# NATIONAL HIV/AIDS SECRETARIAT
## HEALTH SECTOR RESPONSE GROUP



# National Antiretroviral Treatment Guidelines

## Ministry of Health and Sanitation

## Sierra Leone

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# Abbreviations

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

| | |
|---|---|
| **VL** | Viral Load |
| **WHO** | World Health organization |
| **ZDV** | Zidovudine, also known as AZT |

# Introduction

The Global HIV/AIDS epidemic killed more than 3 million people in 2003, and an estimated 5 million acquired the human immunodeficiency virus (HIV) bringing the number to 40 million people living with virus around the world.

In Sub-Saharan Africa, HIV prevalence remained generally at high levels for the past decades. This is due to the fact that high levels of the HIV infections are persisting and are matched with high levels of AIDS mortality. HIV prevalence is maintaining high levels in the general populations at an alarming rate.

The epidemic in Sub-Saharan Africa remains rampant. Its continued escalation will depend on the vigour, scale and effectiveness of prevention, treatment and a care programmes. Urgent actions are required to make a dramatic trend, and anything else will spell failure.

A growing number of countries (many of them in Africa) have begun extending antiretroviral and other AIDS related medications to their citizens. Antiretroviral treatment coverage in Sub-Saharan Africa overall remains dismal despite the efforts of WHO and UNAIDS and partners to bring antiretroviral to 3 million people by 2005.

Since the first case of HIV/AIIDS was identified in 1987, there is an increase in the number of persons living with HIV/AIDS (PLWHAs). A national seroprevalence survey was conducted by CDC in April 2002. After completing initial testing at the Connaught Laboratory in Freetown, a preliminary HIV sero-prevalence of 4.9% was reported for persons aged 12-49 years in surveyed areas of Sierra Leone. Retesting at the CDC laboratory in Atlanta, USA, including Western Blot tests, resulted in a weighted HIV seroprevalence of 0.9% for persons aged 12-49 years surveyed, covering 79% of the population. HIV seroprevalence was higher in Freetown 2.1% than outside Freetown 0.7%.

The advent of potent antiretroviral therapy in 1996 led to revolution in the care of patients with HIV/AIDS. Although ARVs are not a cure for HIV infection, antiretroviral drugs can dramatically reduce HIV related morbidity and mortality and improve quality of life. Moreover, HIV/AIDS is now perceived as a manageable chronic illness.

Majority of people living with HIV/AIDS in developing countries have no access to these drugs. UNAIDS and WHO are committed to increasing access to the drugs which have been shown to be effective in preventing and treating HIV/AIDS.

It is estimated that between 5 and 6 million adults in developing countries are currently in need of ART. Despite the progress made by ECOWAS countries, only some 10,000 people in the region are currently accessing ART in contrast to 1.6 million people that are in need.

The Government of Sierra Leone is accepting the challenge in making ARVs accessible to that in need. To meet this challenge, the development of the National ARV treatment Guidelines is part of the Government's commitment to the treatment of persons living with HIV/AIDS. These guidelines serve to assist health workers in the clinical management of PLWHAs.

These guidelines attempt to summarize the current state of knowledge of HIV disease management and treatment in a resource poor setting and will therefore require regular change and update in the coming years. They are not intended to be an exhaustive document, but rather a useful and practical guide for practitioners.

# 1. Antiretroviral Therapy in Adults

## 1.1 Principles of Antiretroviral Therapy

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

## 1.2 Goals of Antiretroviral Therapy

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

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

The secondary goal is to decrease the incidence through:

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

## 1.3 Strategy

The overall strategy is to:

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

## 1.4 Classes of Antiretrovirals and functions

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

There are currently 16 approved Antiretroviral Drugs for the treatment of HIV that includes **six** Nucleoside Reverse Transcriptase Inhibitors, **one** Nucleotide Reverse Transcriptase Inhibitors, **three** Non-Nucleoside Reverse Transcriptase Inhibitors and **six** Protease Inhibitors.

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

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

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

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

**List of Antiretroviral Drugs and their doses**

***Table 1: Nucleoside reverse transcriptase inhibitors (NRTI).***

| Generic Name | Trade Name | Presentation | Recommended Doses | Diet Restrictions | Side Effects |
|---|---|---|---|---|---|
| Zidovudine | Retrovir® | Capsules 100, 250, 300mg<br>Oral solution 10mg/ml<br>IV formulation : 10mg/ml | 250-300mg BID | None | Myelosuppression : anaemia and/or Neutropenia, Myalgia, Myopathy, Headache, Gastrointestinal Intolerance |
| Didanosine | Videx® | Tablets : 25, 50, 100, 150, 200mg<br>Enteric coated capsules : 125, 200, 250, 400mg | <60kg : 250mg QD or 125 mg BID<br>>60kg : 400 mg QD or<br>200 mg BID | Yes (fasting) | Pancreatitis, Hyperuricemia, Peripheral Neuropathy, Diarrhoea, Nausea |
| Stavudine | Zerit® | Capsules 15, 20, 30, 40mg<br>Oral solution : 1mg/ml | < 60 kg : 30 mg BID<br>≥ 60 kg : 40 mg BID | None | Peripheral Neuropathy, Pancreatitis |
| Lamivudine | Epivir®, 3 TC® | Capsules 150mg<br>Oral solution : 10mg/ml | 150 mg BID | None | Peripheral Neuropathy |
| Abacavir | Ziagen® | Capsules 300mg<br>Oral solution : 20mg/ml | 300 mg BID | None | Hypersensitivity Reaction (2-3%) |

***Table 2: Non-nucleoside reverse transcriptase inhibitors NNRT.***

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

***Table 3: Protease inhibitors (PIs).***

| Generic Name | Trade Name | Presentation | Recommended Doses | Diet Restrictions | Side Effects |
|---|---|---|---|---|---|
| Indinavir | Crixivan® | Capsules 200-400mg | 800 mg TID | Fasting if not boosted | Nephrolithiasis<br>Gastrointestinal intolerance<br>Hyperbilirubinemia |
| Ritonavir | Norvir® | Capsules 100 mg<br>Oral solution 600mg/7.5ml | 600 mg BID | With food | Gastrointestinal intolerance<br>Oral Paresthesia<br>Increase of Transaminases |
| Saquinavir | Invirase®<br>Fortovase® (SGC) | Hard gel capsules 200 mg **or** Soft gel capsules 200 g | (HGC) 600 mg TID **or** (SGC) 1200 mg TID | With food | Gastrointestinal intolerance (Diarrhoea)<br>Headaches |
| Nelfinavir | Viracept® | Tablets 250mg<br>Oral powder 50mg/1g | 750 mg TID or 1250mg BID | With food | Diarrhoea |
| Amprenavir | Agenerase® | Capsules 50mg/150mg<br>Oral solution 15mg/ml | 1200 mg BID | No restrictions | Gastrointestinal intolerance<br>Rash |
| Lopinavir/ Ritonavir | Kaletra® | Capsules 133.3 + 33.3mg<br>Oral solution 80mg+20mg/ml | 400/100mg BID | With food | Digestive intolerance<br>Rash |

***Table 4: Nucleotide analogues (Tenofovir).***

| **Generic Name** | Tenofovir |
|---|---|
| **Trade Name** | Viread™ |
| **Presentation** | Tablets 300mg |
| **Recommended Doses** | 300mg QD |
| **Oral Bioavailability** | 39% |
| **Plasma Half Life** | 16 hours |
| **Cellular Half Life** | 10-50 hours |
| **Diet Restrictions** | With food |
| **Metabolisation** | Hepatic |
| **Excretion** | Renal |
| **Side Effects** | GI disturbances |

## 1.5 When to start Antiretroviral Therapy

### 1.5.1 Conditions necessary to introduce Antiretroviral Drugs (ARVs)

- Access to functioning and affordable health services and support networks into which ARV treatments can be integrated so that the treatments are provided effectively.
- Information and training on safe and effective use of ARVs for health professionals in a position to prescribe ARVs.
- Capacity to diagnose HIV infection and to diagnose and treat concomitant illnesses.
- Assurance of an adequate supply of quality drugs.
- Sufficient resources should be identified to pay for treatment on a long-term basis; patients must be aware that treatment is "for life".
- Functioning laboratory services for monitoring including haematological and bio-chemical tests to detect toxicities, must be available.
- Access to voluntary HIV counselling and testing (VCCT) and follow up counselling services should be assured, including counselling PLWHAs on the necessity of adherence to treatment.

### 1.5.2 Criteria for selection of patients for ART

**Clinic attendance regularity**

Attended HIV Clinic for the last 3 months and on time for the last 4 visits

**Clinic and Biological criteria**

***If CD4 count available:***

- WHO Stage IV irrespective of CD4 count
- WHO Stage I,II,, or III disease with CD4 cell count <200cells/mm3

***If CD4 count is unavailable***

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

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

### 1.5.3 Baseline Clinical Assessment

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

- A medical history
- Physical examination
- Laboratory investigations
- Counselling

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

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

**Laboratory investigations:** In order to be certain of the presence or absence of any underlying co-infection it is essential that maximum laboratory assessment be done, particularly before the initiation of therapy. This is important to ensure that the desired therapeutic response is obtained and adherence is maximized**.**

***Absolute minimum Tests***

Absolute minimum tests are a prerequisite for the introduction of ART. The absolute minimum of laboratory tests required before initiating ART are **an HIV antibody** and a determination of the **haemoglobin level** or that of **haematocrit.**

The rationale is that proof of HIV infection is needed before starting ARV therapy in the first instance, and screening for anaemia is essential before starting Zidovudine-containing regimens**.**

***Basic Test***

Basic recommended tests are commonly used in the clinical setting and are needed to provide effective monitoring of most ARV regimens.

**WBC, Total Lymphocyte Count, ALT, creatinine and blood sugar.**

***Desirable tests***

Desirable tests include those for bilirubin, amylase and serum lipids and CD4 cell testing. These tests, while not absolutely essential, are felt to provide significant information that would be beneficial in the monitoring of ARV**.**

**CD4, Amylase, Bilirubin and Lipids.**

***Optional test***

**Viral Load Testing** is currently considered optional because of resource constraints.

**Counselling for ARV Therapy**

The psychosocial aspects associated with deciding whether to start and then continue on ARV treatment are as important as the medical aspects. Counselling for ARVs is often time consuming and physicians may choose to work with a trained counsellor with specialised skills. If appropriate and informed decisions are to be made, and treatment is to be provided safely and effectively, counselling services must be available to people living with HIV/AIDS (PLHWAs). Those who make the decision to start ARVs will need information, support and encouragement on a regular and long term basis in order to maintain adherence to the regimen.

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

## 1.6 Recommended ARV Regimens

### 1.6.1 First line antiretroviral therapy

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

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

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

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

| Regimen | Comments |
|---|---|
| ZDV+3TC+ EFZ or NVP<br><br>**OR**<br><br>d4T + 3TC+ EFZ or NVP | Give NVP in pregnant women or women for whom effective contraception cannot be assured.<br><br>Give EFZ for patients requiring simultaneous ARV treatment and TB therapy containing Rifampicin. |

- Zidovudine and stavudine (AZT/d4T) should never be used together because of proven antagonism.
- Didanosine and stavudine (ddI/d4T) should be avoided in pregnancy due to risk of lactic acidosis and hepatotoxicity. It is contra-indicated in patients with peripheral neuropathy.
- Efavirenz (EFZ) cannot be used in pregnant women. Women of child bearing age should only receive EFZ in combination with effective contraceptive methods.

### 1.6.2 Second Line Antiretroviral Regimen

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

**For example use**:

- Lamivudine + Stavudine + Indinavir (3TC/d4T/IDV)
- Stavudine + Didanosine+ Kaletra (d4T/ddI+LPV/r)
- Zidovudine + Didanosine + Kaletra (ZDV/ddI+LPV/r)

## 1.7 Follow-Ups and Monitoring of HIV/AIDS Adult Patients during ART

The objective of follow-up is to:

- Monitor ARV adverse effects
- Ensure patient good adherence
- Management of opportunistic infections
- Management of immune reconstitution syndrome
- Diagnosis and management of treatment failure

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

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

### 1.7.1 MONITORING ADULT PATIENTS

#### 1. Patients not receiving Antiretroviral Treatment

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

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

#### 2. Patients on Treatment

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

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

Monitoring will be done using :

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

***Table 6: Recommended schedule for monitoring adult patients***

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

### 1.7.2 Follow-up at Hospital Level

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

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

**Monitoring patient's responses to ART**

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

### 1.7.3 Follow up in a Private Clinic Setting

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

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

### 1.7.4 Follow up at community level

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

## 1.8 ART data collection and management

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

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

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

## 1.9 When to change Antiretroviral Therapy

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

### 1.9.1 Toxicity

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

For example, d4T can be substituted for ZDV for ZDV related symptoms or anemia and NVP can be substituted for EFZ when EFZ related central nervous systems are unremitting. For other toxicities, for which a specific agent cannot be identified as causal, and/ or low grade but intolerable side effects which frequently compromise adherence, a complete regimen switch to the second line drugs is recommended. If an interruption in therapy is indicated to permit resolution of toxicity, the entire regimen should be temporarily interrupted in order to prevent the emergence of drug resistance.

***Table 7: Major potential toxicities of first line ARV regimens and Recommended Drug Substitution***

| Regimen | Toxicity | Drug Substitution |
|---|---|---|
| **d4T/3TC/NVP** | • d4T-related neuropathy or pancreatitis | • Switch d4T to ZDV |
| | • d4T-related lipoatrophy | • Switch d4T to TDF or ABC |
| | • NVP-related severe hepatotoxicity | • Switch NVP to EFZ (except in pregnancy) |
| | • NVP-related severe rash (but not life-threatening) | • Switch NVP to EFZ |
| | • NVP-related life-threatening rash (Stevens-Johnson Syndrome) | • Switch NVP to PI |
| **ZDV/3TC/NVP** | • ZDV-related persistent GI intolerance or severe haematological toxicity | • Switch ZDV to d4T |
| | • NVP-related severe hepatotoxicity | • Switch NVP to EFZ (except in pregnancy; in this situation switch to NFV, LPV/r or ABC) |
| | • NVP-related severe rash (but not life-threatening) | • Switch NVP to EFZ |
| | • NVP-related life-threatening rash (Stevens-Johnson syndrome) | • Switch NVP to PI |
| **d4T/3TC/EFZ** | • d4T-related neuropathy or pancreatitis | • Switch d4T to ZDV |
| | • d4T-related lipoatrophy | • Switch d4T to TDF or ABC |
| | • EFZ-related persistent CNS toxicity | • Switch EFZ to NVP |
| **ZDV/3TC/EFZ** | • ZDV-related persistent GI intolerance or severe haematological toxicity | • Switch ZDV to d4T |
| | • EFZ-related persistent CNS toxicity | • Switch EFZ to NVP |

### 1.9.2 Treatment Failure

The extent to which the goals of therapy are not accomplished indicates the degree of treatment failure. There may therefore be patients whose quality of life is better but whose viral load is not maximally suppressed. For purposes of therapy treatment failure will be deemed to be present if:

- Viral load rebounds by log 0.5
- Viral load becomes detectable again after being undetectable
- CD4+ Cell Count falls again

There may be fluctuations from day to day in laboratory findings. The viral load and CD4+ Cell Count may rise temporarily after inter current infection or a vaccination.

Therefore, changes in treatment should not be made hastily on single reading which might be within the range of biological or laboratory validation.

# 2. Consideration for Specific Categories of Patients

## 2.1 Infants and Children

The pathogenesis of HIV and the underlying principles of ART are similar in adults and children. However, there are specific physiologic, clinical, practical and social issues to consider when treating HIV-infected children with ART.

The laboratory diagnosis of HIV infection in infants aged less than 18 months is difficult because of the presence of maternal antibodies. Virological tests are required in order to make definitive diagnosis of HIV infection in this age group.

### 2.1.1 When to start Therapy in Children

Children who contract HIV infection from their mothers usually become symptomatic in the first 2 years of life. Treatment in these children should be started as early as possible since morbidity and mortality is highest in young children. HIV disease should be thought of in a child who gets recurrent or persistent bacterial infections or oral thrush or fails to thrive despite adequate nutritional support**.**

A classification of HIV infection in children is done on the basis of the following signs and symptoms:

***Table 8: WHO staging system for HIV infection and disease in children***

| |
|---|
| **Clinical Stage I**<br>- Asymptomatic<br>- Generalised lymphoadenopathy |
| **Clinical Stage II**<br>- Unexplained chronic diarrhea > 30 days<br>- Severe persistent or recurrent candidiasis outside the neonatal period<br>- Weight loss or failure to thrive<br>- Persistent fever > 30 days duration in the absence of unknown etiology<br>- Recurrent severe bacterial infections other than septicaemia or meningitis(e.g osteomyelitis, bacterial pneumonia, abscesses) |
| **Clinical Stage III**<br>- AIDS-defining opportunistic infections<br>- Severe failure to thrive(wasting) in the absence of known etiology<br>- Progressive encephalopathy<br>- Malignancy<br>- Recurrent septicaemia or meningitis |

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

***Table 9: Recommendation for starting ART in children***

| Age | HIV diagnostic testing | Treatment recommendation |
|---|---|---|
| < 18 months | • Clinical assessment<br>• +ve HIV test or history in mother<br>• PCR if available | • WHO Paediatric Stage III (AIDS) irrespective of CD4 cell percentage<br>• Paediatric Stage II disease<br>• WHO Paediatric Stage I disease(asymptomatic) or Stage II disease with CD4 cell percentage<20% |
| >18 months | • Clinical assessment<br>• +HIV test | • WHO Paediatric Stage III(AIDS) irrespective of CD4 cell percentage<br>• Paediatric Stage II disease with no CD4 count<br>• WHO Paediatric Stage I disease(asymptomatic) or Stage II disease with CD4 cell percentage<15% |

### 2.1.2 Recommended first line ARV regimens for Infants and Children

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

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

***Table 10: Recommended first line Antiretroviral Regimens for children***

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

### 2.1.3 Recommended second line ARV therapy for infants and children

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

*Table 11: Recommended second line regimen in children*

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

### 2.1.4 TB treatment and ART in children

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

### 2.1.5 Monitoring of Antiretroviral Therapy in Children

#### 2.1.5.1 Viral Load

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

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

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

#### 2.1.5.2 CD4+ Lymphocytes and Percentages

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

#### 2.1.5.3 Height and Weight

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

### 2.1.6 Reasons for changing ARV therapy in infants and children

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

In children, important clinical signs of drug failure include:

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

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

## 2.2 Treatment of HIV Pregnant Women

The timing of initiation of ARV in an ARV-naive pregnant woman is directed by an analysis of the risk of adverse effects on the foetus versus the risk to both mother and child of delaying therapy. Pay extra attention to adherence during and after pregnancy as adherence to ARV can be particularly difficult during this time. Counsel mothers on ARV regarding their infant feeding options as per the National Guidelines on PMTCT.

Women taking ARV who decide to breastfeed should continue taking ARV. The potential impact of antiretroviral therapy on the fœtus and infant is currently poorly understood. It is generally recommended to avoid antiretroviral treatment during the first trimester, to minimise the impact of these drugs on organogenesis. Some agents or combinations must be avoided during pregnancy due to the risk of teratogenicity or toxicity (efavirenz causes teratogenicity in animals, stavudine +didanosine causes toxicity in neonates and mothers and indinavir causes hyperbilirubinemia). The potential risk of mitochondrial toxicity to the foetus and infant as a result of exposure to NRTI's during pregnancy has been suggested. Long-term follow-up of babies born to treated mothers is important.

Vertical transmission of HIV occurs mainly during the last part of pregnancy, and particularly during labour and delivery. Breast feeding is associated with a significant risk of transmission.

Caesarean Section has been shown to reduce HIV transmission, and should be advised except rarely recommended for a women with fully suppressed viraemia, in good obstetrical conditions. The risk of transmission is directly related to maternal clinical stage (plasma viral load). It is therefore recommended to optimally suppress HIV during the last 8-12 weeks of pregnancy. Nevirapine as a single dose at delivery is recommended in the national PMTCT guidelines.

Guidelines for antiretroviral therapy and for initiation of treatment in HIV pregnant women are the same as those proposed for non pregnant women: the woman's clinical, immunologic and virologic status are of primary importance in guiding treatment decisions.

There is currently no data available to clarify whether women who take single dose NVP without other ARV are at increased risk for failure of NNRTI based regimens due to NVP resistance.

### 2.2.1 Treatment Categories of HIV Pregnant Women

***Women becoming pregnant while already treated with ART:***

Current treatment should be maintained whenever feasible, with the exception of some agents and combinations such as efaverenz. In case of unacceptable drug intolerance, treatment may be temporarily withheld during the first trimester.

***Women becoming pregnant while treatment naive and who fulfil the criteria for initiation of ART***

Initiation of therapy should be delayed until 12 weeks of gestation (end of organogenesis) if the clinical and immunological status allows for this delay in treatment.

***Women becoming pregnant while treatment naive, who do not fulfil the criteria for initiation of HAART***

Treatment should be commenced 12 weeks before delivery. Zidovudine reduces the risk of vertical transmission and can be used as combination therapy.

***Women whose follow up starts very lately during pregnancy***

This is a difficult emergency situation which occurs most often in cases of poor psychosocial conditions.

It is recommended that ART be started immediately (even if delivery is imminent). Nevirapine should be included in the regimen, zidovudine should be administered intravenously during labour and delivery, and Caesarean section is strongly recommended.
Recommended ARV drugs for pregnant women are AZT, 3TC, NVP, NFV or SQV/r. However; AZT and 3TC should be included in first line therapy whenever possible. NVP or NFV are the most widely used drugs combined with AZT+3TC. Do not use efavirenz because of the risk of teratogenicity. SQV/r or IDV/r is alternative drugs to combine with AZT+3TC.

### 2.2.2 Risks associated with certain ARVs in a pregnant woman

- ZDV should be avoided close to delivery due to risk of neonatal hyperbilirubinemia.
- Do not use d4T+ddI as a combination because it increases the risk further.
- PIs may increase the risk of gestational diabetes.
- The risk of lactic acidosis/hepatic steatosis is increased during pregnancy.
- It is acceptable to use NNRTIs if a woman has previously received single dose NVP without other ARV for PMTCT.
- Women who are not on ARV at the start of pregnancy should start ARV whenever it is indicated. Some women may want to delay ARV until the end of the 1st trimester to reduce any possible risk of teratogenicity.
- Women on ARV who become pregnant should continue ARV therapy. The ARV regimen should be optimized to ensure the lowest possible maternal HIV viral load at the time of delivery as this is the most important predictor of MTCT. EFV and the combination of ddI+d4T should be changed to other agents.
- Continue ARV during labour.

***Necessary conditions for an HIV infected women wishing to become pregnant***

The woman desirous of becoming pregnant should have high CD4 cell count, no other infection and no use of drugs which are prohibited during pregnancy.

## 2.3 People with Tuberculosis Disease and HIV Co-Infection

Tuberculosis is an entry point for a significant proportion of patients eligible for ART. ART is recommended for all patients with TB who have CD4 cell counts below 200 cells/mm3, and should be considered for patients with CD4 counts below 350 cells/mm3

For those with CD4 40-200/mm3, they should start ART after the intensive TB treatment phase which usually lasts for 2 months. In cases where a person needs TB and HIV treatment concurrently, first line treatment options include ZDV/3TC plus EFZ.

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

***Table 12: Antiretroviral Therapy for individuals with Tuberculosis Co-infection***

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

## 2.4 Immune Reconstitution Syndrome

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

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

Patients co-infected with hepatitis B or C can be safely treated with several ARV regimens. Because of the possibility of additive hepatoxicity, regimens with ddI/d4T and/or NVP should be avoided in patients to have active hepatitis. 3TC and TDF are both active against hepatitis B and may even have a protective effect against new infections.

## 2.6 Opportunistic Infections and Tuberculosis prophylaxis

ART is the most effective approach to reducing the incidence of Opportunistic Infections in HIV-infected patients but it should not replace efforts to provide antimicrobial prophylaxis.

Cotrimoxazole reduces the risk for bacterial infections, pneumocystitis carinii pneumonia and toxoplasmosis and is recommended for all patients who meet the indications for ART. Where facilities are available for CD4 cell count, patients who have maintained a count above 200/mm3 for over 6 months their prophylaxis against PCT, toxoplasmosis and bacterial infections (>400/mm3 for TB) can be safely withdrawn.

# 3. Post Exposure Prophylaxis

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

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

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

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

## 3.1 Prevention of occupational exposure in health facilities

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

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

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

## 3.2 Immediate steps to be taken after an occupational exposure

The immediate steps to be taken after an occupational exposure include:

- Use soap and water to wash any wound or skin site that came into contact with infected blood or fluid
- Flush exposed mucous membranes with water
- Irrigate an open wound with sterile saline or disinfectant solution
- Eyes should be irrigated with clear water, saline or sterile eye irrigants

- Report to the concerned authority
- Counselling- Ascertain the HIV status of the patient and the injured health worker after appropriate counselling
- Use antiretrovirals immediately after exposure. These should be started within 1 hour if possible and at the latest within 72 hours of the exposure.

## 3.3 Recommended regimens for Post-Exposure Prophylaxis

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

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

or

Stavudine30/40 mg bd + Lamivudine 150 mg bd

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

or

Efavirenz 600 mg od at bedtime

or

Nelfinavir 750 mg tds

# 4. Adherence to Antiretroviral Therapy

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

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

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

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

## 4.1 Failure of Regimen to Poor Adherence

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

## 4.2 Strategies to Improve Adherence

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

Annex 1

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

**Clinical Stage 1**

1. Asymptomatic
2. Generalized lymphadenopathy

*Performance scale 1: asymptomatic, normal activity*

**Clinical Stage 11**

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

*And/or performance scale 2: symptomatic, normal activity*

**Clinical Stage 111**

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

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

**Clinical Stage 1V**

1. HIV wasting syndrome – weight loss of more than 10%, and either unexplained chronic diarrhoea for more than 1 month, or chronic weakness or unexplained prolonged fever for more than 1 month
2. Pneumocystis carinii pneumonia
3. Toxoplasmosis of the brain
4. Cryptosporidiosis with diarrhoea for more than 1 month
5. Extrapulmonary cryptococcosis
6. Cytomegalovirus (CMV) disease of an organ other than liver, spleen or lymph nodes
7. Herpes simplex virus (HSV) infection, mucocutaneous for more than 1 month, or visceral of any duration
8. Progressive multifocal leukoencephalopathy (PML)
9. Any disseminated endemic mycosis such as histoplasmosis, coccidioidomycosis

10. Candidiasis of the oesophagus, trachea, bronchi or lungs
11. Atypical mycobacteriosis, disseminated
12. Non-typhoid salmonella septicaemia
13. Extrapulmonary tuberculosis
14. Lymphoma
15. Kaposi's sarcoma
16. HIV encephalopathy – disabling cognitive and/or motor dysfunction interfering with activities of daily living, progressing slowly over weeks or months, in the absence of concurrent illness or condition other than HIV infection that could account for the findings

*And/or Performance Scale 4: Bed-ridden for more than 50% of the day during the last month*

Annex 2

## Fixed – Dose Combinations of ARVs Available on 1 December 2003

| | |
|---|---|
| **Three-drug fixed-dose combinations** | d4T (40 MG)+ 3TC (150 mg) + NVP (200 mg) |
| | d4T (30 mg) + 3TC (150 mg) + NVP ( 200 mg) |
| | ZDV (300 mg) + 3TC (150 mg) + ABC (300 mg) |
| | ZDV (300 mg) + 3TC (150 mg) + NVP (200 mg) |
| **Two-drug fixed-dose combinations** | d4T (30 mg) + 3TC (150 mg) |
| | d4T (40 mg) + 3TC (150 mg) |
| | ZDV (300 mg) + 3TC (150 mg) |

Annex 3

## Antiretroviral Drug Toxicity

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

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

Annex 4

## Recommended Actions for the Maintenance of Antiretroviral Therapy

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