

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



== Draft for comments ==

**NATIONAL GUIDELINES FOR THE
TREATMENT OF HIV INFECTED ADULTS WITH
ANTIRETROVIRAL THERAPY**

Ministry of Health and Sanitation

Sierra Leone

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I. Abbreviations used

3TC	lamivudine
ART	antiretroviral treatment
ARV	antiretroviral drug
AZT	zidovudine
CBC	complete blood count = total & differential white blood cell count, red blood cell count, platelets + haemoglobin
CD4	CD4 cell count
d4T	stavudine
ddI	didanosine
EFV	efavirenz
Hb	haemoglobin
IDV/r	indinavir boosted with ritonavir
NNRTI	Non-nucleoside reverse transcriptase inhibitor
NRTI	Nucleoside reverse transcriptase inhibitor
NVP	nevirapine
OI	opportunistic infection
PI	protease inhibitor
RTV	ritonavir
TLC	total lymphocyte count
TMP-SMX	trimetoprim-sulfamethoxazole (co-trimoxazole)

Some terminology and definitions used

standard first line ART regimen	(2NRTI + 1NNRTI) - AZT + 3TC + NVP or/EFV
alternative first line ART regimen	when side-effects with standard first line treatment, and AZT is replaced by D4T, or nevirapine by efavirenz or boosted PI
Second line ART regimen	In cases of treatment failure (2NRTI + PI)
ARV experienced patient	Patient who took ARVs for at > 2 weeks,
ARV naïve patient	Patient who never took ARVs, or took ARV for < 2 weeks, or pregnant woman receive NVP single dose of NVP in PMTCT.

Goals of Antiretroviral therapy

At the patient level, there are four clinical goals of antiretroviral therapy:

- Reduction in viral load to the lowest possible level for as long as possible.
- Reconstruction of immune competence since depressed cell- mediated immunity accounts for most of the morbidity and mortality.
- Improved quality of Life.
- Clinical benefit.

3:1. 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.

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. Other considerations include choice of an ARV regimen which can be tolerated with low pill burden by using combination formulation that are potent and have less adverse side effects.

In order to reliably suppress HIV viral replication a combination of at least three potent ARV drugs known as Highly Active Antiretroviral Therapy (HAART) are needed to be prescribed. This regimen will reduce HIV viral load which will in turn lead to a gradual restoration of immune function and the risk of HIV related illnesses decreases. However it must be stated that the restoration of immune function is not perfect and some risk of opportunistic infection may persist at least for some time. The only remedy to such risk is the use of OI prophylaxis with concomitant ongoing monitoring while the patient is taking ARV drugs.

Conditions necessary to introduce antiretroviral drugs(ARVs)

- Access to functioning and affordable health services and support networks into which ARV treatments.
- Information and training 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 (VCT) and follow up counselling services should be assured, including counselling PLHA on the necessity of adherence.

1. Classes of ARV drugs:

ARV drugs are divided into 4 main classes.

- 1 Nucleoside Reverse Transcriptase Inhibitors(NRTI)
- 2 Non-nucleoside Reverse Transcriptase Inhibitors(NNRTIs)
- 3 Protease Inhibitors
- 4 Nucleotide analogues

At present only six ARV drugs have been registered by the Sierra Leone Pharmacy board. They include 3 NRTI (Zidovudine, Lamivudine and Stavudine), 1 NNRTI (Nevirapine), and 2 Protease inhibitors (Idinavir and Ritonavir). Meanwhile the ARV drugs included in these guidelines are those that have sufficient potency and ease of use to be acceptable for use in Sierra Leone

1:2. ARV drugs

Table1: Antiretroviral Drugs⁵

Table: Nucleoside reverse transcriptase inhibitors (NRTI).

	Trade name	Presentation	Recommended doses	Plasma half life	Diet restrictions	Side effects
Zidovudine	Retrovir®	Capsules 100, 250, 300mg Oral solution 10mg/ml IV formulation : 10mg/ml	250-300mg BID	1.1h	None	Myelosuppression : anaemia and/or neutropenia, myalgia, myopathy, headache, gastrointestinal intolerance
Didanosine	Videx®	Tablets : 25, 50, 100, 150, 200mg Enteric coated capsules : 125, 200, 250, 400mg	<60kg : 250mg QD or 125 mg BID >60kg : 400 mg QD or 200 mg BID	1.6h	Yes (fasting)	pancreatitis, hyperuricemia, peripheral neuropathy, diarrhoea, nausea
Stavudine	Zerit®	Capsules 15, 20, 30, 40mg Oral solution : 1mg/ml	< 60 kg : 30 mg BID ≥ 60 kg : 40 mg BID	1h	None	peripheral neuropathy, pancreatitis
Lamivudine	Epivir®, 3 TC®	Capsules 150mg Oral solution : 10mg/ml	150 mg BID	3-6h	None	Peripheral neuropathy
Abacavir	Ziagen®	Capsules 300mg Oral solution : 20mg/ml	300 mg BID	1.5h	None	Hypersensitivity reaction (2-3%)

⁵ DDI suspension, D4T suspension and RTV, need to be stored in the fridge. However, WHO recommends a maximum of 30 days at room temp, however; maximum of 14 days will be a fairly pragmatic approach in a Sierra Leone.)

Note: ritonavir SYRUP: not in fridge!

Table 2 : Non-nucleoside reverse transcriptase inhibitors NNRT

ARV	Trade name	Presentation	Recommended doses	Plasma half life	Diet restrictions	Side effects
Nevirapine	Viramune®	Tablets 200mg Oral suspension 50mg/ml	200 mg QD for 14 days then 200 mg BID or 400 mg QD	25-30h	None	Rash, including rare cases of Stevens-Johnson, increase of transaminases and acute hepatitis
Efavirenz	Sustiva® Stocrin®	Capsules 50, 100, 200mg	600 mg QD	40-55h	None	Dizziness, insomnia, somnolence, abnormal dreams, psychosis (1-2%), acute depression, rash

Table 3 : Protease inhibitors (PIs).

	Trade name	Presentation	Recommended doses	Plasma half life	Diet restrictions	Side effects
Indinavir	Crixivan®	Capsules 200-400mg	800 mg TID	1.5-2h	Fasting if not boosted	Nephrolithiasis Gastrointestinal intolerance Hyperbilirubinaemia
Ritonavir	Norvir®	Capsules 100 mg Oral solution 600mg/7.5ml	600 mg BID	3-5h	With food	Gastrointestinal intolerance Oral paresthesia Increase of transaminases
Saquinavir	Invirase® Fortovase® (SGC)	Hard gel capsules 200 mg or Soft gel capsules 200 mg	(HGC) 600 mg TID or (SGC) 1200 mg TID	1-2h	With food	Gastrointestinal intolerance (diarrhoea) Headaches
Nelfinavir	Viracept®	Tablets 250mg Oral powder 50mg/1g	750 mg TID or 1250mg BID	3.5-5h	With food	Diarrhoea
Amprenavir	Agenerase®	Capsules 50mg/150mg Oral	1200 mg BID	9h	No restrictions	Gastrointestinal intolerance Rash

		solution 15mg/ml				
Lopinavir/ Ritonavir	Kaletra®	Capsules 133.3 + 33.3mg Oral solution 80mg+20m g/ml	400/100m g BID	5-6h	With food	Digestive intolerance 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

2. LABORATORY INVESTIGATIONS

In order to be certain of the presences or absences 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 test are a prerequisite for the introduction of ART . The absolute minimum of laboratory test 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 tests.

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 tests.

Viral load testing is currently considered optional because of resource constraints.

3. MANAGEMENT OF PERSON

In Sierra Leone CD4 cell levels will be regarded as the best prognostic markers for progression to AIDS or death. With the treatments currently available, viral eradication is unachievable. Because of the need for life long treatment under our present state of our knowledge, a risk-benefit balance should be established on a case by case basis, between the need to treat to prevent clinical progression and the risks of patient adherence to a long term therapy (side effects, resistance).

3.1 The main issue is “when to start” therapy

Objectives

1. Familiar with criteria for initiating ART
2. Develop skills to recognise treatment success and failure, toxicity, and immune reconstitution
3. Determine baseline and follow-up lab tests, frequency and rationale of testing
4. Interpretation of CD4 cell count result
5. correlate evolution of CD4 cell count with treatment success and failure

When to start treatment

World Health Organisation (WHO) recommends that, for ARV treatment programmes in resource-limited settings, HIV-infected adolescents and adults should start ART when they have:

- WHO stage iv of HIV disease (clinical AIDS), regardless of the CD4 count;
- WHO stages I, II or III of HIV disease, with a CD4 count below 200/mm³;
- WHO stages II or III of HIV disease with TLC below 1200/mm³;

Wherever possible, countries are encouraged to use CD4 cell counts in their ARV treatment programmes and to consider the use of simple low-cost CD4 methodologies that are currently available on order to enable the wider use of such counts in their programmes. CD4 percentage below 15% corresponds to a total CD4 count of less than 200/mm³. However, in cases where CD4 counts cannot be assessed the presence of a total lymphocyte count of 1200/mm³ or below may be used as a substitute indication for treatment in the presence of symptomatic HIV disease (i.e. WHO stages II or III). While the total lymphocyte count correlates relatively poorly with the CD4 count, in combination with clinical staging it is a useful marker of prognosis and survival. An assessment of viral load, e.g. using plasma HIV-1 RNA levels, is not considered an essential preliminary to therapy.

In children, WHO recommends offering ARV combination therapy to HIV-positive infants under the age of 18 months if they have infection that has been virologically proven (using either HIV PCR or immune-complex-dissociated HIV p24 antigen detection or HIV culture) and WHO Paediatric stage III HIV disease (i.e. clinical AIDS) or WHO Paediatric stages I and II disease and a CD4 percentage below 20%. In settings where virological confirmation is not available, ARV combination therapy can be offered to HIV-positive infants who have WHO stage III HIV disease and a CD4 percentage below 20%. For children aged over 18 months who are HIV-antibody positive, WHO recommends ART if they have WHO stage III HIV disease (i.e. clinical AIDS), regardless of the CD4 percentage. For those older children with WHO stage I or II HIV disease. ART is recommended if the CD4 percentage is below 15%.

The first three months of ART are the most important! Major drop in viral load, adherence in the first 3 months is very important. Always ensure a thorough clinical examination on every visit. Discuss lab results with patient.

At each visit ask about symptoms, adherence, HIV and non-HIV related problems, quality of life.
Physical examination, body weight

Clinical signs and symptoms remain the main criteria for starting treatment. In the absence of HIV related conditions, CD4 level is the criteria for commencing therapy. The risk of severe opportunistic infections (OIs) is linked to the level of CD4 cell counts below 200 /ml.

3:2 Considerations for selection of candidate for HAART

Quick checklist include the following considerations: CD4 count cell count

Good adherence, keep last 3 appoint appointment, takes Cotri / fluconazole prophylaxis correctly and on time? Comes to clinic if he/she has problem with health or medication without appointment? Can he/she easily describe or identify medications? Has good understanding about HIV/AIDS (OI, treatment, OI ARV side effects)? No active OI, baseline lab and other necessary investigations and patient to come with treatment assistant.

Clinic attendance regularity

Attended HIV clinic for at least 3 months and on time for the last 4 visits.

Clinical & biological criteria

Symptomatic (WHO stage III & IV), or CD4 <200mm³ and no active OI.

Adherence and social criteria

HIV disclosure, family and social support, adherence to Cotri / Fluco prophylaxis and TB treatment
Counselling, treatment assistant, commitment to lifelong ARV treatment

3.3 Starting ARV therapy

Objective:

- Management of opportunistic infections
- Address important social issues regarding adherence.
- Patient's commitment to life long therapy
- Management of ARV medicines side effects.
- Provide Security Stock (In order to avoid the client running out of medicine if he cannot come to his next appointment on time, one week security stock should be given to clients).

How is antiretroviral therapy initiated?

It is recommended to initiate antiretroviral therapy in naïve patients (i.e. patients who have not yet been treated with antiretrovirals) using a combination of two NRTI with either one PI or NNRTI. For example, zidovudine + lamivudine + indinavir or stavudine + lamivudine + nevirapine or efavirenz.

An alternative initial regimen consists of 2 PIs with 2 NRTIs. The simultaneous initiation of all the drugs is recommended and sequential addition should be avoided.

While choosing the 2 NRTI component of triple drug therapy, the following two-drug combinations should not be used, as they are either antagonistic, or have overlapping toxicities.

1. Zidovudine + Stavudine
2. Zalcitabine + Stavudine
3. Zalcitabine + Didanosine.

3.4 Which antiretroviral regimen to initiate

A number of specific considerations should be taken into account before deciding between regimens. This include previous medical history (diabetes, chronic liver disease, concomitant medications, HBV/HCV co-infection)

3.4.1 Triple Combination Therapy

The treatment of choice is triple combination therapy including at least one protease inhibitor with potent in vivo activity (indinavir, ritonavir and the new formulation saquinavir). An alternative may be triple combination therapy with ritonavir, saquinavir and an NRTI. Less potent regimens are 2 NRTIs = 1 NNRTI. It is generally recommended that the combination should include a drug that penetrates well into the brain such as Zidovudine or stavudine.

Nucleoside analogue combinations that could be used in triple therapy are:

- zidovudine (ZDV) + didanosine (ddI)
- zidovudine (ZDV) + lamivudine (3TC)
- stavudine (d4T) + lamivudine (3TC)
- stavudine (d4T) + didanosine (ddI)

The above are roughly equivalent. Zidovudine (ZDV) and zalcitabine (ddC) in combination are less active and are regarded as second tier.

Certain combinations are not advisable, because of overlapping toxicity:

- didanosine (ddI) + zalcitabine (ddC)
- stavudine (ddT) + zalcitabine (ddC)

or because of an antagonistic effect due to overlapping intracellular phosphorylation pathways:

- zalcitabine (ddC) + lamivudine (3TC)
- stavudine (d4T) + zidavudine (ZDV)

EXAMPLES OF TRIPLE THERAPY REGIMENS INCLUDING A PROTEASE INHIBITOR

Initial regimen	Alternative combination
ZDV + 3TC + PI	d4T + ddI + PI
D4T + 3TC + PI	ZDV + ddI + PI
ZDV + ddI + PI	d4T + 3TC + PI

ZDV- Zidovudine
 3TC- Lamivudine
 d4T- Tavadine

ddI- Didanosine
 PI-Protease Inhibitor

3.4.2 Double Combination Therapy

Double combination therapy (2 NRTIs) produces clinical and virological improvement, but is inferior to triple therapy. However, many patients in industrialised countries continue to take biotherapy either because they do not want to take more complicated tritherapy regimens or if there are contraindications for the use of protease inhibitors. Double therapy can also be used where protease inhibitors are not available or affordable. Double combination therapy with 2 NRTIs is generally well tolerated and is easier to monitor than triple combination therapy.

When double therapy with two nucleoside analogues is failing, adding only a protease inhibitor without changing the NRTIs since the protease inhibitor then behaves as monotherapy. Double combination of one NTRI and one protease inhibitor has a stronger antiviral effect but also leads to resistance against the protease inhibitor.

3.5 Treatment regimens

First line antiretroviral therapy

If possible use a regimen that reduces dose frequency (twice or once a day) and number of pills (drug combination). Simplify need to take medicines at a certain time in relation to food.

With first line therapy it is of vital importance to preserve further therapeutic options. Treatment should therefore be individualized. Suboptimal therapy that does not achieve viral load suppression could affect the efficacy of subsequent treatments because of the risk of cross resistance, creating a need later for more complicated and heavy regimens which may result in poor adherence, cumulative toxicity, and impaired quality of life.

In ARV naïve patient and if regimen containing NVP is used, the maintenance dose is started only after the successful completion of 2-weeks initial treatment with a lead-in dose of nevirapine as below

Standard first-line regimen

Standard first line regimen consists of dual nucleoside component (NRTI backbone) plus a non-nucleoside drug complement (2NRTI + 1NNRTI)

- AZT +d4T + NVP or/ EFV

Table 6: Leading-in dose of Nevirapine in 1st 14 days³

Morning	Evening
AZT + 3TC + NVP	AZT + 3TC

Table 7: Standard first line ART regime.

Combination	Morning	Evening
AZT (300g) + 3TC (15mg) + NVP (200mg)	1 tab	1 tab

Alternative first line regimen

The common clinical reasons for modifying treatment are anaemia (Hgb < 8gm/dl), drug toxicity, drug interaction, evidence of cross-resistance (especially NNsRTI), and combination of cross resistance, oral contraceptive, Pill burden and pregnancy.

Choice of nevirapine (NVP) or efavirenz (EFV)

- ◇ Chose EFV if PHA is taking TB treatment containing rifampycin.
- ◇ Abnormal liver functions.
- ◇ Chose NVP if pregnant woman.

Choice of AZT or d4T

- ◇ Chose d4T if Hg < Hgb < 8gm/dl,
- ◇ Chose AZT if patient has complaints of peripheral severe neuropathy or lactic acidosis

Second line regimen

2NRTI + PI or (2 NRTI + PI or PI/rt)

This regimen is recommended in circumstances involving treatment failure. The principle is to retain the activity of the drug (regimen) against patient virus. The general principle of 2nd line regimens is that they should contain at least 2 new drugs a new NRTI + 1 (boosted) PI, because resistance develops more slowly to PI (normally 4 mutations are required) and also the HIV strains that are resistant to PI are less virulent than the wild type.

The concentration of ritonavir is so low that it cannot even cause resistance against ritonavir.

3.6 Follow-ups of HIV/AIDS patient during ART:

Objective

1. monitor ARV adverse effects
2. ensure patient good adherence
3. management of opportunistic infections,
4. management of immune reconstitution syndrome
5. diagnosis and management of treatment failure

Table 8: Laboratory follow up of patient on ART

Test	Baseline	W2, M1, M3, M9, M15, M21, M27, M33, ...	M6, M18, M30, ...	M12, M24, M36, ...

³ Sometimes nevirapine needs to be stopped during ART (especially first-line) because of either skin rash or development of TB (immune reconstitution syndrome) while the patient is under HAART. It is recommended to stop NVP immediately, but continue with the others (AZT/3TC or 3TC/d4T) for 3 days. This is because NVP has a longer half-life, so it stays longer in the blood after stopping it.

CD4 cell count	X		X	X
CBC	X		X	X
Hb	X	X	X	X
SGPT	X	X	X	X
amylase	X			
creatinine	X			X
random blood sugar	X			X
total cholesterol	X			X
Hepatitis B surface Ag	X			
Hepatitis C Ab	X			

3.7 Changing therapy in case of adverse event or toxicity

If an adverse event or biological toxicity can reasonably be attributed to one agent, it is recommended to replace this drug by another from the same class, which is not expected to induce the same kind of intolerance or/ toxicity.

Exposure to nucleoside analogues can lead to mitochondrial toxicity. Hyperlactatemia should be excluded if a patient develops a syndrome compatible with lactic acidosis such as nausea, abdominal discomfort, weight loss, malaise, liver enlargement). If hyperlactatemia (venous lactate repeatedly > 5 mmol/L (45mg/dl)) with or without acidosis is confirmed, treatment interruption is mandatory. Treatment may be continued with close monitoring, in case of elevated venous lactate levels between 2 and 5 mmol/L (18-45 mg/dl) in the absence of symptoms

The most prevalent side effect of HAART is nevirapine skin rash lipodystrophy that may be caused by both PI's and NRTI's. In the event of fat accumulation resulting from lipodyftrophy, one may consider switching to a non offending agent.

Physical exercise has been shown to reduce the incidence and severity of lipodystrophy and may have some benefit on insulin resistance. In case of increased blood levels of triglycerides and/or cholesterol, exercise and diet are strongly recommended. Reduction of other cardiovascular risks factors (such as smoking) is essential.

Table 9: Managing potentially serious side effects during the first few months of treatment

Drug & side effect	Agent	Monitoring
Neuropathy	ddi (videx) and d4T (zerit), Isoniazid (INH; Ethambutol, metronidazole dapsone	Mild neuropathy Paresthesia only fingertips or toes, or Mild weakness of feet (=Unable to walk on heels or toes). Severe neuropathy (may be irreversible) Paresthesia more severe than fingertips or toes, or Weakness of the feet, more than unable to walk on heels or toes
Hypersentivity rash		Occurs mostly in the first 12 weeks of treatment Mild rash Macules, papules, dry desquamation Severe rash Vesicles, ulcers, moist desquamation, mucous membrane involvement

Hepato-toxicity		At any time: SGPT> 200
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Table 10: Metabolic side effects occurring later during HAART treatment³

Side effect	Probability	Agent responsible	Action to be taken
Mitochondrial toxicity (polyneuropathy, myopathy, cardiomyopathy, hepatic steatosis, lactic acidosis, and pancreatitis)	Rare	Any NRTI, but often associated with d4T	Lactic levels monthly: >2mmol/L = mild Levels > 5 mmol/L. Stop all NRTI and do not re-challenge with this group of class of drugs
Lipodystrophy: Peripheral lipoatrophy together with trunk fat accumulation	Minor degrees are quite common after prolonged treatment with. Prevalence ranges between 1 – 33%	Usually associated with PI containing regimens as well as d4T or any triple combination treatment	Fat distribution (disfiguring) is a “body image” problem. The decision to continue or stop treatment should involve the patient. Perhaps changing the regimen may offer some help
Diabetes mellitus	Rare	Protease inhibitors (PI)	Treat the diabetes as in any other diabetic patient.

3.8 Changing therapy for failure

Reasons for failure are multiple and include problems of adherence, drug-drug interactions, pharmacokinetic issues and the occurrence of resistance. These factors can sequentially accumulate. In case of persistent viral replication under therapy, accumulation of key resistance mutations will increase the level of resistance as well as the risk of cross resistance which is broad within each class of drugs particularly within the NNRTI class.

Potential strategies to overcome resistance include:

Combination of drugs with expected preserved activity, improvement of pharmacokinetics to optimize exposure to drugs and incorporation of previously unused drug classes in a new regimen. The probability of treatment success decreases as the number of key resistance mutations increases.

3.9 Management of failure on first line antiretroviral therapy.

When failure of therapy is suspected, the patient’s evaluation should include:

Interview of the patient to evaluate adherence and compliance to therapy, with a focus on the evaluation and management of side effects and psycho social parameters. Re-explanation to the patient of the objectives and modalities of the treatment and the potential risks of poor adherence. It is also important to exclude potential drug-drug or drug-food interactions and exclusion of an intercurrent infection or recent vaccination.

After these interventions, a second CD4 determination should be performed a few weeks later and treatment adherence should be re-assessed. For those patients whose CD4 level fall <15% the options are: to wait and measure CD4 1-2 months later.

ARV drug pharmacokinetics can be improved by boosting PI with ritonavir (if applicable and feasible)

Potential strategies to overcome treatment failure:

³ David Wilson : : Metabolic side effects occurring later during HAART treatment

If resistance testing is not available, options are to change the whole regimen or to interrupt therapy or change only the drug(s) for which resistance is suspected or documented.
Change the whole regimen because minor resistant variants could be present.

3.10 Management of failure on second or subsequent antiretroviral therapy.

Poor prescription (often consisting of NsRTI) compounded with poor compliance that might lead to the possibility of resistance not only to the NRTI; which they have taken but cross resistance to all drugs of the NRTI group and sometimes with loss of NRTI backbone. There is always a possibility of 'cross resistance' within the NRTI class and resistance also develops very fast within the NNRTI class (Only one mutation is required). It may not be advisable to use NNRTI for patient with an extensive ARV experience (especially if it includes NNRTI) as a second line, because resistant develops very quickly if given to a patient with NRTI resistant virus.

In this situation, which is quite common, the general recommendations are the same as for failure of first line treatment. However, as treatment options tend to decrease with the number of previous failures, the decision to change a failing regimen in this setting should take into account the treatment options remaining, the level of failure- as determined by the degree of decline of CD4 cell count- and the past treatment and resistance history, including tolerability and adherence issues. Many patients who experience treatment failure with their current anti-HIV regimen, but who do not have appropriate remaining treatment options, may derive clinical benefit from continuing their failing regimens. This may be particularly true if they are able to maintain and if their CD4 count remains higher than their nadir CD4 count. One standard recommendation for these patients is **2 new NRTI + 1 (boosted) PI**, because resistance develops more slowly to PI (normally 4 mutations are required) and also the HIV strains that are resistant to PI are less virulent than the wild type. It is often recommended that highly ARV experienced patients may do better with a regimen of **1 NRTI + 1 NNRTI + 1 (boosted) PI**.¹

These considerations emphasize the fact that patients failing multiple therapies should benefit from being managed by practitioners having experience in the care of HIV patients.

Table 11: Key points about 2nd line regarding resistance and cross resistance within ARV groups:

	NRTI	NNRTI	PI
Development of resistance if sub-optimal regimen or poor adherence	Slower	Easily and quickly	Slower
Cross-resistance within group	+	+++	+

Table 12: Advantages and disadvantages of the different possible regimens

	2 NRTI + 1 NNRTI (eg GPO-vir)	2 NRTI + 1 PI (e.g. Combivir + IDV/rtv)	2 PI + 1 NNRTI (eg IDV + RTV + EFV)	1 NRTI + 1 NNRTI + 1 PI (eg 3TC + EFV + IDV/rtv)
if resistance to NRTI is present	regimen will fail quickly	regimen will fail more slowly (because resistance to PI develops more slowly than to NNRTI)	no impact (no NRTI in regimen)	regimen will fail eventually
future options for salvage	regimen with 2 PI	1 NRTI + 1 NNRTI + 1 PI	none	none

¹ Note: A study in Thailand (HIV-NAT 009) has shown another alternative that dual therapy with Indinavir/ritonavir 800/100mg BID and Efavirenz 600mg QD can benefit patients with combination NRTI failure. The median duration of previous combination NRTI therapy in these patients was 4 years. After 48 weeks of Indinavir/ritonavir 800/100mg BID and Efavirenz 600mg QD, 87% of patients had undetectable viral load.^{1, 2}

regimen				
pill burden	1 tablet twice per day	3 tabs/caps twice per day	many caps twice per day	3 tabs am 6 tabs pm
side effects	+/-	++/-	++++ (full dose RTV)	+/-
Storage	no difficulties	RTV needs refrigeration	RTV needs refrigeration	RTV needs refrigeration
Approx. cost	1 US\$ / day	3 to 4 US\$ / day	+++ US\$ / day	5 to 6 US\$ / day
an option in project protocol?	Yes	Yes	Not really (IDV/rtv is an option but not IDV + RTV)	Yes

3.11 What advice do we give patients should do if they forget one dose of ARV and realize later.

Drugs such as AZT and EFV, side effects such as headache and insomnia occur immediately after the drug is taken and are dose related. It is not advisable for patients to take the forgotten dose as soon as they realize they have forgot.

In regimens such as 3TC + d4T + NVP; where side effects are cumulative, rather than occurring immediately after the drug is taken, the principle is to take the forgotten dose as soon as they realize they forgot it. Then the next dose should be taken at the standard time. However; if it is almost time to take the next dose (if it is less than 6 hours away from your next dose) never advice to take a double dose.

Regarding certain PIs the genetic barrier for resistance is quite high. In boosted PI the pharmacological barrier to resistance is also often high. In practical terms this implies that they are more forgiving for forgotten doses, therefore it is important not to advice patients to take a double doses.

It is important to review the patient's commitment to good adherence. It may not be a suitable time to initiate ART, or if already on ART it may be time for the patient to take a drug holiday.

3.12 Therapeutic success or failure

What is therapeutic success?

Clinical success:

Clinical failure is characterized by any or all of the following conditions: general condition is improving, less opportunistic infections (fever, diarrhoea...) and patient is not dying anymore

Immunologic success:

Immunological success is indicated by CD4 cell count steadily increases (>25% increase)

Virological success:

In the case of virological success the Viral load is repeatedly undetectable. Though is not available but it may necessary in certain instances where it may be requested by a patient who can afford the cost.

What is therapeutic failure?

*Virological failure:*²

This will include the following: VL>400copies/ml after 24 weeks HAART, VL>50copies/ml after 48 weeks and Viral rebound

Immunologic failure:

² Not available

This test is available and remains the most reliable marker in a resource poor setting. It is shown by increase less than 25-50 cells/mm³, CD4 cell count returns to baseline or below, CD4 cell count fall by 25% or more, confirmed by 2-repeated measurement at 3 months interval.

Clinical failure:

Clinical signs and symptoms remain one of the important criteria to determine therapeutic failure. It is indicated by occurrence or recurrence of HIV related events, new symptoms, development of an OI, cancer or other HIV related conditions of the same or more severe CDC category, occurring after 6 months of HAART and progression of HIV illness towards next WHO stage

Causes of therapeutic failure.

Frequent reasons for therapeutic failure are due to the following: no optimal regimen, non-adherence, bad absorption drug interaction and drug resistance. Other reasons may include side effects of ARV or other drugs immune reconstitution syndrome, OI or other HIV related problems and Non HIV related problems

4. Immune reconstitution syndrome (IRS).

IRS is associated with risks of seroconversion illness and OIs, particularly in those with low CD4 counts. In TB Immune reconstitution previously quiescent TB infection becomes obvious 2-3 weeks after starting ART by increasing inflammatory response and occurs quite frequently. Symptoms can include fever, lymphadenopathy, worsening pulmonary lesions and expanding lesions of CNS Usually self-limiting, but it can be potentially fatal. In general, ART should not be interrupted, but in case of very bad general state, it might sometimes be more practical to stop but certain opportunistic infections associated with IRS are tuberculosis, CMV retinitis, herpes Zoster meningitis (Cryptococcus or Tuberculosis)

5. Drug interactions

Drugs or food altering the absorption, distribution, and metabolism or elimination ARV drug thus changes ARV plasma concentration.

Objectives

- Personalise dosing schedule for adherence
- Explaining the importance of food requirement for specific ARV drugs.
- Explain to patients certain food or drinks to avoid with certain drugs
- Discuss various options for taking certain ARV drugs opening some capsules or crushing certain tablets
- Know drugs that cannot be co-administered (drug interactions).

Before prescribing any drugs, check whether there are drug interactions with ARVs.

Rifampicin should not be used together with nevirapine, because it decreases the level of NVP.

4. ARV and ARV drug interaction

NNRTI and PI metabolized by P450 CYP3A4 enzyme in liver both classes of drugs themselves can induce or inhibit the enzyme and thus increase or lower the concentration of other drugs: EFV levels are increased by ritonavir, whilst levels of ritonavir are increased by EFV and IDV levels are reduce by EFV.

Stavudine and zidovudine are both thymidine analogues and they are antagonists.

4.1 Other interactions

Interactions with non-ARV's:

- Rifampicin induces hepatic enzyme and thus decreases PI levels to sub therapeutic
- Do not co-administer rifampicin with IDV.
- Do not use with NVP with Rifampicin due to combined hepatotoxicity and reduction of NVP levels by rifampicin

- RTV, NNRTI decreases oestrogen level in oral contraceptives³
- PI and EFV raise the level of benzodiazepines, with prolonged sedation as a result
- Do not co-administer ketokonazole with NVP
- Do not give clarythromycin with EFV
- Do not co-administer DDI and allopurinol.
- Ketoconazole should be substituted for fluconazole. Benzodiazepines should be avoided.
- Magnesium-containing 'milk', such as Maalox^o should never be used.

4.2 ARV drug interactions with food:

ARV drug related to food (meal)

- ddI, IDV, IDV/r – should be taken either 1 hour before or 2 hours after meal
- EFV – should not be taken with fatty food
- ddI not to be taken with antacid.

In practise a newly diagnosed TB patients can start 3TC/d4T/NVP only after completing the first 2 months of the TB treatment in cases of newly diagnosed TB. In instances of a patient developing TB either due to new infection or immune reconstitution syndrome either: (1) interrupt ARVs for 2 months then switch from NVP to EFV in the regimen increase EFV to 800mg.

5. Special consideration

5.1 Treatment of HIV pregnant women

Objectives:

1. Treatment of the woman, irrespective of pregnancy.
2. Prevention of mother to child transmission

Assessment of HIV/AIDS patients

Clinical management: early and accurate diagnosis, including testing, rational treatment and follow-up care

Nursing care: promotion of adequate hygiene practices and nutrition, palliative care, home care and education to care providers at home and family, promoting observance of universal precautions

Counselling and emotional support: psychosocial and spiritual support, including stress and anxiety reduction, risk reduction planning and enabling coping, accepting sero status and disclosure to others, positive living and planning of the future for the family

Social support: information, provision or referral to peer support, welfare services, spiritual support and legal advice

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.

³ Oral contraceptives levels are reduced by EFV, hence patient should use other contraceptive methods, e.g. injectable hormonal contraceptives, or condoms.

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 foetus 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.

5.1.1 Treatment categories of HIV pregnant woman.

Women becoming pregnant while already treated with HAART:

Current treatment should be maintained whenever feasible, with the exception of some agents and combinations such as efavirenz. 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 HAART

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 late 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 are alternative drugs to combine with AZT+3TC.

5.2 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.

7. Prevention of infectious complications in HIV adult patients

1. Indications for initiating prophylaxis of opportunistic infections
2. Interruption of long term suppressive therapy of opportunistic infections
3. Vaccinations

6 Initiation of Antiretroviral therapy (ART) in patients with active opportunistic infections.

Initiation of ART may exacerbate clinical manifestations of latent or mildly symptomatic infections such as CMV infection presenting as anterior chamber vitritis and in the case of other viruses such as viral hepatitis. Simultaneous initiation of ART and specific treatment for certain opportunistic infections may lead to cumulative toxicity or difficult to manage drug interactions. This sometimes occurs with cytomegalovirus disease.

Therefore treat all opportunistic infection adequately before initiating HAART. Do not start HAART in instances of active OI. During the entire course of HAART continuously re-evaluate for OI (immune reconstitution syndrome or new OI).

Recommendations:

The successful outcome of antiretroviral therapy depends largely on the early diagnosis and correct management of opportunistic infections (OI). Any patient presenting with low immunity more often has an existing OI. Inability to diagnose and manage important OI such as TB, CMV, PCP, and cryptococcal and meningitis leads to poor outcome.

Exclude mycobacterial disease, before initiation of ART, in case of suggestive signs or symptoms. If mycobacterial disease is diagnosed (e.g. TB, MAC), treat it for two months before starting ART. If exacerbation of symptoms due to mycobacterial disease suggestive of an immunorestitution syndrome occurs after initiation of ART, start mycobacterial therapy and to consider interruption of ART. Perform fundoscopy in all patients with $CD4 \leq 100$, in order to exclude asymptomatic CMV retinitis. Treat and stabilise CMV disease if diagnosed before starting ART in order to avoid unacceptable toxicity. If a patient is already on HAART and showing sign and symptoms of TB either stop HAART or use EFV to replace NVP and continue with HAART (some expert increases the dose of EFV to 800mg because of drug interaction)

Patients taking antiretroviral treatment (HAART) can develop an opportunistic infection because of any of the following reasons: Low immunity, immune reconstitution syndrome and treatment failure. Antiretroviral therapy is the cornerstone of the therapy for certain opportunistic diseases associated with profound immunosuppression (cryptosporidiosis, progressive multifocal leukoencephalopathy, Kaposi sarcoma and lymphoma). Initiate ART and specific therapy (if available) as soon as possible. In the case of lymphoma, start with specific chemotherapy and delay initiation of ART to second or later cycle, to avoid cumulative toxicity.

6.1 Prophylaxis for opportunistic infections

Table 13: Criteria for initiating and stopping primary prophylaxis against OI's

Opportunistic Infections	Criteria for initiation of primary prophylaxis	Drug regimen	Criteria for interruption of primary prophylaxis
PCP	CD4 < 200 or Symptomatic HIV	Cotrimoxazole 1 DS tablet thrice weekly or 1 regular tablet QD	CD4 > 200 for > 3-6 months on anti HIV treatment

	disease	Dapsone 50-100 mg daily	
TOXOPLASMOSIS	CD4 < 100 and positive IgG for toxo	Cotrimoxazole 1 DS tablet daily Dapsone 50mg/d+ Pyrimethamine 25mg twice weekly	CD4 > 200 for > 3-6 months on anti HIV treatment
TUBERCULOSIS	Positive PPD - No active TB or Contact with a patient with active pulmonary TB and no history of BCG	INH + pyridoxine for 6-9 months	NA
A TYPICAL MYCOBACTERIA	CD4 < 50	Azythromycin 1-1.25 g weekly or Clarithromycin 500mg BID	CD4 > 100 for > 6 months on anti HIV treatment

The immune reconstitution which is observed in most patients in whom ART is initiated allows interruption of primary prophylaxis in selected situations. The decision to stop or re-initiate primary prophylaxis against OI's should be based on CD4 levels.

Follow up of CD4 cell count after interruption of primary prophylaxis is warranted in order to allow for re-initiation of primary prophylaxis in case of immune degradation. This is particularly indicated in case of antiretroviral treatment failure or treatment interruption.

6.2 Recommendations for interruption of long term suppressive therapy of opportunistic infections

PCP: Same as primary prophylaxis i.e. CD4 > 200 for ≥ 6 months on anti HIV treatment

TOXO: Provisional recommendations: CD4 > 200 for ≥ 6 months on anti HIV treatment

MAC: Provisional recommendations: CD4 > 100 for > 6 months on anti HIV treatment

CMV: CD4 > 100 for ≥ 6 months on anti HIV treatment. No active lesion

It should be noted that continuous low dose fluconazole can lead to development of resistant strains not only of Cryptococcus but also of Candida. Usually it is recommended that if primary prophylaxis with fluconazole is prescribed, active Cryptococcal infection is first ruled out by means of a negative Cryptococcal antigen test. Should not be provided for any patient with evidence of existing cryptococcal disease i.e. if patient has fever or any other symptom of unknown cause.

6.3 Management of cotrimoxazole toxicity:

Protocol for oral desensitization to cotrimoxazole adverse effects

Grade 1: Macules or generalized erythema

Grade 2: Papules or dry desquamation

Grade 3: Moist desquamation or vesicles or ulcers

Grade 4: Toxic Epidermal Necrolysis or Stevens-Johnson Syndrome or Rash with Fever or other systemic manifestations

2) Cotrimoxazole Rapid Desensitization

Preparing the suspensions:

A: 40 mg TMP / 200 mg SMX / 5 ml)

Take 1 ml of suspension A, add 9 ml of water to make 10 x dilution

(Suspension B: 4 mg TMP / 20 mg SMX / 5 ml)

Take 1 ml of suspension B, add 9 ml of water to make 10 x dilution

(Suspension C: 0,4 mg TMP / 2 mg SMX / 5 ml)

Take 1 ml of suspension C, add 9 ml of water to make 10 x dilution

(Suspension D: 0,04 mg TMP / 0,2 mg SMX / 5 ml)

Take 1 ml of suspension D, add 9 ml of water to make 10 x dilution

(Suspension E: 0,004 mg TMP / 0,02 mg SMX / 5 ml)

Desensitization process:

<i>Hours</i>	<i>Suspension</i>	<i>Quantity</i>	<i>Dosage (mg)</i>
0	E	5 ml	0,004 / 0,02
1	D	5 ml	0,04 / 0,2
2	C	5 ml	0,4 / 2
3	B	5 ml	4 / 20
4	A	5 ml	40 / 200
5	A	20 ml	160 / 800

Desensitization can be done in outpatient department, in the presence of a doctor.

Before starting, check blood pressure, pulse and respiratory rate and before giving the next solution, each time check pulse and respiratory rate. If pulse increases > 100 and/or respiratory rate > 40, stop immediately. Observe for 30 minutes and if dyspnoea and tachycardia don't improve, refer to the hospital according to the severity of symptoms. If itching, stop immediately and treat accordingly. You can expect 80 % of success of desensitization with this rapid oral process.

7 Treatment of the HIV/AIDS patient with hepatitis V (HBV) and/or hepatitis C (HBC) co-infection

HIV-1, HBV and HCV share similar routes of transmission. Co-infection with HIV-1 and HBV and/or HCV is therefore common. Up to 80% of injecting drug users with HIV-1 infection and up to 77% of homosexual men with HIV-1 infection have markers of past or chronic HBV infection and more than 70% and 7% respectively, have markers of past or chronic HCV infection.

7.1 HIV and HBV

HBV replication is increased in case of HIV co-infection, and results in an increased risk of developing chronic infection (21% compared to 7% in HIV seronegative patients). Patients with a low CD4 cell count clear HBsAg significantly less frequently. Histological and biochemical studies have suggested that the severity of liver disease is reduced in case of HIV and HBV co infection, whereas expression of HBeAg and HBV-DNA are increased. In patients who have cleared the HBsAg from plasma, HBsAg and HBV DNA may reappear in connection with the development of an advanced immunodeficiency.

Recommendations for management are:

Liver biopsy maybe considered to evaluate the degree of liver damage.

Lamivudine dosage of 150mg BID should be used in HIV co infected patients. Use of lamivudine as monotherapy should be avoided.

7.2 HIV and HCV

HCV could impair immune recovery following initiation of ART. On the other hand, there is mounting evidence to show that there is a faster progression of HCV-related liver disease in HIV co-infected individuals. HIV infected patients have a 5 to 20-fold higher risk of developing cirrhosis and liver failure and a 6-fold increased risk of liver carcinoma, when compared to HIV negative individuals infected with HCV. Low CD4 cell counts (i.e. < 200) have been shown to be associated with a faster progression to liver fibrosis.

Liver biopsy is recommended before initiation of therapy.

Treatment of HCV consists of a combination of interferon and ribavirin. Clinical studies are underway to evaluate the potential interaction between ribavirin and nucleoside analogues, as well as the cumulative risk of pancreatitis when ribavirin is used together with didanosine.

Response to treatment depends on age of patient (lower response rate in older patients), race (response rate is lower among blacks when compared to Caucasians), duration of HCV infection (response rate decreases as duration increases), histological findings (response rate decreases as liver damage increases), HCV genotype (genotype 1 response rate is low) and CD4 level (lower response rate in case of low CD4 cell count)

8. Vaccination of the HIV infected patient

Efficacy of vaccination depends on the level of CD4 cells. It is therefore recommended to immunize patients before their CD4 cells drop below 200 or to wait for immune restoration if CD4 levels are below 200 at the start of ART. In patients whose CD4 do not raise above 200 one should nevertheless consider vaccination against pneumococcal infection.

Any vaccination may lead to a transient rise of HIV viral load. This rise is considered to be clinically not relevant.

8:1. Three categories of vaccinations:

8:1:1. Vaccines which should be administered to all HIV patients

<i>Vaccine</i>	<i>Eligibility</i>	<i>Frequency</i>
Tetanus	All patients	Every 10 years

8:1:2 Vaccines which are recommended in selected groups of HIV patients

<i>Vaccine</i>	<i>Eligibility</i>	<i>Frequency</i>
Pneumococcus	Same categories as with HIV negative population including splenectomized patients and patients with past pneumococcal infection	Every 5 years
Influenza	Same categories of patients as in HIV negative population	Yearly
Hepatitis A	Patients at risk (travel,...) HCV co infected patients Homosexual men	Every 10 years
Hepatitis B	Patients with multiple sexual partners HIV infected healthcare worker HCV co-infected patients	Follow level of antibodies

8:1:3. Vaccines whose indications are limited to selected cases/circumstances (travels,...)

This category includes all other vaccines with the exception of :

1. Oral live vaccines which are contraindicated
2. BCG which is contraindicated

Yellow fever vaccine which should be considered only for HIV patients with CD4 above 300 cells who are exposed to substantial risk

9. Promotion of adherence:

Goal:

1. Clinically no OI while on ARV treatment
2. CD4 > 25% after 6 months of ARV treatment.
3. Patient's commitment.
4. Responsible attitude.

9:1. Activities to promote adherence:

Patient centered education strategies:

Ensure patient have good understanding of the treatment and strong support system (treatment assistant). Explain to patient that ARV therapy is not a cure; it can only suppress HIV replication, but does not stop it. If ARV therapy is ceased HIV replication quickly returns to pre-treatment levels and promptly begins to damage the immune system once again. Provide education on how drug resistance occurs and the relationship between adherence and resistance as well as treatment failure and the impact of resistance on future options. Explain to the patient what to do if doses are missed, delayed, or vomited what to do if stopping therapy. Improve their knowledge on relationship between dosing and eating (dietary restrictions, examples of appropriate/inappropriate foods, storage of drugs and about expiry dates as well as importance about refrigeration and drug interactions

9:2. Community centred education strategies:

Create community awareness and education through participation in civic activities such as World AIDS day and related activities. Solicit social support for PHAs through a nurse drug educator and counsellor (for serious problems) and PHA "Lay counsellor" to help patients with individual adherence problems. Develop HHA peer support groups exclusively for HAART therapy focusing on discussions about barriers to adherence, adverse events, disclosure and other psychological issues as well as health promotion.

9:2. Develop basic adherence tools:

Improve the understanding on ARV drug names and what they look like, form of medication (tablet, capsule, liquid etc) dose (number of pills) and dosing frequency and spacing. Develop tools in the form of material support to PHA, Pill boxes, drug identification and flip charts. Train counsellor to assist patients having difficulties with any aspect of HAART and work with treatment assistant to assist patient with adherence issues. Organize periodic home visit for more thorough follow-up of patient having problems. Other will include material support (other social NGOs), provide pillboxes, drug identification charts, daily or weekly schedules and drug samples during consultations

9:3. Developing PLWHA support

PHA group meetings should be interactive ensuring that all the clients in the meeting have a chance to contribute to the session. Most of the interaction should be directly between the group members because clients usually attend meetings for help with their own problems, rather than to support each other. The long term goal is to encourage PHAs to support each other, especially in practical solutions to problems with adherence as follows: Improving adherence and developing PHA support. Drug adherence education with explanations, create a supportive environment, encourage self-help and create a mutually supportive group dynamic, PHA involved more as active participant.