Guidelines for Antiretroviral Therapy in Ghana
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Guidelines for Antiretroviral Therapy in Ghana

Ministry of Health/Ghana Health Service
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FOREWORD

The HIV/AIDS epidemic continues to pose a threat to public health, economy and indeed to national security in some countries. The Government of Ghana has indicated its commitment to effectively respond to this threat.

Comprehensive management of persons infected with HIV and AIDS patients has been shown to reduce mortality in addition to improving the quality of life of the infected. The continuum of care includes general measures as well as specific medication for prevention and treatment of opportunistic infections and the use of Anti–retroviral Therapy. Clinical science and medical treatment of PLWHA's has developed rapidly in this domain.
The Health Sector has the primary mandate of providing care among others for PLWHA's. These guidelines are not intended to provide a state of the art medical care, but a practical approach for managing HIV related illness. This includes criteria for initialisation of therapy, drug combinations on monitoring among others. It also provides technical detail on drug interactions. It takes cognisance of the inadequate laboratory support that will ensure optimum monitoring. It also recognizes the cost implications and therefore recommends drugs that are efficacious, with safe profile and cost effective.

Even though Primary and Secondary Prevention are not addressed in this document, it should be emphasized that these should form an integral part of patient management of every opportunity. 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. KWAKU AFRIYIE
HON. MINISTER OF HEALTH

LIST OF ACRONYMS

AIDS  Acquired Immune Deficiency Syndrome
AFBS  Acid Fast Bacilli
ART   Antiretroviral Therapy
ARV   Antiretrovirals
AZT   Zidovudine
BUE   Blood Urea and Electrolytes
ddC   Zalcitabine
DDI   Didanosine
d4T   Stavudine
CD4   CD4 cells– T4 helper cells
HIV   Human Immune Deficiency Virus
IDV   Indinavir
LIP   Lymphoid Interstitial Pneumonitis
NACP  National HIV/AIDS/STI Control Programme
NGO  Non–governmental Organisation
NFV   Nelfinavir
NRTI  Nucleoside Reverse Transcriptase Inhibitor
NNRTI Non–Nucleoside Reverse Transcriptase Inhibitor
CHAPTER 1

Introduction

The first case of HIV was reported in Ghana in 1986. There has since then been a rapid rise in HIV prevalence in Ghana and by October 2001 a cumulative number of 48,771 cases of AIDS had been reported in the country. Almost 90% of all reported AIDS cases have occurred between the ages of 15 and 49 years. The female to male ratio in 2000 was found to be 2:1 compared to 6:1 in 1987. This suggests that there seems to be evening out of the epidemic between the sexes. The peak age group affected is the 25 to 34 year group accounting for 42.5% of all AIDS cases reported in 1999. The peak age group for males (30 to 34 years) is slightly higher than that for females (25 – 29 years). With a reporting level of about 30%, it is estimated that 350,000 cases of HIV infection have probably already occurred.

Data gathered in the 2000 Sentinel surveillance estimated the prevalence HIV among adults of 3.0%. The prevalence of HIV is expected to rise to a level of about 8% by the year 2005 and may increase to 9% in 2014 or remain more or less stable at about 4% in 2014, based on current trends. The prevalence may depend on the sustainability of the current and future responses to the epidemic. With this trend one can expect the number of adult Ghanaians infected with HIV to rise to about between 560,000 and 1,200,000 by the year 2014. This trend will have serious social and economic consequences for the country and will comprise the overall national development in the medium and long term if not halted.

The impact of HIV/AIDS will be felt in all sectors. In the health sector by 2014 AIDS will be responsible for 28 percent of all deaths and the health expenditure for the management of opportunistic infections will rise to 167 billion cedis. Tuberculosis in particular is an opportunistic infection that is expected to increase due to the rising number of immuno-suppressed individuals. It is expected that there will be 46,000, and 76,000 cases by 2005 and 2015 respectively.

Heterosexual spread remains the main mode of transmission accounting for 75 to 80 % of all transmissions, mother to child transmission or (vertical transmission) accounting for 15% and transmission through blood products accounting for 5%. HIV 1 continues to be the most predominant type of HIV infection accounting for 95.9% of all infections, with HIV 2 accounting for 1.5% of infections and dual infections accounting for 2.6 of infections.

Ghana has instituted a strong national response. This began in 1985 with the setting up of The National Technical Committee on AIDS (NTCA). This was replaced with The National AIDS/STD Control Programme (NACP) based in the Ministry of Health in 1987. NACP has been the co-ordinating body of the national
response even though it is situated in the Ministry of Health. In September 2000 the Ghana AIDS Commission was inaugurated to serve as the coordinating body for all HIV/AIDS related activities in Ghana. The objectives of the plans have been to reduce further transmission of infection and to mitigate the effects of HIV/AIDS on the infected and affected Priority interventions 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. The context of the response has been multisectoral multidisciplinary and expanded. Stakeholders have included government sectors, private sector, NGOs, traditional healers, persons living with HIV/AIDS (PLWHA) and civil society. Presently however with the increasing number of PLWHA, the clinical care and management including the treatment with antiretroviral therapy has become a priority.

The number of HIV infected individuals and those with AIDS are increasing daily. In 2000 over 380,000 individuals are estimated to be infected with HIV in Ghana. Prolonging the life of these individuals to enable them be productive and support their families and the nation as a whole is of Utmost importance

Available care in Ghana

Presently People Living with HIV/AIDS (PLWHA) in Ghana have limited access to clinical care. They are supported counselled, some are provided with prophylaxis and treatment for opportunistic infections. The Ministry of Health in its Five Year Strategic Framework for HIV has planned a continuum of care programme to introduce protocols for prophylaxis and the treatment for opportunistic infections as well as the treatment with antiretroviral drugs. To complement this, the Ministry of Health, various NGOs and Faith based organisations are involved in Home Based Care for People Living with HIV/AIDS and provide them with care and support.

 Though antiretroviral therapy is available its prices are prohibitive for all but the extremely rich. A few individuals are sent medication from family and friends in western countries. The drugs available in Ghana are:

- Combivir (a combination of AZT and Lamivudine)
- Viracept (Nelfinavir)
- Nevirapine (used mainly for the prevention of mother to child transmission)

These are available at $200, and $282 per month for Combivir and Viracept respectively. Nevirapine is presently free and being used for the prevention of mother to child transmission.

There is also limited laboratory support for antiretroviral therapy and Viral load determination and CD4 cost between $85 and $200 for viral load determination and $20 and $50 for CD4 count and are only available in two centres in the capital Accra.

Other investigations that need to be done such as serum chemistries and haematological test are available in most regional hospitals, and full blood count is available in most district hospitals.

Efforts at provision of ART in Ghana

Over the past year various efforts have been made to provide ART in Ghana. Issues addressed include:

- Negotiations for resource mobilisations
- Negotiations with pharmaceutical companies to provide drugs at reduced prices
- Provision of free drugs for particular programmes
- Discussion on the technology transfer between Ghana and Thailand to produce Antiretroviral drugs in Ghana
- Setting up of a multidisciplinary Task Force for Antiretroviral therapy in Ghana.
Purpose

The purpose of this document is to provide guidelines for the introduction, provision and monitoring of Antiretroviral therapy in Ghana. These guidelines need to be updated at regular intervals and as new evidence becomes available.

Goal

The goal of Antiretroviral therapy is to improve the quality of life and reduce HIV–related morbidity and mortality.

Objectives

The objectives are to:

• To provide access to affordable ART
• To assure the continuum of care for PLWHA
• To monitor response to therapy in PLWHA
• To avoid and monitor resistance
• To strengthen comprehensive HIV care.

CHAPTER 2

Antiretroviral therapy

Introduction of ART

Due to the high–cost of antiretroviral drugs, the complexity of the regimen and the need for careful monitoring, specific services and facilities must be in place before considering the introduction of ART into any setting.

The following conditions are essential.

• Assured access to voluntary counselling and testing and follow up counselling
• Identification of sufficient resources to pay for treatment on a long– term basis
• Assurance of adequate and regular supply of good quality drugs for treatment of opportunistic infections
• Assurance of adequate supply of good quality Antiretroviral agents
• Capacity to recognise and appropriately manage common HIV related illnesses and opportunistic infections
• Information and training on safe and effective use of antiretroviral drugs for health professionals in a position to prescribe ART and dispense and regularly update this information
• Reliable laboratory monitoring

• Monitoring efficacy of ART

• Establishment of reliable regulatory mechanisms against misuse and misappropriation of antiretroviral drugs.

• Functional implementation, referral and monitoring system.

Strategies to Achieve effective ART

• Maximise adherence to the antiretroviral regimen
• Rational sequencing of drugs
• Preservation of future treatment options
• Use of resistance testing in selected clinical settings

Initiation

Since the cost of therapy is to be borne by the patient and the therapy is life long the clinician should ascertain that the patient can afford the cost of therapy on a long term basis since termination of therapy will be detrimental to the patient (see counselling).

Before initiation of Antiretroviral therapy a comprehensive medical history including social history and a complete physical examination is required. This is aimed at:

• Assessing the clinical staging of HIV infection
• Identifying past HIV related illnesses
• Identifying current HIV related illnesses that will require treatment
• Identifying co−existing medical condition that influence the choice of therapy
• Assessing financial capacity
• Assessing capacity to adhere.

Initiation Criteria

Antiretroviral therapy should be initiated when the patient satisfies at least one of the following criteria:

Adults (individuals more than 12 years):

• Symptomatic with HIV 1\(^1\) infections in WHO stage 3 and 4\(^2\) (excluding individuals in stage 3 and 4 due to Tuberculosis)

• Patients with CD4 count less than 250 cells/ml

• Patients with Total Lymphocyte count less than 1000

\(^1\) HIV in this text refers to HIV 1
\(^2\) See Appendix 1 for staging

Children (less then 12 years)

• Symptomatic children in categories B and C of HIV positive mothers\(^3\)

• Children of HIV positive mothers

• With or without PCR positive after 24 hours
• Children with antibody test positive at 18 months (the child's treatment is not dependant on the mother's treatment)

3 See Appendix 2 for categories

Exclusion Criteria

Antiretroviral Therapy shall not be initiated under the following circumstances:

• The patient is not motivated
• Treatment is not sustainable, the person is not able to cope with follow up visits
• No biological monitoring possible
• The patient presents with severe hepatic or renal insufficiency
• The patient has an acute opportunistic infection
• The patient has terminal illness

Interruption of Therapy

Interruption of therapy refers to the temporal 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 especially in cases of financial incapacity this may result in resistance. However in triple therapy including Nevirapine, Nevirapine should be stopped abruptly while the other drugs are continued for a period of one week only since the half-life of Nevirapine expends to a period of one week.

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

• Intolerable side effects
• Severe drugs interactions
• First trimester (when the patient so elects) The patient may restart therapy after the first trimester.

Criteria for Changing Therapy

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

• Drug toxicity
• Difficulties in adherence
• Treatment Failure. This can be defined as development of symptomatic diseases not caused by Antiretroviral drug side effects, or immune reconstitution disease or non-HIV related illness, in the presence of weight loss and no CD4 increase.
• In areas where viral load is available, Treatment failure is defined as or insufficient viral load suppression at 6 months after starting ART, or stable or increase in viral by half log (by RT-PCR) after initial suppression. (Note that if after one month after initiation of therapy there is significant increase in viral load then this indicates drug resistance.)
• Severe drug interactions
Recommended ART Regimen

The regime described below is for treatment (patients who have not previously been treated with ART) individuals and is based on evidence from other ART programmes worldwide. The recommendations are based on the effectiveness of the drug, pill burden, toxicity, dosing frequency, food requirements, convenience and drug interaction profiles, resistance to ARV, availability and cost.

The regimen is based on triple therapy. Monotherapy or Dual therapy are contraindicated.

The following triple therapy regimen are recommended

- 2 Nucleoside reverse transcriptase inhibitors (NRTIs) and 1 Protease Inhibitor (PI)
- 2 NRTIs and 1 Non–nucleoside reverse transcriptase inhibitors (NNRTI)
- 2 NRTIs and 2 Pls

One drug/combination is chosen from group A and one form group B

<table>
<thead>
<tr>
<th>Column A</th>
<th>Column B</th>
</tr>
</thead>
<tbody>
<tr>
<td>FIRST LINE DRUGS</td>
<td></td>
</tr>
<tr>
<td>Efavirenz</td>
<td>Stavudine + Lamivudine</td>
</tr>
<tr>
<td>Nevirapine* (as single dose for Prevention for mother to child transmission)</td>
<td>Stavudine + Didanosine</td>
</tr>
<tr>
<td></td>
<td>Zidovudine + Lamivudine</td>
</tr>
<tr>
<td></td>
<td>Zidovudine + Didanosine</td>
</tr>
<tr>
<td>SECOND LINE DRUGS**</td>
<td>Nevirapine (as part of triple therapy)</td>
</tr>
<tr>
<td></td>
<td>As in column B above</td>
</tr>
<tr>
<td></td>
<td>Indinavir</td>
</tr>
<tr>
<td></td>
<td>Nelfinavir</td>
</tr>
</tbody>
</table>

* Nevirapine single dose therapy is being used for the prevention of mother to child transmission programme alone.

** Second line drugs may be used in individuals who fit the criteria for change of therapy. Preferably the whole regimen should be changed if the patient fits this criteria.

<table>
<thead>
<tr>
<th>Drug</th>
<th>Adult dosage</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>300 mg bid</td>
<td>160 mg/m2 8 hourly</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></td>
<td>Greater than 60 kg 200 mg bid or 400 mg daily Less than 60 kg 125 mg bid of 250 mg daily</td>
<td>90 – 150 mg/m2 12 hourly</td>
<td>Neuropathy, Nausea, Diarrhoea dry mouth</td>
<td>Pancreatitis, Lactic Acidosis</td>
<td>Take food One hour before or after food Contains antacid, affects absorption of other drugs</td>
</tr>
<tr>
<td>Didanosine (DDI)</td>
<td>0.75 mg tid</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Drug</td>
<td>Dosage</td>
<td>Side Effects</td>
<td>Interactions</td>
<td>Notes</td>
<td></td>
</tr>
<tr>
<td>--------------</td>
<td>--------</td>
<td>------------------------------------------------------------------------------</td>
<td>------------------------------------------------------------------------------</td>
<td>----------------------------------------------------------------------</td>
<td></td>
</tr>
<tr>
<td>Zalcitabine</td>
<td>0.005–0.01 mg/kg hourly</td>
<td>Peripheral neuropathy, mouth ulcer</td>
<td>Pancreatitis Lactic acidosis</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lamivudine (3TC)</td>
<td>150 mg bid</td>
<td>Few side effects, neutropenia, peripheral neuropathy reported</td>
<td>Lactic acidosis</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stavudine (d4T)</td>
<td>20 – 40 mg twice daily</td>
<td>Peripheral neuropathy</td>
<td>Lactic acidosis</td>
<td>Caution in liver insufficiency</td>
<td></td>
</tr>
<tr>
<td>Abacavir</td>
<td>300 mg tid</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>
<td></td>
</tr>
<tr>
<td>Nelfinavir (NFV)</td>
<td>750 mg tid or 1250 mg bid</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Indinavir (IDV)</td>
<td>800 mg 8 tid</td>
<td>Nausea, Abdominal pain, Headache</td>
<td>Kidney stones, Hyperglycaemia, Lypodystrophy, Abnormal bleeding</td>
<td>Take on an empty stomach, Drink 1.5 litres of liquid per day to avoid kidney problems, Report loin pain or blood in urine</td>
<td></td>
</tr>
<tr>
<td>Ritonavir (RTV)</td>
<td>600 mg bid</td>
<td>Gastrointestinal tolerance first 2 to 4 weeks, Weakness, Skin sensitivity, Peri oral tingling and numbness, Change in taste</td>
<td>Abnormal liver function tests, Major drug interactions, Hyperglycaemia, Lypodystrophy, Abnormal bleeding</td>
<td>Capsule require refrigeration, Easier tolerated if taken with food</td>
<td></td>
</tr>
<tr>
<td>Saquinavir</td>
<td>600 mg tid</td>
<td>Few reported side effects, Should be used as potentiated PI in conjunction with Ritonavir</td>
<td>Diarrhoea, Nausea, Abnormal LFTS</td>
<td>Take high fat meal, Refrigeration for long term storage, Caution in liver disease</td>
<td></td>
</tr>
<tr>
<td>Efavirenz</td>
<td>600 mg daily</td>
<td>Skin rash, Abnormal Liver function test</td>
<td>Neuropsychiatric disturbances</td>
<td>Caution in liver disease</td>
<td></td>
</tr>
<tr>
<td>Nevirapine</td>
<td>200 mg daily x 14 then 200 mg b.d</td>
<td>Skin rash, Abnormal liver function tests</td>
<td>Hepatitis</td>
<td>Caution in liver disease</td>
<td></td>
</tr>
</tbody>
</table>

**Drug Interactions**

Drug interactions may occur in PLWHA taking other medications for prophylaxis and control of opportunistic infections, treatment of other infection and/or disease. Drug interactions may occur between:

- Different antiretroviral drugs prescribed (this has been eliminated to some extent by the choice of regimen above, however new interactions may be defined in the future).
• Between prescribed drugs and alternative or non−prescription medication
• Between drugs and food
• Certain recreational drugs

See appendix 3 for table on drug interactions Some important drug interactions are listed below:

**Recommendations for Antiretroviral Therapy in Patients with Tuberculosis**

In the treatment of tuberculosis some important interactions should be considered. Rifampicin, PIs and NNRTIs are metabolised by the same enzyme system (cytochrome P450) thus Rifampicin 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 extent and can lead to altered blood levels of Rifampicin. This may result ineffective Antiretroviral or anti−tuberculous therapy or drug toxicity. Therefore:

• Treatment for tuberculosis should be in accordance with the National Tuberculosis Programme Guidelines
• If possible antiretroviral therapy should be deferred until the completion of anti−tuberculosis chemotherapy.
• ART should be deferred until the continuation phase of TB treatment where only ethambutol and isoniazid is used in the continuation.

**Other interactions**

Other interactions occur between drugs used in the treatment of opportunistic infections. 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 toxicity.

**Management of Opportunistic Infections**

This should follow established protocols for the management of opportunistic infections. (see Opportunistic infections guidelines). Principal Opportunistic infections need to be treated before the initiation of therapy.

**Clinical Monitoring**

A detailed clinical evaluation is essential prior to initiating ART.

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

1. Assess the clinical staging of HIV infection
2. Identify past HIV related illnesses
3. Identify current HIV related illnesses that will require treatment
4. Identify co−existing medical conditions that may influence the choice of therapy

This can be achieved by:
1. Taking a detailed medical history
2. Carrying out a complete physical examination and
3. Appropriate laboratory investigations.

The Medical History should include:

1. Time of initial HIV diagnosis
2. Current symptoms and concerns
3. Past Medical History including diagnosis of Tuberculosis
4. Drug history including treatment for TB
5. Sexual history and past symptoms of STI
6. Gynaecological history
7. Social history

The physical examination should have the following components

1. Patient's weight
2. Skin and lymph nodes, looking out for the following
   a. Herpes Zoster (old scars and new lesions)
   b. Kaposi's sarcoma
   c. Lymphadenitis
   d. HIV dermatitis
3. Oropharyngeal mucosa
   a. candidiasis
   b. Kaposi's sarcoma
   c. leucoplakia
4. Examination of heart and lungs including Chest X-ray
5. Examination of GIT
6. Examination of CNS & MSS including the mental status, motor sensory deficits
7. Fundoscopy whenever possible for retinitis or papilloedema
8. Detailed examination of Genital Tract including discharge, ulcers, enlarged glands and
growths

Patients on ART should be closely followed to assess adherence to therapy as well as tolerance and efficacy
of the treatment. Intensive follow up should be done in the first few weeks of management. Management of
the PLWHA should be a team approach between the physician, nurse, counsellor, pharmacist and any other
service provider member of the family who will support the patient in 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 four monthly intervals or as necessary. Patients should
also be seen after laboratory tests.

**Monitoring of adherence**

Adherence to ART is essential and a reduction of 80% adherence greatly reduces the effectiveness of
therapy. To improve adherence the initial counselling sessions should be comprehensive resulting in
well-informed decisions and commitment by the patient. In addition there should be accessible knowledge or
information and a supporting committed medical team. Adherence to treatment should be discussed in depth
at each follow up visit.
**Monitoring of tolerance**

Causes of any new symptoms and signs should be identified after initiation of ART.

New symptoms may be due to

- Intercurrent illnesses
- Adverse reactions of antiretroviral drugs
- Opportunistic infections becoming clinically apparent as a result of immune reactivation (these need to be diagnosed and treated)
- Adverse effects from drugs should be explained to patients and appropriate measures taken e.g. adapting the drug regime, providing symptomatic treatment and giving reassurance.

Ancillary drug test done will confirm adverse effects such as anaemia, neutropenia among others. (see laboratory monitoring).

**Monitoring of Efficacy**

Indicators for improvement would be

- Sustained suppression of viral load
- Increase in CD4 count of (100–200 cells per year) (this may be less if initial CD4 <50)
- Increase in total lymphocyte count
- Gain in body weight
- Decrease in frequency/severity of opportunistic infections
- Decrease in occurrence/severity of HIV related malignancies
- Increase in haemoglobin (in patient with Zidovudine haematotoxicity)
- Increase in platelets if low at the start

4 Where viral load has been done

**Laboratory Monitoring**

Initial laboratory evaluation should provide:

1. Confirmation of diagnosis of HIV infection and typing
   - Confirmatory HIV test (and typing 1 and 2)
   - Viral load (not absolutely needed depends on the financial capacity of the patient)

2. Indication of patients’ immune status
   - CD4
   - Total lymphocyte count

3. Information on the patient’s baseline

   - Haematological test    Full blood count and platelets
   - Biochemical test       Blood Urea and Electrolytes (only if clinically indicated)
                            Liver Function tests (if on Nevirapine more regular monitoring is necessary)
Fasting Blood sugar (if treatment includes Pls)

Cholesterol and lipid (if treatment includes Pls)

Urinalysis (Urine R/E)

• Hepatitis B Surface antigen (not needed if the liver function test is normal)

Chest X-ray – if symptoms so indicate

• Sputum for AFBS – if symptoms so indicate

• Supplementary test depending on signs and symptoms at presentation

Histology on skin and lymph node biopsy
Screening for STIs
Pregnancy tests
Abdominal Ultrasound

4 Where viral load has been done

Laboratory Monitoring Regimen

Reasons for testing

The above test should be conducted to:

• Determine whether patient satisfies initiation criteria
• Determine the presence or absence of Opportunistic infections and stage of the infection
• To identify the onset of side effect and toxicity of the ART

Viral load

This test is the most important test and should be done first if resources permit. It indicates the prognosis of HIV infection and the virological response of therapy. This test is for HIV 1 only. Viral load is not essential if there is clinical improvement, good adherence and increase in CD4 count.

Though viral load is not essential for management and follow up. It is recommended that where available and affordable viral load should be done at Month 0, 3, 6, 12 and then yearly. 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

CD4

This is a good indicator of the immune function in HIV infection. Recommendations: Month 0, 6, 12 and then 6 monthly intervals

Chest X-ray

Chest X-ray should be done at Month 0 (if symptoms so indicate) Sputum for AFBS should be done at month 0 (if symptoms so indicate)

Ancillary Tests

Ancillary tests should be done at least at 3 monthly intervals
Test for monitoring of tolerance:
• Full blood count (this may be done at monthly intervals)
• Urine R/E
• Fasting Blood Sugar (if the patient is on PIs)
• BUE and Creatinine
• Liver function tests

Other tests can be done depending on clinical findings

Post Exposure Prophylaxis for Health Care Workers

Post Exposure prophylaxis may reduce 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 24 to 48 hours of exposure.

1. All infection prevention programmes should be in place and health workers should follow procedures at all times to prevent exposure. In the event of possible exposure to HIV the following actions should be taken immediately.

2. All health workers accessing the post exposure prophylaxis package should receive counselling from a trained counsellor throughout the period and thereafter if necessary.

3. Treatment of exposure site: The wound site should be cleaned with soap and water/or in the case of mucous membranes flushed with water.

4. Timing of post–HIV exposure prophylaxis initiation

If therapy is necessary it should be initiated promptly, preferably 1 to 2 hours post exposure.

5. Assessment of exposure risk

Low risk exposure is

- Exposure to a small volume of blood or blood contaminated fluids from asymptomatics HIV–positive patients with low viral load
- An injury with a solid needle

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 seroconversion phase of HIV
- Injury with a hollow bore needle
  - Deep and extensive injury
  - Drug resistance in source patient

6. Post –HIV exposure prophylaxis

Low risk:

- Lamivudine 150 mg 12 hourly x 28 days
- Zidovudine 200 mg 8 hourly x 28 days
High risk:

- Zidovudine 200 mg 8-hourly x 28 days
- Lamivudine 150 mg 12 hourly x 28 days
- Indinavir 800 mg 8 hourly x 28 days
- Nelfinavir 750 mg tid or 1250 mg bid x 28 days

7. Recommended drug toxicity and HIV serology testing after exposure

**Baseline tests:**

- Full blood count
- Liver and renal function tests, Hepatitis Surface Antigen
- HIV serology/(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

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**CHAPTER 3**

**Guidelines on ART Counselling**

**Considerations**

Counselling for ART compliments all ongoing counselling for VCT and PMTCT. Guidelines for VCT and PMTCT are available. The following have been identified.

1. HIV/AIDS Counselling Manual
2. Guidelines for HIV/AIDS Counselling
3. Prevention of Mother–to–Child Transmission of HIV in Ghana.\(^5\)


Counselling for ART should also compliment the general counselling for HIV/AIDS. ART should not be initiated until the patient has had at least 3 counselling sections on ART and the patient fully understands the implications of starting treatment.

Each Physician should identify a full time or part time counsellor who shall receive training in the above. Dispensing of ARVs should be done in the clinic such that the client will have adequate adherence counselling.
**Goals of Counselling**

The patient should understand the following issues to make an informed decision.

- The Goals of Therapy
- ART is not a cure.
- The virus can still be transmitted while on ART and so preventative measures should still be applied.
- ART is a life-long commitment.
- Financial considerations.
- Drug information.
- Adherence.
- Disclosure.
- Emotional and Social Support.

**The Goals of Therapy**

- To make the patient clinically better,
- Sustained and durable suppression of viral load, Reduction of HIV-related morbidity and mortality, Restoration or preservation of immune function.

**ART**

The approach to antiretroviral treatment and the design of therapeutic regimens has been influenced by the following key finding 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 while on ART**

- HIV can still be transmitted even while on ART and so preventive measures should still be applied (e.g. condom use, safe sex etc. See Training Manual).

**ART is 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 the emergence of resistant strains of the virus. The patient may need to be reassessed before the same (or if necessary another) ART regimen is started.
Financial considerations

The counsellor should tell the patient the approximate cost of ART per month (or per year).

The patient must be prepared for the high financial commitment ARV places on her/him. The patient should be reminded that treatment is a lifetime commitment.

The patient must be prepared for the cost of laboratory investigations necessary to monitor the effectiveness and side effects of treatment. This financial commitment must be made in relation to other social, family and business considerations.

The consequences of sub–optimal dosing, drug holidays and non–compliance due to financial constraints should be discussed.

Drug Information

– 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.
– Drug interaction with other drugs (e.g. anti–TB, antifungal).
– Storage of the Drugs.
– Address possible unrealistic expectations of therapy.
– Clinical and laboratory monitoring (for monitoring ART) 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, alcoholic patient etc)

Adherence

This limits the effectiveness of ART. The main reasons for non–adherence of therapy are

– The number and timing of doses
– Number and size of pills (pill burden)
– Food restrictions
– Fear of undesirable side effects.

To overcome this problem a drug time–table should be drawn with the patient. The patient should be reassured about side–effects. An alternate regimen should be discussed if side–effects are intolerable.

Disclosure

The counsellors should encourage the disclosure of the HIV–positive status to a confidant (either the partner, a close relative or friend of the patient) so that this person can be involved in the issues relating to drugs and offer support to the patient.

Emotional and Social Support

All groups involved in HIV/AIDS prevention, treatment and care for patients should be identified so that they can offer social support systems to enhance adherence.
Examples of these groups are given below.

– Family
– Friends
– Religious groups
– Healthcare workers
– Networks of PLWHA
– NGOs in AIDS care

Data Management

The following information should be collected:

Demographic data
Medical History
Social History
Physical Examination
Laboratory Evaluation (operational research into the timing of viral load, CD4)
Drug treatment and adherence

CHAPTER 4

Procurement, Storage and Distribution

Procurement

Goals for ARV Procurement

The strategies and methods by which Anti−retrovirals are procured shall aim to achieve 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.

Criteria for selection of drugs

The WHO has defined some 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 based on the results of efficacy and safety evaluations obtained in controlled clinical trials and epidemiological studies, and on the performance in general use in a variety of medical settings;
• When several drugs are available for the same indication, only the drug and the Pharmaceuticals form that provides the more convenient benefit/risk ratio shall be selected

• When two or more drugs are therapeutically equivalent, the selection shall fall on:
  • the drug that has been more thoroughly investigated
  • the drug with the most favourable pharmacokinetic properties;
  • the drug with the lowest cost, calculated on the basis of the whole course of treatment,
  • the drug with which health workers are already familiar,
  • the drug for which economically convenient manufacturing is available in the country
  • the drug which show better stability at the available storage conditions;

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

**Specification**

Generic (or 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.

**Quantification**

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

\[
\text{Quantity of a drug specified for a standard course of treatment} \times \text{Number of treatment episodes of a given health problem} = \text{Total quantity of the drug required for the given health problem}
\]

This calculation is repeated for each health problem and its corresponding drug. Where a drug is used for more than one health problem, the respective totals are added together to obtain the total quantity required.

**Quality Assurance**

ARVs procured by MOH shall be of acceptable quality and shall be demonstrated by:

• Certification of compliance with good manufacturing practice, issued by a competent regulatory authority.

• Certification of quality following testing by an independent quality control laboratory.

• Subject to requirement in accordance with the Ghana Food and Drugs Board’s Law, which makes it mandatory for all drugs to be registered and a system of post registration surveillance implemented.
Executive Procurement

ARVs shall be procured centrally into the public drug supply system through competitive bidding using centrally consolidated order quantities. A framework rolling three−year contract shall be concluded to ensure uninterrupted supply.

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

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

Storage and Distribution

ART shall be stored centrally and distributed direct to selected treatment centres on a stock rotation basis (First expiry first out). The audit trail shall be transparent to prevent possible leakages.

Dispensing of Art

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

Dispensers shall provide clear and simple instructions to patients on use of ARVs and adverse effects.

A relationship based on confidentiality between the patient and dispenser shall be established.

A prescription register containing the following information shall be maintained by the pharmacy;

- Name of Patient, Age, Address, date of initiation of treatment, prescribers name, Dispensers name and signature, quantity of drug dispensed, date dispensed, patient registration Number, type of patient.

Financing and Sustainability

- Initial capital investment (capitalization stock) shall be funded by GOG, Health Partners and the Civil Society at large. This shall not be done at the expense of other services. User fee shall be charged to recover the variable cost of acquisition of ARVs and other logistic (Diagnostic reagents and treatment monitoring reagents).

- Recapitalisation of the scheme shall be considered when necessary.

- The use of generic drugs, and negotiations with other companies for competitive prices and the introduction of health insurance would go to ensure financial sustainability.

Monitoring and Evaluation

A system for monitoring and evaluation of the scheme shall be implemented at all levels to establish:

- Value for money procurement that achieves lower prices
- Goods availability that accredited treatment sites
- Rational use of ART
- Effective revolving fund
Implementation Arrangements

The ART will be introduced into the country as a phase in programme and as such the following centres will be involved initially:

St. Martin's Hospital Agomanya
Atua Government Hospital
St. Dominic's Hospital, Akwatia
Korle–bu Teaching Hospital, Accra
Komfo Anokye Teaching Hospital, Kumasi

It is envisaged that within the next five years all Regional Hospitals shall be involved in the programme.

Prescribers of ART will need to undergo training in ART. Trainees should have followed up 25 patients before embarking on the management of patients with ART.

A mechanism would be put in place to ensure exchange of information and supervision of prescribing physicians.

APPENDIX 1

OTHER DRUGS USED FOR ART

<table>
<thead>
<tr>
<th>Alternative</th>
<th>Column A</th>
<th>Column B</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abacavir</td>
<td>Didanosine + Lamivudine</td>
<td></td>
</tr>
<tr>
<td>Amprenavir</td>
<td>Zidovudine + Zalcitabine</td>
<td></td>
</tr>
<tr>
<td>Delarvidine</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nelfinavir + Saquinavir</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ritonavir</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Saquinavir</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

The following drugs are not recommended

| Hydroxyurea                                     |
| Ritonavir + Indinavir                           |
| Ritonavir + Nelfinavir                          |

The following drug combinations are contraindicated

| Saquinavir                                      | Stavudine + Zidovudine |
| Saquinavir                                      | Zalcitabine + Lamivudine |
| Saquinavir                                      | Zalcitabine + Stavudine |
| Saquinavir                                      | Zalcitabine + Didanosine |
APPENDIX 2

WHO CLINICAL STAGING SYSTEM FOR HIV INFECTION AND DISEASE

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

**CLINICAL STAGE 1**

- Asymptomatic
- Generalised lymphadenopathy,
- Performance score 1: asymptomatic, normal activity

**CLINICAL STAGE 2**

- Weight loss < 10% body weight (and > 5%)
- Minor mucocutaneous manifestations (seborrheic dermatitis: prurigo, fungal nail infections, recurrent oral ulcerations, angular stomatitis)
- Herpes Zoster within the last 5 years
- Recurrent upper respiratory tract infections (i.e. bacterial sinusitis)
- And/or performance score 2: symptomatic, normal activity

**CLINICAL STAGE 3**

- Weight loss > 10% body weight
- Unexplained chronic diarrhoea > 1 month
- Unexplained prolonged fever (intermittent or constant) > 1 month
- Oral candidiasis
- Oral hairy leukoplakia
- Pulmonary tuberculosis within the previous year
- Severe bacterial infections (i.e. Pneumonia, pyomyositis)
- And/or performance scale 3: bedridden < 50% of the day during the last month

**CLINICAL STAGE 4**

- HIV wasting syndrome (as defined by CDC (i.e. weight loss > 10% body weight, plus either unexplained chronic diarrhoea (> 1 month), or chronic weakness and unexplained prolonged fever (> 1 month))

  - *Pneumocystis carinii* pneumonia
  - Toxoplasmosis of the brain
  - Cryptosporidiosis with diarrhoea > 1 month
  - Cryptococcus (extrapulmonary)
  - Cytomegalovirus of an organ other than the liver, spleen or lymph nodes
  - Herpes simplex virus infection, mucocutaneous > 1 month, or visceral any duration
  - Progressive multifocal leukoencephalopathy
  - Any disseminated endemic mycosis
• Candidiasis of the oesophagus, trachea, bronchi or lungs
• Atypical mycobacteriosis, disseminated
• Non–typhoidal salmonella septicaemia
• Extrapulmonary tuberculosis
• Lymphoma
• Kaposi’s sarcoma
• HIV encephalopathy (as defined by CDC)
• And/or performance scale 4: bed–ridden > 50% of the day during last month

<table>
<thead>
<tr>
<th>LABORATORY STAGE</th>
<th>CLINICAL STAGE OF DISEASE (1–4)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total lymphocyte count x 10^6/l</td>
<td>CD4+</td>
</tr>
<tr>
<td>A</td>
<td>&gt;2000.</td>
</tr>
<tr>
<td>B</td>
<td>1000–2000</td>
</tr>
<tr>
<td>C</td>
<td>&lt;1000</td>
</tr>
</tbody>
</table>

APPENDIX 3

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

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

• Category B: moderately symptomatic Examples of conditions in clinical category B include:
  – Anaemia, neutropenia, or thrombocytopenia
  – Bacterial infections: pneumonia, bacteraemia, (single episode)
  – Candidiasis, oropharyngeal
  – Cardiomyopathy
  – Diarrhoea, recurrent or chronic? Hepatitis
  – Herpes stomatitis, recurrent
  – Lymphoid interstitial pneumonia
  – Nephropathy
  – Persistent fever >1 month
  – Varicella (persistent or complicated primary chickenpox or shingles)

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

APPENDIX 4

DRUG–DRUG INTERACTIONS

<table>
<thead>
<tr>
<th>DRUG</th>
<th>DRUG–DRUG INTERACTIONS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Delvaridine</td>
<td>Rifampicin, Rifabutin, DDI, Antacids, Antiepileptics, PIs</td>
</tr>
<tr>
<td>Didanosine (DDI)</td>
<td>Fluroquinolones, dapsone, isoniazid, itraconazole, ketoconazole, tetracyclines</td>
</tr>
<tr>
<td>Indinavir</td>
<td>Rifabutin, Rifampicin cisapride, terfenadine, astemizole, warfarin</td>
</tr>
<tr>
<td>Nevirapine</td>
<td>PIs, Rifabutin, Rifampicin, Indinavir</td>
</tr>
<tr>
<td>Ritonavir</td>
<td>Alprazolam, clarithromycin, diazepam, erythromycin, ketoconazole, itraconazole, rifabutin, saquinavir, tricycl, antidepressants, oral contraceptives</td>
</tr>
<tr>
<td>saquinavir</td>
<td>Ketoconazole, rifampicin, rifabutin, phenytoin, carbemazepin</td>
</tr>
<tr>
<td>Zalcitabin</td>
<td>Warfarin</td>
</tr>
</tbody>
</table>

This list is not exhaustive.

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