GUIDELINES FOR ANTIRETROVIRAL THERAPY IN GHANA

National HIV/AIDS/ STI Control Programme

Ministry of Health / Ghana Health Service

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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.

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HON. MINISTER OF HEALTH
September 2002

FOREWORD TO SECOND EDITION

LIST OF ACRONYMS

ABC	Abacavir
AFBs	Acid Fast Bacilli
AIDS	Acquired Immune Deficiency Syndrome
ART	Antiretroviral Therapy
ARV	Antiretroviral
AZT	Zidovudine
BUE	Blood Urea and Electrolytes
CD4	CD4 cells- T4 helper cells
D4T	Stavudine
DDI	Didanosine
GAC	Ghana AIDS Commission
GFATM	Global Fund for AIDS Tuberculosis and Malaria
GHS	Ghana Health Service
HAART	Highly Active Antiretroviral Therapy
Hb	Haemoglobin
HBV	Hepatitis B virus
HIV	Human Immunodeficiency Virus
IDV	Indinavir
3TC	Lamivudine
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
PEP	Post Exposure Prophylaxis
PI	Protease Inhibitor
PLWHA	People Living with HIV/AIDS
PMTCT	Prevention of Mother to Child Transmission
RTV	Ritonavir
SOP	Standard Operating Procedures
STD	Sexually Transmitted Disease
STI	Sexually Transmitted Infection
TB	Tuberculosis
TDF	Tenofovir Disoproxil Fumarate
VCT	Voluntary Counselling and Testing
WHO	World Health Organisation
USAID	United States Agency for International Development
START	Support Treatment and Antiretroviral Therapy
FHI	Family Health International

CHAPTER 1

1.1 INTRODUCTION

The first case of AIDS was reported in Ghana in 1986. There has since been a rapid rise in the number of cases as well as the HIV prevalence. By the end of December 2003 a cumulative number of 76,139 cases had been reported in the country. Almost 90% of these cases occurred in persons between the ages of 15 and 49 years. The female to male ratio in 2003 was found to be 1.6 :1, compared to 6:1 in 1987. The peak age group affected is the 30 to 34 year age group accounting for 34.8% of all AIDS cases reported in 2003. The peak age for males (30 to 34 years) is higher than that for females (25 – 29 years). With an estimated reporting level of 30% and with the HIV prevalence of 3.6% in 2003, it is projected that 400,000 cases of HIV infection have probably already occurred.

Sexual spread remains the main mode of transmission accounting for an estimated 80% of all transmissions, mother-to-child (vertical) transmission 15%, blood and blood products 5%. Data gathered in the 2003 Sentinel Survey estimated a median prevalence of HIV infection among antenatal clients of 3.6%. Also in this survey both HIV 1 and 2 were found in the Ghanaian population with HIV 1 occurring in 94%, HIV-2 in 0.5% and dual infections in 5% of all infections .

The response to the epidemic included priority interventions which initially focussed on promotion of safe sex, condom promotion, improved management of STDs, safe blood, infection control, nursing/clinical care and counselling, home based care and prevention of mother-to-child transmission. These interventions were geared towards reducing the number of new infections and improving the quality of life of PLWHA. Since June 2003, antiretroviral therapy has been available in the public health sector in Ghana. This has the added value of reducing HIV-related morbidity and mortality

Access to ART within the continuum of care is now a priority and the Government of Ghana has made a commitment towards providing it. Antiretroviral therapy however is a life long 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
- Use of drug resistance testing in selected clinical settings

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1.2 AVAILABLE CARE IN GHANA

The provision of Antiretroviral therapy in the public health care system started in June 2003 at two pilot sites. The NACP in collaboration with its partners Family Health International and with funding from USAID supported the setting up of two pilot sites in the Manya Krobo district to provide comprehensive care for PLWHA. As part of the comprehensive care programme antiretroviral therapy was provided to PLWHA according to the criteria prescribed by the National ART Guidelines

The comprehensive care programme Support Treatment and Antiretroviral Therapy (START) ensured the provision of Voluntary Counselling and Testing and Prevention of mother to Child Transmission (VCT/PMTCT), Management of Sexually Transmitted Infections, Management of Opportunistic Infections and Antiretroviral therapy. Community activities to encourage behaviour change and promotion of services are also part of the package. These comprehensive care services ensured the holistic management of PLWHA and the provision the effective entry points to care. Lessons learned from this programme were fed into the expansion of the national ART programme for scaling up.

Support from the Global Fund to fight AIDS, Tuberculosis and Malaria (GFATM) and FHI's START programme enabled the scale up of comprehensive care for PLWHAs from the two pilot sites. In December 2003 and February 2004 the Korle-Bu Teaching Hospital and Komfo Anokye Teaching Hospital respectively started providing ART for PLWHA. A total of four treatment sites in the country were thus in place by the end of 2004. The GFATM procured ART drugs for the 2000 patients over a period of two years. By the end of December 2004 a total of 2017 adults and children had accessed treatment from the four sites.

The Government of Ghana is committed to providing ART and comprehensive care to PLWHA. In line with the "3 by 5 initiative" Ghana has plans to provide ART for 30,000 PLWHA. In line with this The NACP and the Ghana Health Service is scaling up ART in all 10 Regional hospitals and some selected district hospitals in Ghana. In addition public-private partnerships programmes are underway to enhance the rapid scale up ART for PLWHA.

To ensure the standardisation and quality of management for PLWHA various guidelines were developed in 2001 and 2002 to guide care. These include:

- National Guidelines on Antiretroviral Therapy
- National Guidelines on Management of Opportunistic Infections
- National Guidelines on VCT
- National Guidelines on PMTCT
- National Guidelines on STI Management
- Logistics Management Guidelines and Protocols

In addition requisite procedures and structures were put in place to provide an enabling environment for the effective management of ART. Furthermore polices 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

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 the Monitoring and evaluation systems (Logistics Management and health information system)
- Procurement of logistics and consumables

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

- Rational selection and sequencing of drug regimen
- Maximising adherence to the selected regimen
- Preservation of future treatment options
- Use of drug resistance testing in selected clinical settings

The regimen used in Ghana is based on Highly Active Antiretroviral Therapy regimen using triple drug regimen. In Ghana, no dual or monotherapy shall be used in the management of PLWHA.

Combinations of drugs in Table 1 below are the drugs currently recommended in the national guidelines for Antiretroviral Therapy in Ghana.

TABLE 1.1 ART AVAILABLE IN GHANA

Nucleoside Reverse Transcriptase Inhibitors (NRTI)	**Nucleotide Reverse Transcriptase Inhibitor (NtRTI)**	**Non-Nucleoside Reverse Transcriptase Inhibitors (NNRTI)**	**Protease Inhibitors (PI)**
Zidovudine	Tenofovir	Nevirapine	Nelfinavir
Lamivudine		Efavirenz	Ritonavir boosted Lopinavir
Stavudine			
Didanosine			
Abacavir			
Emtricitabine			

Where available fixed dose combinations of these drugs are preferred.

The cost of care has been substantially subsidised by the Government of Ghana. A PLWHA currently pays 50,000 cedis (about US $5) for a month's supply ART drugs 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/AIDS drugs and other related commodities in Ghana.

1.3 PURPOSE

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

1.4 OBJECTIVE:

The objective of this document is :

- 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 including counselling in ART
- To provide direction on logistics management and information for Antiretroviral drugs

These objectives facilitate access to affordable ART and assure the continuum of care for PLWHA.

Complementary documents have been developed and combine use will ensure quality care. These documents which should be used as complementary documents to this one include the following:

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 Voluntary counselling And Testing in Ghana', GAC/MOH
3. 'Prevention of Mother-to-Child Transmission of HIV in Ghana', MOH/GHS
4. 'VCT 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. 'Logistics Management of Public Sector Health Commodities in Ghana, SOPs', MOH/GHS
8. 'Manual on Nursing Care for People Living with HIV/AIDS', MOH/GHS
9. 'Guidelines for managing Tuberculosis in Health Facilities' Training / Reference manual
10. *Nutrition Guidelines for PLWHA (these are still under development).

CHAPTER 2

ANTIRETROVIRAL THERAPY IN ADULTS AND ADOLESCENTS (≥13 years)

2.1 INTRODUCTION

The high cost of antiretroviral drugs, the complexity of the regimens, 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 therefore undergo accreditation and be assisted to meet set criteria before they provide ART[1].

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

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

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 its interruption will be detrimental to 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 5).

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

- Assessing the clinical staging of the HIV infection
- Identifying past HIV related illnesses
- Identifying current HIV related illnesses requiring treatment
- Identifying co-existing medical conditions. 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

[1] See National Accreditation Criteria for Antiretroviral Therapy

Antiretroviral therapy may be initiated when the patient satisfies the following the criteria:

1. Patients with CD4 count less than 250 cells /ml
   and / or
2. Symptomatic with HIV infection in WHO stage 3 and 4 [2]. (Where initiation is based solely on WHO staging the CD4 count must be done as soon as possible).

2.3.2 EXCLUSION CRITERIA

Antiretroviral Therapy should not be initiated under the following circumstances:

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 pre-treatment adherence counselling
3. Treatment is not sustainable, e.g. the person is not able to cope with follow up visits
4. No laboratory monitoring is possible
5. The patient presents with severe hepatic or renal insufficiency
6. The patient has an acute opportunistic infection. In this case these acute opportunistic infections must be treated before initiation of antiretroviral therapy.
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:

- 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

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
- Past Medical History including diagnosis of tuberculosis
- Drug history including treatment for TB
- Sexual history and past symptoms of STI
- Gynaecological history (for females)

[2] See Appendix 1 for staging

- Social history

The physical examination should have the following components:

- Patient's weight and height
- Skin and lymph nodes, looking out for the following
  - Herpes Zoster (old scars and new lesions)
  - *Herpes simplex*
  - *Molluscom contangiosum*
  - Kaposi's sarcoma
  - HIV dermatitis
- Oropharyngeal mucosa
  - Candidiasis
  - Leucoplakia
  - Kaposi's sarcoma
- Lymphadenitis/lymphadenopathy
- Examination of Respiratory and Cardiovascular system
- Examination of the abdomen
- Examination of 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
- Determine whether female patients are pregnant
- Determine the presence or absence of opportunistic infections
- Determine of the Stage of HIV infection

Initial laboratory evaluation should provide:

1. Confirmation HIV infection and typing
   - Confirmatory HIV test (and typing 1 and/or 2)
   - Viral load (not absolutely necessary)[3]

2. Indication of patients' immune status
   - CD4 lymphocyte count [4]

[3] **Viral load**

Although this test is important, it cannot be done routinely due to financial and capacity constraints. The viral load at the initiation of therapy indicates the prognosis of HIV infection and during therapy it provides evidence of the virological response to therapy. Viral load monitoring is not critical if there is clinical improvement, good adherence and increase in CD4 count.

Though viral load is not essential for management and follow up, it is recommended that where available and affordable it should be done at month 0, 3, 6 month and then six-monthly. If the viral load is undetectable and there is good adherence to drugs, the frequency of viral load determination can be reduced unless there are clinical indicators of deterioration.

Information on the patient's baseline indicators including:

Other Baseline tests

• Haematological test	Full blood count including total lymphocyte count and platelets
• Biochemical test	Blood Urea and Electrolytes Liver Function tests (if on Nevirapine more frequent monitoring is necessary) Fasting Blood sugar (if treatment includes PIs) Fasting Cholesterol and lipids (if treatment includes PIs)
• Routine examinations	Urinalysis (Urine R/E) Stool R/E
• Respiratory examinations	Chest X-ray Sputum for AFBS- if symptoms so indicate
Supplementary tests These tests are performed depending on signs and symptoms	Hepatitis B Surface antigen screen Histology on skin and lymph node biopsy Screening for STIs Pregnancy tests Abdominal Ultrasound

2.6 RECOMMENDED ART REGIMEN

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. Monotherapy or dual therapy (treatment with one or two drugs only) is contraindicated for treatment of PLWHA.

The following triple therapy regimens are recommended:

- 2 Nucleoside Reverse Transcriptase Inhibitors (NRTIs) and 1 Non-Nucleoside Reverse Transcriptase Inhibitor (NNRTI)

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[4] **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 and once every six months

- 2 NRTIs and 1 Protease Inhibitor (PI)
- 2 NRTIs and 2 PIs. The 2 PIs are considered as one ARV, as the second PI, usually ritonavir, is in low dose and is used to boost the blood level of the first PI.

The Table of the recommended drug combinations are shown below.
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 clinical evidence of treatment failure with the first line regimen. This should be confirmed preferably by CD4 monitoring (where a viral load is possible this should also be performed).In this case the whole regimen should be changed. Dosages of the Regiment will be found in drug information attached in appendix 7.

2.6.1 FIRST LINE DRUGS

TABLE 2.1

	Drugs	Contra-indications	Comments
First choice drugs	**First Option** Zidovudine+ Lamivudine +Nevirapine	Nevirapine is contraindicated in: o liver dysfunction o hypersensitivity Zidovudine is contraindicated in: o severe anaemia	Replace with Efavirenz Replace with stavudine
	Second Option Zidovudine+ Lamivudine+ Efavirenz	Efavirenz is contraindicated in: o Pregnancy o CNS presentations When there is Efavirenz related persistent CNS toxicity	Replace with Nevirapine Replace with Nevirapine
Second Choice drugs	**First Option** Stavudine + Lamivudine+ Nevirapine		Stavudine 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) stavudine should replace zidovudine

	Drugs	Contra-indications	Comments
Second Choice drug	**Second Option** Stavudine + Lamivudine+ Efavirenz	Efavirenz in contraindicated in: o Efavirenz related Persistent CNS toxicity Pregnancy	Stavudine should be used when Zidovudine is contraindicated e.g. anaemia Replace with Nevirapine

2.6.2 SECOND LINE DRUGS

TABLE 2.2

	Drugs	Contra-indications/	Comments
First Alternative	Abacavir*** + Tenofovir* + Nelfinavir Abacavir + Tenofovir + Lopinavir/r**		
Second Alternative	Didanosine + Abacavir + Nelfinavir Didanosine + Abacavir + Lopinavir/r	Contraindicated in hypersensitivity of Abacavir	switch to Tenofovir

Emtricitabine can be used for those with abacavir hypersensitivity

The following triple nucleoside/nucleotide reverse transcriptase inhibitor combinations are **NOT RECOMMENDED** due to known virological failure:

- Didanosine + Lamivudine + Tenofovir
- Abacavir + Lamivudine + Tenofovir
- Abacavir + Lamivudine + Zidovudine (Please note exception in children with HIV/TB co-infection).

* If Tenofovir is given together with Didanosine, the dose of Didanosine should be reduced from 400 mg/daily to 250 mg/daily because of drug interaction which increases levels of ddI.

** Lopinavir/r is a Ritonavir boosted lopinavir which requires secure cold chain. It can however be stored at a maximum temperature of 35^0C for one month. Therefore patients who do not have refrigeration should not be given more than one month's supply

2.6.3 SPECIAL CONDITIONS

TABLE 2.3

The recommended regimen above should be amended in these conditions:

Condition	Recommendation	Comments
Women of childbearing potential	Zidovudine or Stavudine + Lamivudine + Nevirapine	Efavirenz is teratogenic and should not be used unless adequate birth control is assured
Co-infection with Hepatitis B (Core antigen positive)	Regimen should include either Lamivudine or Tenofovir	Lamivudine and Tenofovir are active against hepatitis B and HIV
ART experienced patients	Review drug combination and duration, clinical, immunological and virological response. 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 Nevirapine from PMTCT	This does not preclude the use of Nevirapine for ART	

2.6.4 Recommendations for antiretroviral therapy in patients with Tuberculosis

All HIV positive patients with TB should be considered severely ill and treated in accordance with the National Tuberculosis Programme Guidelines with short course chemotherapy. The regimen should not include thiacetazone in view of the high incidence of Stevens Johnson syndrome in PLWHA taking this drug.

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.

Due to drug-drug interactions the following options may be followed in the treatment of HIV positive patients with known TB co-infection:

1. When possible ART should be deferred until the completion of anti-tuberculosis chemotherapy.

2. For moderately immunocompromised patients, ART should be deferred until the completion of the intensive phase so that the ARV is given without rifampicin.

3. For severely immunocompromised patients (CD4 count<50) both therapies may be initiated at the same time. Nevirapine and Rifampicin are both hepatotoxic and should not be administered together. Therefore, in patients being treated with Rifampicin, in the initial intensive phase of Short course of Tuberculosis treatment, a Nevirapine containing regimen should be replaced with a Efavirenz containing regimen. The usual dose of Efavirenz should be increased from 600 mg to 800 mg to correct for the increased metabolism of Efavirenz in the presence of Rifampicin.

2.7 DRUG INTERACTIONS

Drug interactions may occur between any medications an individual takes. For a PLWHA 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 anti-retroviral drugs
- Between prescribed medicines and alternative or non-prescription medication
- Between medicines and food
- Certain recreational drugs

Some important drug interactions are:

- Trimethoprim-sulfamethoxazole, ganciclovir 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 stavudine, zidovudine and didanosine
- 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 PLWHA should be a team approach between the physician, 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 bi-monthly intervals or as necessary. Patients should also be seen after laboratory tests have been completed.

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 methodologies:

- Self-reports
- Pill counts
- Pharmacy records

2.9.1.2 Monitoring of tolerance

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
- Opportunistic infections becoming clinically apparent as a result of immune reactivation

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.
Ancillary laboratory tests should be done to confirm adverse effects such as anaemia, neutropenia among others (see laboratory monitoring).
Where Opportunistic Infections become clinically apparent as a result of immune reconstitution syndrome. These need to be diagnosed and treated)

2.9.1.3 Monitoring of Efficacy

Indicators for improvement in the patient's condition would be

- Gain in body weight
- Decrease in frequency or severity of opportunistic infections
- Increase in CD4 count of 100-200 cells per year (this may be less if initial CD4 <50)
- Increase in total lymphocyte count
- Increase in platelets if low at the start
- Sustained suppression of viral load [5]

2.9.2 LABORATORY MONITORING

Continuous 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 3 monthly intervals:

- Full blood count including platelet count (patients on Zidovudine may require frequent Hb monitoring -)
- Urine R/E
- Fasting Blood Sugar (if the patient is on PIs)
- BUE and Creatinine
- Liver function tests (ALT, AST)

Other tests can be done depending on clinical findings such as chest X-ray, sputum for AFBs etc.

It is recommended that the CD4 count be done at initiation and once every six months

Though viral load is not essential for management and follow up, it is recommended that where available and affordable it should be done at month 0, 1 month and then six-monthly. It provides evidence of the virological response to therapy. If the viral load is undetectable and there is good adherence to drugs, the frequency of viral load determination can be reduced unless there are clinical indicators of deterioration.. Viral load determination is not essential if there is clinical improvement, good adherence and increase in CD4 count.

[5] 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 drugs interactions
- First trimester of pregnancy (when the patient so elects). The patient may restart therapy after the first trimester
- 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 and virologically by an crease in viral load. Treatment failure may occur at initiation or some time after treatment.

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

Immunologic Failure is the return of CD4 count to pre-therapy baseline or below and/or more than 30% fall from on-therapy CD4 peak level (and /or more than 3% change in CD4%) without other concomitant infection to explain the decrease.

Virologic failure is defined as insufficient viral load suppression at 6 months after starting ART, or stable/increase in viral load by one log or three fold (“half log”)as determined by RT-PCR, after initial suppression.
(Note that if after one month of initiation of therapy there is significant increase in viral load then this indicates drug resistance).

The main reasons for treatment failure are;

1. Poor prescribing
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 PLWHAs. 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 VCT, PMTCT, and Management of Opportunistic Infections, nutritional support, Home Based Care, Care for Orphans vulnerable and 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. PLWHA associations, Home Based Care providers, Social workers and legal workers.

ART sites should form linkages with one an other to facilitate referral and exchange of information (see appendix for some sites in comprehensive care)

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 caused by 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. Clinicians should have a high index of suspicion to clinically detect children who have HIV/AIDS and initiate early management to improve survival.

Definitive diagnosis of HIV infection in children especially in those less than 18 months is complex due to the persistence of maternal antibodies and requires virologic tests. Where virological tests are not done or available, exposed children must be followed up till 18 months when the child will be confirmed either HIV seropositive or negative by antibody testing. A child who tests negative after 18 months is not infected.

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 the negative virologic or antibody test at a single point in time does not exclude the child becoming infected at a later time if breastfeeding is continued.

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:

1. A child < 18 months who is HIV sero-positive or born to HIV positive mother: and • HIV DNA positive by PCR or • A positive viral culture
2. A child < 18 months who is HIV sero-positive or born to HIV positive mother: and • who meets the clinical criteria for AIDS diagnosis based on the WHO staging system (see appendix 2) and • Absolute lymphocyte count less than 2500x 10^6 cells/mm^3 or • CD4 percentage less than 20%.
3. A child ≥18 months who is HIV sero-positive

3.4 INITIATION CRITERIA

3.4.1 INCLUSION CRITERIA

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

TABLE 3.2 INCLUSION CRITERIA FOR ART

Age	**HIV Diagnostic testing**	**Treatment Recommendation**
<18 months	Viral PCR not available HIV antibody sero-positive	Treat if WHO Paediatric stage III and IV disease irrespective of CD4 % For WHO stage II treat if CD4 < 20%
	Positive HIV PCR	Treat if WHO Paediatric stage III and IV irrespective of CD4%
		Treat if WHO Stage II with CD4< 20%
≥18 months	HIV antibody seropositve	WHO Paediatric Stage III and IV irrespective of CD4%
		WHO Stage I - IV with CD4< 15%

EXCLUSION CRITERIA

Antiretroviral therapy shall not be initiated under the following circumstances:
1. Lack of parental or guardian motivation
2. Treatment is not sustainable
3. No basic laboratory test available e.g. full blood count
4. Patient presents with severe hepatic or renal insufficiency
5. The patient has an acute opportunistic infection. (This must be treated before the initiation of ART)
6. Carer or guardian must complete pre-treatment adherence counselling

- **CLINICAL EVALUATION**

A detailed clinical evaluation is essential prior to initiating ART.

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

- 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

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
- Mother's pregnancy and drug, (including ARV) history

Examination should include

- weight
- height
- Head circumference
- Mid Upper arm Circumference in children 1 to 6 yrs of age

(For further details of the clinical evaluation see chapter 2 page 16)

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 Stage of HIV infection

(For details of the laboratory evaluation see chapter 2 page 17)

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 PI
- 2NRTI plus 2PIs

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 (i.e. on ART during pregnancy)
- Therapy for ARV naïve infants and infants exposed to intrapartum Nevirapine shall be the same.
-

3.7.1 FIRST LINE DRUGS

The first line drugs for the Ghana's national guidelines indicated in the table below.

TABLE 3.3

	Drugs	**Contra-indications**	**Comments**
First Choice Drugs	**First Option** Zidovudine+ Lamivudine +Nevirapine	Nevirapine is contraindicated in: liver dysfunction hypersensitivity Zidovudine is contraindicated in: severe anaemia	Replace with Efavirenz Replace with stavudine
	Second Option Zidovudine+ Lamividine+ Efavirenz	Efavirenz is: not indicated in Children less than 3 years Contraindicated in Efavirenz related Persistent CNS toxicity	Replace with Nevirapine Replace with Nevirapine

	Drugs	Contra-indications	Comments
Second Choice Drugs	**First Option** Stavudine + Lamivudine+ Nevirapine		Stavudine should be used when Zidovudine is contraindicated e.g. anaemia
	Second Option Stavudine + Lamivudine+ Efavirenz	Efavirenz is: not indicated in Children less than 3 years Contraindicated in Efavirenz related Persistent CNS toxicity	Stavudine should be used when Zidovudine is contraindicated e.g. anaemia Replace with Nevirapine Replace with Nevirapine

3.7.2 SECOND LINE DRUG

The first line drugs for the Ghana's national guidelines indicated in the table below.

TABLE 3.4

	Drugs	Contra-indications/	comments
First Choice Drugs	1. Didanosine + Abacavir Nelfinavir	In case of hypersensitivity to Abacavir,	switch to Zidovudine or Stavudine
Second Choice Drugs	2. Lopinavir + Didanosine + Abacavir	In case of hypersensitivity to Abacavir	switch to Zidovudine or Stavudine

(For drug dosages and characteristics see Appendix 7)

3.7.3 Treatment experienced

Children born to HAART experienced women or who have themselves received ART in the past should be treated bearing in mind their previous exposure to ART and the possibility of resistance. This should be undertaken in consultation with a specialist in ART.

3.7.4 Treatment in co-infection with Tuberculosis and HIV

Patients with Tuberculosis merit special considerations because co-management of HIV and TB is complicated by Rifampicin drug interactions with NNRTI and PIs, pill burden, adherence and drug toxicity. For children less than 10 kg or under 3 years with TB/HIV dual infection, Abacavir +

(Stavudine or Zidovudine) + Lamivudine are recommended. For more information see Chapter 2.

3.7.5 Treatment Changes

Therapy changes are similar for adults and children (see adult section Chapter 2 for interruption of therapy and criteria for changing therapy). However a few important issues should be taken into consideration

3.7.5.1 Treatment Failure

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 24 weeks).

Clinical and CD4 Count definition of treatment failure in infants and children

Clinical signs of treatment failure	CD4 cell criteria for treatment failure
Lack of growth among children who show an initial response to treatment, or decline in growth among children who show an initial growth response to therapy	Return in CD4 cell percentage (or for children > 6 years of age, absolute CD4 cell count) to pre-therapy baseline or below
Loss of neurodevelopment milestone or development	≥ 50% fall from peak level on therapy of CD4 cell percentage (or for children > 6 years of age, absolute CD4 cell count), in absence of other concurrent infection to explain transient CD4 decrease.
Occurrence of new opportunistic infection or malignancy signifying clinical disease progression	
Recurrence of prior opportunistic infections, such as oral candidiasis refractory to treatment	

3.8 Drug Issues

Drug interactions for children are similar to those of adults. (See chapter 2 and Appendix 8 for further information).

Drug dosing in children is dependant 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 8 for further information)

3.9 Monitoring

3.9.1 Clinical Monitoring

Clinical monitoring of children on ARVs similar to the monitoring in adults. (See Chapter 2)
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;
- And/or decreased frequency of infections (oral thrush, bacterial and/ or 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
- 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 six years of age. See Chapter 2.

3.9.2.1 Monitoring of adherence

In children adherence counselling involves the parents and/or guardian who will be administering the medication. See Chapter 2.

3.9.2.2 Monitoring of Efficacy

See Chapter 2.

CHAPTER 4

POST EXPOSURE PROPHYLAXIS FOR HEALTH CARE WORKERS

4.1 INTRODUCTION

The risk of exposure to blood and blood borne pathogens is slightly greater for health care personnel than people who do not work around blood. Workplace accidents or injuries may occur that expose the health worker to body fluids of a patient. Post Exposure Prophylaxis (PEP) reduces the likelihood of HIV infection after high-risk 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 of exposure and not more than 72 hours of exposure.

4.2 RISK

An exposure that would create such a risk is defined as:

- A percutaneous injury (e.g. a needle stick or cut with a sharp object)

Or

- A mucutaneous membrane of non-intact skin (e.g. skin that is chapped abraded, or affected by dermatitis) contact

And

- The exposure is to infected blood, tissue or other body fluids.

The risk of infection for HIV after a percutaneous injury is approximately 0.3%. 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 disease stage
- A deep percutaneous injury
- An injury with a hollow- bore, blood filled needle.

Transmission rates after mucous membrane on non-intact skin exposures are lower than from percutaneous injuries.

4.3 PREVENTION

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

- Hands should be washed frequently before and after handling all patients.
- Gloves must be worn when any kind of venous or arterial access is being performed.
- Gloves, gowns, boots eye wear and masks should be used appropriately for the patient care.
- Sharps should be used with caution with all patients
    - Sharps should used with a sharps container nearby
    - Sharps should be disposed of in a puncture proof receptacle immediately after use

4.4 STEPS TO PREVENT OCCUPATIONAL TRANSMISSION OF HIV

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

4.4.1 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 water.
- Eyes should be flushed with water or saline.

4.4.2 PEP STEP 2: Assess the exposure risk

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

4.2.2.1 Low risk exposure is:

- Exposure to a small volume of blood or blood contaminated fluids from asymptomatic HIV-positive patients with low viral load
- An injury with a solid needle
- Any superficial injury or muco-cutaneous exposure

4.2.2.2 High-risk exposure is

- Exposure to a large volume of blood or potentially infectious fluids
- Exposure to blood or blood contaminated fluids from a patient with a high viral titre. i.e. in the AIDS phase or early sero-conversion phase of HIV
- Injury with a hollow bore needle
- Deep and extensive injury
- Drug resistance in source patient

4.4.3 PEP STEP 3: Specific PEP management

1. Counselling and Testing:
    - All health workers accessing the post exposure prophylaxis package must receive counselling and testing immediately from a trained counsellor throughout the period and thereafter if necessary.
    - All known source-patients should also be counselled and tested if their status is not known.
    - All exposed individuals should receive counselling from trained counsellors throughout the period and thereafter

2. Timing of post-HIV exposure prophylaxis initiation.
   If therapy is necessary, it should be initiated promptly, preferably within 1-2 hours post–exposure and not more than 72 hours of exposure.
3. Specific treatment for is described on the table below.

Table 4.1: Recommended Post –HIV exposure prophylaxis

RISK LEVEL	RECOMMENDED PROHYLAXIS
Very Low risk	Wash exposed area immediately with soap and water
Low risk	Zidovudine 300mg bid x 28 days Lamivudine 150mg bid x 28 days
High risk	Zidovudine 300mg bid x 28 days Lamivudine 150mg bid x 28 days Nelfinavir 750 mg tid or 1250 mg bid x 28 days Or Lopinavir/r 400mg/100mg 12hrly 28days

4.4.4 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 serology, and to monitor the toxicity of drugs on the personnel. Table 4.2 indicates the laboratory tests that required.

Table 4.2 : Recommended monitoring of drug toxicity and HIV serology of exposed health care personnel after exposure

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

The individual who sero-converts should have access to comprehensive care services and ART if needed as spelt out in the "Workplace HIV/AIDS Policy and Technical Guidelines for the Health Sector"[6] . For further information refer to this document.

[6] Workplace HIV.AIDS Policy and Technical Guidelines for the Health Sector, Ministry of Health, August 2004

4.4.5 PEP STEP 5: Report and Document

All occupational exposures should be reported immediately to the supervisor; circumstances of the exposure and PEP management should be recorded in the exposed person's medical confidential records. Details should include:

- Date and time of exposure
- Details of incident; where and how the exposure occurred, exposure site on the body and type of sharp device, if any.
- Details of the exposure; type and amount of fluid material, severity of the exposure
- Details of the exposure source; whether the source material contained HIV or other blood borne products
- If the source patient is HIV-positive, the stage of the disease, the viral load, whether on ART and the ART resistance information.
- Details about exposed health care worker; medical history, Vaccination including Hepatitis B, known medical conditions and medications, including pregnancy or breast-feeding
- Document counselling, post exposure management and follow up

CHAPTER 5

GUIDELINES ON ART COUNSELLING

5.1 INTRODUCTION

Counselling for ART compliments all ongoing counselling for VCT, PMTCT and follow up counselling for psychosocial support. The following guidelines are available to support general counselling and counselling of ART:

- National Guidelines for the Development and implementation of HIV Voluntary counselling And Testing in Ghana [7]
- Prevention of Mother-to-Child Transmission of HIV in Ghana, [8]
- VCT Training Manual[9]

5.2 GOALS 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
- ART is not a cure.
- The virus can still be transmitted while on ART and so preventative 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 compliment the general counselling for HIV/AIDS. ART should not be initiated until the patient has had at least 2 counselling sessions 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.

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

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

[9] MOH/GHS VCT Training Manual'

Each treatment facility should identify and train at least one full time counsellor. ARV should not be dispensed to any patient unless he/she has had adequate adherence counselling.

5.2.1 The Goals of Therapy

The patient should understand that the goal of therapy is to:

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

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

5.3 Antiretroviral Therapy

The approach to antiretroviral treatment and the design of therapeutic regimens has 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 not only able to consistently suppress HIV replication, but also able to induce a significant delay in 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 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.

5.3.1 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)

5.3.2 Financial considerations

The counsellor should tell the patient the cost of ART per month (or per year). The patient must be prepared for the financial commitment ARV places on her/him. The patient should be reminded that treatment is a lifetime commitment. The consequences of sub-optimal dosing, drug holidays and non-adherence should be discussed.

5.3.3 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, antifungal).
- 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.

5.3.4 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.

5.3.5 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 (either 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.

5.3.6 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 PLWHA
- Other Civil Society Organizations
- NGOs in AIDS care
- Social welfare department
- District Assemblies

5.3.7 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.

CHAPTER 6
Data Management

6.1 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 summary report of ART patients
- ART patient register
- ARV dispensing log adult regimen
- ARV dispensing log paediatric regimen
- Bin card
- Initial patient assessment forms for adults.
- Initial patient assessment forms for children.
- Follow up patient assessment forms for adults.
- Follow up patient assessment for children.

6.2 Health Information Management System (HMIS)

The following patient information should be obtained from each patient:

- Demographic data
- Medical History
- Social History
- Physical Examination
- Laboratory Evaluation
- Drug Treatment
- Adherence
- Side Effects

This information is collected using the initial patient assessment and follow up forms for adults and children. Information collected shall be reported monthly from each site 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.

6.3 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

6.3.1 Essential data for LMIS

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

- **Stock on hand**; quantities of usable stock available at all level of the system at 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 form one facility to another at the same level (e.g. transfer) or a correction for an error in counting. Losses and adjustment s may therefore be negative or a positive number.

6.3.2 LMIS Forms for administering ART in Ghana

The following 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 Adult and Paediatric ARV drugs

CHAPTER 7

PROCUREMENT, STORAGE AND DISTRIBUTION OF ARV DRUGS

7.1 PROCUREMENT

7.1.1 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 purchase price
- Ensure reliability of the supplier to supply good quality products and back them with adequate services.
- Minimize loss of resources, e.g. of funds and goods, resulting from adverse influences on procurement decisions and processes.
- Obtain optimum economy in personnel, time and other resources used in the procurement process.

7.1.2 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.

Issues in the selection of ARVs and drugs for treating opportunistic infections.

- Shall be based on the results of efficacy and safety evaluations obtained in controlled clinical trials and epidemiological studies, and on the performance in general use in a variety of medical settings;

- When several drugs are available for the same indication, only the drug and the pharmaceutical form that provides the most convenient benefit/risk ratio shall be selected

- When two or more drugs are therapeutically equivalent, the selection shall fall on the drug:

    - that has been more thoroughly investigated

    - with the most favourable pharmacokinetic properties;

    - with the lowest cost, calculated on the basis of the whole course of treatment,
    - the drug with which health workers are already familiar,

    - for which economically convenient manufacturing is available in the country

- which shows better stability at the available storage conditions.

A fixed dose combination shall be accepted only if clinical documentation justifies the concomitant use of more than one drug, and the combination provides a proven advantage over single compounds administered separately in therapeutic effect, safety, patients' compliance or cost.

7.1.3 SPECIFICATION

Generic (international non-specific nomenclature) names shall be employed, as the standard means of reference and selected drugs shall conform to the BP, USP and or any other officially accepted pharmacopeal standards.

7.1.3 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 the drug required for the given health problem

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.

7.1.4 QUALITY ASSURANCE

Antiretroviral drugs procured by MOH shall be of acceptable quality and 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.
Subject to requirement in accordance with the Ghana Food and Drugs Board's Law, which makes it mandatory for all drugs to be registered and a system of post registration surveillance implemented.

7.1.4 EXECUTIVE PROCUREMENT

ARVs shall be procured centrally into the public drug supply system through competitive bidding using centrally consolidated order quantities. A framework for awarding a three-year contract shall be established to ensure uninterrupted supply.

All ARVs procured shall bear unique identification marks for easy recognition and scheme protection.

At the scheme inception phase, ARVs shall be for prescription only and not for sale in the Open Market. This is to prevent abuse and development of ARV resistance.

7.2 STORAGE AND DISTRIBUTION

ARVs shall be stored centrally and distributed directly to treatment centres on a stock rotation basis (First expiry first out basis) The audit trail shall be transparent to prevent possible leakages.
At both the central and facility 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.[10]

- ART Patient Register
- Monthly Summary Report of ART Patients
- Bin Card
- ARV Drugs Dispensing Log
- Monthly LMIS Report For ANTIRETROVIRAL DRUGS

7.2.1 DISPENSING OF ARVs

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

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

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

APPENDIX 1

WHO CLINICAL STAGING SYSTEM FOR HIV INFECTION AND DISEASE

Patients with HIV infection who are aged 13 years or older are clinically staged on the basis of the presence of the clinical condition, or performance score, belonging to the highest level. (This staging differs from that used for AIDS surveillance).

WHO CLINICAL STAGING SYSTEM FOR HIV INFECTION AND DISEASE

CLINICAL STAGE 1	• Asymptomatic • Generalised lymphadenopathy, • Performance scale 1: asymptomatic, normal activity
CLINICAL STAGE 2	• Weight loss < 10% body weight (and > 5%) • Minor mucocutaneous manifestations (seborrheic dermatitis: prurigo, fungal nail infections, recurrent oral ulcerations , angular stomatitis) • Herpes Zoster within the last 5 years • Recurrent upper respiratory tract infections (i.e. bacterial sinusitis) • And /or performance scale 2: symptomatic, normal activity
CLINICAL STAGE 3	• Weight loss > 10% body weight • Unexplained chronic diarrhoea > 1 month • Unexplained prolonged fever (intermittent or constant) > 1 month • Oral candidiasis • Oral hairy leukoplakia • Pulmonary tuberculosis within the previous year • Severe bacterial infections (i.e. Pneumonia, pyomyositis) • And /or performance scale 3: bed-ridden < 50% of the day during the last month
CLINICAL STAGE 4	• HIV wasting syndrome (as defined by CDC (i.e. weight loss > 10% body weight, plus either unexplained chronic diarrhoea (. 1 month), or chronic weakness and unexplained prolonged fever (> 1 month) • *Pneunmocysitis carinii* pneumonia • Toxoplasmosis of the brain • Cryptosporidiosis with diarrhoea > 1 month • Cryptococcus (extrapulmonary) • Cytomegalovirus of an organ other than the liver, spleen or lymph nodes • Herpes simplex virus infection, mucocutaneous > 1 month, or visceral any duration

	• Progressive multifocal leukoencephalopathy • Any disseminated endemic mycosis • Candidiasis of the oesophagus, trachea, bronchi or lungs • Atypical mycobacteriosis, disseminated • Non-typhoidal salmonella septicaemia • Extrapulmonary tuberculosis • Lymphoma

APPENDIX 2

PAEDIATRIC STAGING OF HIV/AIDS DISEASE

WHO Paediatric Stage 1	▪ Asymptomatic ▪ Persistent generalized lymphadenopathy (PGL) ▪ Hepatosplenomegaly
WHO Paediataric Stage 2	▪ Popular pruritic eruptions ▪ Seborrheic dermatitis ▪ Fungal nail infection ▪ Angular chelitis ▪ Lineal gingival erythema ▪ Extensive HPV or molluscum infection (<5% of body area/face) ▪ Recurrent oral ulcerations (>1 episodes/6 mths) ▪ Recurrent or chronic upper respiratory infection (URI) otitis media otorrhea, sinusitis (<episodes/6 mths)
WHO Paediatric Stage 3	▪ Unexplained moderate malnutrition (-2SD or Z score) not responding to standard therapy ▪ Unexplained persistent diarrhoea (>14 days) ▪ Unexplained persistent fever (intermittent or constant, >1 mth) ▪ Oral candidiasis (outside neonatal period) ▪ Oral hairy leukoplakia ▪ Pulmonary tuberculosis ▪ Severe recurrent presumed bacterial pneumonia (>2 episodes/12 mths) ▪ Acute necrotizing ulcerative gingivitis/periodonitis ▪ Lymphoid interstitial Pneumonitis (LIP) ▪ Unexplained anemia (<8gm.dL) neutropenia (<1,000/mm^3), or thrombocytopenia (<30,000/mm^3 for > 1mth) ▪ HIV-related cardiomyopathy ▪ HIV-related nephropathy
WHO Paediatric Stage 4 in children <18 months	Symptomatic HIV-antibody positive infant age <18 mths Two more of the following: ▪ Oral candidiasis/Thrush ▪ Severe pneumonia ▪ Failure to thrive ▪ Sepsis Presumptive diagnosis of stage 4 disease in HIV antibody positive infants <18 mths requires confirmation with HIV virologic tests when possible or by antibody tests after age 19 mths.
WHO Paediatric Stage 4 (Any Age)	▪ Unexplained severe wasting or severe malnutrition (3SD or Z score) not responding to standard therapy ▪ Pnemocystis pneumonia ▪ Recurrent severe bacterial infections (> episodes/12 mths excluding pneumonia) ▪ Chronic orolabial or cutaneous HSV (lasting > 1 mo) ▪ Extrapulomonary tuberculosis ▪ Kaposi's sarcoma ▪ Eosphageal candidiasis

	▪ CNS toxoplasmosis ▪ Cryptococcal meningitis ▪ Any disseminated endemic mycosis ▪ Cryptosporidiosis or isosporiasis (with diarrhea >1 mth) ▪ CMV infection of organ other than liver, spleen, lymph nodes (and onset age > 1 mth ▪ Disseminated mycobacterial disease other than tuberculosis ▪ Candida of trachea, bronchi or lungs. ▪ Acquired recto vesico fistula ▪ Cerebral or B cell non-Hodgkins lymphoma ▪ Progressive multifocal leukoencepthalopahy (PML) ▪ HIV encephalopathy

Appendix 3

Centres for diseases Control 1994 revised classification system foe HIV infection in children less than 13 yrs old

- Category N: no symptoms
- Category A: mildly symptomatic
  - Lymphadenopathy
  - Hepatomegaly
  - Splenomegaly
  - Dermatitis
  - Parotitis
  - Recurrent upper respiratory tract infections, sinusitis, or otitis media

- Category B: moderately symptomatic

Examples of conditions in clinical category B include:

  - Anaemia, neutropenia, or thrombocytopenia
  - Bacterial infections: pneumonia, bacteraemia, (single episode)
  - Candidiasis, oropharyngeal
  - Cardiomyopathy
  - Diarrhoea, recurrent or chronic
  - Hepatitis
  - Herpes stomatitis, recurrent
  - Lymphoid interstitial pneumonia
  - Nephropathy
  - Persisitent fever >1 month
  - Varicella (persistent or complicated primary chickenpox or shingles)

- Category C: severely sumptomaic
  - Any condition listed in the 1987 surveillance case definition for AIDS, with exception of LIP. For example
  - Serious bacterial infections, multiple or recurrent
  - Candidiasis (oesophageal, pulmonary)
  - cytomegalovirus diseases with onset of symptoms at age > 1 month
  - cryptosporidiosis or isosporiasis with diarrhoea persisiting 1 month
  - encephalopathy
  - Lymphoma
  - *Mycobaterium tuberculosis,* disseminated or extrapulmonary
  - *Mycobacterium avuim complex,* or *M. kansasii,* disseminated
  - *Pneumocystis carinii* pneumonia
  - Progressive multifocal leukoencephalopathy
  - Toxoplasmosis of the brain with onset at age > 1 month
  - Wasting syndrome

Appendix 4

B Human Immunodeficiency Virus Pediatric Immune Category Classification System Based on Age- Specific CD4 T cell count and Percentage*

	< 12 months		1- 5 years		6-12 years	
	Total Lymphocyte /ml	CD4 %	Total Lymphocyte/ml	CD4 %	Total Lymphocyte /ml	CD4 %
Category 1: No suppression	≥ 1,500	≥ 25%	≥ 1,000	≥ 25%	≥ 500	≥ 25 %
Category 2: Moderate suppression	750- 1,499	15% - 24%	500- 999	15%- 24%	200- 499	15%- 24%
Category 3 Severe suppression	<750	<15%	<500	(< 15%)	<200	< 15%

Modified from CDC. 1994 Revised Classification system for human immunodeficiency virus infection in children less than 13 years of age. MMWR, 1994; 43 (No. RR-12): p. 1-10

APPENDIX 5

DRUG-DRUG INTERACTIONS

DRUG	DRUG-DRUG INTERACTIONS
Delvaridine	Rifampicin, Rifabutin, DDI, Antacids, Antiepileptics, PIs
Didanosine (DDI)	Fluroquinolones, dapsone, isoniazid, itraconazole, ketoconazole, tetracyclines
Indinavir	Rifabutin, Rifampicin,cisapride, terfenadine, astemizole, warfarin
Nevirapine	Protease Inhibitors, Rifabutin, Rifampicin, Indinavir
Ritonavir	Alprazolam, clarithromycin, diazepam, erythromycin, ketaconazole, itraconazole, rifabutin, saquinavir, tricyclic, antidepressnts, oral contraceptives
Saquinavir	Ketoconazole, rifampicin, rifabutin, phenytoin, carbemazepin
Zalcitabine	Warfarin

APPENDIX 6

Drug information

Drug	Adult dosage	Formulations	Adverse effects Minor, frequent	Adverse effects serious, dose limiting	Special instructions
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
Didanosine (DDI)	200 mg bid for wt > 60kg 125 mg bid for wt <60kg	Tablet	Neuropathy Nausea Diarrhoea dry mouth	pancreatitis, Lactic Acidosis	Take drug One hour before or two hours after food Contains antacid, affects absorption of other drugs
Lamivudine (3TC)	150 mg bid	Tablet	Few side effects, neutropenia, peripheral neuropathy reported	Lactic acidosis	
Stavudine (d4T)	30mg bid for wt <60kg, 40 mg bid for wt >60kg	Capsule	Peripheral neuropathy	Lactic acidosis	
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
Nelfinavir (NFV)	750 mg tid or 1250 mg bid	Tablet			

Drug	Adult dosage	Formulations	Adverse effects Minor, frequent	Adverse effects serious, dose limiting	Special instructions
Tenofovir	300 mg daily	Tablet			
Indinavir (IDV)	800 mg tid	Tablet	Nausea, Abdominal pain headache	Kidney stones Hyperglycaemia Lipodystrophy Abnormal bleeding Hyperbilirubinaemia	Take drug One hour before or two hours after food Drink 1.5 litres of liquid per day to avoid kidney stones Report loin pain or blood in urine
Lopinavir/r	400 mg /100 mg bid	Capsule			Lopinavir/r (is a Ritonavir boosted lopinavir which requires secure cold chain
Ritonavir (RTV)	600 mg bid	Tablet	Gastrointestinal tolerance first 2 to 4 weeks. Weakness Skin sensitivity Perioral tingling and numbness Change in taste	Abnormal liver function tests. Major drug interactions Hyperglycaemia Lipodystrophy Abnormal bleeding	Capsule require refrigeration Easier tolerated if taken with food
Saquinavir	600 mg tid	Tablet	Few reported side effects Should be used as potentiated PI in conjunction with Ritonavir	Diarrhoea Nausea Abnormal LFTS	Take high fat meal Refrigeration for long term storage Caution in liver disease
Efavirenz	600 mg daily	Capsule	Skin rash Abnormal Liver function test	Neuropsychiatric disturbances, teratogenicity	Caution in liver disease

Drug	Adult dosage	Formulations	Adverse effects Minor, frequent	Adverse effects serious, dose limiting	Special instructions
Nevirapine	200 mg daily x 14 then 200 mg b.d	Tablet	Skin rash Abnormal liver function tests	Hepatitis	Caution in liver disease

Paediatric Drugs and their characteristics

Drug	Preparations	Dosage for children	Adverse effects Minor, frequent	Adverse effects serious, dose limiting	Special instructions
Zidovudine (AZT)	Syrup: 10mg/ml Capsules:100mg Tablets:300mg	Neonatal dose: Oral: 2mg/kg body weight every 6hrs. Paediatric dose: 240mg/m2 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
Didanosine (DDI)	Paediatric powder for oral solution (when constituted as solution containing antacid: 10mg/ml Chewable	90 – 150 mg/m2 12 hourly (note higher dosage in patients with central nervous system disease)*	Neuropathy Nausea Diarrhoea dry mouth	Pancreatitis, Lactic Acidosis	Keep suspension refrigerated; stable for 30 days; must shake well Take drug one hour before or 2 hours after food Each dose should

Drug	Preparations	Dosage for children	Adverse effects Minor, frequent	Adverse effects serious, dose limiting	Special instructions
	tablets with buffers: 25,50, 100, 150 mg, 200mg				consist of 3 tablets to ensure that adequate buffering is provided to prevent degradation of the drug in gastric secretions.
Lamivudine (3TC)	Tablet 150 mg Paediatric solution 10 mg /ml	4 mg/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
Stavudine (d4T)	Capsule 15, 20, 30, and 40mg Solution 1mg/ml	< 30 kg: 1mg /kg / dose twice daily 30 – 60 kg: 30 mg/dose twice daily Maximum dose: > 60 kg 40 mg/dose twice daily	Peripheral neuropathy	Lactic acidosis Pancreatitis	Caution in liver insufficiency Keep refrigerated: stable for 30 days; must shake well. Needs to be stored in glass bottles Capsules can be opened and mixed with small amounts of food or water (stable in solution for 24 hours if kept

Drug	Preparations	Dosage for children	Adverse effects Minor, frequent	Adverse effects serious, dose limiting	Special instructions
					refrigerated) Do not use with AZT (Antagonistic antiretroviral effect)
Abacavir	Oral solution: 20 mg/ml Tablet 300mg	8 mg/ kg / dose bid	Nausea Poor Appetite Vomiting Fatigue Sleep disturbance	Hypersensitivity reaction Lactic acidosis	Caution in liver or renal disease Discontinue use if symptoms of hypersensitivity
Nelfinavir (NFV)	250 mg	30 mg/kg tid	Diarrhoea	.	Can give with food
Lopinavir/Ritonavir	Capsules: 133.3mg Lopinavir/33.3mg ritonavir Oral solution: 80mg Lopinavir/20mg Ritonavir per ml	6months to 13 years of age: 7 to <15kg: 225 mg/m2 LPV/57.5 mg/m2 ritonavir twice daily or weight- based dosing: 7-15 kg: 12 mg/kg LPV/3mg/kg ritonavir/dose twice daily 15-40 kg: 10mg/kg Lopinavir/ 5mg/kg Ritonavir twice daily		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 increases bitter taste) ; solution stable for 6 hours Because of

Drug	Preparations	Dosage for children	Adverse effects Minor, frequent	Adverse effects serious, dose limiting	Special instructions
		Maximum > 40 kg: 400 mgLPV/100 mg ritonavir (3 capsule or 5 ml) twice daily			difficulties with use of powder, use of crushed tablets preferred (even for infants) if appropriate dose can be given Powder and tablets can be stored at room temperatures Take with food Drug interactions (less than ritonavir containing protease inhibitors

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	200 mg/m2/dose once daily for 2 weeks; then 200 mg/m^2/dose twice daily Maximum dose allowable is 200mg.	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.

Drug	Preparations	Dosage for children	Adverse effects Minor, frequent	Adverse effects serious, dose limiting	Special instructions
Efavirenz	Syrup: 30mg/ml (note syrup requires higher dosing than capsules) Capsules: 50mg, 100mg, 200mg, 600mg	Capsule (liquid) dose for > 3yrs: 10 to 15kg: 200mg once daily 15 to < 20kg: 250mg once daily 20 to < 25kg: 300mg once daily 25 to < 33kg: 350mg once daily 33 to < 40kg: 400mg once daily maximum dose: ≥ 40kg: 600mg once daily	Skin rash	1.CNS toxicity 2.Teratogenic	Only for children over 3 years Capsules may be opened and added to food but has a very peppery taste Avoid high fatty foods Best given at bed time to reduce CNS side effects

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

APPENDIX 7

LIST OF ART SITES IN GHANA

ST. MARTIN DE PORRES HOSPITAL, AGOMANYA
ATUA GOVERNMENT HOSPITAL
KORLE-BU TEACHING HOSPITAL
KOMFO ANOKYE TEACHING HOSPITAL
KOFORIDUA REGIONAL HOSPITAL