

GUIDELINES FOR ANTIRETROVIRAL
THERAPY IN GHANA

National HIV/AIDS/ STI Control Programme

Ministry of Health / Ghana Health Service

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TABLE OF CONTENTS

ACKNOWLEDGEMENTS	2
CONTENTS.....	3
TABLE OF CONTENTS	4
FOREWORD TO FOURTH EDITION	7
FOREWORD TO THIRD EDITION	8
FOREWORD TO FIRST EDITION	10
LIST OF ACRONYMS.....	11
CHAPTER 1	13
1.1 INTRODUCTION	13
1.2 HIV CARE SERVICES IN GHANA	14
1.3 PURPOSE.....	15
1.4 OBJECTIVE:	15
CHAPTER 2 ANTIRETROVIRAL THERAPY IN ADULTS AND ADOLESCENTS (≥13 YEARS).....	17
2.1 INTRODUCTION	17
2.2 INITIATION OF ANTIRETROVIRAL THERAPY.....	18
2.3 INITIATION CRITERIA.....	18
2.3.1 INCLUSION CRITERIA	18
2.3.2 EXCLUSION CRITERIA	18
2.4 CLINICAL EVALUATION	19
2.5 LABORATORY EVALUATION	20
2.6 RECOMMENDED ARVS AND ART REGIMEN	21
2.6.1: FIRST LINE DRUGS.....	23
2.6.2: SECOND LINE DRUGS.....	24
2.6.3: SPECIAL CONDITIONS	25
2.6.4: RECOMMENDATIONS FOR ANTIRETROVIRAL THERAPY IN PATIENTS WITH TUBERCULOSIS	26
2.7 DRUG INTERACTIONS	26
2.8 MANAGEMENT OF OPPORTUNISTIC INFECTIONS.....	27
2.9 MONITORING.....	27
2.9.1 CLINICAL MONITORING	27
2.9.1.1 Monitoring of adherence.....	27
2.9.1.2 Monitoring of Adverse Effects.....	28
2.9.1.3 Monitoring of Efficacy.....	31
2.9.2 LABORATORY MONITORING.....	31
2.10 INTERRUPTION OF THERAPY	32
2.11 CRITERIA FOR CHANGING THERAPY	32
2.11.1 Drug toxicity.....	32
2.11.2 Treatment Failure.....	32
2.12 REFERRALS AND LINKAGES.....	33
CHAPTER 3 ARV IN CHILDREN < 13YEARS	34
3.1 INTRODUCTION.....	34
3.2 DIAGNOSIS OF HIV INFECTION.....	34
3.3 CRITERIA FOR DIAGNOSING HIV INFECTION IN CHILDREN.....	35
3.4 INITIATION CRITERIA	36
3.4.1 INCLUSION CRITERIA.....	36
3.4.2 EXCLUSION CRITERIA.....	36
3.5 CLINICAL EVALUATION.....	37

3.6 LABORATORY EVALUATION.....	37
3.7 RECOMMENDED TREATMENT REGIMEN	38
3.7.1 FIRST LINE DRUGS.....	38
3.7.2 SECOND LINE DRUG	39
3.8 SPECIAL CONSIDERATIONS.....	41
3.9 DRUG ISSUES.....	45
3.10 MONITORING	45
3.10.1 Clinical Monitoring.....	45
3.10.2 Laboratory monitoring.....	46
3.9.2.2 Monitoring of Efficacy.....	46
CHAPTER 4 MANAGEMENT OF HEPATITIS B VIRUS COINFECTION WITH HIV	47
4.1 INTRODUCTION	47
4.2 ASSESSMENT OF ALL HIV+ PATIENTS FOR HEPATITIS B INFECTION	47
4.3 GENERAL MANAGEMENT OF HEPATITIS B VIRUS INFECTION IN HIV	48
4.4 TREATMENT OF HEPATITIS B VIRUS INFECTION IN HIV/HBV CO-IN FECTION.....	49
4.4.3 Monitoring of HIV/HBV treatment.....	49
CHAPTER 5	51
POST EXPOSURE PROPHYLAXIS FOR HEALTH CARE WORKERS AND RAPE SURVIVORS	51
HEALTH CARE WORKERS.....	51
5.1 INTRODUCTION.....	51
5.2 RISK.....	51
5.3 PREVENTION.....	51
5.4 STEPS TO PREVENT OCCUPATIONAL TRANSMISSION OF HIV	52
RAPE SURVIVORS.....	56
5.5: INTRODUCTION	56
5.6: MEDICO-LEGAL FRAMEWORK.....	56
5.7: SERVICE DELIVERY POINTS	57
5.8: CLIENT ENTRY INTO CARE AND REFERRALS.....	57
5.9: ASSESSMENT	58
5.10: EVALUATION OF RISK.....	59
5.11: PROTOCOL FOR PEP AND PREVENTIVE TREATMENT OF STI.....	59
5.12: FOLLOW-UP CARE	60
5.13: DOCUMENTATION.....	61
CHAPTER 6 GUIDELINES ON ART COUNSELLING	62
6.1 INTRODUCTION.....	62
6.2 GOAL OF COUNSELLING IN ART	62
6.2.1 The Goals of Therapy.....	63
6.3 ANTIRETROVIRAL THERAPY.....	63
6.3.1 A life-long commitment	63
6.3.2 Drug Information	64
6.3.3 Understanding Adherence.....	64
6.3.4 Disclosure	65
6.3.5 Emotional and Social Support	65
6.3.6 Nutrition.....	65
CHAPTER 7 DATA MANAGEMENT	66

7.1 INTRODUCTION.....	66
7.2 HEALTH INFORMATION MANAGEMENT SYSTEM (HMIS).....	66
7.3 LOGISTIC MANAGEMENT INFORMATION SYSTEM (LMIS)	67
7.3.1 Essential data for LMIS	67
7.3.2 LMIS Forms for administering ART in Ghana.....	67
CHAPTER 8 PROCUREMENT, STORAGE AND DISTRIBUTION OF ARV DRUGS.....	68
8.1 PROCUREMENT	68
8.1.1 GOALS FOR ARV PROCUREMENT	68
8.1.2 CRITERIA FOR SELECTION OF DRUGS	68
8.1.3 SPECIFICATION.....	69
8.1.4 QUANTIFICATION	69
8.1.5 QUALITY ASSURANCE	69
8.1.6 PROCUREMENT.....	69
8.2 STORAGE AND DISTRIBUTION	70
8.2.1 DISPENSING OF ARVs.....	70
APPENDIX 1 CLINICAL STAGING OF HIV/AIDS FOR ADULTS AND ADOLESCENTS	71
APPENDIX 2	74
A. WHO CLINICAL STAGING OF HIV AND AIDS FOR INFANTS AND CHILDREN	74
B. PRESUMPTIVE DIAGNOSIS OF CLINICAL STAGE 4 HIV IN	76
C. IMMUNOLOGICAL CATEGORIES FOR PAEDIATRIC	77
HIV INFECTION	77
D. IMPLICATION FOR CLINICAL AND IMMUNOLOGICAL.....	78
APPENDIX 3	80
DRUG-DRUG INTERACTIONS.....	80
APPENDIX 4	81
DRUG INFORMATION	81
APPENDIX 5: ALGORITHM FOR THE MANAGEMENT OF HEPATITIS B VIRUS CO- INFECTION WITH HIV	87
APPENDIX 6- PEP FOR RAPE SURVIVORS.....	88
APPENDIX 6.1 FORENSIC EVIDENCE COLLECTION	88
APPENDIX 6.2:	89
DRUG RECOMMENDATION FOR HIV PEP IN ADULTS AND ADOLESCENTS (>40KG) INCLUDING PREGNANT AND LACTATING WOMEN	89
APPENDIX 7: ALGORITHM FOR TB SCREENING IN PLHIV	90
APPENDIX 8 GUIDELINES ON HIV VIRAL LOAD (VL) MONITORING FOR CLIENTS ON ART	91
REFERENCES	95

FOREWORD TO FOURTH EDITION

The HIV and AIDS epidemic remains a threat to the economies of many nations particularly in sub-Saharan Africa. The fast changing dynamics in the comprehensive care of Persons Living With HIV (PLHIV) using Antiretroviral Therapy (ART) has become an inevitable stimulus for regular revision of management guidelines. Recently published guidelines for the care of PLHIV by the World Health Organisation (2010) coupled with emerging new evidence in therapeutic guidelines and important programme and research data makes it imperative for countries including Ghana to update their guidelines for ART. It is against this backdrop that the third edition is being revised to improve therapeutic decisions and overall quality of management of PLHIV.

The highlights of this new edition are as follows:

1. A review of the list of recommended ARVs for use in Ghana to exclude Stavudine, Nelfinavir and Didanosine,
2. A reconstruction of first and second line regimens and options consequent to the above for both adult and paediatric care including salvage therapy,
3. Amendments to treatment of HIV co-morbidities,
4. Revised criteria for initiation of therapy for infants and children,
5. Inclusion of guidelines for viral load testing and
6. The expansion of Post Exposure Prophylaxis to include the management of rape survivors.

It is my expectation that these updated guidelines further facilitate the work of our hardworking service providers to ensure optimal care and support for PLHIV in Ghana.

Dr. Benjamin Kunbuor
Hon. Minister of Health
Republic of Ghana

FOREWORD TO THIRD EDITION

Treatment and support of persons living with HIV and AIDS in Ghana started in mid 2003. Globally the treatment of persons living with HIV has been evolving at a rapid pace with the addition of newer and less toxic formulations since the first efforts at treatment. The last revision of the guidelines was in 2005. Over the three years, knowledge and newer co-morbidities have become important. The national programme thus undertook the exercise of reviewing recent literature including both the World Health Organisation and Centre for Disease Control and Prevention in publications to inform the few but pertinent revisions made.

Critical among these are:

1. A clear listing of antiretrovirals recommended for use in Ghana.
2. The new baseline for the initiation of antiretroviral therapy which stipulates that all persons living with a CD4 count less than 350 cells/ml are eligible for therapy.
3. The inclusion of the management of HIV and Hepatitis B co-morbidity.
4. And a simplified paediatric dosing chart.

Like all the other editions this version is complemented by the new PMTCT guidelines and protocols, the Tuberculosis and HIV co-morbidity clinical guidelines, the new sexually transmitted disease guidelines and the new management of Opportunistic Infections guidelines.

I am sure that all prescribers will use these guidelines to ensure a uniform quality of care for persons living with HIV.

Let me take this opportunity to thank all our development partners who have over the years supported the national effort at providing care and support to persons living with HIV and AIDS. I also recognise the untiring effort of all health staff for their dedication to providing care to persons living with HIV.

Major Courage E.K. Kwashigah (Retired)
Honourable Minister for Health

FOREWORD TO SECOND EDITION

The first edition of the guidelines on antiretroviral therapy was produced in 2002. This was in response to the need to start Highly Active Antiretroviral (HAART) therapy in Ghana, albeit on a pilot sale.

The first client to access HAART in the Public sector was in May 2003 as part of the Family Health International-National AIDS Control Programme (FHI-NACP) collaboration in a Pilot project in the Manya Krobo district of the Eastern Region. The field of Highly Active Antiretroviral therapy is dynamic and rapidly evolving. The World Health Organisation has provided a recent update on antiretroviral therapy for resource limited settings. Recent global updates and new drug formulations have been released. Locally, experience has been gained on the use of antiretroviral therapy and critical lessons learnt since May 2003. These lessons learnt and the aforementioned have informed the decision to revise the first edition.

This second edition clearly defines the first line, alternate first line and second line regimen, a gap identified in the first edition. It includes the use of Fixed Dose Combination (FDC) therapy in the country.

The eligibility criteria for initiating Highly Active Antiretroviral Therapy in Ghana has been clarified and simplified to meet the needs of all service providers.

New chapters on antiretroviral therapy in children, post exposure prophylaxis and adherence counselling have been added as an improvement on the earlier version and the scope of services provided also expanded.

This document is complemented by additional materials developed for the comprehensive care of persons living with HIV/AIDS. These include the National Guidelines on Prevention of Mother-To- Child- Transmission of HIV (PMTCT), the Voluntary Counselling and Testing (VCT) manual and guidelines for the management of Opportunistic Infections (OI). Also included are manuals on the Management of Sexually Transmitted Infections (STI) and HIV/AIDS Logistics Management Information System.

It is the expectation of the Ministry of Health that this treatment guideline would be the basic text that will guide all prescribers of antiretroviral drugs in the country.

The Ministry of Health acknowledges the contribution of the Department For International Development (DFID) of the United Kingdom for financial support and the World Health Organisation (WHO) for technical support in the development of the second edition.

Major Courage E. K. Quashigah (Retired)
Hon. Minister for Health

FOREWORD TO FIRST EDITION

The HIV/AIDS epidemic continues to pose a threat to public health, economy, and indeed to national security in countries. The Government of Ghana has made a commitment to responding to this threat.

Comprehensive management of persons infected with HIV and AIDS patients has been shown to reduce mortality in addition to improving their quality of life of the infected. The continuum of care includes general specific medication for prevention and treatment of opportunistic infections and the use of Anti-retroviral Therapy. Clinical science and medical treatment has developed rapidly in this domain.

The Health Sector has the primary mandate of providing healthcare among 'People living with HIV/AIDS' (PLWHA). These guidelines are not intended towards providing 'state of the art' medical care, but rather a practical approach for management of HIV related illness. This includes criteria for initialisation of therapy, drug combinations on monitoring among others. It provides technical detail on drug interactions. It takes cognisance of the inadequate laboratory support that will ensure optimum monitoring. It also takes recognises the cost implications and therefore recommends drugs that are efficacious, with safe profiles and that are cost effective.

Even though primary and secondary prevention are not addressed in this document, it should be emphasised that these should form an integral part of patient management. Separate guidelines are available for the detailed management of Sexually Transmitted Infections and Management of Opportunistic Infections These are to complement each other in the comprehensive care of infected persons.

It is the hope of the Ghana Health Service that this and other guidelines will together provide adequate guidance to all providers in the clinical management of PLWHA's, both in the public and private sectors and contribute to the improvement in the quality of life of infected individuals.

We gratefully acknowledge the inputs of the task team members for their invaluable contribution. We also acknowledge the numerous documents that were consulted.

Finally, I wish to acknowledge the financial support from the Ministry of Health

Dr Kweku Afriyie
HON. MINISTER OF HEALTH
September 2002

LIST OF ACRONYMS

ABC	Abacavir
AFBs	Acid Fast Bacilli
AFP	Alpha Fetoprotein
AIDS	Acquired Immune Deficiency Syndrome
ALT	Alanine Transferase
ART	Antiretroviral Therapy
ARV	Antiretroviral
ATV	Atazanavir
AZT	Zidovudine
BUE	Blood Urea and Electrolytes
CD4	CD4 cells- T4 helper cells
d4T	Stavudine
DDI	Didanosine
DNA	Deoxyribonucleic Acid
FHI	Family Health International
FTC	Emtricitabine
GAC	Ghana AIDS Commission
GFATM	Global Fund for AIDS Tuberculosis and Malaria
GHS	Ghana Health Service
HAART	Highly Active Antiretroviral Therapy
Hb	Haemoglobin
HBsAb	Hepatitis B surface antibody
HBsAg	Hepatitis B surface antigen
HBIg	Hepatitis B Immunoglobulin
HBV	Hepatitis B virus
HCC	Hepatocellular carcinoma
HBCIgG	Hepatitis B core antibody
HIV	Human Immunodeficiency Virus
IDV	Indinavir
IRS	Immune Reconstitution Syndrome
LFT	Liver Function Test
LIP	Lymphoid Interstitial Pneumonitis
LMIS	Logistics Management Information System
LPV	Lopinavir
LPV/r	Ritonavir boosted lopinavir
MOH	Ministry of Health
NACP	National HIV/AIDS/ STI Control Programme
NFV	Nelfinavir
NGO	Non-Governmental Organisation
NNRTI	Non-Nucleoside Reverse Transcriptase Inhibitor
NtRTI	Nucleotide Reverse Transcriptase Inhibitor
NRTI	Nucleoside Reverse Transcriptase Inhibitor
NTCA	National Technical Committee on AIDS
PCR	Polymerase Chain Reaction
PEG IFN α 2a	Pegylated interferon alfa-2a
PEP	Post Exposure Prophylaxis
PI	Protease Inhibitor
PLHA	People Living with HIV/AIDS
PMTCT	Prevention of Mother- to- Child- Transmission
RFT	Renal Function Test
RTV	Ritonavir
SQR/r	Saquinavir/r
SOP	Standard Operating Procedures
START	Support Treatment and Antiretroviral Therapy
STD	Sexually Transmitted Disease
STI	Sexually Transmitted Infection
TB	Tuberculosis
TDF	Tenofovir Disoproxil Fumarate

USAID	United States Agency for International Development
VCT	Voluntary Counselling and Testing
WHO	World Health Organisation
3TC	Lamivudine

CHAPTER 1

1.1 INTRODUCTION

The first case of AIDS was reported in Ghana in 1986, since then there has been a rise in the number of cases. The estimated adult national HIV prevalence in 2009 was 1.9%. The estimated number of persons living with HIV and AIDS in 2009 was 267,069, made up of 154,612 females and 112,457 males giving a female: male ratio of 1.4:1. In the same year, there were 25,666 children living with HIV and an estimated 3,354 children were newly infected. The annual AIDS deaths were 20,313. Sexual spread remains the main mode of transmission accounting for an estimated 80% of all transmissions, Mother-to-child (vertical) transmission accounts for 15% of infections and blood and blood products 5%.

In the 2009 HIV sentinel survey (HSS), the median prevalence of HIV infection among antenatal clinic clients was 2.9%. This constituted a rise from the previous year's prevalence of 2.2%, following two consecutive drops in 2007 and 2008. Trend analysis of ANC HIV prevalence since 2000 shows three peaks in 2003, 2006 and 2009, the lowest being in 2009. The age group with highest prevalence of 4.0% in 2009 was the 40-44 year group. Also in this survey both HIV 1 and 2 were found in the Ghanaian population, with HIV 1 occurring in 91.8%, HIV-2 in 5.2% and dual HIV-1/2 infections in 3.0% of all infections. Aggregate HIV-2 infection therefore was 8.2% compared to the previous year's figure of 5.5%.

The response to the epidemic included priority interventions which initially focussed on promotion of safe sex, condom use, improved management of STIs, safe blood transfusion, infection prevention and control, nursing/clinical care and counselling, home based care and Prevention of Mother-To-Child Transmission (PMTCT). These interventions were geared towards reducing the number of new infections and improving on the quality of life of Persons Living with HIV (PLHIV). Antiretroviral Therapy (ART) has been available in Ghana since June 2003. The number of treatment sites has increased from 2 to over 138, and the cumulative number of people with HIV infection receiving ART was 33,745 as at December 2009. This has contributed significantly to the reduction of HIV-related morbidity and mortality.

Antiretroviral therapy is a lifelong activity needing distinctive strategies to ensure its effectiveness and prevent development of drug resistance.

These strategies include:

- Capacity building;
- Strengthening the health system to improve logistics management, pharmacy and laboratory services, quality of care, partnerships and linkages;
- Rational selection and sequencing of drug regimen;
- Maximising adherence to the selected regimen;
- Preservation of future treatment options;
- Monitoring of HIV drug resistance alongside the scale- up.

1.2 HIV CARE SERVICES IN GHANA

The provision of antiretroviral therapy in the public health care system started in June 2003 at two pilot sites in the Manya Krobo district. This was part of a comprehensive care package that also included the provision of Counselling and Testing, and Prevention of Mother to Child Transmission (CT/PMTCT), Management of Sexually Transmitted Infections and Opportunistic Infections. To ensure the standardisation and quality of care for PLHIV, guidelines and manuals have been developed to guide service delivery. These include:

- National Guidelines on Antiretroviral Therapy
- National Guidelines on Management of Opportunistic Infections
- National Guidelines on CT
- National Guidelines on PMTCT
- National Guidelines on STI Management
- Logistics Management Guidelines and Protocols
- Guidelines and Protocols for Early Infant Diagnosis in Ghana
- Guidelines on Nutritional Care and Support of PLHIV
- Manual for Integrated Management of Adult and Adolescent Illnesses
- Quality Assurance of HIV Testing in Ghana
- Guidelines for evaluation of HIV Test Kits
- Training Manual for HIV Testing
- National HIV Drug Resistance plan for Ghana

In addition requisite procedures and structures were put in place to provide an enabling environment for the effective management of ART. Furthermore policies to govern ARV procurement were formulated. These include:

- National accreditation criteria for ART to ensure all sites and staff providing ART are accredited
- A Policy directive on importation, sale and distribution of Antiretroviral Drugs
- Technical Working Group on ART to provide technical advice on ARVs and provide direction for the scale up of ART in Ghana

The establishment of ART sites in Ghana has followed the following process:

- Assessment and accreditation of sites
- Provision of guidelines and protocols to standardise treatment
- Training of all cadres of staff in ART and other support services
- Ensuring adequate basic equipment and infrastructure
- Strengthening monitoring and evaluation systems (Logistics Management and health information system)
- Procurement of logistics and consumables

The current ART regimen recommended for the treatment of PLHIV in Ghana are based on the principles of:

- Rational selection and sequencing of drug regimen
- Maximising adherence to the selected regimen
- Preservation of future treatment options

- Use of HIV drug resistance testing in selected clinical settings

Ghana uses triple combination of antiretrovirals (Highly Active Antiretroviral Therapy). No mono or dual therapy shall be used in the treatment of PLHIV.

Lessons learnt from the ART programme since its inception has informed the scale-up of services nationally. Currently, over 138 public and private facilities are providing ART in all regions and about 60% of districts. The number of persons accessing treatment has increased from 2,017 adults and children in four sites in December 2004, to 33,745 by the end of 2009. It is estimated that 123,245 PLHIV (110,494 adults and 12,751 children) shall be put on ART by the year 2015 in line with universal access targets.

The programme is supported by the Global Fund to fight AIDS, Tuberculosis and Malaria (GFATM) and other partners. This support is in the form of capacity building, procurement of drugs and logistics among others.

Considering new evidence and current programme experience, there is a need for regular revision of ART guidelines. The 2002 Guidelines for Antiretroviral Therapy in Ghana, was first revised in 2005 and 2008. The current revision has been necessitated by new WHO guidelines and other emerging evidence.

The cost of care has been substantially subsidised by the Government of Ghana to GH¢ 5 for a month's supply of ARV drugs, OI drugs, laboratory and other investigations, and other services.

In order to ensure continuity of supply, assure the quality of formulations and minimise wastage, leakage, abuse and the development of drug resistance, the Ministry of Health has been mandated as the sole agency for the importation, and distribution of HIV and AIDS drugs and other related commodities in Ghana.

1.3 PURPOSE

The purpose of this document is to provide updated guidelines for use by healthcare workers for the provision of ART and clinical monitoring in Ghana.

1.4 OBJECTIVES:

The objectives of this document are:

- To provide information on ART in Ghana
- To facilitate the provision of standard ART in Ghana
- To provide guidance on monitoring of ART – clinical, laboratory and adherence
- To provide guidance on provision of comprehensive care and counselling in ART
- To provide direction on logistics management and information for Antiretroviral drugs

Complementary documents for HIV treatment, care and support have been developed. The following documents should be used as complementary documents to this one:

1. 'Guidelines for the management of opportunistic infections and other related HIV Diseases'. MOH/GHS
2. 'National Guidelines for the Development and implementation of HIV Counselling and Testing in Ghana', GAC/MOH
3. 'Prevention of Mother-to-Child Transmission (PMTCT) of HIV in Ghana', MOH/GHS
4. 'HIV Counselling and Testing Training Manual' MOH/GHS
5. Sexually transmitted Infections Guidelines for Management. MOH/GHS
6. 'Antiretroviral (ARV) Drugs Logistics Management Information System Guidelines'. MOH/GHS
7. NACP Logistics Management Information System, E-LMIS version 1.0 Manual, Ghana Health Service January 2009
8. 'Logistics Management of Public Sector Health Commodities in Ghana, SOPs', MOH/GHS
9. 'Manual on Nursing Care for People Living with HIV/AIDS', MOH/GHS
10. 'Guidelines for the Clinical Management of TB and HIV Co-infection in Ghana'. Ghana Health Service, August 2007
11. 'Guidelines on Nutritional Care and support for People living with HIV and AIDS', Ghana Health Service, 2006
12. Accreditation for Antiretroviral Therapy in Ghana: National Guidelines and Site Assessment Ghana Health Service. 2006
13. HIV Drug Resistance Plan 2006-2010
14. National HIV/AIDS and STI Policy. Ghana AIDS Commission. August 2004

CHAPTER 2

ANTIRETROVIRAL THERAPY IN ADULTS AND ADOLESCENTS (≥13 years)

2.1 INTRODUCTION

The cost of antiretroviral drugs, the simplicity or complexity of the regimen, the need for careful monitoring and adherence to therapy make it essential that specific services and facilities must be in place before considering the introduction of ART into any setting. Sites shall undergo assessment, and be assisted to meet set criteria before accreditation to provide ART¹. However, accreditation may be suspended or withdrawn if a facility consistently fails to adhere to national standards.

The management of PLHIV is best achieved using a multidisciplinary team approach. The team should ideally comprise the following categories of individuals;

- Clinician
- Nurse
- Pharmacy staff
- Counsellor
- Nutritionist/dietician
- Social worker
- Laboratory staff
- Patient confidante
- Psychosocial support provider

The provision of comprehensive HIV care and the administering of ART aim at attaining the following goals:

- a. The suppression of HIV replication, as reflected in plasma HIV concentration, to as low as possible and for as long as possible
- b. The preservation or enhancement of the immune function (CD4 restoration), thereby preventing or delaying the clinical progression of HIV disease
- c. Improvement in quality of life.
- d. Reduction in HIV related morbidity and mortality
- e. Promotion of growth and neurological development in children.

¹ See National Accreditation Criteria for Antiretroviral Therapy

2.2 INITIATION OF ANTIRETROVIRAL THERAPY

Since therapy is life long, the team should ascertain that the patient is willing and able to sustain therapy as interruption of treatment will be detrimental to the health of the patient. Interruption could lead to development of drug resistance and increase the likelihood of transmission of a resistant virus which would have further public health implications (see Counselling in chapter 6).

A comprehensive medical and social history, a complete physical examination and laboratory evaluation are required before ART can be initiated. This is aimed at:

- Confirming HIV infection
- Assessing the clinical stage of the HIV infection
- Identifying past HIV related illnesses
- Identifying current HIV related illnesses requiring treatment
- Identifying co-existing medical conditions and pregnancy. This may influence the choice of therapy
- Assessing nutritional status
- Assessing capacity to adhere to treatment.

2.3 INITIATION CRITERIA

2.3.1 INCLUSION CRITERIA

Antiretroviral therapy may be initiated when patients, including HIV positive pregnant women, satisfy the following criteria:

1. Patients with CD4 count less than 350 cells /ml and / or
2. Symptomatic with HIV infection in WHO clinical stage 3 and 4 ².
(Where initiation is based solely on WHO clinical staging the CD4 count must be done as soon as possible).

For pregnant women, where the CD4 count is greater than 350, they shall be put on ARV prophylaxis starting from 14 weeks for the purpose of PMTCT. (For ART in pregnancy, refer to the PMTCT Guidelines)

2.3.2 EXCLUSION CRITERIA

Antiretroviral Therapy shall not be initiated whilst the following circumstances prevail:

1. The patient is not motivated. (i.e. the patient shows no real interest or commitment, in starting treatment. In this instance counselling will be continued until motivation is established).
2. Patient does not complete at least 2 sessions of pre-treatment adherence counselling

² See Appendices 1 and 2 for WHO clinical staging

3. Treatment is not sustainable, e.g. the person is not able to cope with follow-up visits, or facility is unable to assure continuity of care.
4. No laboratory monitoring is possible
5. The patient presents with severe hepatic (Liver Function Tests (LFT) > 5 times the upper limit of normal) or end stage renal disease.
6. The patient has an acute opportunistic infection. **In this case these acute opportunistic infections must be treated before initiation of antiretroviral therapy.** (In the case of TB there may be some exceptions. See Section 2.6.4)
7. The patient has a terminal medical condition.

2.4 CLINICAL EVALUATION

A detailed clinical evaluation of the HIV-infected patient is essential prior to initiating ART.

The aims of the evaluation are to:

- Identify past HIV related illnesses
- Identify current HIV related illnesses that will require treatment
- Identify co-existing medical conditions and pregnancy that may influence the choice of therapy
- Assess the clinical stage of HIV infection

These can be achieved by:

- Taking a detailed medical and social history
- Carrying out a complete physical examination
- Conducting appropriate laboratory investigations.

The Medical History should include:

- Date of initial HIV diagnosis
- Current symptoms and concerns including a symptom screen for tuberculosis (See Appendix 6 TB screening algorithm)
- Past Medical History including diagnosis of tuberculosis
- Drug history including treatment for TB and previous ARV exposure
- Sexual history and past symptoms of STI
- Obstetrics and Gynaecological history including family planning
- Social history including family support systems and income

The physical examination should have the following components:

- Patient's weight and height
- Skin looking out for the following
 - Herpes Zoster (old scars and new lesions)
 - *Herpes simplex*
 - *Molluscum contagiosum*
 - Kaposi sarcoma
 - Pruritic papular dermatitis
 - Plane warts
- Oropharyngeal mucosa

- Candidiasis
- Oral hairy Leucoplakia
- Kaposi sarcoma
- Lymphadenitis/lymphadenopathy
- Respiratory and Cardiovascular system
- Genito-urinary system
- Gastrointestinal tract
- Nervous and musculo-skeletal systems including mental status, motor and sensory deficits
- Fundoscopy whenever possible for retinitis or papilloedema
- Detailed examination of Genital Tract for discharge, ulcers, enlarged glands and growths

2.5 LABORATORY EVALUATION

The reasons for investigations are to determine:

- Whether patient satisfies initiation criteria
- Whether female patients are pregnant
- The presence of opportunistic infections
- The immunological stage of HIV infection
- The presence of co-morbid diseases

Initial laboratory evaluation should provide:

1. Confirmation of HIV infection and type
 - Confirmatory HIV test (HIV1, HIV2, HIV1and 2)
 - Viral load (when available).

It is recommended that where available this test should be done at baseline, at six months and yearly thereafter.
2. Indication of patients' immune status
 - CD4 count

This is a good indicator of the immune function in HIV infection. It is recommended that the CD4 count be done at initiation, at six months and yearly thereafter.

Further information on the patient's baseline indicators are as in the table below (Table 2.1):

Table 2.1: Other Baseline tests

Haematological test	Full blood count
Biochemical test	Blood Urea, Creatinine and Electrolytes; Liver Function tests Fasting; Fasting Blood Sugar; Cholesterol and lipid profile
Routine examinations	Urinalysis (Urine R/E) Stool R/E
Respiratory examinations	Sputum for AFBs and throat/nasal swabs for respiratory viruses where necessary Chest X-ray
Serological Test	Hepatitis B Surface antigen screen
Supplementary tests <i>These tests are performed depending on signs and symptoms</i>	Histology on skin and lymph node biopsy Kidney biopsy Screening for STIs Pregnancy tests Paps smear, HPV DNA Abdominal Ultrasound

2.6 RECOMMENDED ARVs AND ART REGIMEN

Table 2.2 below shows the recommended ARVs in Ghana.

TABLE 2.2: RECOMMENDED ARVs IN GHANA

Nucleoside Reverse Transcriptase Inhibitors (NRTI)	Nucleotide Reverse Transcriptase Inhibitor (NtRTI)	Non-Nucleoside Reverse Transcriptase Inhibitors (NNRTI)	Protease Inhibitors (PI)
Zidovudine (AZT/ZDV)	Tenofovir (TDF)	Nevirapine (NVP)	Ritonavir boosted Lopinavir (LPV/r)
Lamivudine (3TC)		Efavirenz (EFV)	Ritonavir boosted Atazanavir (ATV/r)
Abacavir (ABC)			
Emtricitabine (FTC)			

Where available, fixed dose combinations of these drugs are preferred to single dose preparations because they improve adherence to treatment. Some of these fixed dose combinations are AZT/3TC, AZT/3TC/NVP, AZT/3TC/EFV and TDF/FTC.

The regimen described below is for the treatment of ART-naïve persons (i.e. patients who have not previously been treated with ART) and is based on evidence from other ART programmes worldwide and recent local experience. These recommendations are also based on the effectiveness of the drug, pill burden, dosing in relation to food, toxicity, dosing frequency, nutritional requirements, convenience and drug interaction profiles, resistance to ARV, availability and cost.

The regimen is a triple therapy, i.e. three drugs. Mono therapy or dual therapy (treatment with one or two drugs only) is contraindicated for treatment of PLHIV.

The following triple therapy regimens are recommended:

- 2 Nucleoside/tide Reverse Transcriptase Inhibitors (NRTIs) and 1 Non-Nucleoside Reverse Transcriptase Inhibitor (NNRTI)
- 2 NRTIs and 1 boosted Protease Inhibitor (PI)

Table 2.3 below shows the recommended drug combinations used in Ghana. The first line regimen is the first option for treatment of all patients who fit the treatment criteria.

The second line regimen is used when there is evidence of treatment failure with the first line regimen. This should be confirmed preferably by CD4 monitoring and viral load where available. In this case the whole regimen should be changed. Dosages of the regimen will be found in drug information attached in appendix 4.

A third line or salvage therapy is recommended for heavily treatment experienced patients and those who have failed second line treatment. Baseline investigation for such patients should include viral load and drug resistance testing where available. The construction of a salvage therapy must be done in consultation with a specialist.

2.6.1: FIRST LINE DRUGS

TABLE 2.3

	Drugs	Contra-indications	Comments
First choice drugs	First Option Zidovudine + Lamivudine + Nevirapine	Nevirapine is contraindicated in: <ul style="list-style-type: none"> ○ liver dysfunction ○ hypersensitivity Zidovudine is contraindicated in: <ul style="list-style-type: none"> ○ severe anaemia 	Replace with Efavirenz Replace with Tenofovir
	Second Option Zidovudine + Lamivudine + Efavirenz	Efavirenz is contraindicated in: <ul style="list-style-type: none"> ○ First trimester Pregnancy ○ CNS presentations When there is Efavirenz related persistent adverse CNS effect	Replace with Nevirapine Replace with Nevirapine
Second Choice drugs	First Option Tenofovir +(Lamivudine or Emtricitabine) + Nevirapine		Tenofovir should be used when Zidovudine is contraindicated e.g. anaemia (Hb less than 8g/dl) When Hb drops significantly (more than a 25% drop from the baseline value) Tenofovir should replace zidovudine

	Drugs	Contra-indications	Comments
	Second Option Tenofovir + (Lamivudine or Emtricitabine) + Efavirenz	Efavirenz in contraindicated in: <ul style="list-style-type: none"> ○ Efavirenz related Persistent adverse CNS effect ○ Pregnancy 	Tenofovir should be used when Zidovudine is contraindicated e.g. anaemia When Efavirenz is contraindicated replace with Nevirapine

2.6.2: SECOND LINE DRUGS

TABLE 2.4

	Drugs	Contra- indications	Comments
First Alternative	Tenofovir + (Emtricitabine or Lamivudine) + (Lopinavir/r or Atazanavir/r)		If AZT base first line. If LPV/r was used for HIV2 in first line, use ATV/r
Second Alternative	Zidovudine + Lamivudine +(Lopinavir/r or Atazanavir/r)		If TDF base first line. Consider Abacavir if patient has used both Tenofovir and Zidovudine

2.6.3: SPECIAL CONDITIONS

The regimen recommended in Table 2.3 shall be amended in the conditions depicted under Table 2.5 below.

TABLE 2.5: RECOMMENDATIONS FOR SPECIAL CONDITIONS

Condition	Recommendation	Comments
Women of childbearing potential	Zidovudine + Lamivudine + Nevirapine	Efavirenz should not be used in the first trimester
HIV co-infection with Hepatitis B See Chapter 4	The recommended regimen shall be: Lamivudine + Tenofovir + Efavirenz.	Lamivudine and Tenofovir are active against both HBV and HIV. Nevirapine can be used in place of Efavirenz, but with caution because of the risk of hepatotoxicity.
ART experienced patients	Review previous drugs used for ART, duration of use, as well as the clinical, immunological and virological response to the therapy. Conduct resistance testing if available. Change all drugs if there is evidence of resistance	Consultation or referral to an HIV expert.
Dual HIV-1 and HIV -2 or HIV-2 infections	Due to the ineffectiveness of non-nucleoside drugs (Nevirapine and Efavirenz) in HIV-2 infection, combination of nucleosides and protease inhibitors should be used	
Previous exposure to 1. Zidovudine and Lamivudine or 2. Nevirapine for PMTCT prophylaxis	This does not preclude the use of any of these medications – Zidovudine, Lamivudine or Nevirapine for ART	

2.6.4: RECOMMENDATIONS FOR ANTIRETROVIRAL THERAPY IN PATIENTS WITH TUBERCULOSIS

All HIV positive patients with TB shall be treated in accordance with the National Tuberculosis Programme Guidelines with short course chemotherapy (See Guidelines for Clinical Management of TB and HIV co-infection in Ghana). The regimen consists of initiation phase of rifampicin, Isoniazid, pyrazinamide and ethambutol for 2 months and a continuation phase of rifampicin and Isoniazid for 4 months. Streptomycin is now reserved for use in cases of re-treatment.

In the treatment of tuberculosis some important interactions should be considered. Rifampicin, PIs and NNRTIs are metabolised by the same liver enzyme system (cytochrome P450). Thus, Rifampicin, which stimulates the enzyme, can lead to a reduction in the blood levels of the PIs and NNRTIs. PIs and NNRTIs may also inhibit or enhance this enzyme system to different extents and can lead to altered blood levels of Rifampicin. These drug-drug interactions may result in ineffective antiretroviral or anti-tuberculous therapy or drug toxicity.

To reduce the effect of drug-drug interactions, the following options may be followed in the treatment of HIV positive patients with known TB co-infection:

- For Patients not on ART
 1. Start ART in all HIV/TB co- infected individuals irrespective of CD4 count
 2. Start TB treatment followed by ART as soon as TB treatment is tolerated
 3. The ART must be introduced within 8 weeks of TB treatment.
- For patients already on ART
 1. Evaluate ART adherence, assess patient clinically and immunologically.
 2. Maintain patient on ART, but replace Nevirapine with Efavirenz if patient was on Nevirapine.
 3. Start TB treatment as soon as possible.
- For both instances given above:
 1. Use EFV based ART regimen i.e. **AZT+3TC+EFV**
 2. EFV contraindicated or not tolerated, use AZT+3TC+ABC or AZT+3TC+TDF(triple nukes) for the duration of TB treatment and revert to standard first line

2.7 DRUG INTERACTIONS

Drug interactions may occur between any medications an individual takes. For a PLHIV, drugs may be taken for prophylaxis and treatment of opportunistic infections, other infections and/or diseases. Drug interactions may occur between:

- Different antiretroviral drugs prescribed (this has been eliminated to some extent by the choice of regimen above)
- Medicines used for the management of Opportunistic Infections and antiretroviral drugs
- Prescribed and non-prescription medication or alternative medicine
- Between medicines and food
- Certain recreational drugs and prescribed medications

Some important drug interactions:

- Trimethoprim-sulfamethoxazole, ganciclovir, acyclovir and hydroxyurea can have potentially additive haematologic toxicity when given together with zidovudine. Careful haematologic monitoring is necessary.
- Dapsone may lead to additive neurotoxicity with zidovudine
- Ketoconazole and Fluconazole may inhibit the metabolism of Protease Inhibitors and may result in PI toxicity.

See Appendix 3 for table on drug interactions

2.8 MANAGEMENT OF OPPORTUNISTIC INFECTIONS

This should follow established protocols for the management of opportunistic infections. (See Guidelines for Management of Opportunistic infections and other related diseases). Opportunistic infections need to be treated before the initiation of ART.

2.9 MONITORING

2.9.1 CLINICAL MONITORING

Patients on ART should be closely followed-up to assess adherence to therapy as well as tolerance and efficacy of the treatment. Intensive follow up should be done in the first few weeks of management. Management of the PLHIV should be a team approach between the clinician, nurse, counsellor, pharmacist, any other service provider and confidante who will support the patient with his/her management. The patient should be seen a few days (not more than 14 days) after initiation of therapy. After the first few weeks, follow up can be at monthly intervals for the first 3 months, then at intervals of 2 – 3 months and as necessary.

2.9.1.1 Monitoring of adherence

Adherence to ART is essential and more than 95% adherence is required for effectiveness of therapy. To improve adherence, the initial counselling sessions should be comprehensive and should result in well-informed decisions and commitment by the patient. Disclosure to and the use of adherence monitors has been found to be effective in improving adherence. In addition there should be available information and a committed supporting

medical team. Adherence to treatment should be discussed in-depth at each follow-up visit.

2.9.1.1.1 Measurement of adherence

Adherence should be monitored using one of the following methods:

- Self-reports
- Pill counts
- Pharmacy records

2.9.1.2 Monitoring of Adverse Effects

Causes of any new symptoms and signs should be identified after initiation of ART. New symptoms may be due to,

- Intercurrent illnesses
- Adverse reactions to antiretroviral drugs and other drugs
- Opportunistic infections becoming clinically apparent as a result of immune reconstitution.

Where opportunistic infections become clinically apparent as a result of immune reconstitution syndrome, these need to be diagnosed and treated. Patients should be observed at each clinic visit for opportunistic infections and screened for TB every 6 months.

Adverse effects of drugs should be explained to patients and appropriate measures taken e.g. adapting the drug regimen, providing symptomatic treatment and giving reassurance.

Antiretroviral agents are responsible for a broad range of adverse effects from low grade self-limiting to life-threatening side-effects. Differentiating between complications of HIV disease and ART toxicity is sometimes difficult. Alternative explanations for a patient's presenting symptoms should be considered before it is concluded that toxicity is ART-related. Regardless of their severity, adverse events may affect adherence to therapy.

A proactive approach to managing toxicity is recommended. Ancillary laboratory tests should be done to confirm adverse effects such as anaemia, neutropaenia among others (see laboratory monitoring).

TABLE 2.6 COMMON ARV TOXICITIES

HAEMATOLOGICAL TOXICITY	Drug-induced bone marrow suppression, most commonly seen with AZT (anaemia, neutropenia).
MITOCHONDRIAL DYSFUNCTION	Primarily seen with the NRTI drugs, including lactic acidosis, hepatic toxicity, pancreatitis, peripheral neuropathy, lipoatrophy, myopathy.
RENAL TOXICITY	Renal tubular dysfunction is associated with TDF. ATV can also cause nephrolithiasis.
OTHER METABOLIC ABNORMALITIES	More common with PIs. Include hyperlipidaemia, fat accumulation, insulin resistance, diabetes and osteopenia. Lipodystrophy is also associated with Zidovudine. The risk of cardiovascular events with Abacavir is still debatable.
ALLERGIC REACTIONS	Skin rashes and hypersensitivity reactions, more common with the NNRTI drugs but also seen with certain NRTI drugs, such as ABC and some PIs.

TABLE 2.7 GRADING OF ADVERSE EVENTS

GRADE	SEVERITY	ACTION
1	Mild	Transient or mild discomfort: no limitation in activity; no medical intervention/therapy required
2	Moderate	Limitation in activity- some assistance may be needed; minimal or no medical intervention required
3	Severe	Marked limitation in activity- some assistance usually required; medical intervention/therapy required- Hospitalization possible
4	Severe Life-threatening	Extreme limitation in activity - significant assistance required; significant medical intervention/therapy required; hospitalization and home-based care

2.9.1.2.1 Guiding principles in the management of ARV drug toxicity

1. Determine the seriousness of the toxicity.
2. Evaluate concurrent medications and establish whether the toxicity is attributable to an ARV drugs or to a non-ARV medication taken at the same time.
3. Consider other disease processes (e.g. viral hepatitis in an individual on ARV drugs who develops jaundice) because not all problems that arise during treatment are caused by ARV drugs.
4. Manage the adverse event according to severity:
 - Grade 4 (severe life-threatening reactions): Immediately discontinue all ARV drugs, manage the medical event (i.e. symptomatic and supportive therapy) and reintroduce ARV drugs using a modified regimen (i.e. with an ARV substitution for the offending drug) when the patient is stabilized.
 - Grade 3 (severe reactions): Substitute the offending drug without stopping ART.
 - Grade 2 (moderate reactions): Consider continuation of ART as long as feasible. If the patient does not improve on symptomatic therapy, consider single-drug substitutions.
 - Grade 1 (mild reactions) are bothersome but do not require changes in therapy.

5. Stress the maintenance of adherence despite toxicity for mild and moderate reactions.

6. If there is a need to discontinue ART because of life-threatening toxicity, all ARV drugs should be stopped until the patient is stabilized.

2.9.1.3 Monitoring of Efficacy

Indicators for improvement in the patient's condition are:

- Gain in body weight
- Decrease in frequency or severity of opportunistic infections
- Increase in CD4 count of 100-200 cells in the first year (this may be less if initial CD4 <50)
- Improvement in full blood counts
- Sustained suppression of viral load ³

2.9.2 LABORATORY MONITORING

Regular laboratory monitoring is necessary to identify side effects and toxicity of the ART and the immunological status of the patient.

The following ancillary tests should be done at least at 6 monthly intervals:

- Full blood count (patients on Zidovudine may require frequent Hb monitoring)
- Urine R/E
- Fasting Blood Sugar and Lipid profile (if the patient is on PIs)
- BUE and Creatinine
- Liver function tests (ALT, AST)
- TB screening and sputum test for AFBs should be done 6 monthly and chest X-ray done depending on clinical findings.

It is recommended that the CD4 count be done at initiation, at six months and annually thereafter.

It is recommended that HIV viral load testing should be done at initiation and at six months and annually thereafter. It provides evidence of the virological response to therapy. In a case of suspected failure, viral load must be done earlier.

(See Guidelines for Viral Load Monitoring APPENDIX 7)

³ Where viral load has been done

2.10 INTERRUPTION OF THERAPY

Interruption of therapy refers to the temporary or permanent discontinuation of all drugs at the same time. The administration of one or two drugs only should not be done for any reason as this may result in the development of resistant viruses. However the exception occurs when triple therapy includes Nevirapine or Efavirenz, in which case the Nevirapine or Efavirenz should be stopped abruptly while the other drugs are continued for a period of five days since they have long half-lives.

Interruption of therapy should be done by the clinician in consultation with the patient under the following circumstances:

- Intolerable side effects
- Severe drug interactions
- Poor adherence

2.11 CRITERIA FOR CHANGING THERAPY

The physician in consultation with the patient may change antiretroviral therapy under the following circumstances:

- Drug toxicity
- Treatment Failure

2.11.1 Drug toxicity

This refers to the inability of the patient to tolerate the side effects of the medication and/or significant organ dysfunction.

2.11.2 Treatment Failure

This can be defined clinically by disease progression, immunologically by a decrease in CD4 count or virologically by an increase in viral load. Treatment failure may occur soon after initiation as may be in a case of transmitted resistance viruses or may occur some time after treatment.

Virologic failure is defined as plasma HIV RNA >5000 copies/ml 6 months after initiating therapy in persons that are adherent to ART. This should be confirmed with a repeat test at six weeks before a switch to second line. For details on management of failure see Viral Load Monitoring guidelines (Appendix 8).

Note: If after one month of initiation of therapy there is significant increase in viral load then this indicates drug resistance.

Immunologic Failure is the return of CD4 counts to pre-therapy baseline or below and/or more than 50% fall from on-therapy CD4 peak level (and /or more than 50% change in CD4%), or persistent low CD4 of less than 100 cells/ml after one year of therapy without other concomitant infection to explain the low CD4.

Clinical failure is the occurrence of new opportunistic infection or malignancy signifying clinical disease progression, the recurrence of prior opportunistic infection or onset/ recurrence of WHO stage 3 or 4 conditions.

The main reasons for treatment failure are;

1. Poor prescribing practices
2. Poor adherence
3. Pre-existing viral drug resistance
4. Insufficient drug levels (serum and cellular)
5. Insufficient ARV potency.

2.12 REFERRALS AND LINKAGES

ART is only a part of the continuum of care in the comprehensive care package for PLHIV. Strong linkages within and outside the health system with other providers of care and support will further strengthen the effective management of patients. ART should have linkages with other comprehensive care services such as CT, PMTCT, DOTS Centres, Management of Opportunistic Infections, Nutritional Support, Home Based Care and Care for Orphans and Vulnerable Children, Psychosocial Support.

Referrals should follow the normal health system channels and in addition there should be networking with other stakeholders such as those in the community e.g. PLHIV associations, Home Based Care providers, Social workers and legal workers.

ART sites should form linkages with one another to facilitate referral and exchange of information and resources.

CHAPTER 3 **ARV IN CHILDREN < 13YEARS**

3.1 INTRODUCTION

The pathogenesis of Human Immunodeficiency Virus (HIV) infection and the general virologic and immunologic principles underlying the use of antiretroviral therapy are similar for all HIV-infected persons. However there are unique considerations for HIV-infected infants and children. These include:

- In-utero and perinatal exposure to antiretroviral medication in some infected children
- Differences in diagnostic evaluation in perinatal infection
- Differences in immunologic markers (i.e. CD4+ T cell count) in young children
- Changes in pharmacokinetic parameters with age due to the continuing development and maturation of organ systems involved in drug metabolism and clearance
- Differences in the clinical and virologic manifestations of perinatal HIV infection in growing, immunologically immature persons resulting in rapid progression of disease in some children
- Special considerations associated with adherence to treatment.

3.2 DIAGNOSIS OF HIV INFECTION

Early detection of HIV infection is important both for early intervention and optimizing individual therapeutic choices. This would significantly enhance survival and quality of life. Early Infant Diagnosis (EID) via HIV DNA PCR will facilitate early detection of HIV infected infants among all exposed babies for regular follow up and early treatment initiation.

Where virologic tests are not available however, exposed children must be followed up regularly till 18 months when the child's HIV sero-status will be confirmed. A child who tests negative after 18 months is not infected provided breastfeeding has stopped for at least 3 months earlier. In all cases, it is important for clinicians to have a high index of suspicion to clinically detect children who have HIV and AIDS and initiate early management to improve survival.

All infants and children with signs or symptoms suggestive of HIV infection and with other severe illness needing admission (including all cases of failure to thrive, severe malnutrition and

TB diagnosis) should undergo HIV serological testing according to national guidelines.

It should be noted that breastfed infants are at risk of HIV infection from an HIV infected mother during the entire period of breastfeeding, and a negative virologic or antibody test at a single point in time does not preclude the child from becoming infected at a later time if breastfeeding is continued. Extending ARV prophylaxis for infants or mothers during the period of breast feeding is effective in significantly decreasing the risk of HIV transmission.

The guidelines for HIV diagnosis in children less than 13 years using clinical criteria, specifically including AIDS defining conditions are shown below.

3.3 CRITERIA FOR DIAGNOSING HIV INFECTION IN CHILDREN

TABLE 3.1

A child is said to be HIV positive if the following criteria are met:

<p>1. A child < 18 months who is HIV antibody-positive or born to HIV positive mother: And</p> <ul style="list-style-type: none"> • HIV DNA positive by PCR (done at 6 weeks of age or 6 weeks after cessation of breastfeeding)
<p>2. A child < 18 months who is HIV antibody-positive: and</p> <ul style="list-style-type: none"> • who meets the clinical criteria for AIDS diagnosis based on the WHO staging system for a presumptive diagnosis of AIDS (see appendix 2) <p>and/or</p> <ul style="list-style-type: none"> • CD4% < 25% (CD4 750 cells/mm³) <p>Confirm HIV infection with DNA PCR as soon as practicable or at 18 months with HIV antibody test.</p>
<p>3. A child ≥18 months who is HIV antibody-positive</p>

NB: Always record the HIV type (HIV 1, HIV 2 or HIV 1+2) based on mother's antibody for treatment decision making.

3.4 INITIATION CRITERIA

3.4.1 INCLUSION CRITERIA

The criteria for the Initiation of ART for children are dependant on the age of the child, presence of HIV antibody or PCR tests and the CD4 (%). The table below shows the criteria.

TABLE 3.2 INCLUSION CRITERIA FOR ART

Age	HIV Diagnostic testing	Treatment Recommendation
<18 months	DNA PCR not available HIV antibody sero-positive	Treat if WHO Paediatric Presumptive Stage 4 disease irrespective of CD4 %.(Refer Appendix 2(B)) Where CD4% is available, start treatment when CD4% is <25% (CD4 750 cells/mm ³) However, repeat HIV antibody test at 18 months or as soon as virologic test becomes available to confirm infection
	Positive HIV DNA PCR and <24months	Treat all children irrespective of CD4% and WHO clinical staging
≥18 months to 59 months	HIV antibody positive	All WHO Paediatric Stage III and IV irrespective of CD4%
		WHO Stage I and II with CD4% <25% (CD4 750 cells/mm ³) NB: All <24months should be treated.
5-13 years	HIV antibody positive	<ul style="list-style-type: none"> ➤ All WHO Paediatric Stage 3 and IV irrespective of CD4 count ➤ CD4 count < 350 cells/mm³ irrespective of clinical stage

3.4.2 EXCLUSION CRITERIA

Antiretroviral therapy shall not be initiated under the following circumstances:

1. Lack of parental or guardian motivation or when they are in denial
2. Treatment not sustainable
3. No basic laboratory test available for initiation and monitoring of ART e.g. full blood count
4. Patient presents with end stage hepatic or renal insufficiency
5. The patient has an acute opportunistic infection. (This must be treated before the initiation of ART)
6. Caregiver or guardian not completed pre-treatment adherence counselling
7. Lack of a reliable caregiver

3.5 CLINICAL EVALUATION

A detailed clinical evaluation is essential prior to initiating ART.

The aims of evaluation of the HIV-infected Child are to:

- Confirm HIV infection
- Assess the clinical staging of HIV infection
- Identify past HIV related illnesses
- Identify current HIV related illnesses that will require treatment
- Identify co-existing medical conditions that may influence the choice of therapy
- Document past ARV treatment/prophylaxis experience

These can be achieved by:

- Taking a detailed medical and social history
- Carrying out a complete physical examination and
- Appropriate laboratory investigations.

The Medical History should include:

- Date of initial HIV diagnosis
- Current symptoms and concerns
- Immunization history
- Birth and neuro-developmental history
- Nutritional history
- Child's drug (including ARV for PMTCT) history
- History of TB or contact with a TB patient (mother especially)
- Mother's pregnancy and drug, (including ARV) history

Examination should include:

- weight
- height
- weight for height Z-score
- Head circumference
- Mid Upper arm Circumference in children 1 to 5 yrs of age

(For further details of the clinical evaluation see chapter 2)

3.6 LABORATORY EVALUATION

The reasons for investigation are to:

- Determine whether patient satisfies initiation criteria
- Determine the presence or absence of opportunistic infections
- Determine the immunological Stage of HIV infection

(For details of the laboratory evaluation see chapter 2)

3.7 RECOMMENDED TREATMENT REGIMEN

Treatment regimen in children shall be similar to adult regimen. Only triple therapy shall be utilized and shall consist of:

- 2 NRTI plus 1 NNRTI
- 2NRTI plus 1 boosted PI
- Triple NRTI in some special circumstances

The antiretroviral regimen used in paediatric patients may vary depending on the following:

- Antiretroviral naive mother (Patients whose mother has not had any previous exposure to antiretroviral drugs)
- Antiretroviral experienced mother (especially single dose Nevirapine or treatment failure)

3.7.1 FIRST LINE DRUGS

The first line drugs for Ghana are indicated in the table below.

TABLE 3.3: RECOMMENDED FIRST LINE COMBINATIONS

	Drugs	Contra- indications	Comments
First Choice Drugs	First Option Zidovudine + Lamivudine + Nevirapine	Nevirapine is contraindicated in: -liver dysfunction -hypersensitivity	Replace with Efavirenz (if child is more than 3 years and more than 10Kg)
		Zidovudine is contraindicated in: severe anaemia (Hb < 8gm/dl)	Replace with Abacavir
	Second Option Zidovudine + Lamivudine + Efavirenz	Efavirenz is: containdicated in Children less than 3 years or less than 10Kg.	Replace with Nevirapine
		Contraindicated in Efavirenz related Persistent CNS toxicity	Replace with Nevirapine

	Drugs	Contra- indications	Comments
Second Choice Drugs	First Option Abacavir + Lamivudine + Nevirapine		Abacavir should be used when Zidovudine is contraindicated e.g. anaemia
	Second Option Abacavir + Lamivudine + Efavirenz		Abacavir should be used when Zidovudine is contraindicated e.g. anaemia
		Efavirenz is: contraindicated in Children less than 3 years or less than 10Kg	Replace with Nevirapine
		Contraindicated in Efavirenz related Persistent CNS toxicity	Replace with Nevirapine

NOTE:

- Emtricitabine can be used in children over 3 months of age as an alternative to Lamivudine.
- Tenofovir may be used in place of Zidovudine or Abacavir for children more than 12 years of age.

3.7.2 SECOND LINE DRUG

The second line drugs for Ghana are indicated in the table below.

TABLE 3.4: RECOMMENDED SECOND LINE COMBINATIONS

	Initial First-line regimen	Preferred second-line regimen	Contra-indications/caution	Comments
First Choice Drugs	Zidovudine + Lamivudine + Nevirapine or Efavirenz	<p>1a. Abacavir + Lamivudine + Lopinavir/r</p> <p>1b. Tenofovir + (Emtricitabine or Lamivudine) + Lopinavir/r (if child is more than 12 years)</p> <p>{TDF+FTC Fixed-dose combination can be used}</p>	<p>In case of hypersensitivity to Abacavir,</p> <p>In case of renal insufficiency while on Tenofovir</p>	<p>Consider Tenofovir if more than 12 years</p> <p>Adjust dose of Tenofovir according to creatinine clearance</p>
Second Choice Drugs	Abacavir + Lamivudine + Nevirapine or Efavirenz	<p>2a. Zidovudine + Lamivudine + Lopinavir/r</p> <p>2b. Tenofovir + (Emtricitabine or Lamivudine) + Lopinavir/r (if child is more than 12 years)</p> <p>{TDF+FTC Fixed-dose combination can be used}</p>	<p>In case of renal insufficiency while on Tenofovir</p>	<p>Adjust dose of Tenofovir according to creatinine clearance (Refer appendix Sampson)</p>

For drug dosages and characteristics see Appendix 4.

NOTE: Tenofovir is not recommended in pre-pubertal children (less than 12 years) due to safety and toxicity concerns over bone mineralization.

3.7.3 CONSIDERATIONS FOR SALVAGE THERAPY (THIRD-LINE)

In the case of failed second line, salvage therapy may be constructed. The goal in such situations is to attempt to reduce the viral load to undetectable levels and to improve the quality of life of the patient by balancing benefits and risks for the child. It is important to do mutational analysis (genotyping) to know the type of mutations involved to be able to construct a third-line regimen using novel regimen of different classes of ARVs (Integrase Inhibitors, Second generation NNRTIs and PIs) Where the failing regimen is not tolerable, treatment can be stopped and focus should be on prevention of OIs, relief of symptoms and management of pain needs. In all these cases refer to a specialist in ART.

3.7.4 SPECIAL CONSIDERATIONS

3.7.4.1 Previous Exposure to Antiretrovirals

In initiating a child on HAART, it is important to consider issues relating to drug resistance in a child who has gone through PMTCT or born to a mother who is on HAART. This should be undertaken in consultation with a specialist in ART.

3.7.4.2 Treatment of TB/HIV co-infection

Any child with active TB disease should begin TB treatment immediately, and start ART, as soon as tolerated, within the first 8 weeks of TB therapy, irrespective of the CD4 count and clinical stage.

- The preferred first-line ARV regimen for infants and children less than 3 years of age who are taking a rifampicin-containing regimen for TB is:
 - 2NRTIs + NVP (in this case the dose of NVP should be 200mg/m² and no Lead-in dose)
 - Or
 - Triple NRTIs (ABC/AZT/3TC).

Revert to standard first-line upon completion of TB treatment.
For more information see Chapter 2.

- The preferred first-line ARV regimen for children more than 3 years of age who are taking a rifampicin-containing regimen for TB is 2 NRTIs + EFV.

NOTE: Refer Appendix 2(D) for algorithm on diagnosis of tuberculosis in children.

3.7.4.3 Developing TB while on HAART

- In all HIV-infected children on HAART who develop TB, anti-TB therapy should be started immediately while continuing HAART;
- Make adjustments to ART regimen as needed to decrease the potential for toxicities and drug interactions:
 - If on a regimen of 2 NRTIs + NVP, substitute EFV for NVP if the child is 3 years or more in age
 - If on a regimen of 2 NRTIs + NVP and substitution with EFV is not possible, ensure NVP is dosed at the maximum of 200 mg/m² per dose twice daily
 - If on a regimen of LPV/r, consider adding RTV in a 1:1 ratio of LPV: RTV to achieve a full therapeutic dose of LPV.

3.7.4.4 Treatment of HIV and Hepatitis B Co-infection

- For children less than 12 years, it is anticipated that PENTAVALENT vaccine in Ghana will cover all immunized children. However, when a child in this age group is diagnosed with HIV and HBV co-infection, refer to a specialist for initiation of HAART
- For children above 12 years of age with hepatitis B, the preferred regimen is Tenofovir (TDF) + (Emtricitabine (FTC) or Lamivudine (3TC) + NNRTI (Efavirenz preferred).

3.7.4.5 Patients with HIV-2 and HIV 1+2 DUAL Infection

- Use a PI –based regimen in place of NNRTI

3.7.4.6 Treatment Changes

Therapy changes are similar for adults and children (see adult section Chapter 2 for interruption of therapy and criteria for changing therapy).

In children, (in addition to the clinical signs stated for adults in chapter 2) important clinical signs of treatment failure include:

- A lack of growth among children who show an initial growth response to therapy;
- A loss of neurodevelopment milestones
- Development of encephalopathy;
- Recurrence of infections, such as oral candidiasis refractory to treatment.

Before an ARV regimen is thought to be failing, based on clinical criteria, the child should have had a reasonable trial on the ARV therapy (i.e. must have received the ARV for at least 6months).

A switch to a second-line regimen is recommended when:

- Clinical failure is recognized, and/or
- Immunological failure is recognized, and/or
- Virological failure is recognized.

Virological failure is recognized as a persistent VL above 5,000 RNA copies/ml, after at least 6 months on ART, in a treatment-adherent child.

Immunological failure is defined as developing or returning to the following age-related immunological thresholds after at least 24 weeks on HAART, in a treatment-adherent child:

- For children < 2 years, always consult a specialist on switching to second-line
- CD4 count of <250 cells/mm³ or %CD4 <15% for a child >2 years but <5 years of age
- CD4 count of <250 cells/mm³ for a child 5 years of age or older.

Clinical failure is defined as the appearance or reappearance of WHO clinical stage 3 or stage 4 events after at least 6 months on HAART in a treatment-adherent child.

TABLE 3.5 WHO CLINICAL STAGING OF EVENTS TO GUIDE DECISION-MAKING ON SWITCHING TO SECOND-LINE THERAPY FOR TREATMENT FAILURE

New or recurrent clinical event develops after at least 6 months on ART	Management options
No new events or Stage 1 events	Do not switch to new regimen Maintain regular follow-up
Stage 2 events	Treat and manage event Do not switch to a new regimen Assess adherence and offer support Assess nutritional status and offer support Schedule earlier visit for clinical review and CD4 measurement
Stage 3 events	Treat and manage event and monitor response Check if on treatment 6 months or more Assess adherence and offer support Assess nutritional status and offer support Check CD4 where available Institute early follow-up
Stage 4 events	Treat and manage event Check if on treatment 6 months or more Assess adherence and offer support Assess nutritional status and offer support Check CD4 and viral load where available Consider switching regimen

TABLE 3.6 DECISION-MAKING ON SWITCHING TO SECOND-LINE ART FOR TREATMENT FAILURE BASED ON AVAILABILITY OF CD4 MEASUREMENT

New or recurrent clinical event on ART	Availability of CD4 measurement	Management options
	CD4	<p>Consider switching regimen only if two or more values (repeated at 3 month interval) are below the age-related threshold.</p> <p>Increase clinical and CD4 follow-up if CD4 value approaches the age-related threshold.</p> <p>Make effort to measure VL if available.</p>
	CD4	<p>Switching regimen is recommended if CD4 value is below the age-related threshold repeated at 3 month interval and particularly if the child initially had a good immune response to ART.</p> <p>Make effort to measure VL if available.</p> <p>Increase clinical and CD4 follow-up if CD4 value approaches age-related threshold.</p>
Stage 4 event	CD4	<p>Switching regimen is recommended if CD4 value is below the age-related threshold repeated at 3 months interval and particularly if the child initially had a good immune response to ART.</p> <p>Switching may not be necessary where CD4 value is above age-related threshold.</p> <p>Make effort to measure VL.</p>

Decision-making on switching ART using viral load measurement

Children with clinical failure and/or immunological failure may not all have virological failure, and may not need to switch to second-line therapy. However, a delay in switching therapy in a child with high levels of viral replication may lead to greater development of resistance and compromise the virological activity of standard second-line regimens. Therefore, in the context of accurately identifying treatment failure, measurement of viral load is useful. Viral load is recommended where available to confirm clinical and/or immunological failure.

3.8 DRUG ISSUES

Drug interactions for children are similar to those of adults. (See chapter 2 and Appendix 3 for further information). Drug dosing in children is dependent on weight and surface area. Therefore it is necessary to calculate the dosage at each clinical review if the weight and height varies significantly. (See Appendix 4 for further information)

3.9 MONITORING

3.9.1 CLINICAL MONITORING

Clinical monitoring of children on ARVs is similar to the monitoring in adults. (See Chapter 2). Specifically follow up visits for infants are to be done at weeks 2, 4 and then every four weeks for the whole year of infancy.

Important clinical signs of response to ARV therapy in children include:

- Improvement in growth of children previously failing to grow;
- Improvement in neurological symptoms
- Development in children with delayed developmental milestones or encephalopathy;
- Decreased frequency of infections (oral thrush, bacterial and other opportunistic infections).

In addition to the clinical assessment recommended in adults, clinical monitoring of treatment in children should include:

- Nutritional status: mid-upper arm circumference,
- Height, weight and head circumference
- Weight for height Z-score
- Developmental milestones
- Neurological symptoms and signs

3.9.2 LABORATORY MONITORING

Laboratory tests are essentially the same in adults and children except in CD4 assay where the CD4% is the preferred parameter for children up to five years of age. See Chapter 2.

3.9.3 MONITORING OF ADHERENCE

Adherence counselling must involve the child, parents and/or guardian who will be administering the medication. See Chapter 2.

3.9.4 MONITORING OF EFFICACY

See Chapter 2.

CHAPTER 4

MANAGEMENT OF HEPATITIS B VIRUS COINFECTION WITH HIV

4.1 INTRODUCTION

Hepatitis B virus (HBV) infection is common and endemic in Ghana. The routes of transmission of HIV and HBV are very similar, hence the occurrence of HIV and HBV co-infection. The prevalence of HBV infection in Ghana is estimated at 15% of the adult population.

With the advent of HAART and the subsequent improvement in the morbidity and mortality in PLHIV, liver disease from HBV co-infection will become a significant cause of morbidity and mortality as is occurring in countries with a longer treatment experience. HBV does not seem to affect the natural history of HIV infection although there is an increased rate of liver side effects of HAART in those co-infected. HBV reactivation and re-infection seem to be increased in PLHIV.

Observational data demonstrate that individuals with HIV/HBV co-infection have a three to six fold increased risk of developing chronic HBV infection, an increased risk of fibrosis and cirrhosis and a 17-fold increased risk of death compared to HBV-infected individuals without HIV infection. Similarly, observational data support a reduction in liver-related disease with earlier management of HBV with active combination ART. (Ref: WHO Recommendations on ART, 2010).

The rate of response to anti-HBV infection treatment seems to be less in PLHIV than in HIV negative patients. HIV infection also increases the chance of chronicity of HBV infection and progression to cirrhosis and hepatic cell carcinoma. Despite the co-infection, there is increased chance of HBV suppression with sustained control of the disease and significant reduction of the development of cirrhosis and hepatic cell carcinoma with treatment of HBV.

4.2 ASSESSMENT OF ALL HIV+ PATIENTS FOR HEPATITIS B INFECTION

- All PLHIV should be tested for Hepatitis B surface antigen (HBsAg) as part of baseline tests.
- If HBsAg negative, vaccination against HBV is recommended.
 - Start HAART before vaccination to ensure good response.
 - In children if CD4% indicates severe immunosuppression, start HAART before vaccination.

4.3 GENERAL MANAGEMENT OF HEPATITIS B VIRUS INFECTION IN PLHIV

A positive HBsAg test indicates acute or chronic infection of HBV.

4.3.1 ACUTE HBV INFECTION

- The management of acute HBV infection in HIV follows the symptomatic approach as there is no specific treatment of acute HBV infection.
- Repeat HBsAg after 6 months.
 - If negative, acute infection is over
 - If positive, chronic infection indicated. Refer 4.3.2 below.

4.3.2 CHRONIC HBV INFECTION

Chronic HBV infection is defined as a positive HBsAg test result for six months or more. Patients with chronic HBV infection should be evaluated as follows.

1. Assess for liver damage
 - All HIV/HBV co-infected patients should be assessed for liver disease status and risk of progression. This should include a clinical history, examination and blood tests including Liver Function Test (LFT) and clotting studies and HBV infection specific markers if available.
 - Blood Alanine transferase (ALT) level is the most cost effective indicator of liver damage. Patients with normal ALT levels generally do not need treatment or further investigation.
 - If the ALT is increased the HBV viral load may be done, if available. This will help determine whether the liver damage is due to HBV.
2. Screen for liver cancer every 6 months
 - Perform ultrasound
 - Take blood for alpha-fetoprotein (AFP) where testing is available
 - Both tests are needed as AFP is raised in only 60% of cases of liver cancer and ultrasound alone may miss 20% of liver cancers. These tests should be performed regularly and indefinitely. Liver cancer usually develops between 35 and 65 years.
3. Prevent liver damage from other causes
 - Counsel patient to abstain from alcohol
 - Drugs, food supplements and herbal preparations that may injure the liver should be avoided
4. Prevent transmission to others
 - Have family members and sexual contacts screened for HBV infection and vaccinated as appropriate.

- Counsel patient to prevent transmission of HBV to others.
- New born babies should receive hepatitis B Immunoglobulin (HBIG) and hepatitis B vaccine as per national EPI guidelines.

It should be noted that Liver biopsy and HBV viral load are not currently widely available in the country.

4.4 TREATMENT OF HEPATITIS B VIRUS INFECTION IN HIV/HBV CO-INFECTION

While the general rule is that all OIs should be treated first in PLHIV, there is an optimal time for initiating anti-HBV treatment in co-infected patients. Treatment should be individualized according to the status of the patient.

The patient's status is determined by the extent of liver damage and the extent of HBV replication. Another important consideration in the treatment of HBV is whether the PLHIV is on HAART or is due to start HAART as these affect the choice of anti-HBV medicine.

- Start ART in all PLHIV with chronic HBV infection (HIV/HBV co-infected) individuals irrespective of the CD4 cell count or the WHO clinical stage.
- Start TDF and 3TC (or FTC)-containing antiretroviral regimens in all HIV/HBV co-infected individuals.
 - The preferred first line regimen for the treatment of both HIV and HBV is
Efavirenz+Lamivudine+Tenofovir
(EFV + 3TC + TDF)
 - The alternate is
Efavirenz+Emtricitabine+Tenofovir
(EFV + 3TC + TDF)
- The combination of 3TC and TDF **should be continued if there** is good HBV response when HIV resistance to the first line HAART occurs. In such a situation, the second line regimen should consist of 3TC, TDF and LPV/r.

The treatment algorithm for HIV/HBV Co-infection is shown in Appendix 5.

4.4.1 MONITORING OF HIV/HBV TREATMENT

- Patients should be monitored every 6 months by checking ALT levels while on treatment.

- Where facilities are available, viral load for HBV, in addition to ALT levels, may be used to determine the initiation and treatment.
- All patients who have an unexpected rise in ALT should be screened again for HBV.

CHAPTER 5

POST EXPOSURE PROPHYLAXIS FOR HEALTH CARE WORKERS AND RAPE SURVIVORS

5.1 HEALTH CARE WORKERS

5.1.1 INTRODUCTION

The risk of exposure to blood and blood borne pathogens is slightly greater for health care personnel than people who do not work in health care settings. Workplace accidents or injuries that expose the health worker to body fluids of a patient may occur. Post Exposure Prophylaxis (PEP) reduces the likelihood of HIV infection after exposure. PEP may either prevent the establishment of infection or prevent new infection while allowing clearance of already infected cells. PEP is particularly effective within 1 –2 hours and not more than 72 hours after exposure.

5.1.2 RISK

An exposure that would create a risk may be defined as an exposure from infected blood, tissue or other body fluids through:

- A percutaneous injury (e.g. a needle stick or cut with a sharp object),
or
- A mucocutaneous membrane or non-intact skin (e.g. skin that is chapped, abraded, or affected by dermatitis) contact

The risk of infection for HIV after a percutaneous injury is approximately 0.3%. Transmission rates after exposures of mucous membrane or non-intact skin are lower than from percutaneous injuries.

The risk of infection appears higher after:

- Exposure to a large quantity of blood or to other infectious fluids
- Exposure to the blood of a patient in an advanced HIV disease stage
- A deep percutaneous injury
- An injury with a hollow bore, blood filled needle.

5.1.3 PREVENTION

All infection prevention programmes should be in place and health workers should follow Standard Precautions at all times to prevent exposure.

- Hands should be washed properly and frequently before and after handling all patients.
- Gloves must be worn before any kind of invasive procedure or when venous or arterial access is being performed.
- Personal Protective Equipments (Gloves, gowns, boots eye wear and masks) should be used appropriately for patient care.
- Sharps should be used with caution with all patients
 - Sharps should be disposed of in a puncture proof receptacle immediately after use. These should be available nearby.

5.1.4 STEPS TO PREVENT OCCUPATIONAL TRANSMISSION OF HIV

In the event of possible exposure to HIV the following actions should be taken:

5.1.4.1 PEP STEP 1: TREATMENT OF EXPOSURE SITE:

- The wound site should be cleaned with soap and water
- In the case of mucous membranes, exposed area should be flushed with plenty of water.
- Eyes should be flushed with water or saline.

5.1.4.2 PEP STEP 2: ASSESS THE LEVEL OF RISK

The risk of exposure should be assessed in terms of possible transmission of HIV infection. Exposure to HIV may be classified in three categories as described below:

5.1.4.2.1 Very Low risk exposure

- Exposure of potentially infectious material to intact skin.

5.1.4.2.2 Low risk exposure

- Exposure to a small volume of blood or body fluids contaminated with blood from asymptomatic HIV-positive patients.
- An injury with a solid needle.
- Any superficial injury or mucocutaneous exposure.

5.1.4.2.3 High-risk exposure

- Exposure to a large volume of blood or potentially infectious fluids

- Exposure to blood or body fluids contaminated with blood from a patient with a high viral load. i.e. patients in the AIDS phase or early sero-conversion phase of HIV infection.
- Injury with a hollow bore needle
- Deep and extensive injury from a contaminated sharp instrument.
- Exposure to blood from an HIV Drug resistant patient.

5.1.4.3 PEP STEP 3: Specific PEP management

5.1.4.3.1 Counselling and Testing:

- All health care workers accessing PEP must receive counselling and testing immediately from a trained counsellor. This should continue throughout the PEP period and thereafter if necessary. Where an exposed individual declines to test for HIV infection after counselling, this must be documented.
 - Counsellor must emphasize safe sex including condom use.
 - All known source-patients shall also be counselled and tested for HIV infection if this is not known.
2. Timing of PEP initiation.
If therapy is necessary, it should be initiated promptly, preferably within 1-2 hours post-exposure and not more than 72 hours after exposure.
 3. Specific treatment for PEP is described in the table below.

Table 5.1: Recommended PEP

RISK LEVEL	RECOMMENDED PROPHYLAXIS
Very Low risk	Wash exposed area immediately with soap and water
Low risk	Zidovudine 300mg 12 hourly x 28 days Lamivudine 150mg 12 hourly x 28 days
High risk	Zidovudine 300mg 12hourly x 28 days

	Lamivudine 150mg 12 hourly x 28 days Lopinavir/r 400mg/100mg 12hourly x 28days
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NB: If the source patient is HIV/HBV co-infected then use a TDF containing regimen.

5.4.4 PEP STEP 4: Follow up

During the period of prophylaxis a number of base-line and follow-up investigations need to be done to determine HIV sero-status, and to monitor the level of drug toxicity. Table 5.2 indicates these laboratory tests.

Table 5.2: Recommended monitoring of drug toxicity and HIV serology of exposed health care personnel.

Baseline tests:	Full blood count Liver and renal function tests, Hepatitis B Surface Antigen HIV serology or PCR if available
Two weeks:	Full blood count Liver and renal function tests
Six weeks:	HIV serology
Three months:	HIV serology
Six months:	HIV serology

Individuals who sero-convert should have access to comprehensive care and ART services as spelt out in the “Workplace HIV and AIDS Policy and Technical Guidelines for the Health Sector”⁴. For further information refer to this document.

5.4.5 PEP STEP 5: Reporting and Documentation

All occupational exposures should be reported immediately to the supervisor; circumstances of the exposure and PEP management should be recorded. Details should include:

- Date and time of exposure

⁴ Workplace HIV/AIDS Policy and Technical Guidelines for the Health Sector, Ministry of Health, August 2004

- Where and how the exposure occurred, exposure site on the body and type of sharp device. Type and estimated amount of exposure fluid, severity (depth/extent) of the exposure
- Source of exposure and whether the source material contained HIV or blood.
- Clinical status of source patient.
- Relevant information about exposed health care worker(medical conditions, vaccination including Hepatitis B, and medications, pregnancy or breast-feeding)
- Document counselling, post exposure management and follow up

RAPE SURVIVORS

5.5: INTRODUCTION

Ghana has in recent times seen an upsurge of violent crime including sexual violence of various forms such as rape and defilement. Rape and defilement are violent traumatic experiences for the survivors who are affected physically, emotionally and socially. Survivors may react in different ways to such traumatic experiences and they may have to be handled and managed cautiously in order not to aggravate their psychological trauma. Survivors could be women or men, boys or girls; but most often, women and girls are the victims and the perpetrators are usually men.

It is important to recognize that rape and defilement are criminal offences in Ghana. Survivors and the general public should be encouraged to report such occurrences to law enforcement agencies. The healthcare provider must therefore be abreast with the legal requirements regarding the management of the survivor. This includes documentation and reporting as well as the provision of emergency contraception, abortion, counselling, testing and prevention of STIs such as HIV infection. Healthcare workers must understand that their duty is to provide basic medical and psychological intervention to survivors and referral to relevant agencies for other needed services.

5.6: MEDICO-LEGAL FRAMEWORK

- These guidelines are to be used in the context of the clinical management of survivors of sexual assault within the regular healthcare setting. This includes screening and treatment of sexually transmitted infections (STIs), provision of PEP for HIV and the rendering of psychological support.
- These guidelines focus on adult female victims of sexual assault but the principles are the same in the management of adult male victims as well as for minors.
- This document should not to be used as an absolute guide for a forensic examination and the collection of specimens for prosecution. Such a requirement will need a referral to a gynaecologist, a clinician trained in forensic medicine, or other specialist.
- There are no conclusive data on the effectiveness of PEP in preventing transmission of HIV after the occurrence of rape. Experience with prophylaxis relating to occupational exposure and prevention of mother-to-child transmission (PMTCT) however suggest that starting PEP as soon as possible and indeed within 72 hours after the rape is most beneficial.

- The identification of a sexually transmitted infection (STI), counselling and testing for HIV in the aftermath of rape is important.
- Healthcare providers must appreciate that the establishment of the case of rape is a legal matter to be determined by a court of competent jurisdiction and not a decision for the healthcare worker to make. The healthcare worker is providing a service with the presumption that there has been an alleged case of rape or defilement which may or may not be proven.
- Although only a small percentage of alleged rape cases actually go on trial, it is important that the healthcare worker keeps detailed and accurate documentation in the event of the need to testify in court.
- For the purpose of these guidelines, the term “rape” means “rape, defilement or non-consensual unnatural carnal knowledge”.

5.7: SERVICE DELIVERY POINTS

- i. Service is to be provided within the existing healthcare service delivery system where PEP is administered.
- ii. Establishment of linkages and referral to and from gynaecologists, clinicians trained in forensic medicine or other medical practitioners and psychosocial service providers.

5.8: CLIENT ENTRY INTO CARE AND REFERRALS

- i. A Client who reports directly to a facility following an alleged incident of rape is:**
To be assessed by a clinician and appropriately counselled for the administration of needed interventions. Client may be referred to the following for further care and action:
 - a. PEP focal person
 - b. Gynaecologist
 - c. Family planning service provider
 - d. Psychosocial service provider
 - e. The Ghana Police Service
- ii. Client referred from another service provider who has already assessed and examined the client and is just referring the client for PEP:**
PEP provider must be satisfied that the client has indeed been attended to by the said service provider and appropriately referred as evidenced by a referral note, and then proceed to provide PEP.

- iii. Client referred from the Ghana Police Service or a Court of competent jurisdiction:**
Assess and manage as under (i) above.

5.9: ASSESSMENT

- i. Take accurate and detailed history, considering the fact that this could be very sensitive and emotionally traumatic for the client.
- ii. Ensure right to privacy, confidentiality, information and non-discrimination.
- iii. Clarify the kind of sexual assault and orifices involved in the assault.
- iv. Determine whether the perpetrator constitutes a high risk or otherwise
- v. Find out the sexual history of the client both before and after the assault.
- vi. Assess the overall risk of client
- vii. Perform all relevant physical and genital examinations, and collect forensic evidence as may be required by law if you are the clinician primarily responsible for the case. (See Appendix)
- viii. Offer counselling and testing for HIV and screen for other STIs including Syphilis, Hepatitis B where screening tests are available.
 - a. Where client is found to be HIV positive, she/he must be counselled and referred to an ART centre for comprehensive HIV care and support services.
 - b. Treat any STIs found or suspected on screening.
- ix. In the case of a child survivor:
 - a. History should be taken from both the minor and the parent or legal guardian.
 - b. It is preferable to have the parent or guardian wait outside during the interview and have an independent trusted person/chaperone present. Avoid asking leading questions
 - c. For the examination either a parent and/or chaperone must be present.
 - d. Document all findings of the assessment and interventions including the outcome of the HIV test, STI and Hepatitis B screening.
- x. Where the client declines to undertake the HIV test, document this refusal and make client fill and sign The National PEP and Management Record Form for Rape Survivors indicating the refusal.

5.10: EVALUATION OF RISK

The following factors must be considered in the assessment of risk:

- a. Perpetrator is unknown or HIV status of perpetrator is unknown.
- b. Perpetrator's HIV status is known to be positive.
- c. Perpetrator is an injection drug user or armed robber.
- d. Where the alleged sexual violation involved anal penetration.
- e. Where the survivor was allegedly raped by more than one person.
- f. Vaginal penetration with associated genital injuries.
- g. Where survivor is a minor.

5.11: PROTOCOL FOR PEP AND PREVENTIVE TREATMENT OF STI

i. Survivor Presents within 72 Hours of the Incident

- a. Prevent HIV Transmission through the provision of PEP using three ARVs according to national protocol and as spelt out under Appendix.
- b. Treat STIs according to national guidelines.
- c. If HBsAg result is negative prevent Hepatitis B infection by initiating the appropriate vaccination protocol.
- d. Pregnancy can be prevented by providing emergency contraception, using as appropriate, either oral contraceptive pills or intrauterine device (IUD) in accordance with the provision of the "National Reproductive Health Service Policy and Standards, Second Edition, December 2003". Pregnancy test must be done to first exclude an existing pregnancy.
- e. Clean and treat any tears, cuts, abrasions and other injuries. If there are major contaminated wounds consider giving antibiotic cover. Also give tetanus prophylaxis (tetanus toxoid – TT) where there are wounds or break in mucosa.

ii. Survivor Presents More than 72 Hours after the Incident

- a. PEP is not required as it would not be effective. Client must be offered CT and appropriate follow up instituted.

- b. Assess and examine for STIs and provide treatment according to national STI treatment guidelines.
- c. If HBsAg test result is negative recommend vaccination against Hepatitis B infection, using the appropriate protocol.
- d. If the survivor presents after 72 hours but within 120 hours provide emergency contraception, using as appropriate, either oral contraceptive pills or intrauterine device (IUD) in accordance with the provisions of the “National Reproductive Health Service Policy and Standards, Second Edition, December 2003”. Pregnancy test must be done to first exclude an existing pregnancy.
- e. Treat or refer all wounds, abscesses and other injuries and complications. Vaccinate against tetanus if client has not been fully vaccinated.

5.12: FOLLOW-UP CARE

- i. For Survivors who received PEP.**
 - a. One-week follow-up visit:
 - i. Evaluate PEP, STI and other treatment.
 - ii. Evaluate for STI and provide treatment as appropriate.
 - iii. Discuss CT for future HIV testing.
 - b. Six-week and three-month follow-up visits:
 - i. Offer CT for HIV
 - ii. Evaluate for STIs and treat as appropriate
 - iii. Evaluate for pregnancy and provide counselling
- ii. For Survivors who do not receive PEP.**
 - a. Two-week follow-up visit:
 - i. Check if STI and/or other treatment have been adhered to.
 - ii. Evaluate for pregnancy and provide counselling
 - iii. Discuss CT for future HIV testing
 - b. Three-month follow-up visit:
 - i. Offer CT for HIV
 - ii. Evaluate for STIs and treat as appropriate
 - iii. Assess pregnancy status

In all cases evaluate mental and emotional status at every visit, and refer or manage as needed. For minors assess the safety of their environment (Place of residence and school etc) for possible re-location.

5.13: DOCUMENTATION

- i. All information gathered from history, referral notes, assessments, and from physical and genital examination must be clearly documented, dated, signed and appropriately filed under strict confidentiality.
- ii. Document all referrals to and from or within your facility
- iii. Fill all forms required under these guidelines and according to national policies and guidelines.
- iv. Note that proper documentation will facilitate testimony in a court of law.

CHAPTER 6

GUIDELINES ON ART COUNSELLING

6.1 INTRODUCTION

Counselling for ART complements all ongoing counselling for CT, PMTCT and follow up counselling for psychosocial support. The following guidelines are available to support general counselling and counselling of clients on ART:

- National Guidelines for the Development and implementation of HIV Counselling And Testing in Ghana⁵
- National Guidelines for Prevention of Mother-to-Child Transmission of HIV⁶
- CT Training Manual⁷

6.2 GOAL OF COUNSELLING IN ART

The goal of counselling is to help the patient to understand issues in order to make an informed decision to start and also to adhere to a life-long treatment. Patients need to be counselled both prior to initiation of ART and during therapy and indeed counselling should be ongoing.

Specifically the patient should understand the following issues described in these guidelines:

- The Goals of therapy
- The fact that ART is not a cure.
- The virus can still be transmitted while on ART and so preventive measures should still be applied.
- ART is a life-long commitment.
- Financial considerations.
- Drug information.
- Adherence to drug therapy.
- Disclosure.
- Emotional and Social Support.
- Nutrition

Counselling sessions for ART should also complement the general counselling for HIV and AIDS. ART should not be initiated until the patient has had at least 2 counselling sessions

⁵ Ministry of Health/Ghana Health Service/Ghana AIDS Commission, National Guidelines for the Development and implementation of HIV Voluntary counselling And Testing in Ghana

⁶ Ministry of Health/ Ghana Health Service, Prevention of Mother-to-Child Transmission of HIV in Ghana Manual for Health Workers, Ghana 2001

⁷ MOH/GHS VCT Training Manual'

on ART and he/she fully understands the implications of starting treatment.

Patients who are not motivated and/or who do not complete pre-treatment adherence counselling should continue to be supported by the adherence counselling team to become motivated and committed to life long therapy.

ARV should not be dispensed to any patient unless he/she has had adequate adherence counselling.

6.2.1 The Goals of Therapy

The patient should understand that the goals of therapy are to:

- make the patient clinically better,
- produce sustained and durable suppression of viral load
- reduce HIV-related morbidity and mortality,
- restore or preserve immune function and to prevent opportunistic infections.

All these lead to an improved quality of life for HIV infected individuals.

6.3 Antiretroviral Therapy

The approach to antiretroviral treatment and the design of therapeutic regimens have been influenced by the following key findings from studies on the pathogenesis of HIV infection.

- Demonstration that a continuous high-level of replication of HIV is present from the early stages of infection.
- Demonstration that the measured concentration of plasma viral load is predictive of the subsequent risk of disease progression and death.
- Proof that combination antiretroviral treatment is able to consistently suppress HIV replication and also able to significantly delay disease progression to AIDS.
- Since ongoing replication of HIV drives the disease process, the ideal target of antiretroviral treatment is to obtain timely and sustained suppression of viral replication.
- It should be made known to the patient that ART is not a cure. It only suppresses viral replication and makes the patient clinically better.
- Transmission of HIV can occur while on ART and so preventive measures should still be applied including safe sex such as male and female condom use.

6.3.1 A life-long commitment

Once the patient starts ART, treatment should continue for the lifetime of the patient. Stopping treatment leads to a sudden increase in the viral load and increases the emergence of resistant strains of the virus. The patient who interrupts treatment

needs to be reassessed before the reintroduction of ART. (Refer chapter 2, Special considerations)

6.3.2 Drug Information

The following consist of the minimum information that every patient must have before starting ART:

- How ARVs work
- Type of drug(s)
- Dose of drug(s)
- Frequency of administration of drugs (dosing regimen).
- Dosing in relation to meal times, fluid intake, timing with other drugs (i.e. drug timetable).
- Drug interaction with other drugs (e.g. anti-TB, antifungals).
- Storage of the drugs.
- Possible unrealistic expectations of therapy.
- Consequences of non-compliance to the treatment regimen
- Clinical and laboratory monitoring of the effect of ART on patient and the viruses
- Side-effects of the medication.
- Management of side-effects.
- Possibility of treatment failure and the need to change the medication.
- Criteria for cessation or changing of therapy.
- Life-style considerations (e.g. poor nutrition, alcohol abuse etc)
- The need for the patient to keep all drugs for him/herself and not to share his/her ART medication with others (e.g. spouse, friends or relatives).

6.3.3 Understanding Adherence

Adherence is taking medications exactly as prescribed i.e. the right dose at the right time and under the right conditions. Missing just a single dose can lead to development of resistant strains of the virus and reduce the effectiveness of treatment.

The main reasons for non-adherence to therapy are

- Forgetfulness
- The number and timing of doses
- Number and size of pills (pill burden)
- Food restrictions
- Perceived or actual side effects.
- Missed appointments for drug refills

Strategies used to overcome the problem of non-adherence, include use of drug time-tables, adherence monitors, pill boxes and continued adherence counselling. The patient should be

reassured about side-effects and an alternate regimen should be discussed if side-effects are intolerable.

6.3.4 Disclosure

Disclosure and use of adherence monitors have been found to be effective in improving adherence. The counsellors should strongly encourage the disclosure of the HIV-positive status to a confidant (the partner, a close relative or friend of the patient) so that this person (as an adherence monitor) can be involved in the issues relating to treatment and offer support to the patient.

6.3.5 Emotional and Social Support

All groups involved in HIV/AIDS prevention activities and the provision of treatment and care for patients should be identified and linkages established to offer social support systems to enhance adherence. Examples of these groups are given below:

- Family
- Friends
- Religious groups
- Healthcare workers
- Networks of PLHIV
- Other Civil Society Organizations
- NGOs in AIDS care
- Social welfare department
- District Assemblies

6.3.6 Nutrition

Good nutrition plays a key role in the management of the patient. Malnutrition may lead to an increased susceptibility to infections. The patient must be educated to have a diet of clean nutritious food, adequate fruits and vegetables and adequate water intake everyday. (Refer to the 'Guidelines on Nutritional Care and Support of PLHIV', GHS 2006)

CHAPTER 7

Data Management

7.1 Introduction

Data management forms an important component of the entire clinical care programme. Good data management practices ensure availability of information for patient care, programming, quantification and forecasting of drugs and consumables. Forms to be utilised for management of data include:

- Monthly facility report of HIV Test usage
- Monthly report for HIV test kits and consumable laboratory supplies
- Monthly LMIS report for ARVs
- Monthly Assessment of stock status and order calculation work sheet (Adult and Paediatric)
- Monthly summary report of ART patients
- ART client booklet (Includes patient register, Initial and follow-up assessment forms for adults and children and HIV exposed baby follow-up form)
- ARV dispensing log adult regimen
- ARV dispensing log paediatric regimen
- Bin card

7.2 Health Information Management System (HMIS)

The following patient information should be obtained from each patient:

- Demographic data
- Medical History (including a diagnosis & screening for TB)
- Obstetrics and Gynaecological history including family planning
- Sexual history including STI
- Social History
- Physical Examination
- Laboratory Evaluation
- Drug Treatment
- Adherence
- Side Effects of ARVs

This information is collected using the client booklet for adults and children and captured into an electronic data base. Information collated shall be sent on a monthly basis from each site to the Regional Health Directorate for onward transmission to the NACP. This information shall be collated at the national level for decision making and programming purposes. Feedback

will be provided by NACP to the sites and all relevant stakeholders.

7.3 Logistic Management Information System (LMIS)

The LMIS is a collection of manual and/or electronic forms and procedures that gather and organize logistics data, making it possible to procure the right quantity of commodities, track the distribution of products throughout the system, and control the inventory of stocks.

The purpose of an LMIS is to improve management decisions that govern the logistics system. LMIS provides the basis for quantifying products to be procured, adjusting stock position, monitoring losses and wastage rates, quantifying the amount to be dispensed to users, identifying irrational use and assuring accountability. This data enables health managers to make critical decisions to ensure the reliable and secure delivery of supplies at all levels of the system

7.3.1 Essential data for LMIS

Three essential data sets to be collected to run any supply system are;

- **Stock on hand**; quantities of usable stock available at all levels of the system at a point in time.
- **Consumption**: the average quantity of commodities dispensed to users during a particular time period.
- **Losses and adjustments**: Losses are the quantities of commodities removed from the distribution system for any reason other than consumption by client (expiry, damage theft etc). Adjustments may include receipt or issue of supplies from one facility to another at the same level (e.g. transfer) or a correction for an error in counting. Losses and adjustments may therefore be a negative or a positive number.

7.3.2 LMIS Forms for administering ART in Ghana

The following manual and electronic LMIS forms have been designed for use at all sites administering ART

- ART Patient Register
- Bin Card
- ARV Drug Dispensing Log Book
- Monthly Summary Report of ART patients
- Monthly LMIS Report for ARV drugs Adult Regimen
- Monthly LMIS report for ARV drugs Paediatric Regimen
- Monthly Assessment of Stock status and order calculation worksheet for Adult and Paediatric ARV drugs

CHAPTER 8

PROCUREMENT, STORAGE AND DISTRIBUTION OF ARV DRUGS

8.1 PROCUREMENT

8.1.1 GOALS FOR ARV PROCUREMENT

The strategies and methods by which anti-retroviral drugs are procured shall aim at achieving the following goals:

- Obtain the lowest possible price
- Obtain safe, efficacious and quality products in adequate quantities.
- Minimize loss of resources through mis-procurement and product expiry.
- Cost-effective use of personnel, time and other resources.

8.1.2 CRITERIA FOR SELECTION OF DRUGS

The World Health Organisation has defined the criteria, which are suggested as guidelines for the selection of essential drugs. In the preparation of this protocol the same criteria have been adopted.

The selection of ARVs and drugs for treating opportunistic infections shall be guided by the following:

- Current scientific evidence on efficacy and safety.
- The ability of the drug and the pharmaceutical form to provide the most convenient benefit/risk ratio.
- The cost/benefit ratio of the drug and the pharmaceutical form.
- The familiarity of health workers with the drug and pharmaceutical form.
- Availability of an economically convenient manufacturing of the drug in the country.
- Stability of the drug and pharmaceutical form at the available storage conditions.

A fixed dose combination shall be accepted when it provides a proven advantage over single compounds administered separately in therapeutic effect, safety, patients' adherence, or cost.

8.1.3 SPECIFICATION

Generic (international non-specific nomenclature) names shall be employed, as the standard means of reference and selected medicines shall conform to the British and United States Pharmacopoea and or any other officially accepted pharmacopoeal standards.

8.1.4 QUANTIFICATION

Quantification of needs at all levels i.e. national and selected treatment centres etc shall be based on the expected number of manageable cases and the agreed treatment schedules defined for each health problem.

Quantity of a drug specified for a standard course of treatment	X	Number of treatment episodes of a given health problem	=	Total quantity of drug required for the given health problem
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This calculation is repeated for each health problem and its corresponding drug. Where a drug is used for more than one health problem, the respective totals are added together to obtain the total quantity required.

Logistic (consumption) data and service data shall inform the estimation of drugs.

8.1.5 QUALITY ASSURANCE

Antiretroviral medicines procured by MOH shall be of acceptable quality which shall be demonstrated by:

- Certification of compliance with good manufacturing practice, issued by a competent regulatory authority.
- Certification of quality following testing by an independent quality control laboratory.
- Compliance with the Ghana Food and Drugs Board's Law, which makes it mandatory for all medicines to be registered and to have a system of post registration surveillance.

8.1.6 PROCUREMENT

ARVs shall be procured by the Ministry of Health in accordance with the Public Procurement Act (Act 663).

Procurement shall be based on competitive and transparent procurement methods in order to achieve the lowest price possible for quality-assured products, except in the case of small or emergency orders. In addition procurement should be effected in the largest possible quantities reasonable under the requirements of the programme in order to achieve economies of scale. A framework for awarding a three-year contract with scheduled delivery may be established to ensure uninterrupted supply.

ARVs shall be classified as Programme medicines and shall be by prescription only and not be for sale in the open market.

8.2 STORAGE AND DISTRIBUTION

ARVs shall be stored at the Central Medical Store and shall be collected by the Regional Medical Stores from where treatment centres shall collect their respective consignments on a stock rotation basis (first expiry first out basis). Tertiary institutions shall collect their products from the Central Medical Store. The audit trail shall be transparent to prevent possible leakages. At all levels ARVs shall be stored at appropriate temperature under lock and key.

The following Logistics Management Information System (LMIS) forms shall be used at the various levels of the distribution chain.⁸

- ART Patient Register
- Monthly Summary Report of ART Patients
- Bin/Tally Cards
- ARV Dispensing Log
- Monthly LMIS Report For Anti-Retroviral medicines

8.2.1 DISPENSING OF ARVs

Persons specifically trained in communication skills and adherence counselling for People Living with HIV shall dispense ARVs.

All patients shall be provided with clear and simple instructions on the use of ARVs and their side effects.

⁸ Refer Ministry of Health/Ghana Health Service, July 2004. Antiretroviral (ARV) Drugs Logistics Management Information System (LMIS) Guidelines

APPENDIX 1
CLINICAL STAGING OF HIV/AIDS FOR ADULTS AND
ADOLESCENTS

Stages	
Clinical Stage 1	<ul style="list-style-type: none"> • Asymptomatic • Persistent generalized lymphadenopathy
Clinical Stage 2	<ul style="list-style-type: none"> • Moderate explained weight loss (<10% of presumed or measured body weight) • Recurrent respiratory tract infections (RTIs, Sinusitis, bronchitis, otitis media, pharyngitis) • Herpes zoster • Angular cheilitis • Recurrent oral ulcerations • Papular pruritic eruptions • Seborrhoeic dermatitis • Fungal nail infections of fingers.
Clinical Stage 3	<ul style="list-style-type: none"> • Severe weight loss (>10% of presumed or measured body weight) • Unexplained chronic diarrhoea for longer than one month • Unexplained persistent fever (intermittent or constant for longer than one month) • Persistent oral candidiasis • Oral hairy leukoplakia • Pulmonary tuberculosis • Severe bacterial infections (e.g. pneumonia, empyema, meningitis, pyomyositis, bone or joint infection, bacteraemia, severe pelvic inflammatory disease) • Acute necrotizing ulcerative stomatitis, gingivitis or periodontitis • Unexplained anaemia (<8g/dl), neutropenia (<500/mm³) and/or chronic thrombocytopenia (<50 000/mm³) for more than one month.
Clinical Stage 4	<ul style="list-style-type: none"> • HIV wasting syndrome. • <i>Pneumocystis jiroveci</i> pneumonia • Recurrent severe bacterial pneumonia. • Chronic herpes simplex infection (orolabial, genital or anorectal of more than one month's duration or visceral at any site) • Oesophageal candidiasis (or candidiasis of trachea, bronchi or lungs) • Extrapulmonary Tuberculosis • Kaposi sarcoma • Cytomegalovirus disease (retinitis or infection of

	<p>other organs excluding Liver, spleen and lymph nodes)</p> <ul style="list-style-type: none">• Central nervous system toxoplasmosis• HIV encephalopathy• Extrapulmonary cryptococosis including meningitis• Disseminated non-tuberculous mycobacteria infection.• Progressive multifocal leukoencephalopathy (PML)• Chronic Cryptosporidiosis• Chronic Isosporiasis• Disseminated mycosis(histoplasmosis, coccidiomycosis)• Recurrent septicaemia (Including nontyphoidal <i>Salmonella</i>)• Lymphoma (cerebral or B cell non-Hodgkin)• Invasive cervical carcinoma• Atypical disseminated leishmaniasis• Symptomatic HIV-associated nephropathy or HIV-associated cardiomyopathy.
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IMMUNOLOGICAL STAGING OF HIV INFECTION

In addition to clinical staging, immunological staging can be done based on CD4 count measurement. This supports and reinforces treatment decision-making.

The table below classifies the immunological staging.

For clinical purposes long term prognosis has shown to be related to the nadir or lowest-ever value of CD4. It should be noted that the immunological staging of disease reverses with successful ART.

CD4 LEVEL IN RELATION TO THE SEVERITY OF IMMUNOSUPPRESSION

Not significant immunosuppression	>500/mm ³
Mild immunosuppression	350 – 499mm ³
Advanced immunosuppression	250 – 349/mm ³
Severe immunosuppression.	<250/mm ³

APPENDIX 2

A. WHO CLINICAL STAGING OF HIV AND AIDS FOR INFANTS AND CHILDREN

PERSONS AGED UNDER 13 YEARS WITH CONFIRMED LABORATORY EVIDENCE OF HIV INFECTION

Stage	
Clinical Stage 1	<ul style="list-style-type: none"> • Asymptomatic • Persistent Generalized Lymphadenopathy
Clinical Stage 2	<ul style="list-style-type: none"> • Unexplained Hepatosplenomegaly • Papular pruritic eruptions • Extensive warts virus infection • Extensive molluscum contagiosum • Recurrent oral ulcerations • Unexplained persistent parotid enlargement • Lineal gingival erythema (LGE) • Herpes zoster • Recurrent or chronic URTIs(Otitis media, otorrhoea, sinusitis, tonsillitis) • Fungal nail infections
Clinical Stage 3	<ul style="list-style-type: none"> • Unexplained moderate malnutrition not adequately responding to standard therapy • Unexplained persistent diarrhoea (14 days or more) • Unexplained persistent fever (Above 37.5°C, intermittent or constant, for longer than one month) • Persistent oral candidiasis (After first 6 weeks of life) • Oral hairy leukoplakia • Acute necrotizing ulcerative gingivitis/periodontitis • Lymph node TB • Pulmonary TB • Severe recurrent bacterial pneumonia. • Symptomatic Lymphoid interstitial pneumonitis • Chronic HIV-associated lung disease including bronchiectasis • Unexplained anaemia (<8g/dl), neutropenia (<1000/mm³) or chronic thrombocytopenia (<50 000/mm³) for more than one month.
Clinical Stage 4	<ul style="list-style-type: none"> • Unexplained severe wasting or severe malnutrition not adequately responding to

	<p>standard therapy.</p> <ul style="list-style-type: none"> • Pneumocystis pneumonia • Recurrent severe presumed bacterial infections (e.g. empyema, pyomyositis, bone or joint infection, meningitis, but excluding pneumonia) • Chronic herpes simplex infection (orolabial or cutaneous of more than one month's duration or visceral at any site) • Extrapulmonary TB • Kaposi sarcoma • Oesophageal candidiasis or candidiasis of trachea, bronchi or lungs • CNS toxoplasmosis (outside the neonatal period) • HIV encephalopathy • Cytomegalovirus(CMV) infection; retinitis or CMV infection affecting another organ with onset at age more than one month) • Extrapulmonary cryptococcosis including meningitis • Disseminated endemic mycosis (e.g. extrapulmonary histoplasmosis, coccidiomycosis, penicilliosis) • Chronic Cryptosporidiosis (with diarrhoea) • Chronic Isosporiasis • Disseminated non-tuberculous mycobacteria infection • Cerebral or B cell non-Hodgkin lymphoma • Progressive multifocal leukoencephalopathy (PML) • HIV-associated cardiomyopathy or nephropathy.
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B. PRESUMPTIVE DIAGNOSIS OF CLINICAL STAGE 4 HIV IN CHILDREN AGED UNDER 18 MONTHS

The presumptive diagnosis is designed for use where access to confirmatory diagnostic testing for HIV infection by means of virological testing for infants and children aged under 18 months is not readily available. **It is not recommended for use by clinical care providers who are not trained in ART or experienced in HIV care.** It should be accompanied by immediate efforts to confirm the HIV diagnosis with HIV DNA PCR. Presumptive diagnosis of clinical stage 4 disease suggests severe immunosuppression, and ART is indicated.

PRESUMPTIVE CLINICAL STAGE 4 IN INFANTS AND CHILDREN AGED UNDER 18 MONTHS WHERE VIROLOGICAL CONFIRMATION OF HIV INFECTION IS NOT AVAILABLE

A presumptive diagnosis of stage 4 clinical disease should be made if

An infant is HIV-antibody positive (ELISA or rapid test), aged under 18 months and symptomatic with two or more of the following:

- oral thrush
- severe pneumonia
- severe wasting/malnutrition
- severe sepsis

Other factors that support the diagnosis of clinical stage 4 HIV infection in an HIV-Seropositive infant are:

- recent HIV related maternal death
- advanced HIV disease in the mother
- CD4% < 20%

Confirmation of the diagnosis of HIV infection should be sought as soon as possible.

C. IMMUNOLOGICAL CATEGORIES FOR PAEDIATRIC HIV INFECTION

Immunological staging for children is also possible. The absolute CD4 count and the percentage values in healthy infants who are not infected with HIV are considerably higher than those observed in uninfected adults, and slowly decline to adult values by the age of 5 years. In considering absolute counts or percentages, therefore, age must be taken into account as a variable. The absolute CD4 count associated with a specific level of immunosuppression tend to change with age, whereas the CD4 percentage related to immunological damage does not vary as much. Currently, therefore, the measurement of the CD4 percentage is recommended in children less than 5 years of age. CD4 testing is not essential for the initiation of ART, and should only be used in conjunction with the clinical stage. As for adults, immunological staging assists clinical decision making and provides a link with monitoring and surveillance definitions. It is usually reversed by successful ART.

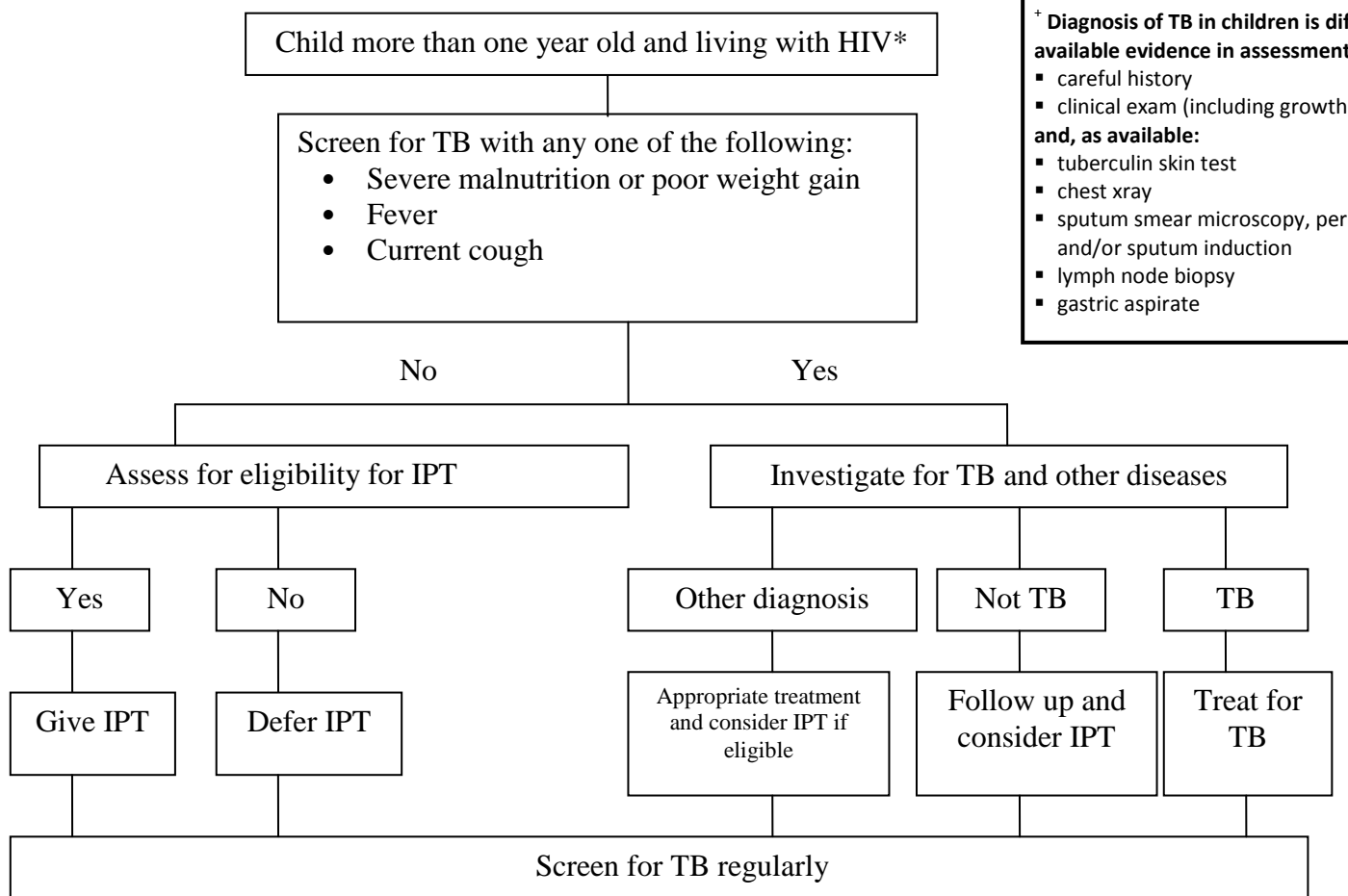
CD4 LEVEL IN RELATION TO THE SEVERITY OF IMMUNOSUPPRESSION

Classification of HIV associated immune deficiency	Age-related CD4 values			
	<11 months (%)	12-35 months (%)	36-59 months (%)	≥5 yrs (cells/mm ³)
Not Significant	>35	>30	>25	>500
Mild	30-35	25-30	22-25	350-499
Advanced	25-30	20-25	15-20	200 - 349
Severe	<25	<20	<15	<200 or <15%

CD4% Formula:

$$\text{CD4\%} = \frac{\text{ABSOLUTE CD4 COUNT}}{\text{TOTAL LYMPHOCYTE COUNT}} \times 100$$

D. ALGORITHM FOR DIAGNOSIS OF TUBERCULOSIS IN CHILDREN



E. IMPLICATION FOR CLINICAL AND IMMUNOLOGICAL CRITERIA FOR INITIATING ART

The need for ART should be considered in all HIV infected children. All children with stages 3 or stage 4 diseases (advanced HIV defined clinically) should start ART following discussion with their families. For children less than 2 years with confirmed HIV infection, ART should be initiated.

CLINICAL AND IMMUNOLOGICAL CRITERIA FOR INITIATING ART IN INFANTS AND CHILDREN

Clinical Stages	Treatment Recommendation
Stage 3 and 4	Treat
Presumptive Stage 3 and 4	Treat
Stage 1 and 2	Treat if < 24 months of age with confirmed HIV infection
Stages 1 and 2	Where CD4 available treat under the following conditions: Under 24 months treat irrespective of CD4% 24 – 59 months: CD4% < 25 (<750 cells/mm ³) 5 years and above: CD4 < 350 cells/mm ³
Note: co-trimoxazole prophylaxis should be given to all HIV-exposed infants and children until HIV infection is excluded and to all HIV-infected infants and children.	

CD4 can be used to monitor responses to treatment, although it is not essential. Absolute CD4 values also fluctuate with intercurrent illness and with physiological and test variability, so the trend over two or three repeated measurements is usually more informative than individual values.

RECOMMENDATIONS FOR IMPLEMENTATION

The following recommendations concern the use of the revised clinical staging and HIV and AIDS case definitions for clinical management and case-reporting.

- This revised clinical staging should be used as guidance on which clinical and immunological stages require or are eligible for ART treatment and support patient follow up.
- All infants and children less than 24 months with clinical stage 2, 3 or stage 4 diseases should be reported as having advanced HIV and AIDS which immediately requires or will soon require ART.
- Adolescents and adults with clinical stage 3 or stage 4 diseases should be reported as having advanced HIV and AIDS which immediately requires or will soon require ART.
- HIV and AIDS reporting for surveillance should preserve patient confidentiality in accordance with existing national recommendations.

APPENDIX 3

DRUG-DRUG INTERACTIONS

DRUG	DRUG-DRUG INTERACTIONS
Abacavir	Methadone, Phenobarbital, Phenytoin, Rifampicin
Atazanavir	
Efavirenz	Nevirapine, Antiarrhythmics (Lidocaine, amiodarone), Antiepileptics (Phenytoin, Carbamazepine, Primidone), Antihistamines (Astemizole, Terfenadine, Loratidine), Benzodiazepine, Ergometrine, Grapefruit juice, Indinavir, Lopinavir, Methadone, Nevirapine, Phenobarbital, Rifampicin, Ritonavir, Oral Contraceptives (oestrogen-based), Phenobarbital, Benzodiazepine, Saquinavir, St. John's Worts (Herbal)
Emtricitabine	Lamivudine
Lamivudine	Emtricitabine,
Lopinavir/Ritonavir	Artemether+Lumefantrine, Alprazolam, Amiodarone, , Astemizole, Carbamazepine, Chlorpheniramine, Clarithromycin, Dexamethasone, Diazepam, Efavirenz, Erythromycin, Itraconazole, Ketoconazole, Lidocaine, Loratidine, Metronidazole, Nelfinavir, Oral contraceptives, Phenobarbitalone, Phenytoin, Rifabutin, Rifampicin, Quinidine, Saquinavir, Simvastatin, St. John's worts, Tenofovir, Terfenadine, Tricyclic antidepressants,
Nevirapine	Carbamazepine, Cocaine, Efavirenz, Fluconazole, Indinavir, Levonorgestrol, Medroxyprogesterone, Methadone, Norethisterone, Oral contraceptives (oestrogens and progestogens), Phenytoin, Protease Inhibitors, Rifabutin, Rifampicin, Indinavir, Efavirenz, Saquinavir, St. John's worts, Warfarin, Carbamazepine, Phenytoin, Cocaine.
Tenofovir	Acyclovir, Aminoglycosides, Amphotericin B, Didanosine, Lopinavir, Pentamidine, Probenecid, Salicylates, Vancomycin
Zidovudine	Cytotoxics (Doxorubicin etc) Fluconazole, Ganciclovir, Ibuprofen, Interferon, Methadone, Phenytoin, Pyrimethamine, Ribavirin, Rifampicin, Stavudine, Valproic Acid

APPENDIX 4

DRUG INFORMATION

Drug	Adult dosage	Formulations	Adverse effects Minor, frequent	Adverse effects serious, dose limiting	Special instructions
Abacavir	300 mg bid	Tablet	Nausea, Poor Appetite, Vomiting Fatigue Sleep disturbance	Hypersensitivity reaction Lactic acidosis	Caution in liver or renal disease Discontinue use in symptoms of hypersensitivity
Efavirenz	600 mg daily	Capsule/ Tablet	Elevated Liver enzyme Skin rash CNS disturbances	Suicidal ideations, Mania Teratogenicity	Caution in liver disease
Emtricitabine	200mg daily	Capsule	Few side effects, rash, peripheral neuropathy reported	Lactic acidosis Hepatomegaly with steatosis	Caution in liver or renal disease Exacerbation of hepatitis in patients with chronic hepatitis B may occur on discontinuation of emtricitabine
Lamivudine (3TC)	150 mg bid	Tablet	Few side effects, neutropenia, peripheral neuropathy reported	Lactic acidosis (Rare)	
Lopinavir/ritonavir	400 mg /100 mg bid	Tablet	Diarrhoea, nausea, dyslipidemia, lipodystrophy, headache	Hypersensitivity Pancreatitis Diabetes Mellitus	
Nevirapine	200 mg daily		Skin rash	Hypersensitivity	Caution in liver

Drug	Adult dosage	Formulations	Adverse effects Minor, frequent	Adverse effects serious, dose limiting	Special instructions
	for 14 to 28 days then 200 mg bid	Tablet		Hepatotoxicity	disease
Tenofovir	300 mg daily	Tablet		Nephrotoxicity (Rare)	To be taken with a meal
Zidovudine (AZT)	300 mg bid	Tablet	Nausea Headache Fatigue Muscle pains	Anaemia, Neutropenia, gastrointestinal intolerance, Lactic acidosis	Caution in: pre-existing anaemia Liver and renal insufficiency

Paediatric Drugs and their characteristics

Drug	Preparations	Dosage for children	Adverse effects Minor, frequent	Adverse effects serious, dose limiting	Special instructions
Abacavir	Oral solution: 20 mg/ml Tablet:300mg	3 months to 16 years: 8 mg/ kg / dose bid (maximum, 600mg daily)	Nausea Poor Appetite Vomiting Fatigue Sleep disturbance	Hypersensitivity reaction Lactic acidosis	Caution in liver or renal disease Discontinue use if symptoms of hypersensitivity

Drug	Preparations	Dosage for children	Adverse effects Minor, frequent	Adverse effects serious, dose limiting	Special instructions
Efavirenz	<p>Capsules: 50mg, 100mg, 200mg, 600mg</p> <p>Oral solution: 30mg/ml note syrup requires higher dosing than capsules)</p>	<p>Capsule/Tablet</p> <ul style="list-style-type: none"> • 40 kg and over, 600 mg once daily; • over 3 years/10–14 kg, 200 mg once daily; • 15–19 kg, 250 mg once daily; • 20–24 kg, 300 mg once daily; • 25–32 kg, 350 mg once daily; • 33–39 kg, 400 mg once daily <p>As oral solution</p> <ul style="list-style-type: none"> • 40 kg and over, 720 mg once daily; • over 3 years/10–15 kg, 270 mg once daily; • 15–20 kg, 300 mg once daily; • 20–24 kg, 360 mg once daily; • 25–32 kg, 450 mg once daily; • 33–39 kg, 510 mg 	<p>Elevated Liver enzyme Skin rash CNS disturbances</p>		<p>Only for children over 3 years</p> <p>Capsules may be opened and added to food but has a very peppery taste</p> <p>Avoid high fatty foods</p> <p>Best given at bed time to reduce CNS side effects</p>

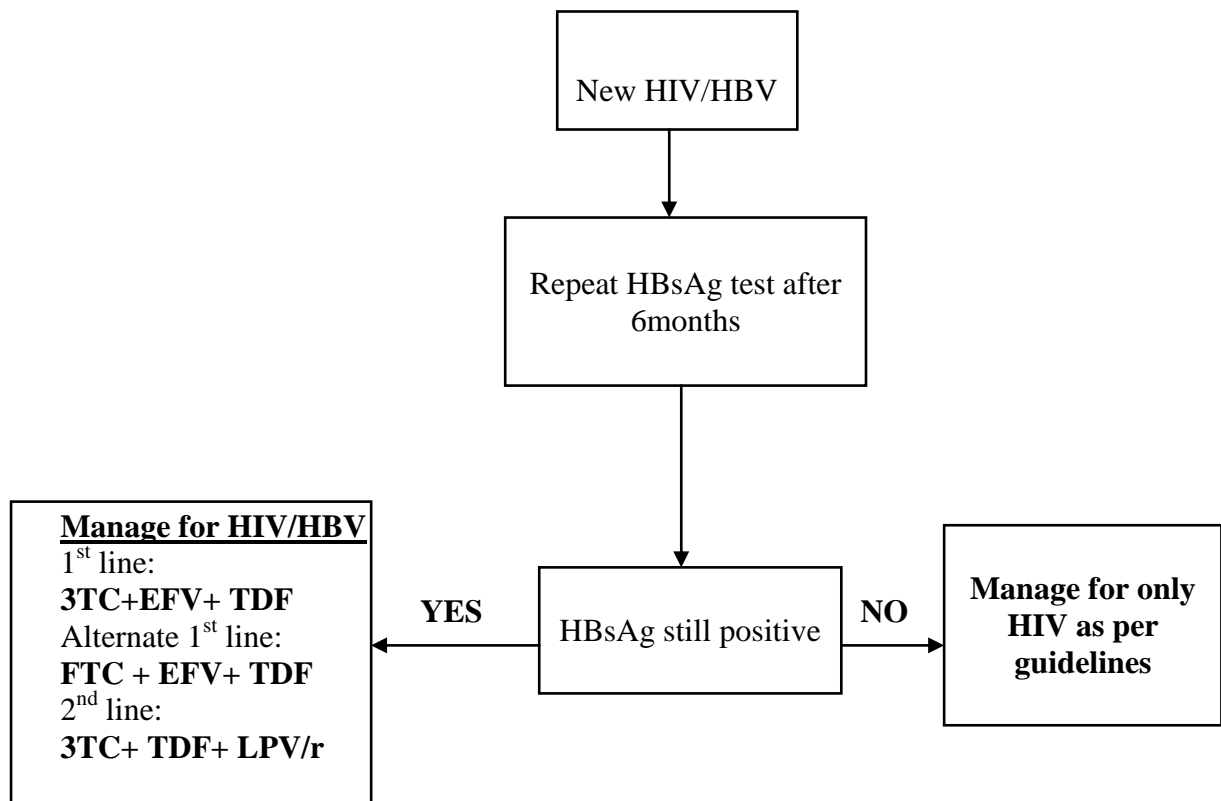
Drug	Preparations	Dosage for children	Adverse effects Minor, frequent	Adverse effects serious, dose limiting	Special instructions
		once daily			
Emtricitabine (FTC)	Oral solution: 10mg/ml	<ul style="list-style-type: none"> Over 33 kg, 1 capsule (200 mg) or 24 ml (240 mg) oral solution once daily 4 months–18 years, under 33 kg, 6 mg/kg oral solution once daily 	Few side effects, rash, peripheral neuropathy reported	Lactic acidosis Hepatomegaly with steatosis	Caution in liver or renal disease Exacerbation of hepatitis in patients with chronic hepatitis B may occur on discontinuation of emtricitabine
Lamivudine (3TC)	Tablet:150 mg Oral Solution: 10 mg /ml	<ul style="list-style-type: none"> Infants under 1 month: 2mg/kg 12hourly Child over 1 month: 4mg/kg 12 hourly 	Few side effects, neutropenia, peripheral neuropathy reported	Lactic acidosis	Store at room temperature can be administered with food. Decreased dosage with renal impairment
Lopinavir/ Ritonavir (LPV/r)	Lopinavir/ Ritonavir tablet: 200mg/50mg Oral solution: Lopinavir/ Ritonavir:80/20mg per ml	<p><u>Surface area</u></p> <ul style="list-style-type: none"> 6months–13 years: lopinavir, 225 mg/m² + ritonavir, 56.25 mg/m² twice daily <p><u>Weight based</u></p> <ul style="list-style-type: none"> 7–15 kg, lopinavir, 12 mg/kg + ritonavir, 3 mg/kg twice daily; 	Diarrhoea, nausea, dyslipidemia, lipodystrophy, headache	Hypersensitivity Pancreatitis Diabetes Mellitus	Preferably oral solution and capsules should be refrigerate; must be reconstituted immediately prior to administration in water, milk, formula, pudding, etc- do not use acidic food or juices

Drug	Preparations	Dosage for children	Adverse effects Minor, frequent	Adverse effects serious, dose limiting	Special instructions
		<ul style="list-style-type: none"> • 15–40 kg, lopinavir, 10 mg/kg+ ritonavir, 2.5 mg/kg twice daily). • > 40 kg: Lopinavir 400 mg/Ritonavir 100 mg twice daily 			<p>increases bitter taste) ; solution stable for 6 hours</p> <p>Because of difficulties with use of powder, use of crushed tablets preferred (even for infants) if appropriate dose can be given</p> <p>Powder and tablets can be stored at room temperatures Take with food</p> <p>Drug interactions (less than ritonavir containing protease inhibitors</p>

Drug	Preparations	Dosage for children	Adverse effects Minor, frequent	Adverse effects serious, dose limiting	Special instructions
Nevirapine (NVP)	Oral suspension: 10mg/ml Tablet: 200 mg	<ul style="list-style-type: none"> • 200 mg/m²/dose once daily for 14 to 28 days; then • 200 mg/m²/dose twice daily 	Skin rash	Hypersensitivity Hepatotoxicity	If Rifampicin co-administration, avoid use Store suspension at room temperature; must shake well Can give with food can be crushed and combined with small amount of water or food and immediately administered warn parents about Rash.
Zidovudine (AZT)	Syrup: 10mg/ml Capsules:100mg Tablets:300mg	Neonatal dose: Oral: 4mg/kg body weight 12hrly. Paediatric dose: 240mg/m ² every 12 hrs Max-300mg every 12hrs	Nausea Headache Fatigue Muscle pains	Anaemia, Neutropenia, gastrointestinal intolerance, Lactic acidosis	Caution in: pre-existing anaemia Liver and renal insufficiency. Can be administered with food Store at room temperature

* Adolescent dose is same as adult dosage see adult section.

APPENDIX 5: ALGORITHM FOR THE MANAGEMENT OF HEPATITIS B VIRUS CO-INFECTION WITH HIV



APPENDIX 6- PEP FOR RAPE SURVIVORS

APPENDIX 6.1 FORENSIC EVIDENCE COLLECTION

It is ideal to document injuries and collect samples, such as blood, hair, saliva and sperm within 72 hours of the incident. Whenever possible, this should be done during the medical examination following the order below:

a. Inspection of the Body

- i. Examine the survivor's clothing under good light before she undresses
- ii. Collect any foreign debris on clothes, body or in hair
- iii. Let survivor undress while standing on a sheet of paper to collect any debris that fall
- iv. Examine the upper part of body first followed by the lower half
- v. Collect torn and stained items of clothing if possible
- vi. Document all injuries in as much detail as possible
- vii. Take samples on body or from the mouth for semen analysis in the event of ejaculation into survivor's mouth
- viii. Collect samples for DNA analysis from where there could be the assailants saliva or semen on the skin, using cotton tipped-swab moistened with sterile water
- ix. Take blood and urine for toxicology testing if survivor was drugged

b. Inspection of the Perineum and Vulva

Inspect and collect samples for DNA analysis from around the anus, perineum and vulva using separate cotton-tipped swabs moistened with sterile water

c. Examination of the Vagina and/or Rectum (depending on the site of penetration or attempted penetration)

- i. Lubricate speculum with normal saline or clean water
- ii. Using a cotton-tipped swab, collect fluid from the posterior fornix for examination of sperm
 - a. Use a wet mount to examine and take note of any motile sperms
 - b. In addition to the first slide a second slide could be made and both air-dried for future examinations
- iii. Take specimen from the posterior fornix and the endocervical canal for DNA analysis. Let them dry at room temperature
- iv. Collect separate samples from the cervix and the vagina for acid phosphatase analysis
- v. Obtain samples from the rectum for similar examinations, if indicated

d. Maintaining the Chain of Evidence

- i. All evidence collected must be well processed, labelled, stored and transported properly; and documentation must include a signature of everyone who has possession of the evidence at any time, from the person who collects it to the one who takes it to the courtroom.

- ii. Evidence should be kept in a safe, secured place, and should be released to the relevant authority at the request of the survivor, the police with the consent of the survivor or at the request of a court of competent jurisdiction.

APPENDIX 6.2:

DRUG RECOMMENDATION FOR HIV PEP IN ADULTS AND ADOLESCENTS (>40KG) INCLUDING PREGNANT AND LACTATING WOMEN

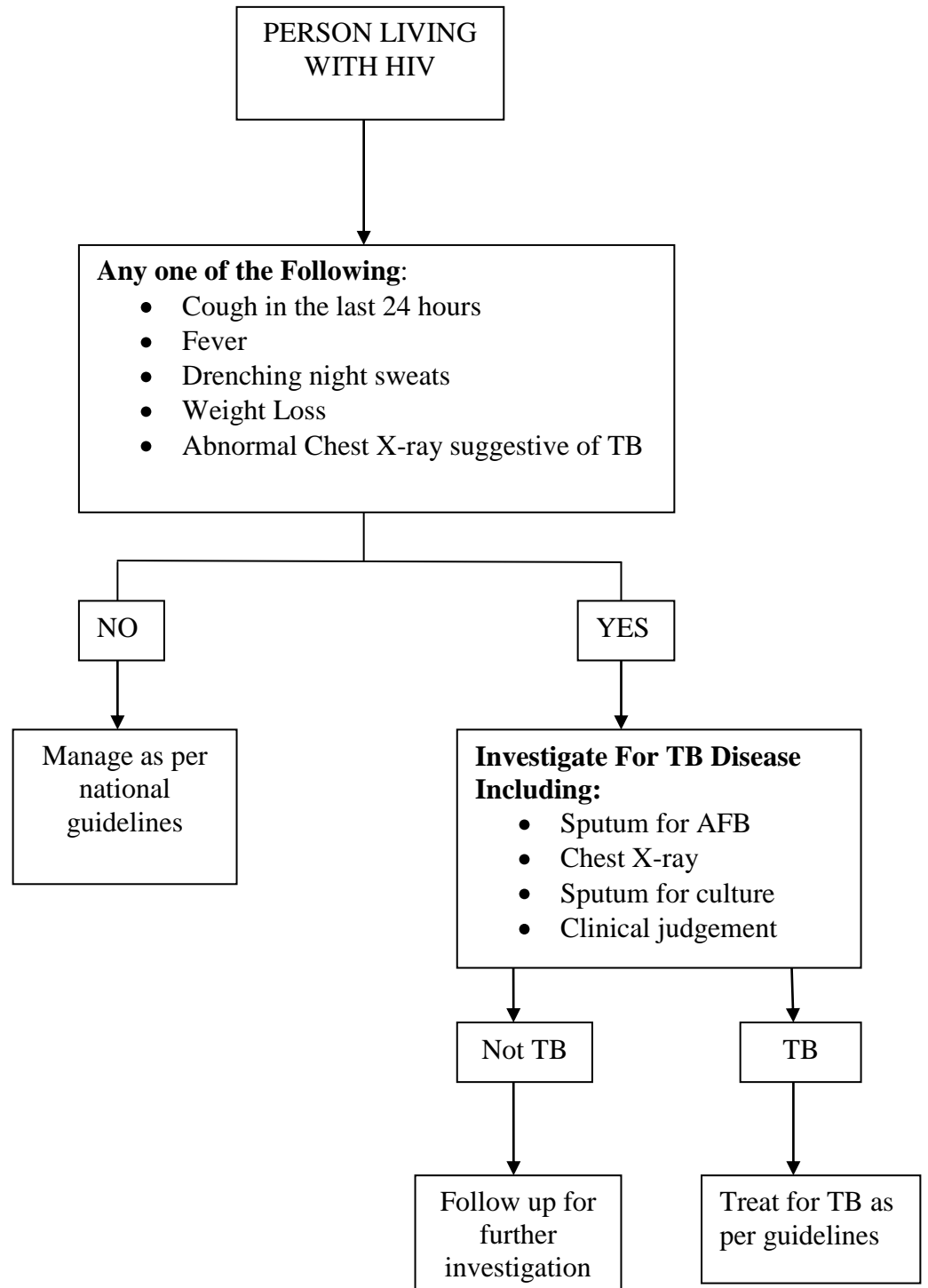
DRUG RECOMMENDATION
Zidovudine 300mg 12 hourly for 28 days plus Lamivudine 150mg 12 hourly for 28 days plus Lopinavir/r 400mg/100mg 12hourly x 28 days

F. DRUG RECOMMENDATION FOR HIV PEP IN CHILDREN

Recommended drugs in children are the same as in the case of the adult but dosing must be according to age and body weight as outlined below:

WEIGHT OR AGE	STRENGTH	DOSING
<2 years or 5 – 9kg	Zidovudine syrup 10mg/ml plus Lamivudine syrup 10mg/ml plus Lopinavir/r (80mg/20mg)/ml syrup	7.5mls 12 hourly 2.5mls 12 hourly (14mg/3mg)/kg bd
10–19kg	Zidovudine 300mg tablet plus Lamivudine 150mg tablet plus Lopinavir/r (80mg/20mg)/ml syrup	½ tablet 12 hourly ½ tablet 12 hourly (12mg/3mg)/kg bd
20- 39kg	Zidovudine 100mg capsule plus Lamivudine 150mg tablet plus Lopinavir/r (80mg/20mg)/ml syrup or 200mg/50mg tablet	2 capsules 12 hourly 1 tablet 12 hourly (10mg/2.5mg)/kg bd

APPENDIX 7: ALGORITHM FOR TB SCREENING IN PLHIV



APPENDIX 8

Guidelines on HIV Viral Load (VL) Monitoring for Clients on ART

What is an HIV viral load test?

An HIV viral load test measures the amount of specific HIV RNA in plasma (blood). It is known that in HIV infection, HIV viral RNA levels in plasma can predict disease progression to AIDS. The Viral Load (VL) of a person living with HIV correlates with response to antiretroviral therapy (ART) and can be used to monitor the clinical outcome of ART. A goal of ART is to achieve undetectable virus within 16 – 24 weeks after initiation of therapy.

The best way to use an HIV viral load test is to determine a baseline level of viral RNA and relate levels over time to the patient's clinical outcome. This will determine the effectiveness of antiretroviral drugs administered.

In the Guidelines for ART in Ghana, viral load is not a pre-requisite for initiating ART but it is recommended, where available, to monitor the progress of persons on ART.

How is HIV viral load measured?

The polymerase chain reaction (PCR) is a standard method for measuring the quantity of viral RNA. The results of the PCR test are reported as copies of HIV RNA per milliliter of plasma (copies/ml). Some ultra sensitive assays can accurately detect a minimum range of 1 to 50 RNA copies/ml. A value of <50 copies/ml is said to be undetectable, one of the goals of ART.

Interpretation of VL

Health workers who are managing persons living with HIV (PLHIV) can use the results of a viral load test for a specific client to make decisions about the effectiveness of an ART regimen.

- Effective ART will bring down VL levels to below level of detection.

What is virologic failure?

- It is defined as confirmed plasma HIV RNA >5000 copies/ml 6 months after initiating therapy in persons that are adherent to ART.

Observations about VL measurements:

- Viral loads are affected by laboratory variation and assay fluctuations and there is a 10-30 percent variation in a test result if the same sample is repeated on the same assay in the same laboratory.
 - For example, 100,000copies/ml is not significantly different from 130,000copies/ml.
- Patient variables such as acute illness and recent vaccinations may require deferral of viral load testing for at least 4 weeks.
- At least two VL measurements usually should be performed on separate visits four weeks apart before antiretroviral drug therapy is changed.
- It is important to allow sufficient time on therapy (more than six months) before judging effectiveness of ARVs.

General recommendations for the evaluation and management of treatment failure.

- Review clinical status and ART history.
- Evaluate adherence, tolerability, drug-drug interactions, drug-food interactions and psychosocial issues
- Request VL if virologic failure is suspected
- Identify suitable drug combinations available according to national guidelines and switch therapy if virologic failure is confirmed.

When to request VL

1. ***Six months after starting ART and subsequently after every 12 months.***
2. ***Subsequently during management, VL may be requested under the following conditions or situations:***
 - a. ***If the CD4 is declining:***
 - For Children above 5years and Adults
 - Fall of CD4 count to pre-therapy baseline (or below); or
 - 50% fall from the on-treatment peak value (if known); or
 - Persistent CD4 levels below 100 cells/mm³ for more than one year on ART.
 - For Children 5 years and below
 - Fall of CD4% to pre-therapy baseline (or below); or
 - 50% fall from the on-treatment peak value (if known).
 - b. ***If Clinical disease is progressing,***
 - New or recurrent WHO stage 4 condition

Management of virologic failure

Management of virologic failure should be a team approach. Consultation with other colleagues is strongly recommended for an informed decision.

If viral load is >5000 copies/ml after 6 months of ART.

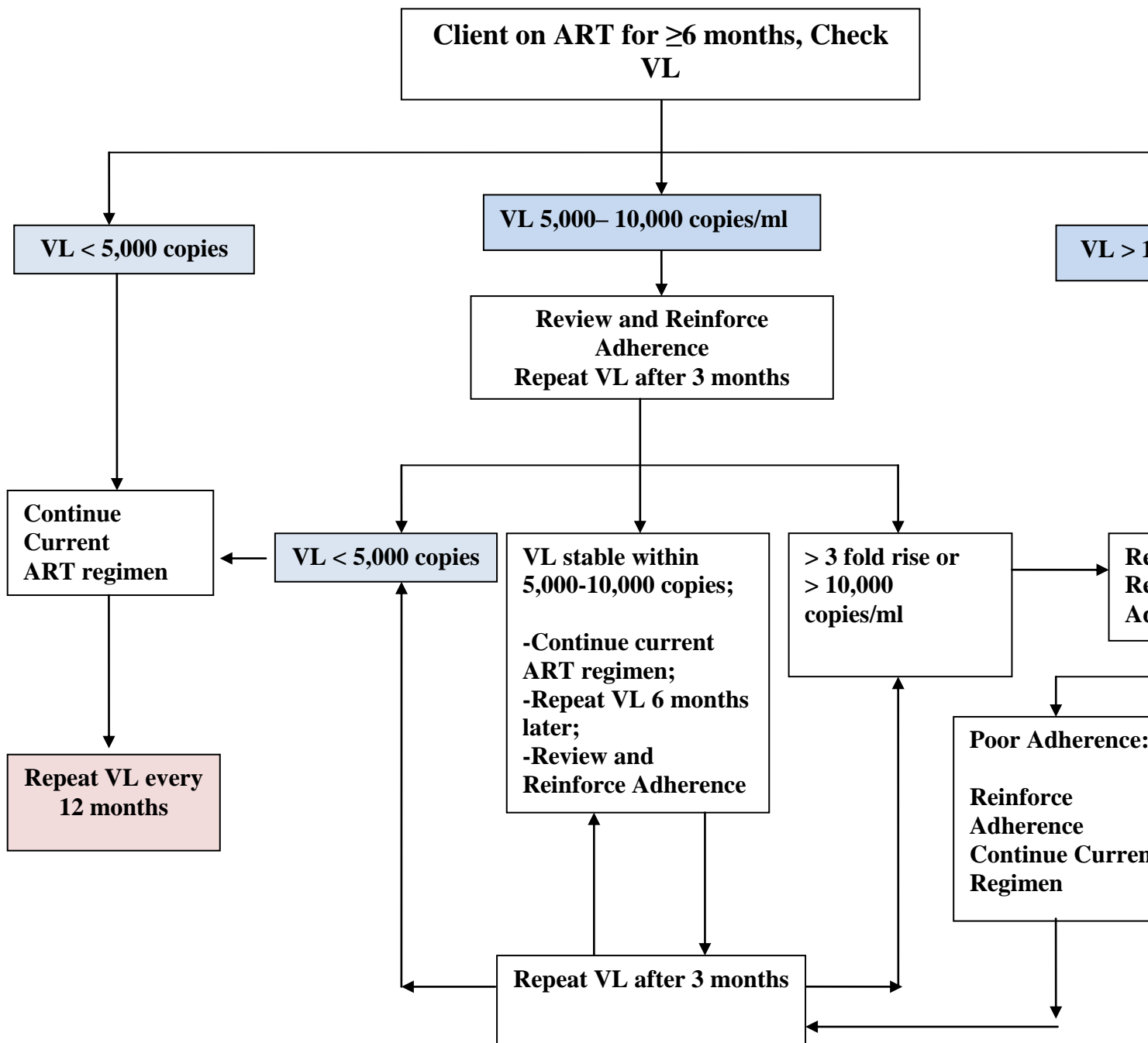
1. Review and reinforce adherence of patient to ART
2. Repeat VL after 3 months while continuing the current ART regimen.
3. If VL increases more than three fold or is >10,000 copies/ml ***then go to the next point.***

If viral load is >10,000 copies/ml (after 6 months or more on ART)

1. Review and reinforce adherence of patient to ART
2. Where adherence is satisfactory, change ART regimen as soon as possible to the next line of recommended drugs.
3. Where client is poorly adherent, efforts must be made to improve adherence while maintaining the current ART regimen. Repeat VL after 3 months while continuing the current ART regimen.

NB:

1. The goal of switching therapy is to achieve plasma HIV RNA < 50 copies/ml as soon as possible, hopefully within 3 months. This will re-establish maximal and sustained virologic response.
2. In some clients with possible drug resistance due to prior exposure to ARVs, viral suppression may be difficult or impossible to achieve with the prescribed regimen. Management of such clients is complex and referral for expert advice is recommended. The goal of treatment is preservation of immune function and prevention of clinical progression.



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