Recommended Doses	Diet Restrict - ions	Side Effects	Storage Require-ments
Zidovudine	Retrovir ®	Capsules 100, 250, 300mg Oral solution 10mg/ml IV formulation: 10mg/ml	250-300mg BID	None	Myelosuppression : anaemia and/or Neutropenia, Myalgia, Myopathy, Headache, Gastrointestinal Intolerance	Room temperature
Didanosine	Videx®	Tablets : 25, 50, 100, 150, 200mg Enteric coated capsules : 125, 200, 250, 400mg	<60kg : 250mg QD or 125 mg BID >60kg : 400 mg QD or 200 mg BID	Yes (fasting)	Pancreatitis, Hyperuricemia, Peripheral Neuropathy, Diarrhoea, Nausea	Room temperature for tablets and capsules. Oral solutions for children is stable after reconstitution for 30 days if refrigerated

Generic Name	Trade Name	Presentation	Recommended Doses	Diet Restrict - ions	Side Effects	Storage Require-ments
Stavudine	Zerit®	Capsules 15, 20, 30, 40mg Oral solution : 1mg/ml	< 60 kg : 30 mg BID ≥ 60 kg : 40 mg BID	None	Peripheral Neuropathy, Pancreatitis	Room temperature. Oral solutions should be kept refrigerated.
Lamivudine	Epivir®, 3 TC®	Capsules 150mg Oral solution : 10mg/ml	150 mg BID	None	Peripheral Neuropathy	Room temperature
Abacavir	Ziagen®	Capsules 300mg Oral solution : 20mg/ml	300 mg BID	None	Hypersensitivity Reaction (2-3%)	Room temperature
Emtricatabine		200mg tablet	200mg daily			Room temperature

Table 2: Non-nucleoside reverse transcriptase inhibitors NNRT.

Generic Name	Trade Name	Presentation	Recommended Doses	Diet Restrict -ions	Side Effects	Storage Require-ments
Nevirapine	Viramune ®	Tablets 200mg Oral suspension 50mg/ml	200 mg QD for14 days then 200 mg BID or 400 mg QD	None	Rash, including rare cases of Stevens-Johnson, increase of Transaminases and Acute Hepatitis	Room temperature
Efavirenz	Sustiva® Stocrin®	Capsules 50, 100, 200mg	600 mg QD	None	Dizziness, Insomnia, Somnolence, Abnormal Dreams, Psychosis (1-2%), Acute Depression, Rash	Room temperature

Table 3: Protease inhibitors (PIs).

Generic Name	Trade Name	Presenta-tion	Recommen-ded Doses	Diet Restrict-ions	Side Effects	Storage Requirements
Indinavir	Crixivan®	Capsules 200-400mg	800 mg TID	Fasting if not boosted	Nephrolithiasis Gastrointestinal intolerance Hyperbilirubin emia	Room temperature
Ritonavir	Norvir®	Capsules 100 mg	600 mg BID	With food	Gastrointestinal intolerance	Refrigerate capsules until

		Oral solution 600mg/7.5ml			Oral Paresthesia Increase of Transaminases	dispensed. Stable at room temperature for 30 days. Store oral solutions at room temperature.
Saquinavir	Invirase® Fortovase® (SGC)	Hard gel capsules 200 mg **or** Soft gel capsules 200 g	(HGC) 600 mg TID **or** (SGC) 1200 mg TID	With food	Gastrointestinal intolerance (Diarrhoea) Headaches	Room temperature
Nelfinavir	Viracept®	Tablets 250mg Oral powder 50mg/1g	750 mg TID or 1250mg BID	With food	Diarrhoea	Room temperature
Amprenavir	Agenerase ®	Capsules 50mg/150mg Oral solution 15mg/ml	1200 mg BID	No restrictions	Gastrointestinal intolerance Rash	Room temperature
Lopinavir/ Ritonavir	Kaletra®	Capsules 133.3 + 33.3mg Oral solution 80mg+20mg/ ml	400/100mg BID	With food	Digestive intolerance Rash	Refrigerate for long term storage. Stable for 30 days at room temperature.

1.5 When to start Antiretroviral Therapy in Adults and Adolescents

The process of initiating ART involves assessing:

- Readiness to commence therapy
- Understand its implication that it is a life long therapy
- Understanding the importance of adherence to treatment
- Toxicity
- Access to nutritional support
- Family and peer support

1.5.1 Conditions necessary to introduce Antiretroviral Drugs (ARVs)

- Access to functioning and affordable health services and support networks into which ARV treatments can be integrated so that the treatments are provided effectively.
- Information and training on safe and effective use of ARVs for health professionals in a position to prescribe ARVs.
- Capacity to diagnose HIV infection and to diagnose and treat concomitant illnesses.
- Assurance of an adequate supply of quality drugs.
- Sufficient resources should be identified to pay for treatment on a long-term basis; patients must be aware that treatment is “for life”.

- Functioning laboratory services for monitoring including haematological and bio-chemical tests to detect toxicities, must be available.
- Access to voluntary HIV counselling and testing (VCCT) and follow up counselling services should be assured, including counselling PLWHAs on the necessity of adherence to treatment.

1.5.2 Criteria for selection of adult and adolescent patients for ART

- All patients with a history of AIDS-defining illness or severe symptoms of HIV regardless of CD4 cell count
- All asymptomatic patients with CD4 cell count of < 350 cells
- WHO stage III irrespective of CD4 cell count
- WHO stage IV irrespective of CD4 cell count

If CD4 count is unavailable

- WHO Stage IV disease irrespective of absolute lymphocyte count
- WHO Stage II or III disease with absolute lymphocyte count<1,000-2,000 cells/mm3

* Before starting ART, the patient should make the final decision regarding acceptance of treatment.

1.6 Baseline Clinical Assessment

Before any patient is enrolled on a long time ARV therapy, he/she should undergo a baseline clinical assessment to include the following:

- Medical History
- Physical Examination
- Laboratory Investigations
- Counselling

1.6.1 Baseline Medical History should include the essential demographic characteristics, the past medical history including major illnesses (e.g. Tuberculosis), hospitalizations and surgeries, the length of time since the diagnosis of HIV infection, and current medications and symptoms. In the case of women, current or planned pregnancy and the access to contraceptive services should be reviewed.

1.6.2 The Baseline Physical Examination should include vital signs, weight and details of any abnormalities of the eyes (including fungi if possible), Oropharynx, Lymph Nodes, Lungs, Heart, Abdomen, Extremities, Nervous System and Genital Tract.

1.6.3 Clinical Staging should form part of baseline assessment on entering into a care and treatment program.

1.6.4 WHO Staging System for HIV Infection and Disease in Adults and Adolescents

Clinical Stage I

1. Asymptomatic

2. Generalized lymphadenopathy

Performance scale 1: asymptomatic, normal activity

Clinical Stage II

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

And/or performance scale 2: symptomatic, normal activity

Clinical Stage III

1. Weight loss >10% of body weight
2. Unexplained chronic diarrhoea, >1 month
3. Unexplained prolonged fever (intermittent or constant), >1 month
4. Oral candidiasis (thrush)
5. Oral hairy leukoplakia
6. Pulmonary tuberculosis within the past year
7. Severe bacterial infections such as pneumonias, pyomyositis

And/or Performance Scale 3: Bed-ridden for less than 50% of the day during the last month

Clinical Stage IV

1. HIV wasting syndrome – weight loss of more than 10%, and either unexplained chronic diarrhoea for more than 1 month, or chronic weakness or unexplained prolonged fever for more than 1 month
2. Pneumocystis carinii pneumonia
3. Toxoplasmosis of the brain
4. Cryptosporidiosis with diarrhoea for more than 1 month
5. Extrapulmonary cryptococcosis
6. Cytomegalovirus (CMV) disease of an organ other than liver, spleen or lymph nodes
7. Herpes simplex virus (HSV) infection, mucocutaneous for more than 1 month, or visceral of any duration
8. Progressive multifocal leukoencephalopathy (PML)
9. Any disseminated endemic mycosis such as histoplasmosis, coccidioidomycosis
10. Candidiasis of the oesophagus, trachea, bronchi or lungs
11. Atypical mycobacteriosis, disseminated
12. Non-typhoid salmonella septicaemia
13. Extrapulmonary tuberculosis
14. Lymphoma
15. Kaposi's sarcoma
16. HIV encephalopathy – disabling cognitive and/or motor dysfunction interfering with activities of daily living, progressing slowly over weeks or months, in the

absence of concurrent illness or condition other than HIV infection that could account for the findings

1.7 HIV Related Clinical Events in Adults and Adolescents

A number of clinical events have been identified during the various stages of HIV infection. These events have been recognised to be useful in the clinical and definitive diagnosis of HIV infection.

Table 4: Criteria for HIV- Related Clinical Events in Adults and Adolescent

CLINICAL EVENT	CLINICAL DIAGNOSIS	DEFINITIVE DIAGNOSIS
CLINICAL STAGE 1		
Asymptomatic	No HIV-related symptoms reported and no signs on examination	Not applicable
Persistent generalized lymphadenopathy	Painless enlarged lymph nodes >1 cm , in two or more non-contiguous sites (excluding inguinal) in absence of known cause and persisting for three months or longer	Histology
CLINICAL STAGE 2		
Moderate unexplained weight loss (under 10% of body weight)	Reported unexplained weight loss. In pregnancy, failure to gain weight	Documented weight loss (under 10% of Body weight)
Recurrent bacterial upper respiratory tract infections (current event plus one or more in last six months	Symptoms complex, e.g. unilateral face pain with nasal discharge (Sinusitis), painful inflamed eardrum (Otitis media), or tonsillopharyngitis without features of viral infection (e.g Coryza, cough)	Laboratory studies if available, e.g. culture of suitable body fluid
Herpes Zoster	Painful vesicular rash in dermatomal distribution of a nerve supply does not cross midline	Clinical diagnosis
Angular cheilitis	Splits or cracks at the angle of the mouth not attributable to iron or vitamin deficiency, and usually responding to antifungal treatment	Clinical diagnosis
Recurrent oral ulcerations (two or more episodes in last six months	Aphthus ulcerations, typically painful with a halo of inflammation and a yellow-grey pseudomembrane	Clinical diagnosis

Papular pruretic eruption	Papular pruretic lesions, often with marked post inflammatory pigmentation	Clinical diagnosis
Seborrhoeic dermatitis	Itchy scaly skin condition, particularly affecting hairy areas (scalp, axillae, upper trunk and groin)	Clinical diagnosis
Fungal nail infections	Paronychia (painful red and swollen nail bed) or onycholysis (separation of nail from nail bed) of the fingernails (white discolouration, especially involving proximal part of nail plate, with thickening and separation of nail from nail bed)	Fungal culture of nail/nail plate material
CLINICAL STAGE 3		
Severe unexplained weight loss (more than 10% of body weight)	Reported unexplained weight loss (over 10% of body weight) and visible thinning of face, waist and extremities with obvious wasting or body mass index below 18.5. In pregnancy, weight loss may be masked	Documented loss of >10% of body weight
Unexplained chronic diarrhoea for longer than one month	Chronic diarrhoea (loose or watery stools three or more times daily) reported for longer than one month	Not required but confirmed if three or more stools observed and documented as unformed, and two or more stool tests reveal no pathogens
Unexplained persistent fever (intermittent or constant and lasting for longer than one month)	Reports of fever or night sweats for more than one month, either intermittent or constant with reported lack of response to antibiotics or antimalarials, without other obvious foci of disease reported or found on examination. Malaria must be excluded in malarious areas.	Documented fever exceeding 37.6 degrees C with negative blood culture, negative Ziehl-Neilsen (ZN) stain, negative malaria slide, normal or unchanged chest X-ray (CXR) and no other obvious focus of infection
Oral Candidiasis	Persistent or recurring creamy white curd-like plagues which can be scraped off (pseudomembranous), or red patches on tongue, palate or lining of mouth, usually painful or tender (erythematous form)	Clinical diagnosis

Oral hairy leukoplakia	Fine white small linear or corrugated lesions on lateral border of the tongue, which do not scrape off	Clinical diagnosis
Pulmonary TB (current)	Chronic symptoms (lasting at least two to three weeks): cough, haemoptysis, shortness of breath, chest pain, weight loss, fever, night sweats, PLUS either positive sputum smear OR negative sputum smear AND compatible chest radiograph (including but not restricted to upper low infiltrates, cavitation, pulmonary fibrosis and shrinkage). No evidence of extra pulmonary disease.	Isolation of M tuberculosis on sputum culture or histology of long biopsy (together with compatible symptoms).
Severe bacteria infection (e.g. pneumonia, meningitis, empyema, pyomyositis, bone or joint infection, bacteraemia, severe pelvic inflammatory disease)	Fever accompanied by specific symptoms or signs that localise infection, and response to appropriate antibiotic	Isolation of bacteria from appropriate clinical specimens (usually sterile sites).
Acute necrotizing ulcerative gingivitis or necrotizing ulcerative periodontitis	Severe pain, ulcerated gingival papillae, loosening of teeth, spontaneous bleeding, bad odour, rapid loss of bone and/or soft tissue.	Clinical diagnosis
Unexplained anaemia (below 8g/dl), neutropenia (below 0.5 $x10^9$/l) or chronic (more than one month) thrombocytopenia ($50x10^9$)/l	N presumptive clinical diagnosis	Diagnosed on laboratory testing and not explained by other non-HIV conditions. Not responding to standard therapy with haematinics antimalarials or antihelmintics as outlined in relevant national treatment guideline, WHO IMCI guidelines or other relevant guidelines.
CLINICAL STAGE 4		
HIV wastage syndrome	Unexplained involuntary weight loss (over 10% of body weight) with obvious wasting or body mass index below 18.5 PLUS EITHER unexplained chronic diarrhoea (loose or watery stools three or more	Documented weight loss (over 10% of body weight plus two or more unformed stools negative for pathogens or documented temperature exceeding 37.6 C with no other cause of

	times daily) reported for longer than one month. OR reports of fever or night sweats for more than one month without other cause and lack of response to antibiotics or antimalarials. Malaria must be excluded in malarious areas.	disease, negative stool culture, negative malarial slide and normal or unchanged chest x-ray
Pneumocystis pneumonia	Dyspnoea on exertion or unproductive cough of recent onset (within the past three months) tachypnoea and fever, AND chest x-ray evidence of diffused bilateral interstitial infiltrates, AND no evidence of bacteria and pneumonia, bilateral crepitations on auscultation with or without reduced air entry	Cytology or immunofluorescent microscopy of induced sputum or bronchoalveolar lavage or histology of lung tissue.
Recurrent bacteria pneumonia (this episode or one or more episodes in last six months)	Current episode plus one or more episodes in last six months. Acute onset (under two weeks) of symptoms (e.g. fever, cough, dyspnoea, and chest pain) PLUS new consolidation on clinical examination or chest x-ray. Response to antibiotics	Positive culture or antigen test of a compatible organism
Chronic herpes simplex virus infection of more than one month	Painful progressive anogenital or orolabial ulceration, lesions caused by recurrent herpes simplex virus infection and reported for more than one month. History of previous episodes. Visceral herpes simplex virus requires definitive diagnosis	Positive culture or DNA (by PCR) of herpes simplex virus or compatible cytology/histology
Oesophageal candidiasis	Recent onset of retrosternal pain or difficulty on swallowing (food and fluids) together with oral candidiasis	Macroscopic appearance at endoscopy or bronchoscopy or by microscopy/histology
Extra pulmonary TB	Systemic illness (e.g fever,night sweats, weakness and weight loss). Other evidence of extra pulmonary or disseminated TB varies by site: Pleura, pericardial, peritoneal involvement, meningitis,	M. tuberculosis isolation or compatible histology from appropriate site OR radiological evidence of miliary TB on chest x-ray.

	mediastinal or abdominal lymphadenopathy or osteitis. Discrete peripheral lymph node M. tuberculosis infection is considered a less severe form of extra pulmonary tuberculosis	
Kaposi sacoma	Typical appearance in skin or oropharynx of persistent, initially flat patches with a pink or blood –bruised colour,skin lesions that usually develop into violaceous plaques or nodles	Macroscopic adherence at endoscopy or bronchoscopy, or by histology.
CMV disease (other than liver spleen or lymph node	Retinitis only: may be diagnosed by experienced clinicians. Typical eye lesions on fundoscopic examination: discrete patches of retinal whitening with distinct borders, spreading centrifugally, often following blood vessels, associated with retinal vasculitis, haemorrhage and necrosis	Compatible histology or CMV demonstrated in CSF by culture or DNA (by PCR)
CMS toxoplasmosis	Recent onset of a focal neurological abnormality or reduced level of consciousness AND response within ten days to specific therapy.	Positive serum toxoplasma antibody AND (if available) single/multiple intracranial mass lesion on neuroimaging (CT or MRI)
HIV encephalopathy	Clinical finding of disabling cognitive and /or motor dysfunction interfering with activities of daily living, progressive over weeks or months in the presence of a concurrent illness or condition, other than HIV infection, which might explain the findings.	Diagnosis of exclusion, and, if available neuroimaging (CT or MRI).
Extrapulmonary cryptococcosis (including meningistis)	Meningitis: usually subacute, fever with increasingly severe headache, meningism, confusion, behavioural changes that respond to criptococcal therapy	Isolation of Cryptococcus neoformanas from extrapulmonary site or positive cryptococcal antigen test (CRAG) on CSF/blood.

Disseminated non-tuberculous mycrobacteria infection	No presumptive clinical diagnosis	Diagnosed by finding a typical mycrobacterial specimens from stool, blood, body fluid or other body tissue, excluding lung.
Progressive multifocal leukoencephalopathy (PML)	No presumptive clinical diagnosis	Progressive neurological disorder (cognitive dysfunction, gait/speech disorder, visual loss, limb weakness and cranial nerve palsies) together with hypodense white matter lesions on neuroimaging or positive polyomavirus JC (JCV) PCR on CSF.
Cryptosporidiosis (with diarrhoea lasting more than one month.	No presumptive clinical diagnosis	Cyst identified on modified ZN microscopic examination of unformed stool
Chronic isosporiasis	No presumptive clinical diagnosis	Identification of isospora
Disseminated mycosis (coccidiomycosis, histoplasmosis)	No presumptive clinical diagnosis	Histology, antigen detection or culture from clinical specimen or blood culture
Recurrent non-typhoid salmonella bacteraemia	No presumptive clinical diagnosis	Blood culture
Lymphoma (cerebral or B cell non-hodgkin) or other solid HIV associated tumors	No presumptive clinical diagnosis	Histology of relevant specimen or, for CNS tumors, neuroimaging techniques
Invasive cervical carcinoma	No presumptive clinical diagnosis	Histology or cytology
Visceral leishmaniasis	No presumptive clinical diagnosis	Histology (amastigotes visualized) or culture from any appropriate clinical specimen
HIV- associated nephropathy	No presumptive clinical diagnosis	Renal biopsy
HIV-associated cardiomyopathy	No presumptive clinical diagnosis	Cardiomegaly and evidence of poor left ventricular function confirmed by echocardiography

Source: revised WHO clinical staging and immunological classification of HIV and case definition of HIV for surveillance, 2006 (in press)

1.8 Clinical Monitoring and Laboratory Tests

Clinical monitoring and laboratory tests are used as indicators of the progress of HIV disease and of antiretroviral treatment. These tests include CD4 count, viral load and other blood tests.

HIV causes gradual change in the human body. If HIV is not treated, these changes can lead to worsening health and eventually to AIDS. Keeping track of these changes in the body is known as medical monitoring, which depends on clinical assessment and laboratory tests.

1.8.1 Laboratory Monitoring Before Treatment

A wide variety of laboratory tests are used in medical monitoring. Some are used to confirm an HIV diagnosis, and/or to detect co-infections such as tuberculosis. Various blood tests directly measure viral activity or monitor HIV-related changes in he function of the immune system. Other tests are used to estimate the risk of toxicity due to antirectoviral treatment and can be used to guide the choice of treatment. The setting and availability of technical and financial resources will determine which test can be used.

- The minimum test required for laboratory monitoring before or during antirectoviral therapy are: HIV antibody tests, redblood cell and white blood cell counts and pregnancy tests. These tests can be done in any medical laboratory.

- If resources are better a CD4 blood test can be done which shows how much damage HIV has caused to the immune system, or if the immune system is starting to recover as a result of treatment. The count is low when the immune system is damage and should gradually increase when the system is recovering. Treatment should be started in any patient with a CD4 count of less than 350.

- In well-resource hospital laboratories a viral load test can be used to show how active the virus is in the person's body, and to predict how quickly disease is likely to appear. It increases when the virus is active and should decrease as a result of treatment.

These tests are very useful tools for predicting he future cause of HIV and the risk of developing AIDS. However, they are at present too expensive to use in most resource limited settings, especially those with high HIV prevalence.

1.8.2 Monitoring in Resource Limited Settings

Laboratory tests provide additional information that is useful when considering ART or monitoring progress. These laboratory tests can be grouped into four categories.

i. Absolute Minimum Test

Absolute minimum tests are essential for introduction of antiretroviral therapy. These tests include an HIV antibody test to confirm HIV infection and a blood test measuring haemoglobin or haematocrit levels to screen for anaemia, which may be due to nutritional deficiencies or treatable parasitic diseases.

ii. Basic Tests

Basic tests are used to provide effective monitoring of most antiretroviral regiments and are needed to identify potential toxic reactions and then to trigger changes in drug regiment. Basic laboratory test include:

- White blood cell count and differential to permit assessment neutropenic side effects of antirectoviral theraphy
- Serum alanine or aspartate aminotransferase level, to assess the possibility of hepatitis co-infection and to monitor for toxicity o deliver.
- Serum creatinine and or blood urea nitrogen, to assess baseline kidney function.
- Serum glucose. This is to measure blood sugar levels.
- Pregnancy tests for women. Pregnancy tests for women are needed to prevent transmission of HIV to a child.

iii. Desirable Tests

Desirable tests are not absolutely essential but can provide significant information that would be helpful in the monitoring of antiretroviral therapy in resource limited settings. Treatment must be commenced in all asymptomatic patients with CD4 counts below 350 cells. These tests include: CD4 cell count, which are the best indicator of immunologic response to treatment, bilirubil test, serum amylase and serum lipids. These tests are used to assess the risk or development of some potential side effects of antiretroviral therapy.

iv. Optional Test

Viral load testing is considered an optional test in resource limited settings because of cost constraints. Virus load refers to the amount (the number of copies) of HIV genetic material (RNA) circulating in the blood plasma (the fluid that carries blood cells). Where resources permit, regular viral load monitoring is a direct measure of the effectiveness of antiretroviral therapy in reducing levels of virus in a patient's blood. Virus load test result can range from 50 copies to more than one million copies. A viral load greater than 100,000 is usually considered to be high. If there are high levels of virus in the blood there are also likely to be high levels of virus in semen and vaginal fluid. Therefore, with high virus loads are likely to be more infectious.

1.8.3 Monitoring Adult Patients

i. Patients not receiving Antiretroviral Treatment

These patients will be monitored periodically to assess disease progression using only the CD4+ Cell Count as follows:

a. If CD4+ Cell Count 201-400/ml – check CD4+ Cell Count every 3 months
b. If CD4+ Cell Count >400/ml – check CD4 Cell Count every 6 months

Counselling for ARV Therapy

The psychosocial aspects associated with deciding whether to start and then continue on ARV treatment are as important as the medical aspects. Counselling for ARVs is often time consuming and physicians may choose to work with a trained counsellor with specialised

skills. If appropriate and informed decisions are to be made, and treatment is to be provided safely and effectively, counselling services must be available to people living with HIV/AIDS (PLHWAs). Those who make the decision to start ARVs will need information, support and encouragement on a regular and long term basis in order to maintain adherence to the regimen.

Where ARVs are readily available, the possibility of obtaining these treatments is an incentive to seek out counselling and testing. It has been shown that one of the main barriers to knowing one's HIV status, particularly in high prevalence areas, is the lack of perceived benefit for those who fear they might be seropositive.

1.9 Recommended ARV Regimens

1.9.1 First Line Antiretroviral Therapy

It is recommended to initiate Antiretroviral Therapy in naïve patients (i.e. patients who have not yet been treated with ARVs) using a combination of two NRTIs with one PI or one NNRTI.

For example: Zidovudine + Lamivudine + Indinavir
Stavudine + Lamivudine + Nevirapine
Stavudine + Lamivudine + Efavirenz
Zidovudine + Lamivudine + Nevirapine
Zidovudine + Lamivudine + Efavirenz

Fixed combinations containing the above drugs are strongly recommended because they are cheaper, user friendly and facilitate better adherence because of low pill burden.

Table 5: Recommended First Line Antiretroviral Regimes for adults and adolescents in Sierra Leone

Regimen	Comments
ZDV+3TC+ EFZ or NVP **OR** d4T + 3TC+ EFZ or NVP Alternative Regimen ZDV + ABC + 3TC	Give NVP in pregnant women or women for whom effective contraception cannot be assured. NVP is recommended in women with CD4 count < or = 250 and with males with CD4 cell count < or = 400 Give EFZ for patients requiring simultaneous ARV treatment and TB therapy containing Rifampicin. EFZ is recommended except during first trimester of pregnancy or women with high reproductive potential

- Zidovudine and stavudine (AZT/d4T) should never be used together because of proven antagonism.
- Didanosine and stavudine (ddI/d4T) should be avoided in pregnancy due to risk of lactic acidosis and hepatotoxicity. It is contra-indicated in patients with peripheral neuropathy.

- Efavirenz (EFZ) cannot be used in pregnant women. Women of child bearing age should only receive EFZ in combination with effective contraceptive methods.

1.9.2 Second Line Antiretroviral Regimen

This regimen is recommended in circumstances involving treatment failure. The principle is to retain the activity of the drug regimen against the virus. The general principle of second line regimen is that they should contain at least 2 new drugs (new NRTI) plus 1 PI, because resistance develops more slowly to PI.

Table 6: Second Line Antiretroviral Regimen P1-Based Regimen: 10R 2 P1 + 2nrtis

REGIMEN	COMMENTS
Zidovudine + Indinavir boosted with Ritonavir + Lamivudine Alternate Regimen Zidovudine + Lopinavir boosted with Ritonavir + Lamivudine	

1.9.3 Follow-Ups and Monitoring of HIV/AIDS Adult and Adolescent Patients during ART

The objective of follow-up is to:

- Clinical assessment as same as pre-ART
- Assessment of clinical stage
- Counseling to assist patients with adherence to treatment
- Patients response to treatment
- Manage opportunistic infections
- Assess symptoms of drug toxicity
- Diagnose and manage treatment failure

Once ART is started, follow-up and monitoring should be scheduled as follows:

- First visit one month after initiation of ART
- Every three/four months thereafter
- If possible, monthly visits are encouraged for better adherence

Patients on Treatment

The ideal intervals for monitoring patients have not been determined because the cost of monitoring could be higher than the cost of purchasing ARV regimens. Determination of the minimum schedule that could be used without compromising care, especially in our setting remains an important area of study.

Taking into consideration the timing of expected toxicities and changes in measures of treatment efficacy, the schedules are considered pragmatic, while awaiting clinical trials data.

Monitoring will be done using:

- **viral load** and CD4+ Cell Counts to assess treatment efficacy,
- **by clinical examination** to assess toxicity, adherence, clinical failures and
- **by blood chemistry and haematology** to assess drug toxicity).

Table 7: Recommended schedule for monitoring adult patients

1	**Plasma HIV RNA (Viral load)** • At start of Therapy • At 3 months to assess initial efficacy • Every 6 months thereafter
2	**CD4+ Cell Count** - Every 3-4 months
3	**Blood Chemistry (LFTs, Urea+ Creatinine) and Haematology (FBC)** • At start of Therapy • At 2 weeks to assess toxicity for Nevirapine • Every 3 months thereafter
4	**Clinical Monitoring** • 1 Week by Doctor) • 2 Weeks – for Chemistry (by Doctor or other Health Worker) • 1 month by Doctor • 3 months by Doctor • 3 months thereafter

Follow-up at Hospital Level

As ART becomes more available, many district hospitals will be starting patients on ARVs and also undertake their follow up.

The role of hospitals in follow up should include the following:

Monitoring patient's responses to ART

- Symptoms checklist to detect intercurrent illnesses, HIV disease progression or adverse events to ART.
- Weight. This should be recorded at every visit.
- Haematology and biochemistry investigations should be done at least every 6-12 months and when there are symptoms suggestive of severe toxicity to ARV drugs
- CD4 cell count if facilities are available should be done every 6-12 months or earlier if patient is not responding to ART.
- Provide continuous counseling to ensure adherence to ART.

Follow up in a Private Clinic Setting

Some patients may prefer to be followed up in private clinics even when they have obtained their drugs from a public setting. This is acceptable as long as:

- The private clinic has the expertise and knowledge to manage ART
- The link exists for consultations with other experienced ART providers
- The clinic follows the National ARV guidelines and standard of care

Follow up at Community Level

Community based organizations are important in providing continuous support to patients on ART. This demystifies ART and ensures better adherence to treatment. However, there should be an effective referral network between these organizations and ART services.

1.10 ART Data Collection and Management

Data on ART need to be collected to guide the monitoring and evaluation process. The data should be collected by all those involved in the implementation of ART.

Data on the following information should be collected:

- Number of patients accessing ART from the facility including their age, sex etc.
- Total number of patients screened for ART and those who qualify
- Number who attend clinics and how many default
- Nature of side and toxic effects
- Number of patients who develop treatment failures and their reasons
- Information on adherence

The data collected should be forwarded to the district medical officer for transmission to the HIV/AIDS health Sector Response. At the district level, the information should be used to identify bottlenecks and find solutions. At the Health Sector Response level, the data will be used to improve policies and guidelines on the progamme at national level.

1.11 When to change Antiretroviral Therapy

It may be necessary to change ART because of either toxicity or treatment failure.

Toxicity

Toxicity is related to the inability to tolerate the side effects of medication and to the significant organ dysfunction that may result. This can be monitored clinically on the basis of patient reporting and physical examination, and there may also be a limited number of laboratory tests, depending on the specific combination regimen that is utilized.

For example, d4T can be substituted for ZDV for ZDV related symptoms or anemia and NVP can be substituted for EFZ when EFZ related central nervous systems are unremitting. For other toxicities, for which a specific agent cannot be identified as causal, and/ or low grade but

intolerable side effects which frequently compromise adherence, a complete regimen switch to the second line drugs is recommended. If an interruption in therapy is indicated to permit resolution of toxicity, the entire regimen should be temporarily interrupted in order to prevent the emergence of drug resistance.

Table 8: Drug Substitution because of Toxicity of First-line ARV's and Recommended Substitutions

ARV Drug	Common associated Toxicity	Suggested substitute
ABC	Hypersensitivity reaction	AZT or TDF or d4T
ZDV	Severe anemia or neutropenia Severe GI intolerance	TDF or D4t or ABC
	Lactic acidosis	TDF or ABC
d4T	Lactic acidosis Lipoatrophy/metabolic syndrome	TDF or ABC
	Peripheral neuropathy	AZT or TDF or ABC
TDF	Renal toxicity (renal tubular dysfunction)	AZT or ABC or d4T
EFZ	Persistent & severe CNS toxicity	NVP or TDF or ABC (or any PI)
	Potential teratogenicity (first trimester of pregnancy or women not using adequate contraception)	NVP or ABC (or any PI)
NVP	Hepatitis	EFV or TDF or ABC (or any PI)
	Hypersensitivity reaction	TDF or ABC (or any PI)
	Severe or life-threatening rash (Stevens-Johnson Syndrome)	

Treatment Failure

Antiretroviral treatment failure can be defined as a sub-optimal response to therapy

Treatment Failure can be assessed by 3 criteria:

- Virological
- Immunological
- Clinical Progression

Virological failure can be defined as incomplete or lack of HIV RNA response to Antiretroviral therapy

- Incomplete virological response
  - Repeated HIV RNA > 400 copies/ul after 24 weeks or > 50 copies after 48 wks, <u>in a treatment naive initiating therapy</u>

Immunological Failure

- Failure to increase CD cell count by 25-50 cell/mm3 above baseline count over the first year of therapy
- Or decrease below baseline value mean. Mean increases of CD4 cell count in treatment naïve patient are approximately 150 cells over the first year

Clinical Progression refers to the occurrence or recurrence of HIV-related events WHO stage 3 or 4 (after 3 months on an antiretroviral regimen)

On the basis of Clinical Criteria, ARV regimen failure cannot be diagnosed until there is First-line therapy lasting 3-6 months & treatment failure assessment done.

Assessment of Antiretroviral Treatment Failure

- Cause of treatment failure should be explored
- Review Medical History
- Physical examination for signs of clinical progression (physical exam, laboratory or radiologic
- Antiretroviral treatment history
- Medication taking history (including adherence, dosing frequency, concomitant medication, co-morbidity)
- Assess adherence, tolerability & pharmacokinetic issues

Discontinuation or interruption of Antiretroviral Therapy

- Unplanned interruption of ART may become necessary because of;
  - Serious drug toxicity
  - Intervening illness
  - Surgery that precludes oral therapy
  - Antiretroviral medication unavailability
- Planned treatment discontinuation and interruption may be used as a strategy in several situations
  - Patients who have achieved viral suppression
  - Reduce long term toxicity
  - In some patient who experience treatment failure

Short term interruption

- Drug Toxicity
- Inter-recurrent illness which precludes oral intake such as gastroenteritis, Pancreatitis, and prolonged vomiting
- Non availability of drugs

Long term therapy interruption

Is not recommended.

1.12 People with Tuberculosis Disease and HIV Co-Infection

Tuberculosis is an entry point for a significant proportion of patients eligible for ART. ART is recommended for all patients with TB who have CD4 cell counts below 200 cells/mm3, and should be considered for patients with CD4 counts below 350 cells/mm^3.
For those with CD4 40-200/mm3, they should start ART after the intensive TB treatment phase which usually lasts for 2 months. In cases where a person needs TB and HIV treatment concurrently, first line treatment options include ZDV/3TC plus EFZ.

For women of child bearing age (without contraception), pregnant women, and children with TB, either SQV/r or ABC+ (d4T or ZDV) + 3TC is recommended. Except for SQV/r, PIs are not indicated during TB treatment with Rifampicin.

Table 9: Antiretroviral Therapy for individuals with Tuberculosis Co-infection

Situation	Recommended Treatment
Pulmonary TB and CD4 cell count<50/mm3 or extra pulmonary TB or WHO stage IV	Start TB therapy Plus one of these regimens: • ZDV/3TC/EFZ • d4T/3TC/EFZ
Pulmonary TB and CD4 50-200/mm3 or total lymphocyte count<1200/mm3	Start TB therapy for 2 months then start one of these regimens: • ZDV/3TC/EFZ • d4T/3TC/EFZ
Pulmonary TB and CD4>200/mm3 or total lymphocyte count>1200/mm3	Treat TB first. Monitor clinically or do CD4 counts if available. Start ART when indicated: • ZDV/3TC/EFZ • d4T/3TC/EFZ

1.13 Immune Reconstitution Syndrome

For many opportunistic infections, including Tb, There can be a transient worsening of infection 2-3 weeks after the initiation of ART. This is called the Immune Reconstitution Syndrome. For patients with Tb, this syndrome has been reported in 30% of cases in the developed world. The syndrome is characterized by fevers, lymphadenopathy, worsening pulmonary lesions and expanding lesions of the central nervous system. These reactions are typically self limiting, although they may require the use of corticosteroids to reduce the inflammation of the CNS or severe respiratory symptoms. The initiation of ART can also unmask previously undiagnosed infections by augmenting the inflammatory response**.** In general, ART should not be interrupted if the immune reconstitution syndrome occurs.

1.14 Treatment of HIV/AIDS patients with hepatitis B and/or hepatitis C Co-infection

Patients co-infected with hepatitis B or C can be safely treated with several ARV regimens. Because of the possibility of additive hepatoxicity, regimens with ddI/d4T and/or NVP should

be avoided in patients to have active hepatitis. 3TC and TDF are both active against hepatitis B and may even have a protective effect against new infections.

2. Antiretroviral Therapy in Children

The goal of ART for children is to increase survival and to decrease HIV related morbidity.

At present the majority of children are diagnosed on the basis of symptomatic HIV disease and the positive HIV antibody test of the mother or the child.
The pathogenesis of HIV and the underlying principles of ART are similar in adults and children. However, there are specific physiologic, clinical, practical and social issues to consider when treating HIV-infected children with ART. Moreover, there are age related issues which need to be addressed, especially in infants and adolescents dosages.

The laboratory diagnosis of HIV infection in infants aged less than 18 months is difficult because of the presence of maternal antibodies which remain in the child's body up to the age of 15-18 months. Rapid testing may be less reliable in these children and should not routinely be performed. Virological tests such as polymerase chain reaction (PCR), DNA and RNA assays are required in order to make definitive diagnosis of HIV infection in this age group. Details on these tests can be found in the national paediatric care guidelines.

However, in children aged 18 months or more, HIV diagnosis can be made with antibody test, including rapid antibody test following standard testing algorithms used for adults.

2.1 When to start Therapy in Children

Children requiring ART need to meet both medical and psychosocial criteria before starting therapy.

- Medical criteria:
    - Recurrent hospitalizations (>2 admissions per year) for HIV related disease or prolonged hospitalization (> 4 weeks
    - WHO paediatric clinical stage 4 disease (irrespective of CD4);
    - WHO paediatric clinical stage 3 disease (irrespective of CD4, although it may add guidance); for children aged over 12 months with tuberculosis, lymphocytic interstitial pneumonia, oral hairy leukoplakia or thrombocytopaenia, ART initiation may be delayed if CD4 is above threshold values (see annex--) for initiating ART;
    - WHO paediatric clinical stage 2 disease *and* CD4 *or* TLC (see annex--_) value at or below threshold (see annex---)
    - WHO paediatric clinical stage 1 disease *and* CD4 value at or below threshold.(see annex---)
    - If virological testing is not available to confirm HIV infection, HIV antibody-positive infants and children aged under 18 months should be considered for ART if they have clinically diagnosed presumed severe HIV disease (see annex---)

Psychosocial criteria

These are extremely important for the success of paediatric ART. The principle is that adherence must be guaranteed.

- An identifiable adult who is able to administer medications, including care and support for orphans;
- Demonstrated reliability in the adult care giver, i.e. has attended 3 or more scheduled visits to the services points and the immunization record of the child is up to date
- Supportive social environment – no discrimination or less stigmatization of the child;
- Disclosure to another adult living in the same household is highly encouraged so that there is someone else who can assist with the child's ART;
- Previous record of nutritional support supplements or other chronic care regimens such as DOTS may help to identify children who are at risk of poor adherence.
- Referral or outreach services may need to be arranged for patients in remote areas;
- Always ask about the health of care giver and the other members of the family as well as the socio-economic status.

Table 10: WHO staging system for HIV infection and disease in children

Clinical Event	**Clinical Diagnosis**	**Definitive Diagnosis**
Clinical Stage 1		
Asymptomatic	No symptoms reported and no signs on examination	Not required
PGL	Swollen or enlarged lymph nodes >1 cm at two or more non-contiguous sites, without known cause.	Not required. (Histology, germinal centre hyperplasia, lymph node structure preserved.)
Clinical Stage 2		
Hepatosplenomegaly	Unexplained enlarged liver or spleen	Not required.
Papular pruritic eruptions	Persistent papular pruritic vescular lesions, scabies should be excluded.	
Seborrhoeic dermatitis	Itchy scaly skin condition particularly affecting scalp, face, upper trunk and perineum. Also common in uninfected children and in babies	Not required.
Fungal nail infections	Fungal paronychia (painful red and swollen nail bed) or onycholysis (painless separation of the nail from the nail bed). Proximal white subungual onchomycosis is	Culture of nail scrape.

	uncommon without immunodeficiency.	
Angular cheilitis	Splits or cracks on lips at the angle of the mouth with depigmentation, usually responding to antifungal treatment but may recur. Also common in nutritional deficiency, e.g. of B vitamins.	Not required.
LGE	Erythematous band that follows the contour of the free gingival line; may be associated with spontaneous bleeding. Uncommon in HIV-uninfected children.	Not required.
Human papilloma virus infection (extensive facial, more than 5% of body area or disfiguring	Characteristic skin lesions; warts; small fleshy grainy bumps, often rough, on sole of feet are flat (plantar warts). Also common in uninfected children.	Not required.
Molluscum contagiosum infection (extensive facial, more than 5% of body area or disfiguring	Characteristic skin lesions: small flesh-coloured, pearly or pink, dome-shaped or umbilicated growths may be inflamed or red. Also common in uninfected children	Not required.
Recurrent oral ulcerations (two or more in six months)	Aphthous ulceration, typically with a halo of inflammation and yellow-grew pseudomembrane	Not required.
Parotid enlargement	Asymptomatic bilateral swelling that may spontaneously resolve and recur, in absence of other known cause, usually painless. Uncommon in HIV-uninfected children.	Not required.
Herpes Zoster	Painful rash with fluid-filled blisters, dermatomal distribution, can be haemorrhagic on erythematous background,	Viral culture, histology, EM of lesion fluid.

	and can become large and confluent. Does not cross the midlines. Note: severe persistent herpes zoster may have worse prognosis	
Recurrent RTI (twice or more in any six-month period)	Symptom complex, e.g. fever with unilateral face pain and nasal discharge (sinusitis) or painful swollen eardrum (otitis media), sore throat with productive cough (bronchitis), sore throat (Pharyngitis) and barking croup-like cough (LTB). Persistent or recurrent ear discharge.	Not required but may be confirmed by laboratory or X-ray studies where available, especially for sinus, and culture or appropriate specimens.
Clinical Stage 3		
Unexplained moderate malnutrition (very low weight-for-age: up to -2 standard deviation (SDs) (3,4); not responding adequately to standard therapy.	Unexplained weight loss or failure to gain weight not explained by poor or inadequate feeding or other infections, and not adequately responding within two weeks to standard management,	Documented loss of body weight, failure to gain weight on standard management and no other cause identified during investigation.
Unexplained persistent diarrhea (14 days and above)	Unexplained persistent diarrhea (loose or watery stool, three or more times daily), not responding to standard treatment.	Not required, but confirmed if stools observed and documented as unformed. Culture and microscopy reveal no pathogens.
Unexplained persistent fever (intermittent or constant and for longer than one month)	Reports of fever or night sweats for longer than one month, either intermittent or constant, with reported lack of response to antibiotics or antimalarials. No other obvious foci of disease reported or found on examination. Malaria must be excluded in malarious areas.	Not required but confirmed if documented fever of >37.5°C with negative blood culture, negative malaria slide and normal or unchanged CXR, and no other obvious foci of disease.
Oral candidiasis (outside first 6 weeks of live)	Persistent creamy white to yellow soft small plagues on red or normally coloured mucosa, easily scraped off (pseudomembranous), or red patches on tongue, palate or lining of mouth, usually painful or tender, responding	Microscopy or culture.

	to antifungal treatment	
Oral hairy leukoplakia	Fine small linear patches on lateral borders of tongue, generally bilaterally, which do not scrape off	Not required.
Pulmonary TB	Non specific symptoms, e.g. chronic cough, fever, night sweats, anorexia and weight loss. In the older child also productive cough and haemoptysis. Response to standard anti-TB treatment in one month. Note: diagnosis should be made in accordance with national guidelines	Abnormal XCR plus positive sputum smear or culture.
Severe recurrent presumed bacterial pneumonia	Cough with fast breathing, chest indrawing, nasal flaring, wheezing, and gruntin. Crackles or consolidation on auscultation. Responds to course of antibiotic	Not required bur confirmed by isolation of bacteria from appropriate clinical specimens.
Acute necrotizing ulcerative gingivitis or stomatitis, or acute necrotizing ulcerative periodontitis	Severe pain, ulcerated gingival papillae, loosening of teeth, spontaneous bleeding, bad odour, and rapid loss of bone and/or soft tissue.	Not required.
Symptomatic LIP	No presumptive clinical diagnosis	CXR: bilateral reticulonodular interstitial pulmonary infiltrates present for more than two months with no response to antibiotic treatment and no other pathogen found. Oxygen saturation persistently <90%. May present with cor pulmonale and may have increased exercise-induced fatigue. Frequently confused with miliary TB.
Chronic HIV-associated lung disease (including brochiectasis)	No presumptive clinical diagnosis	History of cough productive of copious amounts of purulent sputum, with or without clubbing, halitosis, and crepitations and/or wheezes on auscultation;

		CXR may show honeycomb appearance (small cysts) and/or persistent areas of opacification and/or widespread lung destruction with fibrosis and loss of volume, CT scan of chest may be used to confirm.
Unexplained anaemia (<8g/dl), and or neutropenia (<500/mm^3) for longer than one month	No presumptive clinical diagnosis	Diagnosed on laboratory testing, not explained by other non-HIV conditions, or not responding to standard therapy with haematinics, antimalarials or anthelmintics as outlined in IMCI.
Unexplained severe wasting or severe malnutrition not adequately responding to standard therapy	Persistent weight loss not explained by poor or inadequate feeding, other infections not adequately responding in two weeks to standard therapy. Characterized by: visible severe wasting of muscles, with or without oedema of both feet, and/or weight-for-height of -3 SDs, as defined by WHO IMCI guidelines.	Documented loss of weight or failure to gain weight.
Pneumocystis pneumonia (PCP)	Dry cough, progressive shortness of breath, cyanosis, tachypnoea and fever; chest indrawing or stridor. Response to high-dose co-trimoxazole +/- prednisolone. (severe or very severe pneumonia as in IMCI). Usually of sudden onset and very severe in infants under six months of age.	Microscopy of induced sputum or BAL, or histology of lung tissue. CXR shows typical bilateral perihilar diffuse infiltrates.
Recurrent severe presumed bacterial infection (two or more episodes in one year), e.g. meningitis, empyema, pyomyositis, bone or joint infection, bacteraemia	Fever accompanied by specific symptoms or signs that localize infection. Responds to antibiotics.	Not required but confirmed by bacteria isolated from appropriate clinical specimens and includes recurrent non-typhoidal salmonella septicaemia.
Chronic herpes simplex virus infection (chronic orolabial or intraoral lesions of more than one month or visceral of any	Severe and progressive painful orolabial or skin lesions attributable to recurrent HSV reported for	Visceral HSV requires confirmation. Suggestive symptoms of organ damage, e.g. bronchitis pneumonitis,

duration)	more than one month. History of previous episodes. Scarring from previous episodes may be evident.	oesophagitis, colitis, encephalitis, supported by histology or culture.
Oesophageal candidiasis	Chest pain and dysphagia (difficulty in swallowing), odynophagia (pain on swallowing food and fluids), or retrosternal pain worse on swallowing (food and fluids) +/- oral Candida. Responds to antifungal treatment. May be difficult to detect in young children. Suspect if oral Candida observed and if refusal occurs or if there are difficulties or crying when feeding	Not required but confirmed by macroscopic appearance at endoscopy, microscopy of specimen from tissue or macroscopic appearance at bronchoscopy or histology.
Extrapulmonary TB	TB not limited to lungs. Systemic illness usually with prolonged fever, night sweats, weight loss. Clinical features of organs involved, e.g. focal lymphadenopathy, cold abscess, sterile pyuria, pericarditis, ascites, pleural, effusion, meningitis, arthritis, orchitis, lupus vulgaris. Responds to standard anti-TB therapy. Note: simply lymph gland extrapulmonary TB may have a better prognosis	Mycobacterium TB isolated form blood culture or other specimen except sputum or BAL. Positive AFB on microscopy or culture on relevant specimens. Biopsy and histology. X-ray.
Kaposi's sarcoma	Typical appearance in skin or oropharynx, initially flat patches with a pink or blood-bruise colour, usually developing into nodules.	Typical red-purple lesions seen on bronchoscopy or endoscopy. Biopsy.
CMV retinitis and CMV infection of organs other than liver, spleen or lymph nodes, with onset at age over 1 month	No presumptive clinical diagnosis. Clinically, disease suspected if there are typical eye lesions on serial fundoscopic examination; discrete patches of retinal whitening with distinct borders, spreading centrifugally, often following	Symptoms and signs of organ involvement, e.g. typical eye lesions on fundoscopy or pneumonitis not responding to Co-trimoxazole or antibiotics. Histology or detection of antigen from affected tissue.

	blood vessels, associated with retinal vasculitis, haemorrhage and necrosis	
CNS toxoplasmosis (outside the neonatal period)	Fever, headache, focal neurological signs, convulsions. Response to high-dose co-trimoxazole or pyrimethamine and sulphadiazine or clindamycin	CT scan showing single/multiple lesions with mass effect/enhancing with contrast. CSF results normal or non specific. Resolution of findings after treatment if patient survives.
Cryptococcal Meningitis	Meningitis: usually subacute, fever with increasing severe headache, irritability, meningism, confusion, behavioural changes. Responds to antifungal therapy	CSF: microscopy (India ink or Gram stain) Positive serum CRAG test.
HIV encephalopathy	At lease one of the following, progressing over at least two months in the absence of another illness: ▪ gross discrepancy between the actual and developmental age, failure to attain, or loss of, developmental milestones, loss of intellectual ability; or ▪ progressive impaired brain growth demonstrated by stagnation of head circumference; or ▪ acquired symmetric motor deficit accompanied by two or more of the following: paresis, pathological reflexes, ataxia, gait disturbances.	Brain CT scan or MRI to exclude other causes.
Any disseminated mycosis (e.g. histoplasmosis, coccidiomycosis, penicilliosis)	No presumptive clinical diagnosis	Organ-specific and non specific symptoms, e.g. may cause skin rash, or cough, shortness of breath, fever, anaemia, weight loss.

		Diagnosis confirmed by direct microscopy, histology or antigen detection in relevant specimens. CXR may show infiltrates or nodules.
Candidiasis of the trachea, bronchi or lungs	No presumptive clinical diagnosis	Macroscopic appearance at endoscopy. Microscopy and culture of specimen from endoscopic tissue.
Disseminated mycobacteriosis, other than TB	No presumptive clinical diagnosis	Nonspecific clinical symptoms including progressive weight loss, fever, anaemia, night sweats, fatigue or diarrhea; Plus Culture of atypical mycobacteria species from stool, blood, body fluid or other body tissue, excluding lung.
Cryptosporidiosis (with diarrhoea lasting more than one month)	No presumptive clinical diagnosis.	Chronic diarrhoea, often profuse and watery, with weight loss, ± abdominal pain, nausea, vomiting, but usually mild or no fever. Confirmed by microscopic examination on modified ZN stain.
Isosporiasis	No presumptive clinical diagnosis.	Chronic diarrhoea, often profuse and watery, with weight loss, ± abdominal pain, nausea, vomiting, Isosporiasis responds to high-dose co-trimoxazole.
Cerebral or B cell non-hodgkin lymphoma	No presumptive clinical diagnosis	Symptoms consistent with lymphoma: lymphadenopathy, hepatosplenomegaly, pancytopenia, besides other nonspecific or organ-specific symptoms. No response clinically to antitoxoplasma or anti-TB treatment. CNS imaging: at least one lesion with mass effect on brain scan, and no response to

		antitoxoplasma and anti-TB treatment. Cytology. Histology. Response to chemotherapy.
PML	No presumptive clinical diagnosis	Progressive focal neurological signs without headache or fever. Cortical blindness and cerebellar signs. Convulsions are rare, MRI or CT scan.
Acquired HIV-associated rectal fistula, including rectovaginal fistula		Further information and evidence relating to this condition and its definition are being sought. Case reports from African countries suggest that it is highly specific to HIV and that the prognosis is poor. Clinical features suggestive, exclusion of other causes, faecal discharge through the vagina or urethra, or urine discharge through the rectum in an HIV-infected child usually following an episode of diarrhoea.
HIV-associated nephropathy	No presumptive clinical diagnosis	Further information and evidence relating to this condition and its definition are being sought. Symptoms and signs suggestive of renal disease, with no other obvious cause identified. Early morning urine protein/creatinine ratio of >200mg/mmol in absence of a urinary tract infection and absence of an axillary temperature of 38.0°C. Renal biopsy and histology.
HIV-associated cardiomyopathy	No presumptive clinical diagnosis.	Further information and evidence relating to this condition and its definition are being sought. Exclusion of other causes of congestive cardiac failure. The left ventricle and right ventricle are enlarged. The end-

		diastolic and end-systolic dimensions of the left or right ventricle are increases (2 SDs from the mean for body surface area), with a reduced fractional shortening and ejection fraction (2SDs from the mean). Echocardiography check.

*Interim WHO Clinical Staging of HIV/AIDS and HIV/AIDS Case Definitions for Surveillance

Children with a positive Virological test or positive serological test at the age >18 months with the presence of WHO stage III HIV disease is an indication to start therapy. For children of infected mothers who are <18 months, stage III disease is an indication for urgent CD4 testing or referral if CD4 testing is not available. For children with WHO stage I or II HIV disease, criteria for starting treatment depend on the age of the child, availability of CD4 testing, and a positive HIV diagnosis.

2.2 Recommended first line ARV regimens for Infants and Children

ARVs available for adults are also available in formulations specifically designed for children.

The preferred first line option for children includes (d4T or ZDV) + 3TC plus an NNTRI (NVP or EFZ). However EFZ cannot be used in children under 3 years or weighing less than 10 kg.

Table 11: Recommended first line Antiretroviral Regimens for children

Regimen	Comments
ZDV/3TC+EFZ or NVP or d4T/3TC+EFZ or NVP	If < 3yrs or <10 kg use NVP If>3 yrs or >10 kg, use NVP or EFZ

2.3 Recommended second line ARV therapy for infants and children

Second line therapy for children in the event of failure of a first line regimen includes a change in the nucleoside backbone (e.g. from ZDV+3TC to ABC + ddI). The use of PIs other than LPV/r and NFV is more problematic in children because of a lack of suitable paediatric drug formulations for IDV and SQV.

Table 12: Recommended second line regimen in children

First Line Regimens	Second Line Regimen for Treatment Failure	Alternative Second Line Regimen for Treatment Failure
ZDV/3TC d4T/3TC	d4T/ddI+LPV/r (Kaletra) ZDV/ddI + LPV/r	d4T/ddI+NFV ZDV/ddI+NFV

2.4 TB treatment and ART in children

As a result of the interaction between rifampicin and the PIs and the NNRTIs, one needs to modify the TB treatment or both. EFZ would be the NNRTI of choice for children who require ARV therapy but need or are receiving anti-TB therapy containing rifampicin. For children under 3 years of age who require ARV therapy while receiving anti-TB therapy, the use of a triple NRTI regimen(ZDV/3TC/ABC) should be considered while the TB therapy is being administered. Monitoring for ABC hypersensitivity should be assured.

2.5 Monitoring of Antiretroviral Therapy in Children

2.5.1 Viral Load

The percentage of children on triple therapy who achieve and maintain a plasma viral load of below 400 copies/ml varies from approximately 25% to 75%.

Because ART is a lifelong commitment, it may be preferable not to switch ARVs until the CD4% or count consistently drops or evidence of clinical failure has occurred. Such evidence includes:

- failure to thrive
- reappearance of ' refractory' oral candidiasis
- other intercurrent disease such as cryptosporidial diarrhea, invasive bacterial sepsis or neurodevelopment deterioration**.**

2.5.2 CD4+ Lymphocytes and Percentages

CD4 counts are useful for monitoring response to ARVs. A falling CD4 count or CD4% may be a more important reason to change therapy than a rising viral load. CD4 counts or CD4% may temporarily lowered due to intercurrent infections or vaccinations and can take up to a month to recover.

2.5.3 Height and Weight

The 'Road to Health' chart is a valuable tool for monitoring the well-being of children. Failure to maintain growth is suggestive of progressive HIV disease or superimposed infection such as tuberculosis**.**

2.6 Reasons for changing ARV therapy in infants and children

The principles on which to change therapy in children are similar to those in adults.

In children, important clinical signs of drug failure include:

- Lack of growth in children who show an initial response to treatment
- Decline in growth among children who show an initial growth response to therapy
- Loss of neurodevelopment milestiones
- Development of encephalopathy
- The recurrence of infections such as oral candidiasis that is refractory to treatment

Because of age-related declines in CD4 absolute cell counts until age of 8 years, it is difficult to use such counts for assessing therapy failure in younger children. However, for children aged 8 years or more, similar CD4 cell count criteria to those used for adults are appropriate. Because the CD4 cell percentage varies less with age it can be used to gauge treatment response regardless of age.

2.7 Monitoring of Antiretroviral Therapy in Children

Following confirmation of HIV infection status the baseline *clinical assessment* for infants and children should include:

- clinical staging of HIV disease
- identification of concomitant medical conditions (e.g. TB, pregnancy in adolescent girls);
- detailing of concomitant medications, including co-trimoxazole and traditional or herbal therapies;
- weight, height, head circumference and other measures of growth;
- developmental status;
- nutritional status, including assessment of quality and quantity of intake;
- for those eligible for ART, assessment of children's and caregiver's preparedness for therapy.

The *laboratory assessment* for infants and children at baseline should include:

- confirmation of HIV infection status (virological or antibody testing according to age; Section IV);
- measurement of CD4count or percentage, where available;
- haemoglobin measurement: in infants and children initiated on ZDV-containing first-line regimens;
- white blood cell count (WBC);
- pregnancy test for sexually active adolescent girls;
- screening for TB and malaria (and diagnostic testing where clinically indicated), and for other major treatable HIV coinfections and HIV-related opportunistic diseases as clinically indicated

The frequency of clinical monitoring depends on the response to ART but should be at a minimum be at weeks 2, 4, 8 and 12 after starting ART and then every 2-3 months once the child has stabilized on therapy. In infants and children who were started on ART on the basis of a presumptive clinical diagnosis of severe HIV disease, HIV infection status should be confirmed as soon as possible.

Laboratory assessment of CD4 values is desirable every six months or more frequently if clinically indicated (Table 13). The TLC is not suitable for the monitoring of therapy because a change in its value does not reliably predict treatment success [104].

In infants and children initiated on AZT-containing first-line regimens the measurement of haemoglobin should be performed during the first few months of treatment (at weeks 4, 8 and 12 after initiation of ART) or in a symptom-directed approach. Tests of liver function (i.e. liver enzymes) are recommended during the first few months of treatment in infants and children receiving nevirapine or who have co-infection with hepatitis viruses or are on hepatotoxic medications. When choosing other laboratory parameters, clinical symptoms should be taken into consideration for assessing the response to therapy. Some routine monitoring tests may be advisable in accordance with the specific drugs used, but laboratory monitoring of adverse events should largely be directed by clinical symptoms. It should be noted that an inability to perform laboratory monitoring should not prevent children from receiving ART.

3.0 Considerations in women of childbearing potential or pregnant women

3.1 Women of childbearing potential

- The choice of ART for women with the potential to become pregnant requires consideration of the possibility that the ARV drugs may be received early in the first trimester, before recognition of pregnancy and during the primary period of foetal organ development.
- The ARV drug of most concern is EFV.
- EFV should be avoided in women of childbearing potential who are not receiving adequate contraception.
- Women who are receiving ARV and do not wish to become pregnant should have effective and appropriate contraceptive methods available in order to reduce the likelihood of unintended pregnancy.
- Women for whom effective contraception can be assured, EFV remains a viable option for the NNRTI component of the regimen.

3.1.1 Interaction of ART with hormonal contraceptives

- ARV drugs that can affect liver enzymes include the PIs and, to a lesser extent, the NNRTIs.
- It is recommended that women receiving EFV use a reliable method of barrier contraception in addition to, or instead of, oral contraception.
- The use of condoms is recommended for all women regardless of hormonal contraceptive use, as condoms offer protection against other sexually transmitted diseases as well as HIV super infection.
- Additional or alternative contraceptive approaches should be used in order to avoid pregnancy in women receiving PI and NNRTI drugs.

3.2 Pregnant women

3.2.1 Initiating ART in pregnant women

- ART is recommended for pregnant women in accordance with the same eligibility criteria as for non-pregnant adults.
- It should be initiated in pregnant women with WHO clinical stage 3 or stage 4 disease, or in those with WHO clinical stage 1 or 2 disease and CD4 count below 200 cells/mm3.
- It is recommended that any pregnant woman with a CD4 count below 350 cells/mm3 and WHO clinical stage 3 disease should initiate ART.
- Viral suppression may be compromised if NNRTI-based ART is initiated less than six months following exposure to single dose NVP.
- Women with CD4 counts between 200 and 350cells/mm3 require therapy to begin within the first year postpartum.
- It is desirable to initiate ART after the first trimester in order to minimize the potential for teratogenicity.
- Once started, ART should be continued postpartum.

3.2.2 Choice of firstline ARVs in pregnant women

The choice of ARV in pregnant women is complex and require several competing factors influencing risk and benefits to be weighed. These include:

- What treatment is recommended for the woman in question.
- What is and is not known about the effects of the drugs on the pregnant woman and her infant.

3.2.2.1 Choice of NRTI

- The preferred NRTIs for use in pregnant women are AZT and 3TC.
- Alternative NRTI drugs for use in pregnancy includes ABC, d4T and ddI.
- However the dual NRTI combination of d4T/ddI should be avoided in pregnancy. It should be employed only if no other alternatives exist.
- This is particularly important because of the increased risk of lactic acidosis with this combination in pregnant women.
- TDF exposure has not demonstrated gross congenital abnormalities but have shown decreased fetal growth and a reduction in fetal bone porosity within two months of the commencement of maternal therapy.
- TDF should only be considered as a component of initial ART in pregnant women if other alternatives are not available or are contraindicated.
- However, if a woman receiving TDF becomes pregnant, the regimen must be continued. Alternatively, AZT could be substituted for TDF during the pregnancy.

3.2.2.2 Choice of NNRTI

- NVP is the NNRTI of choice in pregnancy.
- However, symptomatic NVP-associated hepatic toxicity or serious rash are frequent in women especially those with higher CD4 count.

- It is not known if pregnancy further predisposes these women to such toxicities.
- NVP could be substituted for EFV with close monitoring.

3.2.2.3 Choice of PI for secondline ART in pregnancy

- The protease inhibitors for which the most experience and safety data in pregnancy have been obtained are SQV/r and NFV.
- ATV/r or FPV/ should be used only if no alternative is available.

Table 13: Approaches to initial therapy in women with CD4 counts in the range 250 to 350 cells/mm3

APPROACH	ADVANTAGES	DISADVANTAGES
Initiation of NVP-based therapy with close observation over first 12 weeks	Reserves PI for second-line regimen. Consistent with standard recommendations	Potential elevated risk of severe hepatic toxicity
Initiation of EFV-based therapy with assurance of effective contraception	Reserves PI for second-line regimen. Consistent with standard recommendations. Less risk of hepatic toxicity.	Potential risk of teratogenicity if pregnancy occurs
Initiation of triple NRTI therapy*	Reserves PI for second-line regimen. Less risk of hepatic toxicity.	Studies suggest less potent than NNRTI-based regimens. Unknown safety of TDF in pregnancy.
Delaying of therapy until CD4 count drops below 250 cells/mm3	If not on ARVs no risk of hepatic toxicity	Risk of disease progression, particularly if symptomatic
Initiation of PI-based therapy	Less risk of hepatic toxicity	No second-line treatment options exist

***** AZT/3TC/ABC or AZT/3TC/TDF

3.3 Women who are Breastfeeding

- In most resource limited settings, breastfeeding continues to be the most feasible, safe, accessible, affordable and sustainable option supporting adequate nutrition for HIV-exposed infants.
- Breastfeeding is also an important route of postnatal HIV transmission.
- ART is recommended for postpartum breastfeeding women who meet the WHO criteria for the initiation of therapy for their own health.
- This group of infected women who have high viral loads and suppressed immune systems are at high risk of transmitting HIV to their infants through breastfeeding.

4. Co-trimoxazole prophylaxis in HIV infection

Co-trimoxazole is a broad spectrum antimicrobial agent that targets a range of aerobic gram-positive and gram –negative organisms, fungi and protozoa. Prophylaxtic co-trimoxazole administration to HIV-positive patients, has been shown to be helpful in improving the quality of life and reduce mortality among HIV infected patients. For a patient to benefit from prophylaxis, he/she must be:

- Symptomatic HIV patient
- Asymptomatic HIV patient with lymphocyte count < 1,200/mm3
- Be motivated to adhere to treatment
- HIV positive patient with active TB
- A pregnant HIV- positive woman after the first trimester
- Any child born to an HIV-infected woman after 6 weeks of age
- Any child identified as HIV-positive within he first year of life

4.1 Steps to initiate co-trimoxazole prophylaxis

- Verify HIV status
- Take medical history
- Conduct physical examination
- Screen for contraindications to co-trimoxazole administration
- Known allergy to sulphur-containing drugs
- Seriously ill patients (for specialised medical care)
- Counsel patient on drug adherence and side effects of the drug

4.2 Co-trimoxazole monitoring and evaluation:

- Collection of baseline data for each patient to help evaluate ongoing benefit
- Monitor for changes in local antimicrobial drug sensitivity
- Monitor impact on closely related sulfadoxine/pyrimethamine's activity for malaria. Does it increase resistance?

4.3 Recommended dose for co-trimoxazole prophylaxis

a. Adults:
Co-trimoxazole 960mg daily (two single strength tablets) for life

b. Children:
co-trimoxazole syrup should be given once daily. If syrup is unavailable, co-trimoxazole tablets may be crushed. The recommended dose is 60mg/kg body weight.

4.4 Safety of Co-trimoxazole

- The most common reactions are rash, fever, nausea, low white blood cells (leukopenia) and hepatitis.
- Patients should see their health care provider if they experience a rash.
- Rash could lead to fatal allergy called Stevens-Johnson syndrome.

- In such a case stop drug or reduce dose. Reinitiate and desensitize by gradually escalating dose.
- Monitor closely risk of toxic shock.
- Monitor for immune reconstitution reaction with ART.

4.5 Co-trimoxazole drug interaction

- May decrease the effectiveness of oral contraceptives
- May not work if taken with vitamin supplements containing folic acid. In such cases use leucovorin (folinic acid) instead.
- Donot take with sulfadoxine-pyrimethamine (fansidar), especially if pregnant, and coadministration could cause severe folic deficiency and possibly birth defects.

4.6 Co-trimoxazole alternatives

- Dapsone (100mg/day or atovaquone (with or without pyrimethamine and leucovorin) for PCP infection.
- This alternatives however do not provide the same protection against other organisms.

4.7 When to discontinue co-trimoxazole prtophylaxis

- Occurrence of side effects
- Total lymphocyte count above 4000/mm3
- Children testing HIV- negative when older than 18 months.

5.0 Supportive Management

5.1 Nutrition:

It is known that good nutrition can contribute to the well-being of the person with HIV/AIDS at all stages of the disease and may even prolong life. It is important to have nutritional counseling early in the disease and subsequently when receiving ART.

5.1.1 Relationship between HIV/AIDS and Nutrition

- The increase activity of the immune system in reacting to the virus uses more energy and nutrients
- Anxiety about the disease leads to a further weakening of the immune system and a need for more nutrients
- Opportunistic infections also increase metabolic rates thereby increasing food nutrients
- Illness and depression cause poor appetite
- Mouth and throat infections creates difficulty with eating
- Medications can cause poor sense of taste and nausea

5.1.2 Benefits of good nutrition

- Keeps weight stable
- Prevents muscle loss
- Replaces lost nutrients
- Improves wound healing
- Allows patient to better deal with medication and treatment
- Increase strength
- Improves feeling of well being
- Enhances the immune system

5.1.3 Food choices for People Living with HIV/AIDS

- Eat a variety of foods
- Make carbohydrates the basis for each meal as it is high in energy
- Eat a lot of fresh fruits and vegetables as they supply vitamins
- Daily eggs, meat fish and milk provide protein for muscles
- Include beans and groundnut since they are high in protein
- Sugars, fats and oils provide extra energy
- Use salt sparingly to replace loss through diarrhoea
- Drink lots of water to replace water loss
- Do not drink alcohol
- Food should be hygienically prepared
- Adhere to food instructions related to ARVs or other medications

5.2 Psychosocial Support

As HIV infection progresses towards AIDS, the people living with the virus will have increased requirements for medical care and psychosocial support. This leads to an immense strain on families, communities and health care services. As people in their most economically productive age are mostly affected, the loss of an income earner may have severe economic and social consequences for families. It is thus imperative that comprehensive care for people living with AIDS and their families must include services providing a combination of food, clothing, shelter, job opportunities, transportation and care for affected families.

6.0 Post Exposure Prophylaxis

Medical personnel caring for HIV infected patients may be at risk of acquiring HIV infection through contact with HIV-infected blood and body fluids. In persons who have been accidentally exposed to HIV through needle stick inoculation or through contamination of mucous membranes by secretions, like rape victims, it has been shown that immediate administration of antiretrovirals may prevent infection from occurring.

It should be emphasized that, the risk varies with on the type of exposure. A percutaneous injury resulting from a needle prick has a risk of 0.3 % (3 in a 1000) may result in HIV infection. The risk after a mucous membrane exposure is estimated to be lower; about 0.09%. This includes contact with the mucous membranes of the eyes, nose and mouth, or contact with chapped, abraded or inflamed skin.

The following types of exposures to HIV infected materials should be considered for post-exposure prophylaxis:

- Needle-stick injury or injury with a sharp object on a patient
- Mucosal exposure of the mouth or eye by splashing fluids
- Intact skin exposed to a large volume of blood or potentially infectious secretions
- Broken skin exposed to a small volume of blood or secretions

6.1 Prevention of occupational exposure in health facilities

All health facilities in the private and public sector should adopt a policy for the prevention of occupational accidental exposure to blood borne pathogens. Health facilities should implement universal precautions for the prevention of exposure to potentially infectious material.

The programme should include:

- Training of all employees in handling and safe disposal of infectious materials.
- Provision of guidelines for prevention and control of infections within the facilities.
- Provision of equipment and supplies necessary for prevention and control of infections such as, educational materials, disposable gloves, disposable needles and syringes and sharp bins.

All personnel should be made aware of the risks involved in proper handling of such material and the steps necessary for preventing exposure should be clearly displayed in posters. Messages should promote avoiding recapping of needles, using sharp boxes for disposal of sharp objects, and exercising caution in performing any risky procedures.

6.2 Immediate steps to be taken after an occupational exposure

Post exposure prophylaxis must be initiated within 72 hours of exposure.
The immediate steps to be taken after an occupational exposure include:

- Use soap and water to wash any wound or skin site that came into contact with infected blood or fluid
- Flush exposed mucous membranes with water
- Irrigate an open wound with sterile saline or disinfectant solution
- Eyes should be irrigated with clear water, saline or sterile eye irrigants
- Report to the concerned authority
- Counselling- Ascertain the HIV status of the patient and the injured health worker after appropriate counselling
- Use antiretrovirals immediately after exposure. These should be started within 1 hour if possible and at the latest within 72 hours of the exposure.

6.3 Recommended regimens for Post-Exposure Prophylaxis

Immediately after exposure, all exposed individuals should take the following:

(A) Basic (28 days) Zidovudine 300 mg tds +lamivudine 150 mg bd

or

Stavudine30/40 mg bd + Lamivudine 150 mg bd

(B) Expanded (28 days) as above, plus Indinavir 800 mg qid

or

Efavirenz 600 mg od at bedtime

or

Nelfinavir 750 mg tds

7.0 Adherence to Antiretroviral Therapy

ARV drug adherence is well recognized as a key component of treatment success. Conversely, poor adherence can lead to treatment failure, the evolution of drug resistance and subsequent immunologic and clinical failure.

The proper education of patients before initiation of therapy is essential for the success of adherence strategies. Such education should cover basic information about HIV and its manifestations, the benefits and side effects of ARV medications, how the medication should be taken and the importance of not missing any doses.

After the initiation of therapy, it is essential to maintain support for adherence. This should involve adherence assessments whenever there is a visit to a health centre, reinforcement of adherence principles to the patients by treatment supporters, and the continuous involvement of relatives, friends and/or community support personnel.

It is recommended that each patient that enters a treatment programme should complete a personal adherence plan. The adherence plan should include the identification of a companion that will assist the patient to adhere to his/or drugs. The companion will be charged with checking the client on a daily basis to observe and document at least one of the doses being taken. In order for this strategy to succeed, each companion should receive orientation to ARV at least once.

7.1 Failure of Regimen due to Poor Adherence

Each time a patient fails a drug regimen – the questions of adherence to the drug regimen must be raised and carefully enquired into. Poor adherence (poor compliance) is a common reason for treatment failure. This emphasises the need for adherence counselling and adherence monitoring at all stages of HIV treatment.
If poor adherence is considered the underlying cause for treatment failure, then treatment should be stopped until the reasons for poor adherence have been addressed.

7.2 Strategies to Improve Adherence

- **Establish trust with patient and family**
- **Serve as Educator and source of Information**
- **Provide ongoing support and monitoring**
- **Utilise Health Team approach**
- **Provide training to support antiretroviral therapy**
- **Intensify management in periods of low adherence by more frequent visits**
- **Recruitment**

Annex 1

Fixed – Dose Combinations of ARVs Available on 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 (300 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 (300 mg) + 3TC (150 mg)

Annex 2

Antiretroviral Drug Toxicity

Antiretroviral Drug	Primary Toxicities	Minor Toxicities	Monitoring/Management
Zidovudine (ZDV)	Haematological (Anaemia, granulocytosis, thrombocytopenia, macrocytosis), hepatic, myopathy	Blue to black discoloration of nails, nausea and headache	For severe anaemia: • Reduce dose or change to d4T or transfuse For myopathy: • Discontinue if CPK high
Lamivudine (3TC)	Painful peripheral neuropathy, pancreatitis	Skin rash, headache	Do serum amylase. Discontinue if elevated. Restart when resolved or change to ABC
Stavudine (d4T)	Painful peripheral neuropathy, lactic acidosis, pancreatitis, hepatitis	Insomnia, anxiety, panic attacks	Severe peripheral neuropathy, abnormal serum amylase and transaminases, discontinue therapy
Didanosine (ddI)	Pancreatitis, painful peripheral neuropathy	Abdominal cramps, diarrhoea	Discontinue if neuropathy severe, raised serum amylase and transaminases
Abacavir (ABC)	Hypersensitivity reaction,	Lactic acidosis	Discontinue therapy and don't restart when resolved
Nevirapine (NVP)	Skin rash, hepatoxicity		Low-dose over first 2 weeks minimizes rash occurrence. If mild or moderate continue cautiously or substitute with EFZ. If severe discontinue NVP. Also discontinue permanently if hepatitis confirmed
Efavirenz (EFZ)	Nightmares, rash, hepatitis	Dizziness,	Rash in 10% but rarely severe <1%; CNS symptoms often resolve 2-4 weeks. Discontinue if hepatitis is confirmed.
Lopinavir/Rotinavir (Kaletra)	Diarrhea, skin rash	Headache, weakness	Diarrhoea rarely severe

Nelfinavir (NFV)	Diarrhoea, lipid, glucose & liver abnormalities,		Diarrhoea occurs 10-30% at start of therapy but often resolves on its own
Indinavir (IDV)	Nephrolithiasis, hepatitis, lipid, glucose abnormalities	Headache, rash, retinoid-like effects, alopecia,	Ensure adequate rehydration (1.5 L/day). Monitor liver enzymes

Annex 3

Recommended Actions for the Maintenance of Antiretroviral Therapy

Timeframe	Recommended action
1 month after initiating therapy	▪ Conduct a general examination
	▪ Conduct laboratory monitoring as available*
	▪ Monitor drug toxicity
	▪ Reinforce adherence issues
	▪ Reinforce patient's role in decision-making and treatment success
3 months after initiating therapy	▪ Conduct a general examination
	▪ Conduct laboratory monitoring as available 1
	▪ Monitor drug toxicity
	▪ Switch regimen only if necessary
	▪ Reinforce adherence issues
Every 3 months thereafter	▪ Conduct a general examination
	▪ Conduct laboratory monitoring as available 1
	▪ Monitor drug toxicity
	▪ Switch regimen only if necessary
	▪ Reinforce adherence issues
	▪ Reinforce patient's role in decision-making and treatment success
	▪ If the patient's results remain stable, schedule next visit every 4 to 6 months