GUIDELINES FOR ANTIRETROVIRAL THERAPY IN GHANA

National HIV/AIDS/ STI Control Programme
Ministry of Health / Ghana Health Service
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Dr. George Amofa Director Public Health GHS
Dr. Henrietta Odoi- Agyarko Deputy Director Family Health MOH
Dr. Kwaku Yeboah NACP GHS
Dr. Mokowa Adu-Gymafi NACP GHS
Dr. Agnes Dzokoto NACP, GHS
Ms. Evelyn Quaye NACP GHS
Dr. Margaret Lartey Department of Medicine Korle-Bu Teaching Hospital
Dr. Jennifer Welbeck Department of Child Health Korle-Bu Teaching Hospital
Dr. Priscillia Nortey Pharmacy Department, Korle-Bu Teaching Hospital
Mrs. Veronica Bekoe Public Health Reference Laboratory
Mr. Ben Botchwey Food and Drugs Board
Mr. Hayford Procurement Unit, MoH
Mr. Adjei Procurement Unit, MoH
Dr. Kwame Essah Family Health International
Dr. Joseph Amuzu World Health Organisation
Dr. William Ampofo Noguchi Memorial Institute for Medical Research

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Dr. Nii Akwei Addo NACP GHS
Dr. Agnes Dzokoto NACP, GHS
Dr. Margaret Lartey Department of Medicine Korle-Bu Teaching Hospital
Prof. Adukwei Hesse Department of Medicine Korle-Bu Teaching Hospital
Dr. Adwoa Adjei Department of Medicine Korle-Bu Teaching Hospital
Dr. Lorna Renner Department of Child Health Korle-Bu Teaching Hospital
Dr. Priscillia Nortey Pharmacy Department, Korle- Bu Teaching Hospital
Dr. Nanama Acquaye Department of Paediatrics, Ridge Hospital
Dr. Kwesi Torpey Family Health International
Dr. William Ampofo Noguchi Memorial Institute for Medical Research
Dr. Victor Bampo DFID Ghana
Dr. Morkor Newman World Health Organisation
Mrs. Joycelyn Azeez Procurement Unit, MoH
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Dr. Nii Akwei Addo National AIDS/STI Control Programme (NACP), GHS
Dr. Nii Nortey Hanson Nortey National Tuberculosis Programme, GHS
Dr. Margaret Laracey Department of Medicine Korle-Bu Teaching Hospital
Prof. Adukwei Hesse Executive Healthcare Consult
Prof. Bamenla Goka Department of Child Health, Korle-Bu Teaching Hospital
Dr. Lorna Renner Department of Child Health Korle-Bu Teaching Hospital
Dr. Priscillia Nortey Pharmacy Department, Korle-Bu Teaching Hospital
Dr. Richard Amenya Ghana AIDS Commission
Ms. Phyllis Ocran National AIDS/STI Control Programme, GHS
Dr. Bernard Dornoo NACP/World Health Organisation
Dr. Sylvia Deganus Tema General Hospital
Dr. Sally-Ann Ohene NACP/World Health Organisation
Dr. Stephen Ayisi-Addo NACP/World Health Organisation

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FOREWORD TO THIRD EDITION

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**

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<thead>
<tr>
<th>Acronym</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>ABC</td>
<td>Abacavir</td>
</tr>
<tr>
<td>AFBs</td>
<td>Acid Fast Bacilli</td>
</tr>
<tr>
<td>AFP</td>
<td>Alpha Fetoprotein</td>
</tr>
<tr>
<td>AIDS</td>
<td>Acquired Immune Deficiency Syndrome</td>
</tr>
<tr>
<td>ALT</td>
<td>Alanine Transferase</td>
</tr>
<tr>
<td>ART</td>
<td>Antiretroviral Therapy</td>
</tr>
<tr>
<td>ARV</td>
<td>Antiretroviral</td>
</tr>
<tr>
<td>AZT</td>
<td>Zidovudine</td>
</tr>
<tr>
<td>BUE</td>
<td>Blood Urea and Electrolytes</td>
</tr>
<tr>
<td>CD4</td>
<td>CD4 cells- T4 helper cells</td>
</tr>
<tr>
<td>d4T</td>
<td>Stavudine</td>
</tr>
<tr>
<td>DDI</td>
<td>Didanosine</td>
</tr>
<tr>
<td>DNA</td>
<td>Deoxyribonucleic Acid</td>
</tr>
<tr>
<td>FHI</td>
<td>Family Health International</td>
</tr>
<tr>
<td>FTC</td>
<td>Emtricitabine</td>
</tr>
<tr>
<td>GAC</td>
<td>Ghana AIDS Commission</td>
</tr>
<tr>
<td>GFATM</td>
<td>Global Fund for AIDS Tuberculosis and Malaria</td>
</tr>
<tr>
<td>GHS</td>
<td>Ghana Health Service</td>
</tr>
<tr>
<td>HAART</td>
<td>Highly Active Antiretroviral Therapy</td>
</tr>
<tr>
<td>Hb</td>
<td>Haemoglobin</td>
</tr>
<tr>
<td>HBsAb</td>
<td>Hepatitis B surface antibody</td>
</tr>
<tr>
<td>HBsAg</td>
<td>Hepatitis B surface antigen</td>
</tr>
<tr>
<td>HBlg</td>
<td>Hepatitis B Immunoglobulin</td>
</tr>
<tr>
<td>HBV</td>
<td>Hepatitis B virus</td>
</tr>
<tr>
<td>HCC</td>
<td>Hepatocellular carcinoma</td>
</tr>
<tr>
<td>HBCIgG</td>
<td>Hepatitis B core antibody</td>
</tr>
<tr>
<td>HIV</td>
<td>Human Immunodeficiency Virus</td>
</tr>
<tr>
<td>IDV</td>
<td>Indinavir</td>
</tr>
<tr>
<td>IRS</td>
<td>Immune Reconstitution Syndrome</td>
</tr>
<tr>
<td>LFT</td>
<td>Liver Function Test</td>
</tr>
<tr>
<td>LIP</td>
<td>Lymphoid Interstitial Pneumonitis</td>
</tr>
<tr>
<td>LMIS</td>
<td>Logistics Management Information System</td>
</tr>
<tr>
<td>LPV</td>
<td>Lopinavir</td>
</tr>
<tr>
<td>LPV/r</td>
<td>Ritonavir boosted lopinavir</td>
</tr>
<tr>
<td>MOH</td>
<td>Ministry of Health</td>
</tr>
<tr>
<td>NACP</td>
<td>National HIV/AIDS/STI Control Programme</td>
</tr>
<tr>
<td>NFV</td>
<td>Nelfinavir</td>
</tr>
<tr>
<td>NGO</td>
<td>Non-Governmental Organisation</td>
</tr>
<tr>
<td>NNRTI</td>
<td>Non-Nucleoside Reverse Transcriptase Inhibitor</td>
</tr>
<tr>
<td>NRTI</td>
<td>Nucleotide Reverse Transcriptase Inhibitor</td>
</tr>
<tr>
<td>NRTI</td>
<td>Nucleoside Reverse Transcriptase Inhibitor</td>
</tr>
<tr>
<td>NTCA</td>
<td>National Technical Committee on AIDS</td>
</tr>
<tr>
<td>PCR</td>
<td>Polymerase Chain Reaction</td>
</tr>
<tr>
<td>PEG IFN α2a</td>
<td>Peginterferon alfa-2a</td>
</tr>
<tr>
<td>PEP</td>
<td>Post Exposure Prophylaxis</td>
</tr>
<tr>
<td>PI</td>
<td>Protease Inhibitor</td>
</tr>
<tr>
<td>PLWHA</td>
<td>People Living with HIV/AIDS</td>
</tr>
<tr>
<td>PMTCT</td>
<td>Prevention of Mother to Child Transmission</td>
</tr>
<tr>
<td>RFT</td>
<td>Renal Function Test</td>
</tr>
<tr>
<td>RTV</td>
<td>Ritonavir</td>
</tr>
<tr>
<td>SQR/r</td>
<td>Saquinavir/r</td>
</tr>
<tr>
<td>SOP</td>
<td>Standard Operating Procedures</td>
</tr>
<tr>
<td>STD</td>
<td>Sexually Transmitted Disease</td>
</tr>
<tr>
<td>STI</td>
<td>Sexually Transmitted Infection</td>
</tr>
<tr>
<td>TB</td>
<td>Tuberculosis</td>
</tr>
<tr>
<td>TDF</td>
<td>Tenofovir Disoproxil Fumarate</td>
</tr>
<tr>
<td>VCT</td>
<td>Voluntary Counselling and Testing</td>
</tr>
<tr>
<td>WHO</td>
<td>World Health Organisation</td>
</tr>
<tr>
<td>Abbreviation</td>
<td>Full Form</td>
</tr>
<tr>
<td>--------------</td>
<td>-----------------------------------------------</td>
</tr>
<tr>
<td>USAID</td>
<td>United States Agency for International Development</td>
</tr>
<tr>
<td>START</td>
<td>Support Treatment and Antiretroviral Therapy</td>
</tr>
<tr>
<td>3TC</td>
<td>Lamivudine</td>
</tr>
</tbody>
</table>
CHAPTER 1

1 INTRODUCTION

The first case of AIDS was reported in Ghana in 1986. There has been a rise in the number of cases as well as the HIV prevalence since then. In 2007 the estimated adult national HIV prevalence was 1.9% with an estimated 264,481 persons living with HIV and AIDS. This is made up of 153,851 females and 110,666 males giving a female: male ratio of 1.4:1. In the same year, there were 16,947 children living with HIV and an estimated 2,959 babies were born HIV positive. The cumulative AIDS death was 180,899. 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 2007 HIV sentinel survey (HSS), the median prevalence of HIV infection among antenatal clinic clients was 2.6%. The peak age groups affected were the 25 – 29 and 35 – 39 year olds, each with an HIV prevalence of 3.5%. Also in this survey both HIV 1 and 2 were found in the Ghanaian population, with HIV 1 occurring in 96.8%, HIV-2 in 1.4% and dual infections in 1.8% 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 persons living with HIV (PLHIV). Since June 2003, antiretroviral therapy (ART) has been available in Ghana and is being scaled up. This has the added value of reducing HIV-related morbidity and mortality.

Antiretroviral therapy 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;
- 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 Management of Opportunistic Infections. To ensure the standardisation and quality of management for PLHIV, 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 CT
- 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 PLHIV.

Lessons learned from this programme were fed into the expansion of the national ART programme for scaling up. Since then, there has been roll out of comprehensive care including ART to regional, district and private hospitals.
according to a national scale up plan. Currently, over 90 facilities are providing ART across the country. A total of 2017 adults and children had accessed treatment from four sites by December 2004. By the end of 2007, the cumulative number of PLHIV initiated on ART exceeded 13,000. In line with the call for universal access to treatment, care and support for PLHIV, Ghana plans to put 70,000 PLHIV on ART by the year 2010.

Support from the Global Fund to fight AIDS, Tuberculosis and Malaria (GFATM) and other partners have facilitated this process. This support has been in the form of capacity building, procurement of drugs and logistics among others.

Considering new evidence and programmatic experience that has been gained, there is a need for regular revision of ART guidelines. The 2002 Guidelines for Antiretroviral Therapy in Ghana, was first revised in 2005 and the current 2008 revision has been necessary in line with emerging available evidence,

Combinations of drugs in Table 1.1 below are the drugs currently recommended in the national guidelines for Antiretroviral Therapy in Ghana.

**TABLE 1.1: RECOMMENDED ARVs IN GHANA**

<table>
<thead>
<tr>
<th>Nucleoside Reverse Transcriptase Inhibitors (NRTI)</th>
<th>Nucleotide Reverse Transcriptase Inhibitor (NtRTI)</th>
<th>Non-Nucleoside Reverse Transcriptase Inhibitors (NNRTI)</th>
<th>Protease Inhibitors (PI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Zidovudine (AZT/ZDV)</td>
<td>Tenofovir (TDF)</td>
<td>Nevirapine (NVP)</td>
<td>Nelfinavir (NFV)</td>
</tr>
<tr>
<td>Lamivudine (3TC)</td>
<td></td>
<td>Efavirenz (EFV)</td>
<td>Ritonavir boosted Lopinavir (LPV/r)</td>
</tr>
<tr>
<td>Stavudine (d4T)</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Didanosine (DDI)</td>
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<td></td>
<td></td>
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<tr>
<td>Abacavir (ABC)</td>
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<td></td>
<td></td>
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<tr>
<td>Emtricitabine (FTC)</td>
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</tbody>
</table>

Where available, fixed dose combinations of these drugs are preferred to single dose preparations. Not only are they cheaper, they also improve adherence to treatment.

The cost of care has been substantially subsidised by the Government of Ghana to GH¢ 5 (about US $5) for a month’s supply of ARV drugs, OI 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 clinical 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 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. These documents should be used as complementary documents
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
Counselling and Testing in Ghana’, GAC/MOH
3. ‘Prevention of Mother-to-Child Transmission (PMTCT) of HIV in
Ghana’, MOH/GHS
4. ‘CT 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 the Clinical Management of TB and HIV Co-infection in
Ghana’. Ghana Health Service, August 2007
10. ‘Guidelines on Nutritional Care and support for People living with HIV
and AIDS’, Ghana Health Service, 2006
11. Accreditation for Antiretroviral Therapy in Ghana: National Guidelines
and Site Assessment Ghana Health Service. 2006
12. HIV Drug Resistance Plan
2004
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 undergo assessment, and be assisted to meet set criteria before accreditation to provide ART. 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

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.

1 See National Accreditation Criteria for Antiretroviral Therapy
2.3 INITIATION CRITERIA

2.3.1 INCLUSION CRITERIA

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

1. Patients with CD4 count less than 350 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).

For pregnant women, where the CD4 count is greater than 350, they shall be put on ARV prophylaxis starting from 28 weeks for the purpose of PMTCT. (For ART in pregnancy, see the PMTCT Guidelines)

2.3.2 EXCLUSION CRITERIA

Antiretroviral Therapy shall 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 at least 2 sessions of 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 (Liver Function Tests (LFT) > 5 times the upper limit of normal) or renal insufficiency (Renal Function Tests > 3 times the upper limit of normal).
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 some exceptions. See 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:

- 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

---

\(^2\) See Appendices 1 and 2 for WHO clinical staging
• Carrying out a complete physical examination and
• 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 for TB Screening Questionnaire)
• Past Medical History including diagnosis of tuberculosis
• Drug history including treatment for TB
• Sexual history and past symptoms of STI
• Gynaecological history (for females)
• Social history

The physical examination should have the following components:
• Patient’s weight and height
• Skin and lymph nodes, looking out for the following
  o Herpes Zoster (old scars and new lesions)
  o Herpes simplex
  o Molluscom contagiosum
  o Kaposi’s sarcoma
  o HIV dermatitis
• Oropharyngeal mucosa
  o Candidiasis
  o Leucoplakia
  o 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 (when available)\(^3\)

2. Indication of patients’ immune status
• CD4 count \(^4\)

Information on the patient’s baseline indicators including:

**Other Baseline tests**

| Haematological test          | Full blood count including total lymphocyte count and platelets
|                            | The basic minimum test for pregnant women who are taking ARV combination prophylaxis for PMTCT is Haemoglobin
| 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     | Sputum for AFBs for all patients
|                            | Chest X-ray
| Supplementary tests          | Hepatitis B Surface antigen screen
| These tests are performed depending on signs and symptoms | 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.

\(^3\) **Viral load**
Although this test is important, it may not always be available due to capacity constraints. The viral load at the initiation of therapy has a bearing on the severity of HIV infection at the start of therapy. During therapy it provides evidence of the virologic response to therapy.

It is recommended that where available it should be done at baseline 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.

\(^4\) **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.
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 PLHIV.

The following triple therapy regimens are recommended:
- 2 Nucleoside Reverse Transcriptase Inhibitors (NRTIs) and 1 Non-Nucleoside Reverse Transcriptase Inhibitor (NNRTI)
- 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 Regimen will be found in drug information attached in appendix 4.

2.6.1
# FIRST LINE DRUGS

## TABLE 2.1

<table>
<thead>
<tr>
<th>Drugs</th>
<th>Contra-indications</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>First choice drugs</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>First Option</strong></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
| Zidovudine + Lamivudine + Nevirapine | Nevirapine is contraindicated in:  
  - liver dysfunction  
  - hypersensitivity  
  Zidovudine is contraindicated in:  
  - severe anaemia          | Replace withEfavirenz              |
| **Second Option**      |                                                        |                                    |
| Zidovudine + Lamivudine + Efavirenz | Efavirenz is contraindicated in:  
  - Pregnancy  
  - CNS presentations  
  When there is Efavirenz related persistent CNS toxicity | 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 |                                    |
### 2.6.2 SECOND LINE DRUGS
#### TABLE 2.2

<table>
<thead>
<tr>
<th>Drugs</th>
<th>Contra-indications</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Second Option</strong>&lt;br&gt;Stavudine + Lamivudine + Efavirenz</td>
<td>Efavirenz in contraindicated in:&lt;br&gt;○ Efavirenz related Persistent CNS toxicity&lt;br&gt;○ Pregnancy</td>
<td>Stavudine should be used when Zidovudine is contraindicated e.g. anaemia&lt;br&gt;When Efavirenz is contraindicated replace with Nevirapine</td>
</tr>
</tbody>
</table>

### 2.6.3 SPECIAL CONDITIONS

The regimen recommended in Table 2.2 shall be amended in the following conditions.

---

* 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 ddl.
<table>
<thead>
<tr>
<th>Condition</th>
<th>Recommendation</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Women of childbearing potential</td>
<td>Zidovudine or Stavudine + Lamivudine + Nevirapine</td>
<td>Efavirenz is teratogenic and should not be used unless adequate birth control is assured</td>
</tr>
<tr>
<td>HIV co-infection with Hepatitis B See Chapter 4</td>
<td>The recommended regimen shall be Lamivudine, Tenofovir and Efavirenz. Patient should be eligible for ART before starting treatment.</td>
<td>Lamivudine and Tenofovir are active against both hepatitis B and HIV. Nevirapine should not be used because of the risk of hepatotoxicity.</td>
</tr>
<tr>
<td>ART experienced patients</td>
<td>Review previous drugs used for ART, duration 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</td>
<td>Consultation or referral to an HIV expert.</td>
</tr>
<tr>
<td>Dual HIV-1 and HIV-2 or HIV-2 infections</td>
<td>Due to the ineffectiveness of non-nucleoside drugs (Nevirapine and Efavirenz) in HIV-2 infection, combination of nucleosides and protease inhibitors should be used</td>
<td></td>
</tr>
<tr>
<td>Previous exposure to 1. Zidovudine and Lamivudine or 2. Nevirapine for PMTCT prophylaxis or treatment</td>
<td>This does not preclude the use of any of these medications – Zidovudine, Lamivudine or Nevirapine for ART</td>
<td></td>
</tr>
</tbody>
</table>

### 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 does not include thiacetazone in view of the high incidence of Stevens Johnson syndrome in PLHIV taking this drug and also
avoids Streptomycin injections in new cases due to the risk of needle stick injuries to health workers.

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. Presently anti-tuberculous therapy in Ghana uses Rifampicin throughout the treatment.

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:

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

2. For moderately immune-compromised patients, ART should be deferred until the completion of the intensive phase.

3. For severely immune-compromised patients (CD4 count<50) both therapies may be initiated at the same time. Nevirapine and Rifampicin are both hepatotoxic and as much as possible should not be administered together. Therefore in TB/HIV co-infected patients Nevirapine should be replaced with Efavirenz.

4. In the light of current evidence, the dose of Efavirenz can be maintained at 600 mg even in the presence of Rifampicin. There is no longer the need to increase the dose to 800mg.

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 anti-retroviral drugs
- Prescribed medicines and alternative or non-prescription medication
- Between medicines and food
Certain recreational drugs

Some important drug interactions:
- 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 PLHIV 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 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 methodologies:
- 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
• Opportunistic infections becoming clinically apparent as a result of immune reactivation

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 screen 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 intolerances that may be 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, neutropenia among others (see laboratory monitoring).
## Common ARV toxicities

<table>
<thead>
<tr>
<th>HAEMATOLOGICAL TOXICITY</th>
<th>Drug-induced bone marrow suppression, most commonly seen with AZT (anaemia, neutropenia).</th>
</tr>
</thead>
<tbody>
<tr>
<td>MITOCHONDRIAL DYSFUNCTION</td>
<td>Primarily seen with the NRTI drugs, including lactic acidosis, hepatic toxicity, pancreatitis, peripheral neuropathy, lipoatrophy, myopathy.</td>
</tr>
<tr>
<td>RENAL TOXICITY</td>
<td>Nephrolithiasis, commonly seen with Indinavir (IDV). Renal tubular dysfunction is associated with TDF.</td>
</tr>
<tr>
<td>OTHER METABOLIC ABNORMALITIES</td>
<td>More common with PIs. Include hyperlipidaemia, fat accumulation, insulin resistance, diabetes and osteopenia.</td>
</tr>
<tr>
<td>ALLERGIC REACTIONS</td>
<td>Skin rashes and hypersensitivity reactions, more common with the NNRTI drugs but also seen with certain NRTI drugs, such as ABC and some PIs.</td>
</tr>
</tbody>
</table>

# Estimating Severity Grading

<table>
<thead>
<tr>
<th>GRADE</th>
<th>SEVERITY</th>
<th>ACTION</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Mild</td>
<td>Transient or mild discomfort: no limitation in activity; no medical intervention/therapy required</td>
</tr>
<tr>
<td>2</td>
<td>Moderate</td>
<td>Limitation in activity- some assistance may be needed; minimal or no medical intervention required</td>
</tr>
<tr>
<td>3</td>
<td>Severe</td>
<td>Marked limitation in activity- some assistance usually required; medical intervention/therapy required- Hospitalization possible</td>
</tr>
<tr>
<td>4</td>
<td>Severe Life-threatening</td>
<td>Extreme limitation in activity - significant assistance required; significant medical intervention/therapy required; hospitalization and home-based care</td>
</tr>
</tbody>
</table>
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 drug or 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. In general:
   - 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)
- Increase in total lymphocyte count
- Increase in platelets if low at the start
- Sustained suppression of viral load

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

---

5 Where viral load has been done
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)
- Lipid profile (blood cholesterol and triglycerides, yearly)

Other tests such as sputum 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 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 initiation 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.

2.10 **INTERUPTION OF THERAPY**

Interuption 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.

Interuption 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 or virologically by an increase 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 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.

**Virologic failure** is defined as confirmed plasma HIV RNA >50 copies/ml 6 months after initiating therapy in persons that are adherent to ART.

An alternate definition to guide client management and switching to second line medications in resource limited settings is a plasma HIV-1 RNA level above 10,000 copies/ml in a person who has been on a regimen for more than 6 months without other concomitant infection to explain the rise or non-suppression of the viral load and in whom drug adherence is determined to be sufficient. For details on management of failure see Viral Load Monitoring guidelines.

(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 PLHIVs. 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 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. 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.
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 and 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 virologic 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:
   • 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 25% (Child <12months)
   • CD4 percentage less than 20% (Child 12-18months).

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 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

<table>
<thead>
<tr>
<th>Age</th>
<th>HIV Diagnostic testing</th>
<th>Treatment Recommendation</th>
</tr>
</thead>
</table>
| <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;
               |                                                            | • <25%(Child<12months)
               |                                                            | • <20 %( Child 12-18months).
|              | Positive HIV PCR                                            | <12months Treat irrespective of stage and CD4%               |
|              |                                                            | 12-18months Treat if WHO Stage I and II with CD4< 20%        |
WHO Paediatric Stage III and IV irrespective of CD4%

<table>
<thead>
<tr>
<th>≥18 months</th>
<th>HIV antibody seropositive</th>
<th>WHO Paediatric Stage III and IV irrespective of CD4%</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>WHO Stage I and II with CD4</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• &lt; 20% or 750cells/mm³</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(child 18-35months)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• &lt; 15% or 350 cells/mm³</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(child &gt;35months)</td>
</tr>
</tbody>
</table>

### 3.4.2 EXCLUSION CRITERIA

Antiretroviral therapy shall not be initiated under the following circumstances:

1. Lack of parental or guardian motivation
2. Treatment 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 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 client 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
- Document past ARV treatment 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
- Head circumference
- Mid Upper arm Circumference in children 1 to 6 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 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 PI (Includes boosted PI)

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 prophylaxis due to PMTCT intervention 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**

<table>
<thead>
<tr>
<th>Drugs</th>
<th>Contra-indications</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>First Choice Drugs</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>First Option</strong></td>
<td>Zidovudine + Lamivudine + Nevirapine</td>
<td>Nevirapine is contraindicated in:</td>
</tr>
<tr>
<td></td>
<td></td>
<td>liver dysfunction</td>
</tr>
<tr>
<td></td>
<td></td>
<td>hypersensitivity</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Replace with Efavirenz</td>
</tr>
<tr>
<td></td>
<td>Zidovudine is contraindicated in:</td>
<td>Replace with stavudine</td>
</tr>
<tr>
<td></td>
<td>severe anaemia</td>
<td></td>
</tr>
<tr>
<td><strong>Second Option</strong></td>
<td>Efavirenz is:</td>
<td>Replace with Nevirapine</td>
</tr>
<tr>
<td></td>
<td>not indicated in Children less than 3 years</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Contraindicated in Efavirenz related Persistent CNS toxicity</td>
<td>Replace with Nevirapine</td>
</tr>
<tr>
<td><strong>Second Choice Drugs</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>First Option</strong></td>
<td>Stavudine + Lamivudine + Nevirapine</td>
<td>Stavudine should be used when Zidovudine is</td>
</tr>
<tr>
<td></td>
<td></td>
<td>contraindicated e.g. anaemia</td>
</tr>
<tr>
<td><strong>Second Option</strong></td>
<td>Stavudine + Lamivudine + Efavirenz</td>
<td>Stavudine should be used when Zidovudine is</td>
</tr>
<tr>
<td></td>
<td></td>
<td>contraindicated e.g. anaemia</td>
</tr>
<tr>
<td></td>
<td>Efavirenz is:</td>
<td>Replace with Nevirapine</td>
</tr>
<tr>
<td></td>
<td>not indicated in Children less than 3 years</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Contraindicated in Efavirenz related Persistent CNS toxicity</td>
<td>Replace with Nevirapine</td>
</tr>
<tr>
<td>NB: Emtricitabine can be used in children over 3 months of age as an alternative to Lamivudine</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
3.7.2 SECOND LINE DRUG
The second line drugs for Ghana’s national guidelines are indicated in the table below.

TABLE 3.4

<table>
<thead>
<tr>
<th>First Choice Drugs</th>
<th>Drugs</th>
<th>Contra-indications/</th>
<th>comments</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1. Didanosine + Abacavir</td>
<td>In case of hypersensitivity to Abacavir,</td>
<td>Switch to Zidovudine or Stavudine</td>
</tr>
<tr>
<td></td>
<td>Nelfinavir</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>2. Lopinavir/Ritonavir +</td>
<td>In case of hypersensitivity to Abacavir,</td>
<td>Switch to Zidovudine or Stavudine</td>
</tr>
<tr>
<td>Second Choice</td>
<td>Didanosine + Abacavir</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Drugs</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

(For drug dosages and characteristics see Appendix 7)
NB: Tenofovir is not recommended in pre-pubertal children due to safety and toxicity concerns.

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). 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

<table>
<thead>
<tr>
<th>Clinical signs of treatment failure</th>
<th>CD4 cell criteria for treatment failure</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lack of growth among children who show an initial response to treatment, or decline in growth among</td>
<td>Return in CD4 cell percentage (or for children &gt; 5 years of age, absolute CD4 cell count) to pre-</td>
</tr>
<tr>
<td>children who show an initial growth response to therapy.</td>
<td>therapy baseline or below</td>
</tr>
<tr>
<td>Loss of neurodevelopment milestones or development</td>
<td>≥ 50% fall from peak level on therapy of CD4 cell percentage (or for children &gt; 5 years of age, absolute</td>
</tr>
<tr>
<td></td>
<td>CD4 cell count), in absence of other concurrent infection to explain transient CD4 decrease.</td>
</tr>
<tr>
<td>Occurrence of new opportunistic infection or malignancy signifying clinical disease progression</td>
<td></td>
</tr>
<tr>
<td>Recurrence of previous opportunistic infections, such as oral candidiasis refractory to treatment</td>
<td></td>
</tr>
</tbody>
</table>

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 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 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)

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 five years of age. See Chapter 2.

3.9.2.1 Monitoring of adherence
Adherence counselling must involve the child, 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
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. Its coinfection with HIV is therefore not surprising. No data of the prevalence of HIV/HBV coinfection in Ghana is available. 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 PLWHIV, liver disease from HBV coinfection 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 coinfected. HBV reactivation and reinfection seem to be increased in PLWHIV.

The rate of response to anti-HBV infection treatment seem to be less in PLWHIV than HIV negative patients. HIV infection also increases the chance of chronicity of HBV infection and progression to cirrhosis and hepatic cell carcinoma. Despite the coinfection, 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 have hepatitis B surface antigen (HBsAg) within a month of diagnosis.
• If HBsAg is negative do Hepatitis B surface antibody (HBsAb) test.
• If HBsAg and HBsAb negative, vaccinate against HBV.
  o Where CD4 counts <350 in adults start HAART before vaccination to ensure good response.
  o In children if CD% indicates severe immuno-suppression, start HAART before vaccination.
• Where possible the HBV status should be checked before starting HAART as this knowledge will inform the choice of drugs (see below).

4.3 GENERAL MANAGEMENT OF HEPATITIS B VIRUS INFECTION IN HIV

HBsAg positive indicates acute or chronic infection

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.
  o If negative, acute infection is over
  o If positive, chronic infection (see below)

4.3.2 Chronic HBV infection
Chronic HBV infection is defined as HBsAg+ for six months or more.

1. Assess for liver damage
   - All HIV/HBV coinfected patients should be assessed for liver disease status and risk of progression. This should include a clinical history, examination and blood tests including LFT and clotting studies (and HBV serology if available)
   - Blood ALT level is the most cost effective indicator of liver damage. Patients with normal ALT levels generally do not need treatment nor further investigation.
   - If the ALT is increased the HBV Deoxyribonucleic Acid (DNA) level (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 alfa-fetoprotein (AFP) where 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 at birth in addition to the (PMTCT intervention).

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 PLWHIV, there is an optimal time for initiating anti-HBV treatment in coinfected patients. Treatment should be individualised 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.

The treatment algorithm is shown in Appendix 5.

4.4.1 Treatment of HBV infection in patients not eligible for HAART

When to treat:
- The primary determinant of the optimal time to start treatment is when there is evidence of liver damage
• Alanine transferase (ALT) >1.5x upper limit of normal (>45 in men, >30 in women) and/or
• High hepatitis B viral load (HBV-DNA >10^5 copies/ml).
• Patients with normal ALT are less likely to have significant liver damage and less likely to respond to treatment.
• Remember that in coinfected patients, elevated ALT may be caused by many conditions some of which are improved immunity to HBV (IRS), hepatotoxicity from HAART drugs and infection with other hepatotoxic viruses.

What to treat with:
1. Specific anti-HBV treatment with
   • Pegylated interferon alfa-2a (PEG IFN α2a) injection once a week for 48 weeks or
   • Entecavir or adefovir where available.
   These lack any activity against HIV and therefore will not compromise the patient’s later HIV drug treatment.

2. Early HAART
   • In case of non-availability of specific anti-HBV, HAART may be initiated between CD4 level 350 and 500. The HAART regimen is discussed below.

Lamivudine should not be given alone to treat HBV infection because of the high rate of development of resistance by both HBV and HIV. It can however, be given in combination in HAART as below. Similarly tenofovir must only be given as part of, or in addition to, an effective HAART regime.

4.4.2 Treatment of HBV infection in patients who are eligible for HAART or on HAART.
   In this case both treatments are required.

When to treat:
• It is policy that any PLHIV coinfected with HBV requiring HAART (CD4 <350) shall be treated for both viruses irrespective of whether there is evidence of liver damage (raised ALT). It is therefore important that the HBsAg status in all PLWHIV be known before initiation of HAART.

What to treat with:
• The first line HAART regimen should contain at least one antiviral agent that has activity against both HIV and HBV.
  o These are Lamivudine (3TC), Tenofovir (TDF) and Emtricitabine (FTC).
FTC and 3TC have the same anti-HIV and anti-HBV actions, same development of resistance, are interchangeable, and should not be used together.

Lamivudine should not be used as monotherapy to treat HBV because this results in development of significant resistance within one year and this increases each year so that by the 4th year of treatment 70-90% of patients have resistant HBV.

- A combination of TDF and 3TC is recommended primarily to prevent development of HBV resistance.
- In view of the hepatotoxicity of Nevirapine, particularly in cases of high ALT levels and also in cases of high CD4 counts (>250 in women and >400 in men), EFV is preferred.
  - Therefore avoid nevirapine in cases of HIV/HBV coinfection.
- The first line preferred regimen for the treatment of both HIV and HBV is therefore Efavirenz+Lamivudine+Tenofovir (EFV, 3TC and TDF).
  - The alternate is Efavirenz+Tenofovir+Emtricitabine.
  - (TDF and FTC are co-formulated as Truvada®) and may be preferred if there is the likelihood of lamivudine resistance.
- The combination of 3TC and TDF should be continued if there is good HBV response when HIV resistance to the first line HAART occurs.
  - The new second line HIV drug regimen, (which could consist of up to three new drugs) should be added to 3TC and TDF.
- For patients who are already on a particular HAART regimen and are stable on this treatment, it may preferable to add adefovir or entecavir rather than switch to tenofovir+lamivudine to cover both viruses.

4.4.3 Duration of treatment and monitoring

- Treatment of HBV co-infection with HIV is long term; treatment duration is 48 weeks in the case of PEG IFN α2a and at least 4 years for those on oral anti-hepatitis B virus medicines.
- Patients should be monitored every 6 months by checking ALT levels while on treatment.
- HBV treatment may be stopped 12 months after ALT levels have returned to normal. Note that treatment cannot be stopped in cases where tenofovir and lamivudine are being used to treat both viruses unless HIV resistance to these drugs have been demonstrated.
- Where facilities are available, HBV DNA (HB viral load), in addition to ALT levels, may be used to determine the initiation and end of treatment.
- Monitoring of serum ALT every 6 months should continue after cessation of treatment. Patients who relapse can be retreated.
- All patients who have an unexpected rise in ALT should be screened again for HBV.
CHAPTER 5

POST EXPOSURE PROPHYLAXIS FOR HEALTH CARE WORKERS

5.1 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 after exposure.

5.2 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 mucocutaneous membrane or 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.

5.3 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 patient care.
- Sharps should be used with caution with all patients
  - Sharps should be used with a sharps container nearby
  - Sharps should be disposed of in a puncture proof receptacle immediately after use
5.4 STEPS TO PREVENT OCCUPATIONAL TRANSMISSION OF HIV

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

5.4.1 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.

5.4.2 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:

5.4.2.1 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

5.4.2.2 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

5.4.3 PEP STEP 3: Specific PEP management

1. Counselling and Testing:
   - All exposed individuals including 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. Where an exposed individual declines to test after counselling, this must be documented.
   - All known source-patients shall also be counselled and tested if their status is not known.

   - 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 on the table below.
Table 5.1: Recommended Post–HIV exposure prophylaxis

<table>
<thead>
<tr>
<th>RISK LEVEL</th>
<th>RECOMMENDED PROPHYLAXIS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Very Low risk</td>
<td>Wash exposed area immediately with soap and water</td>
</tr>
</tbody>
</table>
| 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 28 days |

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

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

<table>
<thead>
<tr>
<th>Time</th>
<th>Tests</th>
</tr>
</thead>
</table>
| 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 and 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
5.4.5 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 6

GUIDELINES ON ART COUNSELLING

6.1 INTRODUCTION

Counselling for ART compliments 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 ART:

- National Guidelines for the Development and implementation of HIV Counselling And Testing in Ghana
- Prevention of Mother-to-Child Transmission of HIV in Ghana,
- CT Training Manual

6.2 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 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 compliment the general counselling for HIV and 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
9 MOH/GHS VCT Training Manual
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 goal of therapy is 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 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.

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)

6.3.3 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.

6.3.4 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.

6.3.5 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 (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.

6.3.6 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
o Religious groups
  o Healthcare workers
  o Networks of PLHIV
  o Other Civil Society Organizations
  o NGOs in AIDS care
  o Social welfare department
  o District Assemblies

6.3.7 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. (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 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.

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)
- 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 sent on a monthly basis from each site to the Regional Medical Stores 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 minimal and essential data 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 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 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 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.

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 drugs shall conform to the BP, USP and or any other officially accepted pharmacopeal 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.

<table>
<thead>
<tr>
<th>Quantity of a drug</th>
<th>X</th>
<th>Number of treatment episodes</th>
<th>=</th>
<th>Total quantity of the drug required for the given health problem</th>
</tr>
</thead>
<tbody>
<tr>
<td>Specified for a Standard course of treatment</td>
<td>of a given health problem</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

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 drugs 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 drugs 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 existing procurement laws into the national drug supply system. This shall be by competitive bidding using centrally consolidated order quantities. A framework for awarding a three-year contract with scheduled delivery shall be established to ensure uninterrupted supply.

ARVs shall be prescription only drugs and shall not be for sale in the open market. This is to prevent abuse and development of ARV resistance.
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). 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.\(^\text{10}\)

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

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.

---

\(^{10}\) 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

<table>
<thead>
<tr>
<th>Stages</th>
<th>Characteristics</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clinical Stage I</td>
<td>Asymptomatic</td>
</tr>
<tr>
<td></td>
<td>Persistent generalized lymphadenopathy (PGL)</td>
</tr>
<tr>
<td>Clinical Stage 2</td>
<td>Moderate explained weight loss (&lt;10% of presumed or measured body weight)</td>
</tr>
<tr>
<td></td>
<td>Recurrent respiratory tract infections (RTIs, Sinusitis, bronchitis, otitis media, pharyngitis)</td>
</tr>
<tr>
<td></td>
<td>Herpes zoster</td>
</tr>
<tr>
<td></td>
<td>Angular cheilitis</td>
</tr>
<tr>
<td></td>
<td>Recurrent oral ulcerations</td>
</tr>
<tr>
<td></td>
<td>Papular pruritic eruptions</td>
</tr>
<tr>
<td></td>
<td>Seborrhoeic dermatitis</td>
</tr>
<tr>
<td></td>
<td>Fungal nail infections of fingers.</td>
</tr>
<tr>
<td>Clinical Stage 3</td>
<td>Conditions where a presumptive diagnosis can be made on the basis of clinical signs or simple investigations.</td>
</tr>
<tr>
<td></td>
<td>Severe weight loss (&gt;10% of presumed or measured body weight)</td>
</tr>
<tr>
<td></td>
<td>Unexplained chronic diarrhoea for longer than one month</td>
</tr>
<tr>
<td></td>
<td>Unexplained persistent fever (intermittent or constant for longer than one month)</td>
</tr>
<tr>
<td></td>
<td>Oral candidiasis</td>
</tr>
<tr>
<td></td>
<td>Oral hairy leukoplakia</td>
</tr>
<tr>
<td></td>
<td>Pulmonary tuberculosis (TB) diagnosed in last two years</td>
</tr>
<tr>
<td></td>
<td>Severe presumed bacterial infections (e.g. pneumonia, empyema, pyomyositis, bone or joint infection, meningitis, bacteraemia)</td>
</tr>
<tr>
<td></td>
<td>Acute necrotizing ulcerative stomatitis, gingivitis or periodontitis</td>
</tr>
<tr>
<td></td>
<td><strong>Conditions where confirmatory diagnostic testing is necessary</strong></td>
</tr>
<tr>
<td></td>
<td>Unexplained anaemia (&lt;g/dl), and or neutropenia (&lt;500/mm$^3$) and or thrombocytopenia (&lt;50 000/mm$^3$) for more than one month.</td>
</tr>
<tr>
<td>Clinical Stage 4</td>
<td><strong>Conditions where a presumptive diagnosis can be made on the basis of clinical signs or simple investigations.</strong></td>
</tr>
<tr>
<td></td>
<td>HIV wasting syndrome</td>
</tr>
<tr>
<td></td>
<td>Pneumocystis pneumonia</td>
</tr>
<tr>
<td></td>
<td>Recurrent severe or radiological bacterial pneumonia.</td>
</tr>
<tr>
<td></td>
<td>Chronic herpes simplex infection (or labial, genital or anorectal of more than one month’s duration)</td>
</tr>
<tr>
<td>Conditions where confirmatory diagnostic testing is necessary</td>
<td></td>
</tr>
<tr>
<td>---------------------------------------------------------------</td>
<td></td>
</tr>
<tr>
<td>Extrapulmonary cryptococcosis including meningitis</td>
<td></td>
</tr>
<tr>
<td>Disseminated non-tuberculous mycobacteria infection.</td>
<td></td>
</tr>
<tr>
<td>Progressive multifocal leukoencephalopathy (PML)</td>
<td></td>
</tr>
<tr>
<td>Candida of trachea, bronchi or lungs</td>
<td></td>
</tr>
<tr>
<td>Cryptosporidiosis</td>
<td></td>
</tr>
<tr>
<td>Isosporiasis</td>
<td></td>
</tr>
<tr>
<td>Visceral herpes simplex infection</td>
<td></td>
</tr>
<tr>
<td>Cytomegalovirus (CMV) infection (retinitis or of an organ other than liver, spleen or lymph nodes)</td>
<td></td>
</tr>
<tr>
<td>Any disseminated mycosis (e.g., histoplasmosis, coccidiomycosis, penicilliosis)</td>
<td></td>
</tr>
<tr>
<td>Recurrent non-typhoidal salmonella septicaemia</td>
<td></td>
</tr>
<tr>
<td>Lymphoma (cerebral or B cell non-Hodgkin)</td>
<td></td>
</tr>
<tr>
<td>Invasive cervical carcinoma</td>
<td></td>
</tr>
<tr>
<td>Visceral leishmaniasis</td>
<td></td>
</tr>
</tbody>
</table>
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

<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Not significant immunosuppression</td>
<td>&gt;500/mm$^3$</td>
</tr>
<tr>
<td>Mild immunosuppression</td>
<td>350 – 499/mm$^3$</td>
</tr>
<tr>
<td>Advanced immunosuppression</td>
<td>250 – 349/mm$^3$</td>
</tr>
<tr>
<td>Severe immunosuppression</td>
<td>&lt;250/mm$^3$</td>
</tr>
</tbody>
</table>
# APPENDIX 2

**WHO CLINICAL STAGING OF HIV AND AIDS FOR INFANTS AND CHILDREN**

**PERSONS AGED UNDER 15 YEARS WITH CONFIRMED LABORATORY EVIDENCE OF HIV INFECTION**

<table>
<thead>
<tr>
<th>Stage</th>
<th>Clinical Stage 1</th>
<th>Clinical Stage 2</th>
<th>Clinical Stage 3</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Asymptomatic</td>
<td>Hepatosplenomegaly</td>
<td>Conditions where a presumptive diagnosis can be made on the basis of clinical signs or simple investigations</td>
</tr>
<tr>
<td></td>
<td>PGL</td>
<td>Papular pruritic eruptions</td>
<td>Moderate unexplained malnutrition not adequately responding to standard therapy</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Seborrhoeic dermatitis</td>
<td>Unexplained persistent diarrhoea (14 days or more)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Extensive human papilloma virus infection</td>
<td>Unexplained persistent fever (intermittent or constant, for longer than one month)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Extensive molluscum contagiosum</td>
<td>Oral candidiasis (outside neonatal period)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Fungal nail infections</td>
<td>Oral hairy leukoplakia</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Recurrent oral ulcerations</td>
<td>Acute necrotizing ulcerative gingivitis/periodontitis</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Lineal gingival erythema (LGE)</td>
<td>Pulmonary TB</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Angular Cheilitis</td>
<td>Severe recurrent presumed bacterial pneumonia.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Parotid enlargement</td>
<td><strong>Conditions where confirmatory diagnostic testing is necessary</strong></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Herpes zoster</td>
<td>Chronic HIV-associated lung disease including bronchiectasis</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Recurrent of chronic RTIs (Otitis media, otorrhoea, sinusitis)</td>
<td>Lymphoid interstitial pneumonitis (LIP)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Unexplained anaemia (&lt;8g/dl), and or neutropenia (&lt;1000/mm³) and or thrombocytopenia (&lt;50 000/mm³) for more than one month.</td>
</tr>
</tbody>
</table>
be made on the basis of clinical signs or simple investigations

Unexplained severe wasting or severe malnutrition not adequately responding to standard therapy. Pneumocystis pneumonia
Recurrent severe presumed bacterial infections (e.g. empyema, pyomyositis, one or joint infection, meningitis, but excluding pneumonia)
Chronic herpes simplex infection; (orolabial or cutaneous of more than one month’s duration)
Extrapulmonary TB
Kaposi’s sarcoma
Oesophageal candidiasis
CNS toxoplasmosis (outside the neonatal period)

Conditions where confirmatory diagnosis testing is necessary.

CMV infection (CMV retinitis or infection of organs other than liver, spleen or lymph nodes; onset at age one month or more)
Extrapulmonary cryptococcosis including meningitis
Any disseminated endemic mycosis (e.g. extrapulmonary histoplasmosis, coccidiomycosis, penicilliosis)
Cryptosporidiosis
Isosporiasis
Disseminated non-tuberculous mycobacteria infection
Candida of trachea, bronchi or lungs
Visceral herpes simplex infection
Acquired HIV associated rectal fistula
Cerebral or B cell non-Hodgkin lymphoma
Progressive multifocal leukoencephalopathy (PML)
HIV-associated cardiomyopathy or HIV-associated nephropathy.
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 the best nationally or locally available test for age. 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

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

<table>
<thead>
<tr>
<th>Classification of HIV associated immune deficiency</th>
<th>Age-related CD4 values</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>&lt;11 months (%)</td>
</tr>
<tr>
<td>Not Significant</td>
<td>&gt;35</td>
</tr>
<tr>
<td>Mild</td>
<td>30-35</td>
</tr>
<tr>
<td>Advanced</td>
<td>25-30</td>
</tr>
<tr>
<td>Severe</td>
<td>&lt;25</td>
</tr>
</tbody>
</table>
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.

CLINICAL AND IMMUNOLOGICAL CRITERIA FOR INITIATING ART IN INFANTS AND CHILDREN

<table>
<thead>
<tr>
<th>Clinical Stages</th>
<th>Treatment Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stage 4</td>
<td>Treat</td>
</tr>
<tr>
<td>Presumptive Stage 4</td>
<td>Treat</td>
</tr>
<tr>
<td>Stage 3</td>
<td>Consider treatment for all ages. Children aged less than 2 years usually require ART.</td>
</tr>
</tbody>
</table>
| Stages 1 and 2  | Where CD4 available treat under the following conditions:  
|                 | Under 12 months: CD4 % < 25 (<1500 cells/mm³)  
|                 | 12 – 35 months: CD4% < 20 (<750 cells/mm³)  
|                 | 36 – 59 months: CD4 % <15 (<350 cells/mm³)  
|                 | 5 years and above: CD4 < 350 cells/mm³ |

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 cotrimoxazole prophylaxis and ART treatment and support patient follow up.

- All infants, children, 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 or international recommendations.
## APPENDIX 3

### DRUG-DRUG INTERACTIONS

<table>
<thead>
<tr>
<th>DRUG</th>
<th>DRUG-DRUG INTERACTIONS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lamivudine</td>
<td>Emtricitabine,</td>
</tr>
<tr>
<td>Zidovudine</td>
<td>Stavudine, Ganciclovir, Interferon, Ribavirin, Cytotoxics (Doxorubicin etc)</td>
</tr>
<tr>
<td>Stavudine</td>
<td>Dapsone, Isoniazid, Pentamidine, Vinca alkaloids.</td>
</tr>
<tr>
<td>Efavirenz</td>
<td>Nevirapine, Antiarrhythmics (Lidocaine, amiodarone), Antiepileptics (Phenytoin, Carbamazepine, Primidone), Antihistamines (Astemizole, Terfenadine, Loratidine), Phenobarbital, Benzodiazepine, St. John’s Worts (Herbal)</td>
</tr>
<tr>
<td>Didanosine (DDI)</td>
<td>Allopurinol, Pentamidine, Ribavirin, Fluoroquinolones, Dapsone, isoniazid,itraconazole, ketoconazole, tetracyclines</td>
</tr>
<tr>
<td>Tenofovir</td>
<td>Amphotericin B, Aminoglycosides, Pentamidine, Acyclovir, Probenecid, Salicylates, Vancomycin</td>
</tr>
<tr>
<td>Nevirapine</td>
<td>Protease Inhibitors, Rifabutin, Rifampicin, Indinavir, Efavirenz, St. John’s worts, Carbamazepine, Phenytoin, Cocaine</td>
</tr>
<tr>
<td>Lopinavir/Ritonavir</td>
<td>Metronidazole, Alprazolam, clarithromycin, diazepam, erythromycin, ketoconazole,itraconazole, rifabutin, Rifampicin, saquinavir, tricyclic, antidepressants, oral contraceptives, Amiodarone, Quinidine, Lidocaine, St. John’s worts, Astemizole, Loratidine, Terfenadine, Phenobarbitone,</td>
</tr>
<tr>
<td>Nelfinavir</td>
<td>Lidocaine, Amiodarone, St. John’s worts, Astemizole, Loratidine, Rifampicin, Atovastatin, Lovastatin, Simvastatin</td>
</tr>
</tbody>
</table>
## APPENDIX 4

### Drug information

<table>
<thead>
<tr>
<th>Drug</th>
<th>Adult dosage</th>
<th>Formulations</th>
<th>Adverse effects Minor, frequent</th>
<th>Adverse effects serious, dose limiting</th>
<th>Special instructions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Zidovudine (AZT)</td>
<td>300 mg bid</td>
<td>Tablet</td>
<td>Nausea Headache Fatigue Muscle pains</td>
<td>Anaemia, Neutropenia, gastrointestinal intolerance, Lactic acidosis</td>
<td>Caution in: pre-existing anaemia Liver and renal insufficiency</td>
</tr>
<tr>
<td>Didanosine (DDI)</td>
<td>200 mg bid for wt &gt; 60kg 125 mg bid for wt &lt;60kg</td>
<td>Tablet</td>
<td>Neuropathy Nausea Diarrhoea dry mouth</td>
<td>pancreatitis, Lactic Acidosis</td>
<td>Take drug One hour before or two hours after food Contains antacid, affects absorption of other drugs</td>
</tr>
<tr>
<td>Lamivudine (3TC)</td>
<td>150 mg bid</td>
<td>Tablet</td>
<td>Few side effects, neutropenia, peripheral neuropathy reported</td>
<td>Lactic acidosis (Rare)</td>
<td></td>
</tr>
<tr>
<td>Stavudine (d4T)</td>
<td>30 mg bid for wt &lt;60kg, 40 mg bid for wt &gt;60kg</td>
<td>Capsule</td>
<td>Peripheral neuropathy, lipoatrophy</td>
<td>Lactic acidosis, pancreatitis</td>
<td></td>
</tr>
<tr>
<td>Abacavir</td>
<td>300 mg bid</td>
<td>Tablet</td>
<td>Nausea, Poor Appetite, Vomiting Fatigue Sleep disturbance</td>
<td>Hypersensitivity reaction Lactic acidosis</td>
<td>Caution in liver or renal disease Discontinue use in symptoms of hypersensitivity</td>
</tr>
<tr>
<td>Nelfinavir (NFV)</td>
<td>750 mg tid or 1250 mg bid</td>
<td>Tablet</td>
<td>Diarrhoea, lipodystrophy, reduced glucose tolerance</td>
<td></td>
<td>Should be taken with meals</td>
</tr>
<tr>
<td>Drug</td>
<td>Adult dosage</td>
<td>Formulations</td>
<td>Adverse effects Minor, frequent</td>
<td>Adverse effects serious, dose limiting</td>
<td>Special instructions</td>
</tr>
<tr>
<td>----------------------</td>
<td>--------------------</td>
<td>--------------------</td>
<td>-------------------------------------------------------------------------------------------------</td>
<td>-------------------------------------------------------------------------------------------------</td>
<td>--------------------------------------------------------------------------------------------------</td>
</tr>
<tr>
<td>Tenofovir</td>
<td>300 mg daily</td>
<td>Tablet</td>
<td>Diarrhoea, nausea, dyslipidemia, lipodystrophy, headache</td>
<td>Nephrotoxicity (Rare)</td>
<td>To be taken with a meal</td>
</tr>
<tr>
<td>Lopinavir/ritonavir</td>
<td>400 mg /100 mg bid</td>
<td>Capsule/Tablet</td>
<td>Diarrhoea, nausea, dyslipidemia, lipodystrophy, headache</td>
<td></td>
<td>Lopinavir/r (is a Ritonavir boosted lopinavir which requires secure cold chain)</td>
</tr>
<tr>
<td>Ritonavir (RTV)</td>
<td>600 mg bid</td>
<td>Tablet</td>
<td>Gastrointestinal tolerance first 2 to 4 weeks. Weakness, Skin sensitivity, Perioral tingling, numbness, Change in taste</td>
<td>Abnormal liver function tests. Major drug interactions, Hyperglycaemia, Lipodystrophy, Abnormal bleeding</td>
<td>Capsule require refrigeration Easier tolerated if taken with food</td>
</tr>
<tr>
<td>Efavirenz</td>
<td>600 mg daily</td>
<td>Capsule</td>
<td>Skin rash, Abnormal Liver function test</td>
<td>Neuropsychiatric disturbances, teratogenicity</td>
<td>Caution in liver disease</td>
</tr>
<tr>
<td>Nevirapine</td>
<td>200 mg daily x 14then 200 mg b.d</td>
<td>Tablet</td>
<td>Skin rash, Abnormal liver function tests</td>
<td>Hepatitis</td>
<td>Caution in liver disease</td>
</tr>
</tbody>
</table>
### Paediatric Drugs and their characteristics

<table>
<thead>
<tr>
<th>Drug</th>
<th>Preparations</th>
<th>Dosage for children</th>
<th>Adverse effects Minor, frequent</th>
<th>Adverse effects serious, dose limiting</th>
<th>Special instructions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Zidovudine (AZT)</td>
<td>Syrup: 10mg/ml Capsules:100mg Tablets:300mg</td>
<td>Neonatal dose: Oral: 4mg/kg body weight 12hrly. Paediatric dose: 240mg/m² every 12 hrs Max-300mg every 12hrs</td>
<td>Nausea Headache Fatigue Muscle pains</td>
<td>Anaemia, Neutropenia, gastrointestinal intolerance, Lactic acidosis</td>
<td>Caution in: pre-existing anaemia Liver and renal insufficiency. Can be administered with food Store at room temperature</td>
</tr>
<tr>
<td>Didanosine (DDI)</td>
<td>Paediatric powder for oral solution (when constituted as solution containing antacid: 10mg/ml Chewable tablets with buffers: 25,50, 100, 150 mg, 200mg</td>
<td>90 – 150 mg/m² 12 hourly (note higher dosage in patients with central nervous system disease)*</td>
<td>Neuropathy Nausea Diarrhoea dry mouth</td>
<td>Pancreatitis, Lactic Acidosis</td>
<td>Keep suspension refrigerated; stable for 30 days; must shake well Take drug one hour before or 2 hours after food Each dose should consist of 3 tablets to ensure that adequate buffering is provided to prevent degradation of the drug in gastric secretions.</td>
</tr>
<tr>
<td>Drug</td>
<td>Preparations</td>
<td>Dosage for children</td>
<td>Adverse effects Minor, frequent</td>
<td>Adverse effects serious, dose limiting</td>
<td>Special instructions</td>
</tr>
<tr>
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<td>----------------------------------------------------------</td>
</tr>
</tbody>
</table>
| Lamivudine (3TC) | Tablet 150 mg  
Paediatric solution 10 mg /ml | 2mg/kg 12hourly for Neonates . 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, 30mg  
Solution 1mg/ml | < 30 kg: 1mg /kg / dose twice daily  
>30kg: 30mg/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 refrigerated)  
Do not use with AZT (Antagonistic antiretroviral effect) |
<p>| Abacavir  | Oral solution: 20 mg/ml | 8 mg/ kg / dose bid | Nausea Poor Appetite Vomiting Fatigue | Hypersensitivity reaction  Lactic acidosis | Caution in liver or renal disease Discontinue use if |</p>
<table>
<thead>
<tr>
<th>Drug</th>
<th>Preparations</th>
<th>Dosage for children</th>
<th>Adverse effects</th>
<th>Adverse effects serious, dose limiting</th>
<th>Special instructions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nelfinavir (NFV)</td>
<td>Tablet 300mg</td>
<td>Sleep disturbance</td>
<td></td>
<td></td>
<td>symptoms of hypersensitivity</td>
</tr>
<tr>
<td></td>
<td>Table 250 mg</td>
<td>55-65mg/kg bid</td>
<td>Diarrhoea</td>
<td></td>
<td>Can give with food</td>
</tr>
<tr>
<td>Lopinavir/Ritonavir</td>
<td>Lopinavir/ritonavir and.200mg/50mg Tablets and 133.3mg/33.3mg Capsules</td>
<td>6months to 13 years of age: 7 to &lt;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</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Oral solution: 80mg Lopinavir/20mg Ritonavir per ml</td>
<td>Max 40 kg: 400 mg LPV/100 mg ritonavir (3 capsule or 5 ml) twice daily</td>
<td>Hypersensitivity Pancreatitis Diabetes Mellitus</td>
<td></td>
<td>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 difficulties with use of powder, use of crushed tablets preferred ( even for infants) if appropriate dose can be given</td>
</tr>
<tr>
<td>Drug</td>
<td>Preparations</td>
<td>Dosage for children</td>
<td>Adverse effects Minor, frequent</td>
<td>Adverse effects serious, dose limiting</td>
<td>Special instructions</td>
</tr>
<tr>
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<td>-------------------------------------------------------------------------------------</td>
<td>---------------------------------</td>
<td>----------------------------------------</td>
<td>------------------------------------------------------------</td>
</tr>
<tr>
<td>Nevirapine (NVP)</td>
<td>Oral suspension: 10mg/ml (Neonate) &lt;br/&gt; Tablet: 200 mg</td>
<td>2mg/kg bid &lt;br/&gt; 200 mg/m²/dose once daily for 2 weeks; then 200 mg/m²/dose twice daily &lt;br/&gt; Maximum dose allowable is 200mg.</td>
<td>Rash</td>
<td>Hypersensitivity Hepatotoxicity</td>
<td>If Rifampicin co-administration, avoid use &lt;br/&gt; Store suspension at room temperature; must shake well &lt;br/&gt; Can give with food can be crushed and combined with small amount of water or food and immediately administered &lt;br/&gt; warn parents about Rash.</td>
</tr>
<tr>
<td>Drug</td>
<td>Preparations</td>
<td>Dosage for children</td>
<td>Adverse effects Minor, frequent</td>
<td>Adverse effects serious, dose limiting</td>
<td>Special instructions</td>
</tr>
<tr>
<td>------------</td>
<td>------------------------------------------------------------------------------</td>
<td>--------------------------------------------------------------------------------------</td>
<td>---------------------------------</td>
<td>---------------------------------------</td>
<td>-----------------------------------------------------------</td>
</tr>
<tr>
<td>Efavirenz</td>
<td>Syrup: 30mg/ml (note syrup requires higher dosing than capsules)</td>
<td>Capsule (liquid) dose for &gt; 3yrs: 10 to 15kg: 200mg once daily 15 to &lt; 20kg: 250mg once daily 20 to &lt; 25kg: 300mg once daily 25 to &lt; 33kg: 350mg once daily 33 to &lt; 40kg: 400mg once daily maximum dose: &gt; 40kg: 600mg once daily</td>
<td>Skin rash</td>
<td>1. CNS toxicity 2. Teratogenic</td>
<td>Only for children over 3 years</td>
</tr>
<tr>
<td></td>
<td>Capsules: 50mg, 100mg, 200mg, 600mg</td>
<td></td>
<td></td>
<td></td>
<td>Capsules may be opened and added to food but has a very peppery taste</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Avoid high fatty foods</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Best given at bed time to reduce CNS side effects</td>
</tr>
</tbody>
</table>

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

- Kaposi's sarcoma HIV encephalopathy (as defined by CDC) APPENDIX 2
APPENDIX 5  ALGORITHM FOR THE MANAGEMENT OF HEPATITIS B VIRUS CO-INFECTION WITH HIV

HIV/HBV\(^1\)

- **HAART**
  - Efavirenz
  - Lamivudine
  - Tenofovir

Indication for HAART
- CD4 ≤ 350

**Yes**

No

**ALT\(^2\) elevated? ± Other Tests\(^3\)**

**Yes**

- Monitor ALT every 3 months
- Screen for HCC\(^4\) every 6 months with:
  - Ultrasound of liver
  - α-Feto-protein

**No**

- PEG IFN α2a\(^5\) for 48 weeks
- Early HAART including:
  - Tenofovir + Lamivudine
  - Entecavir / Adefovir

---

\(^1\) Chronic Hepatitis B infection is defined as HBs Ag + >6 months (± Hepatitis B Core antibody (HBCIgG) where this can be done)

\(^2\) ALT is elevated when it is >1.5 upper times the upper limit of normal (>45IU/L for men and >30 IU/L for women).

\(^3\) In centres where facilities are available, the following tests may be done in the evaluation of the patient:
  - HBV DNA viral load
  - HBcAg
  - HBCIgG

\(^4\) HCC - Hepatocellular carcinoma. All patients >20 years of age should be regularly screened for HCC.

\(^5\) PEG IFN α2a is peginterferon alfa-2a which has superseded interferon
APPENDIX 6

TB SCREENING QUESTIONNAIRE

NAME: …………………………………………………………………………………………………………

AGE: ……………… SEX: …………….. DATE: ………………………………..

SYMPTOM SCREEN
Do you have any of the following symptoms? (Please grade the symptoms as indicated)

<table>
<thead>
<tr>
<th>Symptom</th>
<th>No</th>
<th>Yes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cough for more than 2 weeks</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>Coughing up blood</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>Sputum production</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>Loss of weight in last 3 months</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Loss of appetite recently</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Fever for more than 1 week</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Chest pain</td>
<td>0</td>
<td>1</td>
</tr>
</tbody>
</table>

Total Score: (max 10)

PAST MEDICAL HISTORY
Exposure to a TB patient? YES NO
Have you been treated for TB in the past 5 years? YES NO
When: ………………… (year)
Duration: …………… (months)

<table>
<thead>
<tr>
<th>Variable</th>
<th>Conclusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cough for &gt; 2 weeks</td>
<td>Suspect</td>
</tr>
<tr>
<td>Score of 7 or more on symptom screen</td>
<td>Suspect</td>
</tr>
<tr>
<td>Previous TB treatment in last 5 years</td>
<td>Suspect</td>
</tr>
</tbody>
</table>

CONCLUSION (Circle) SUSPECT NON SUSPECT

REQUEST SPUTUM SMEAR MICROSCOPY FOR ALL SUSPECTS

RESULTS

<table>
<thead>
<tr>
<th>SPUTUM 1: Date………………</th>
<th>POS</th>
<th>NEG</th>
<th>REF</th>
<th>NPC</th>
<th>DEA</th>
<th>ILL</th>
</tr>
</thead>
<tbody>
<tr>
<td>SPUTUM 2: Date………………</td>
<td>POS</td>
<td>NEG</td>
<td>REF</td>
<td>NPC</td>
<td>DEA</td>
<td>ILL</td>
</tr>
<tr>
<td>SPUTUM 3: Date………………</td>
<td>POS</td>
<td>NEG</td>
<td>REF</td>
<td>NPC</td>
<td>DEA</td>
<td>ILL</td>
</tr>
</tbody>
</table>

POS: positive smear result  NEG: negative smear result  REF: refused to provide a sputum specimen
NPC: non productive cough  DEA: died before sputum collection  ILL: too ill to provide sputum
TB SCREENING QUESTIONNAIRE FOR PRISONS

NAME: ……………………………………………………..  ID No. ………………
AGE: ………………..    SEX: .......................         DATE: ………………………………...
Date of Imprisonment……………… Date of Arrival in this Institution…………………...
Expected Date of Discharge ………………………………………………………………..

SYMPTOM SCREEN
Do you have any of the following symptoms?  (Please grade the symptoms as indicated)

<table>
<thead>
<tr>
<th>Symptom</th>
<th>No</th>
<th>Yes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cough for more than 2 weeks</td>
<td>0</td>
<td>2</td>
</tr>
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<td>Coughing up blood</td>
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<td>1</td>
</tr>
<tr>
<td>Fever for more than 1 week</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Chest pain</td>
<td>0</td>
<td>1</td>
</tr>
</tbody>
</table>

Total Score: (max 10)

PAST MEDICAL HISTORY
Exposure to a TB patient?    YES  NO
Tested Positive for HIV?    YES  NO
Have you been treated for TB in the past 5 years?
   When: …………… (year)
   Duration: …………. (months)
   Which drugs:   H  R  E  S  Z  other
Weight: ………………kg   Height: …………m   BMI: ………….kg/m²

Variable                   Conclusion
Cough for > 2 weeks         Suspect
Score of 7 or more on symptom screen    Suspect
Previous TB treatment in last 5 years    Suspect

CONCLUSION (Circle)   SUSPECT   NON SUSPECT

REQUEST SPUTUM SMEAR MICROSCOPY FOR ALL SUSPECTS

RESULTS

SPUTUM 1: Date……………. POS   NEG   REF   TRF   NPC   REL   DEA   ILL
SPUTUM 2: Date……………. POS   NEG   REF   TRF   NPC   REL   DEA   ILL
SPUTUM 3: Date……………. POS   NEG   REF   TRF   NPC   REL   DEA   ILL

POS: positive smear result   NEG: negative smear result   REF: refused to provide a sputum specimen
TRF: transferred to another facility before sputum collection   NPC: non productive cough
REL: released before sputum collection   DEA: died before sputum collection   ILL: too ill to provide sputum
REFERENCES
6. Hepatitis Treatment Guidelines.