National Anti-retroviral Therapy Guidelines

National Centre
and STD Control
Nepal

NATIONAL ANTI-RETROVIRAL THERAPY GUIDELINES

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Government of Nepal
Ministry of Health & Population
National Centre for AIDS & STD Control (NCASC)
Teku, Kathmandu

Medical knowledge is constantly and rapidly changing, particularly in relation to HIV/AIDS. Readers are strongly advised to confirm that the information (especially with regards to drug doses and usage) complies with the latest standards of practice.

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Foreword

Within 3 decades of its discovery, HIV AIDS has become the number one killer infectious disease of mankind. While on one hand the disease is taking young lives, on the other it is tearing the social fabric apart, thereby perpetuating a vicious cycle of poverty and disease that seems to ignite it in the first place.

At 0.49 per cent prevalence levels in the country, our HIV caseload is hardly modest. While preventive efforts to bring down prevalence levels are ongoing, the importance of treatment, care and support of those that have already been infected cannot be over emphasized. The government of Nepal has made an effort to rapidly scale up Anti-retroviral therapy, so that treatment may be readily accessible to those in need. Anti retroviral therapy is today available at 25 ART centers in the country and we intend to rapidly scale up the number of such centers in the near future.

These guidelines are part of the ongoing effort to rapidly scale up antiretroviral therapy throughout the country. These guidelines are meant for use by doctors, nurses and paramedics that are actively involved in care of the patients. A lot of effort has gone into the preparation of these guidelines, and we have been able to incorporate lessons learnt from our experience with ART during the last 5 years, when the first edition of the guidelines came out.

I would like to take this opportunity to thank Prof. Sashi Sharma, Lead consultant, the members of the Technical Experts Group as well as the Technical Working Group for the incessant effort they have put in bringing out these guidelines. I would also like to thank our partner organizations- the WHO, UNDP, and FHI as well as all the other individuals and organizations for their time and effort in bringing out these guidelines.

Dr. Krishna Kumar Rai
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Abbreviations

AIDS acquired immune deficiency syndrome
ALC absolute lymphocyte count
ALT alanine aminotransferase (also known as SGPT)
APV amprenavir
ARV anti-retroviral
ART anti-retroviral therapy
CBC complete blood count
CD cluster of differentiation
CMV cytomegalovirus
d4T stavudine
DC differential leucocyte count
ddI didanosine
EFV efavirenz
ELISA enzyme linked immunosorbent assay
HCW health care worker
HIV human immunodeficiency virus
IDV indinavir
LPV lopinavir
LPV/r lopinavir boosted with ritonavir
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 jiroveci pneumonia
PCR polymerase chain reaction
PI protease Inhibitor
/r low dose ritonavir
RTV ritonavir
SGPT serum glutamic pyruvic transaminase (also known as ALT).
SQV saquinavir
RT reverse transcriptase
STI sexually transmitted infections
TB tuberculosis
TDF tenofovir disoproxil fumarate
TC total leucocyte count
VCT voluntary counseling and testing (of HIV)
VL viral load
WHO world health organization
ZDV zidovudine, (also known as AZT)

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I. Background

1981 in the USA. Since then, AIDS has become the most humans. More than 60 million people have been infected and about 33 million people are estimated to be currently living with HIV, among whom one-third are between 15-24 years of age. Initially, the epidemic was concentrated in the African continent. But it continues to spread in Asia, particularly in South Asia. In South and South East Asia, there are approximately 4 million people living with HIV/AIDS. In Nepal, the first case of HIV/AIDS was diagnosed in 1988. The major mode of transmission in Nepal is heterosexual. The available data show that there is a high prevalence of HIV in high-risk groups such as injecting drug users and female sex workers. Currently, it is estimated that there are approximately 70,000 people living with HIV/AIDS in Nepal, with an estimated 3,000 deaths (2002) annually.

In 1986, antiretroviral therapy was initially introduced in other countries with the first drug Zidovudine (ZDV). Over the next few years, other antiretroviral drugs (NRTIs, NNRTIs and PIs) were introduced. Initially, mono and dual therapies were used but the problem of resistance emerged. At present, 3 or more ARV drugs are recommended worldwide for the treatment of people with HIV infection. Since the use of combination therapy, this disease has been transformed into a chronic condition. However, the use of antiretroviral therapy is not the final answer to HIV/AIDS prevention and care programs. The delivery of effective care and antiretroviral treatment for people living with HIV/AIDS in the poorest countries is considered an urgent priority and is a complementary program to HIV transmission prevention programs. Initially, antiretroviral therapy was very expensive and so, unaffordable in most developing countries. As drugs are increasingly affordable, the development of guidelines on the appropriate and rational use of ART has become relevant in developing countries.

These current guidelines are intended basically for use by medical doctors who prescribe ARV therapy to the people infected with HIV/AIDS. Guidelines for the treatment and management of HIV infection have been produced in a number of countries of Europe, USA, Australia, India, Thailand, etc. and by WHO/UNAIDS. While these guidelines attempt to represent the current state of knowledge, it is inevitable that as HIV/AIDS is a rapidly evolving medical field new information will change therapeutic choices and preferences. This should be kept in mind while using these guidelines.

II. Principles of Antiretroviral Therapy

- Maximal and durable suppression of viral load.
- Restoration and/or preservation of immunologic function.
- Reduction of HIV-related morbidity and mortality.
- Improvement of quality of life of HIV infected persons.
- Prevention of Mother to Child Transmission (PMTCT).
- Post Exposure Prophylaxis (PEP).

Preconditions for starting Antiretroviral Therapy

The following specific facilities and services are desirable before starting Antiretroviral Therapy

- Availability of HIV voluntary counseling and testing (VCT) services along with follow up counseling services.
- Medical services capable of managing common HIV-related infections including opportunistic infections and STIs.
- Routine laboratory services, preferably with access to CD4+ lymphocyte count and PCR facility for viral load count. Lack of viral load testing and even CD4 testing should not preclude initiation of ART.
- Access to antiretroviral drugs and other drugs to treat OI and other associated diseases.

It is recommended that medical doctors who are trained in clinical management of HIV AIDS initiate and supervise Anti-retroviral Therapy.

Evaluation of patients before starting Antiretroviral Therapy

A detailed evaluation is essential prior to initiating antiretroviral therapy and should aim to:

- Assess the clinical stage of HIV infection.
- Identify past HIV-related illnesses.
- Identify current HIV-related illnesses that will require treatment.

- Identify co-existing medical conditions and treatments that may influence the choice of therapy.

Before initiating therapy, the following evaluations should be performed:

- A history including past illnesses with emphasis on OIs and other conditions.
- Psychological and psychiatric history.
- Assessment of family and social support.
- Practices regarding safe sex and injecting drug use.
- Physical examination

Physical examination and lab tests before initiating ARV Therapy:

Body weight of the patient

Skin: look for Herpes Zoster, HIV dermatitis and other skins conditions.

Lymphadenopathy.

Oropharyngeal mucosa: look for Candidiasis, and hairy leucoplakia, Kaposi sarcoma.

Examination of abdomen, heart, lungs, neurological, musculoskeletal and genitourinary systems.

Laboratory Tests:

TC, DC, Hb%

ALT/SGPT ï If needed LFT (Liver function test)

Serum creatinine ï If needed Kidney function test (Urea, Electrolytes)

Blood sugar level

Chest X ray, Sputum for AFB

Hepatitis B and Hepatitis C

Urine pregnancy test as indicated in female

Urinalysis to assess for proteinuria

CD4 cell count

For women, cervical pap smear or other method of cervical cancer screening, if available.

III. Indications for Antiretroviral Therapy

oviral therapy in adults and adolescents with documented
v.

If CD4 testing available:

It is recommended to document baseline CD4 counts and to offer ART to patients with:

WHO Stage 4 disease, irrespective of CD4 cell count

WHO Stage 3 disease, irrespective of CD4 cell count

WHO Stage 1 or 2 disease with CD4 cell counts less than 350/mm^3

If CD4 testing unavailable:

It is recommended to offer ART to patients with:

WHO Stage 4 disease

WHO Stage 3 disease

Note: WHO stage 1 and 2, treatment is not recommended when CD4 testing is not available

Consider ART initiation in those with active Hepatitis B or C and those with HIV-related nephropathy

Note: In co-infection with other diseases, treatment of tuberculosis and some other opportunistic infections the priority may be to start OI treatment before antiretroviral therapy. However, recent evidence suggests that ART should be started early in the setting of acute AIDS-related OIs if there are no major contraindications to doing so. Waiting to complete OI treatment before initiating ART appears to be associated with a higher risk of AIDS-related disease progression and/or death without any significant benefit in terms of safety or virological response.

r Adults and Adolescents

- Asymptomatic
- Persistent generalized lymphadenopathy

Clinical Stage 2

- Unexplained moderate weight loss (<10% of presumed or measured body weight)[a]
- Recurrent respiratory tract infections (sinusitis, tonsillitis, otitis media and pharyngitis)
- Herpes zoster
- Angular chelitis
- Recurrent oral ulceration
- Papular pruritic eruptions
- Seborrhoeic dermatitis
- Fungal nail infections

Clinical Stage 3[b]

- Unexplained severe weight loss (>10% of presumed or measured body weight)
- Unexplained chronic diarrhea for longer than one month
- Unexplained persistent fever (above 37.5°C intermittent or constant, for longer than 1 month)
- Persistent oral candidiasis
- Oral hairy leukoplakia
- Pulmonary tuberculosis
- Severe bacterial infections (such as pneumonia, empyema, pyomyositis, bone or joint infection, meningitis or bacteraemia)
- Acute necrotizing ulcerative stomatitis, gingivitis or periodontitis
- Unexplained anaemia (<8 g/dl), neutropaenia (<0.5 × 10^9 per litre) and/or chronic thrombocytopaenia (<50 × 10^9 per litre)

Clinical Stage 4[c]

- HIV wasting syndrome
- Pneumocystis pneumonia
- Recurrent severe bacterial pneumonia
- Chronic herpes simplex infection (orolabial, genital or anorectal of more than one monthôs duration or visceral at any site)
- Oesophageal candidiasis (or candidiasis of trachea, bronchi or lungs)
- Extrapulmonary tuberculosis
- Kaposiôs sarcoma
- Cytomegalovirus infection (retinitis or infection of other organs)
- Central nervous system toxoplasmosis
- HIV encephalopathy
- Extrapulmonary cryptococcosis including meningitis
- Disseminated non-tuberculous mycobacterial infection
- Progressive multifocal leukoencephalopathy
- Chronic cryptosporidiosis
- Chronic isosporiasis
- Disseminated mycosis (extrapulmonary histoplasmosis or coccidiomycosis)
- Recurrent septicaemia (including non-typhoidal *Salmonella*)
- Lymphoma (cerebral or B-cell non-Hodgkins)
- Invasive cervical carcinomas
- Atypical disseminated leishmaniasis
- Symptomatic HIV-associated.nephropathy or symptomatic HIV-associated cardiomyopathy

a. Assessment of body weight in pregnant woman needs to consider the expected weight gain of pregnancy.
b. Unexplained refers to where the condition is not explained by other causes.
c. Some additional specific conditions can also be included in regional classifications (such as penicilliosis in Asia).

nd their actions

Categories of approved antiretroviral drugs include the following:

1. A. Nucleoside analog reverse transcriptase inhibitors (NsRTI).

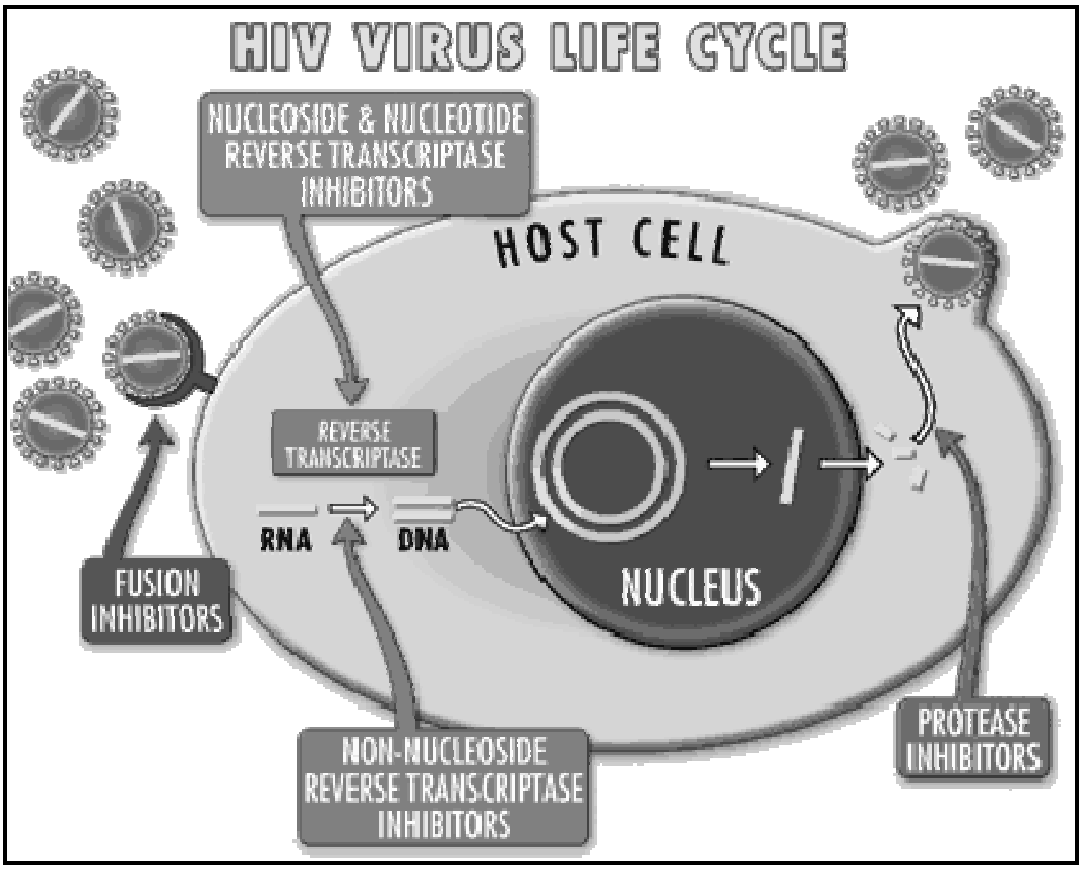
   B. Nucleotide analog reverse transcriptase inhibitors (NtRTI).

2. Non-nucleoside analog reverse transcriptase inhibitors (NNRTIs)

3. Protease inhibitors (PIs)

4. New class of drugs: Fusion inhibitors (FI), CCR5 Antagonists, Integrase Strand Transfer Inhibitors (INSTI)

MECHANISM AND SITE OF ACTION OF ANTIRETROVIRAL AGENTS



The first effective class of antiretroviral drugs was the **Nucleoside analogues**. They act by incorporating themselves into the DNA of the virus, thereby stopping the building process. The resulting DNA is incomplete and cannot create new virus. **Nucleotide analogues** work in the same way as nucleosides, but they have a nonpeptidic chemical structure.

Non-nucleoside reverse transcriptase inhibitors (NNRTIs) stop HIV production by binding onto reverse transcriptase and preventing the conversion of RNA to DNA. These drugs are called "non-nucleoside" inhibitors because even though they work at the same stage as nucleoside analogues, they are not nucleoside analogueS.

Protease inhibitors work at the last stage of the viral reproduction cycle. They prevent HIV from being successfully assembled and released from the infected CD4 cell. **Fusion Inhibitors** work to prevent fusion and entry of the virus to the target cell (CD4). **Integrase Inhibitors** work to prevent the integration of the HIV proviral DNA into the human DNA. **CCR5 Antagonists** work by blocking co-receptors needed for the virus to enter the cell.

			Adverse effects	Interaction with other antiretroviral therapy
Abacavir (ABC)	300 mg twice daily or 600mg OD	Take without regards to meal	Hypersensitivity reaction in 3 to 5% (can be fatal), fever, rash, fatigue, nausea, vomiting, anorexia, respiratory symptoms (sore throat, cough, shortness of breath)	Rechallenge after reaction can be fatal. Some studies show that ABC has been associated with increased cardiovascular risk; these drugs should be used with caution in high risk patients. This was not substantiated in other studies
Didanosine (ddI)	**Weight < 60kg**: 250mg once daily **Weight ≥ 60kg**: 400mg once daily; If given **with TDF**: <60kg 200mg once daily >60kg 250mg once daily	Take on empty stomach (1/2 hour before or 2 hours after meal)	Pancreatitis Peripheral neuropathy Lactic acidosis with hepatic steatosis (rare but potentially life-threatening toxicity) Potential association with noncirrhotic portal hypertension	Avoid TDF and ddI concomitant use. If no other alternatives, use only in treatment experienced patients on boosted PIs, with reduced ddI dose. Try to avoid use with d4T due to increased toxicity. Recent studies show that ddI has been associated with increased cardiovascular risk; these drugs should be used with caution in high risk patients**.**
Lamivudine (3TC)	150 mg twice daily Or 300 mg once daily	Take without regards to meals	Minimal toxicity	None Severe acute exacerbation of hepatitis may occur in HBV-coinfected patients who discontinue 3TC.

			Adverse effects	Interaction with other antiretroviral therapy
Stavudine (d4T)	30 mg twice Daily	Take without regards to meals	Pancreatitis, peripheral neuropathy, lipoatrophy, lactic acidosis with hepatic steatosis (rare but potentially life-threatening toxicity), Hyperlipidemia , Rapidly progressive ascending neuromuscular weakness (rare)	Antagonist with ZDV Try not to use with ddI due to increased toxicity
Zidovudine (ZDV, AZT)	300 mg twice daily	Take without regards to meals	Anaemia, neutropenia, bone marrow suppression, gastrointestinal intolerance, headache, insomnia, myopathy, lactic acidosis, skin & nail hyperpigmentation.	Antagonist with d4T
Tenofovir (TDF) NtRTI	300 mg OD	Take without regards to meal	Asthenia, headache, diarrhea, nausea, vomiting, and flatulence Renal insufficiency, Fanconi syndrome Dosage adjustment in renal insufficiency recommended Osteomalacia Potential for decrease in bone mineral density Severe acute exacerbation of hepatitis may occur in HBV-coinfected patients who discontinue TDF.	Avoid TDF and ddI concomitant use. If no other alternatives, use only in treatment experienced patients on boosted PIs, with reduced ddI dose (<60 kg= 200mg , >60kg = 250mg). Serum creatinine and urinalysis for proteinuria should be monitored at baseline and follow-up.

ñClass side effectò: All nucleoside analogs have been associated with lactic acidosis and hepatic steatosis.

Table 2: Non-Nucleoside Reverse Transcriptase Inhibitors (NNRTIs)

Generic Name	Dose	Food Effect	Adverse Effect
Nevirapine(NVP)	200 mg once daily for 14 days followed by 200 mg twice daily	Take without regards to meals	Hepatitis (usually within 12 wks), life-threatening hepatic toxicity Contraindicated as initial therapy for women if CD4 count is >250 due to increased hepatotoxicity in this group Skin rash occasionally progressing to severe conditions including TEN and

			Stevens Johnson syndrome.
Efavirenz (EFV)	600 mg once daily (bed time administration is suggested to decrease CNS side effects)	Avoid taking after high fat meals	CNS symptoms (dizziness, somnolence, insomnia, confusion, hallucinations, agitation), teratogenicity, and personality change. Rash occurs, but less common than NVP

ÅPatients who develop hepatic toxicity while treated with Nevirapine should not be restarted on that drug.
ÅEfavirenz is contraindicated in the first trimester of pregnancy.

Table 3: Protease Inhibitors (PIs)

Generic Name	Dose	Food Effect	Adverse Effect
Lopinavir/ritonavir (LPV/r) Heat stable tablets	200mg Lopinavir/50mg Ritonavir Fixed dose tablets 2 tablets twice daily	With or without food	Diarrhea, nausea, vomiting, abnormal lipid profiles, glucose intolerance In rare instance when LPV/r is given in combination with NVP or EFV in treatment experienced patients increase LPV/r dose to 3 tablets bid (600/150mg bid)
Saquinavir/ritonavr (SQV/r) Requires refrigeration Less potent than other PIs.	1000mg saquinavir + 100 mg ritonavir twice daily	No food effect when taken with ritonavir	Diarrhea, nausea, vomiting, headache, photosensitivity
Atazanavir/ritonavir	300mg Atazanavir + 100mg ritonavir once daily	Take with food	Hyperbilirubinemia. Less lipid problems than LPV/r Hyperglycemia, Fat maldistribution, Nephrolithiasis Interaction with acid blocking agents. Dosing changes when given with acid-blockers
Indinavir/ritonavir (IDV/r)	800 mg/100mg r BD	Take with food	Nephrolithiasis, increase indirect bilirubin, headache. Rash, diarrhea, nausea, mood disorder, altered taste. Less well tolerated. Not preferred in hot climates.

ñClass side effectò: All PIs can produce increased bleeding in hemophilia, GI intolerance, altered taste, increased liver function test and bone disorder, and all have been associated with metabolic abnormalities, such as hyperglycemia, insulin resistance, and increase in triglycerides, cholesterol and body fat distribution (lipodystrophy).

adverse effects of antiretroviral drugs

Adverse Effect	Major ARVs	Recommendations
Acute pancreatitis	d4T and ddI	Discontinue ART. Give supportive treatment and conduct laboratory monitoring. Resume ART with an NRTI with low pancreatic toxicity risk. AZT, ABC, TDF and 3TC are less likely to cause this type of toxicity.
Diarrhoea	ddI (buffered formulation), NVF, LPV/r and SQV/r	Usually self-limited, without need to discontinue ART. Symptomatic treatment should be offered.
Drug eruptions (mild to severe, including Stevens-Johnson syndrome or toxic epidermal necrolysis)	NVP, EFV (rarely)	In very mild cases, antihistamines and strict observation; there may be regression without need to change ART. If mild/moderate rash, non-progressing and without mucosal involvement or systemic signs, consider a single NNRTI substitution (i.e. from NVP to EFV). In moderate and severe cases, discontinue ART and give supportive treatment. After resolution, resume ART with three NRTIs or two NRTIs + PI.
Dyslipidaemia, insulin resistance and hyperglycaemia	PIs	Consider replacing the suspected PI by drugs with less risk of metabolic toxicity. Adequate diet, physical exercise and antilipaemic drugs should be considered.
GI intolerance, with taste changes, nausea, vomiting, abdominal pain and diarrhoea.	All ARVs (less frequent with d4T, 3TC, FTC and ABC)	Usually self-limited, without need to discontinue ART. Symptomatic treatment should be offered.
Haematological toxicities (particularly anaemia and leukopenia)	AZT	If severe (Hg <6.5 g% and/or ANC <500 cells/mm3), replace by an ARV with minimal or no bone marrow toxicity (e.g. TDF or ABC) and consider blood transfusion.
Hepatitis	All ARVs (particularly with NVP and ritonavir-boosted PIs)	Intense elevations of ALT associated with clinical features have been described with NVP; however, changes of varying intensity may be observed with all ARVs, mediated by different mechanisms. If ALT is at more than five times the basal level, discontinue ART and monitor. After resolution, replace the drug most likely associated with the condition.
Hyperbilirubinaemia (indirect)	ATV	Generally asymptomatic but can cause scleral icterus (without ALT elevations). Replace ATV with other PI.
Hypersensitivity reaction with respiratory symptoms, fever and without mucosal involvement.	ABC	Discontinue ABC and do not restart. Symptomatic treatment. Re-exposure may lead to a severe and potentially life-threatening reaction.

		Recommendations
Lactic acidosis	All NRTIs (particularly d4T and ddI)	Discontinue ART and give supportive treatment. After clinical resolution, resume ART, replacing the offending NRTI. ABC, TDF and 3TC are less likely to cause this type of toxicity.
Lipoatrophy and lipodystrophy	All NRTIs (particularly d4T)	Early replacement of the suspected ARV drug (e.g. d4T with TDF or ABC). Consider aesthetic treatment and physical exercises.
Neuropsychiatric changes (sleep disturbances; depression; behavioural, concentration and personality changes)	EFV	Usually self-limited, without the need to discontinue ART. Symptomatic treatment if required. If a previous psychiatric disturbance has occurred there is a higher risk of a more severe reaction. Effects may be enhanced by alcohol and other psychoactive drugs.
Renal toxicity (nephrolithiasis)	IDV	If using IDV, interrupt it and offer hydration, laboratory monitoring and symptomatic treatment (50% recurrence rate). Consider replacing IDV with another PI.
Renal toxicity (renal tubular dysfunction)	TDF	Discontinue TDF and give supportive treatment. After clinical resolution, resume ART, replacing the offending drug.
Peripheral neuropathy	d4T and ddI	Consider replacement by an NRTI with minimal or no neurotoxicity (AZT, TDF or ABC). Symptomatic treatment should be considered.

l Regimen

The choice of regimen depends on

- Cost of therapy
- Availability
- Affordability of drugs
- Convenience and likelihood of adherence.
- Regimen potency, tolerability and adverse effect profile
- Possible drug interactions and potential for alternate treatment options in the event that the initial drug regimen fails.

Antiretroviral therapy with single or dual drug regimen is not recommended except for the prevention of mother to child transmission and post exposure prophylaxis of HIV.

The combination of a either an NNRTI or a protease inhibitor with 2 NRTIs is potent and causes durable suppression of viral replication. Combination of ritonavir with another PI results in a boosting effect by increasing plasma concentration of these drugs, thereby reducing their doses frequency and pill burden. Currently, several regimens with acceptable antiviral potency are available. These regimes are composed of three or four drugs. Two NsRTIs generally form the backbone of most combinations (see box below).

or

2. 2NRTI + PI

or

3. 2NRTI + 1NRTI (Abacavir) (triple NRTI therapy= ZDV+3TC+ABC; do not use other triple NRTI options)

Possible NRTI combination include:

Zidovudine + Lamivudine (ZDV/3TC)
Tenofovir + Lamivudine (TDF/3TC)
Zidovudine + Didanosine (ZDV/ddI)
Didanosine + Lamivudine (ddI/3TC)
Abacavir + Lamivudine (ABC/3TC)

ZDV and d4T should not be used together due to their antagonistic effects.

Didanosine and Stavudine should not be used together due to high risk of toxicity.

Some patients will have started Stavudine + Lamivudine (d4T/3TC) in the past, this should no longer be used as a first line regimen for new patients as it is ñphased-outò of Nepal due to high risk of toxicity of stavudine.

The common recommended regimens are further given in table 5.

Table 5: First-Line ARV Regimens in Adults and Adolescents

ARV regimen	Major potential toxicities	Usage in women (of childbearing age or pregnant)	Usage in TB co-infection [a]
ZDV/3TC/NVP	ZDV-related GI intolerance, anaemia, and neutropenia, NVP-related hepatoxicity and severe rash	Yes	Use with caution in rifampicin-based regimens [a]

	Fanconi syndrome. HBV-exacerbation on discontinuation. NVP-related hepatotoxicity and severe rash	Yes	Use with caution in rifampicin-based regimens [a]
ZDV/3TC/EFV	ZDV-related GI intolerance, anaemia & neutropenia, EFV-related CNS toxicity & potential for teratogenicity	Only during 2nd and 3rd trimester. EFV should not be given to women in the first trimester of pregnancy or women of childbearing potential, unless effective contraception can be assured	Yes
TDF/3TC/EFV	**Tenofovir related** renal insufficiency, Fanconi syndrome. HBV-exacerbation on discontinuation. NVP-related hepatotoxicity and severe rash	Only during 2nd and 3rd trimester. EFV should not be given to women in the first trimester of pregnancy or women of childbearing potential, unless effective contraception can be assured	Yes
d4T combinations that first line patients may still be on. (New patients should not be started on stavudine containing regimens)			
d4T/3TC/NVP	d4T-related neuropathy, pancreatitis and lipoatrophy, NVP-related hepatotoxicity and severe rash	Yes	Use with caution in rifampicin-based regimens [a]
d4T/3TC/EFV	d4T-related neuropathy, pancreatitis & lipoatrophy, EFV-related CNS toxicity and potential for teratogenicity	Only during 2nd and 3rd trimester. EFV should not be given to pregnant women in the first trimester of pregnancy or women of childbearing potential, unless effective contraception can be assured	Yes

[a] See Section (Tuberculosis and Antiretroviral Therapy).
[b] See Section (Antiretroviral Therapy in Pregnancy and breast feeding).

For group O HIV-1 sub-type or HIV-2 infections, only the triple NsRTI and PI based regimen should be used because of inherent resistance of those viruses to NNRTI compounds. PI based regimen is the preferred option.

) instead of Zidovudine (ZDV):

- ZDV is preferred in most cases
- TDF should be used in the case of anemia or if ZDV is otherwise not tolerated.
- TDF does not require hemoglobin monitoring.
- ZDV may cause nausea, headache, anemia and neutropenia.
- WHO has recommended that Stavudine (d4T) be ñphased outò due to unacceptable rates of toxicity.
- Patients started or switched to Stavudine (d4T) for anemia, should switch to Zidovudine after 6-12 months of stable Hb above threshold, to avoid d4T toxicities.
- Abacavir can be used in the place of Tenofovir.

Some other considerations for NRTIs:

- Do not combine ñd-drugsò (ddI (didanosine), d4T).
- Do not give single d-drugs with pre-existing polyneuropathy.
- Do not combine 3TC and FTC.
- Do not combine ddI and TDF unless no other options exist. Dose of ddI must be reduced.

The choice between Nevirapine (NVP) and Efavirenz (EFV):

- NVP and EFV are both potent NNRTIs.
- The major toxicities associated with EFV are central nervous system (CNS) related, metabolic toxicity, teratogenicity and rash. The CNS symptoms typically abate within the first month of therapy.
- NVP has higher incidence of rash, which may be severe and life threatening. NVP has also a higher risk of hepatotoxicity.

Thus for most patients ZDV/3TC/NVP will be preferred as a first line ART. In patients with Hb less than 7gm% the regimen of choice should be TDF/3TC/NVP. In a female patient who is in the first trimester of pregnancy or likely to be pregnant, EFV should be avoided. In a patient with a certain side effects, an alternative drug should be used.

ens

Triple NRTI-based first-line regimens such as ZDV+3TC+ABC can be recommended in specific circumstances where both NNRTIs are contraindicated or too complex to manage. ZDV+3TC+TDF has not been well studied, but might be an alternative if no other options exist. Other triple NRTI combinations should not be used. Triple NRTIs have the advantage that they still preserve the PI class for second-line ART. These regimens can be used in the following circumstances:

- intolerance or resistance to NNRTIs;
- psychiatric disorders;
- women starting ART with CD4 >250, since great risk of NVP toxicity.
- pre-existing liver disease ï an increase of the ALT level by more than 3ï 5 fold and established cirrhosis;
- coinfection with HBV or HCV;
- HIV-2 infection due to intrinsic resistance to NNRTI class; and
- cotreatment of TB in women of child-bearing age and where adequate contraception cannot be guaranteed, and when NVP and boosted PIs cannot be used.

ZDV+3TC+ABC has short-term inferior virological efficacy at least in patients with high initial viral loads, but comparative immunological efficacy to ZDV+3TC+EFV regimen (CD4 recovery). ZDV+3TC+TDF is a promising regimen (especially in the management of tuberculosis and HIV co-infection; management of hepatitis C and HIV co-infection; and management of hepatitis B and HIV co-infection), but there are limited data to date. Other triple NRTI-based regimens, such as ZDV+TDF+ABC or TDF+3TC+ddI have unacceptably high virological failure rates and high incidence of the K65R mutation and should not be used.

Boosted PIs are usually reserved for second-line ART. They can exceptionally be used as part of first-line ART in combination with two NRTIs when triple NRTI regimen is not available or deemed inappropriate and when there are contraindications to NNRTIs (i.e. neither EFV nor NVP can be prescribed) including:

more than 3ï 5 fold;

- cirrhosis;
- pregnancy with CD4 count of 250ï 350 cells/mm3, particularly in the 1st trimester of pregnancy (as EFV is contraindicated);
- HIV-2 infection due to intrinsic resistance to NNRTI class;

If a first-line ART regimen containing a PI fails, there are very limited options for subsequent regimens within the public sector in Nepal. A failing PI regimen has, in consequence, more resistance patterns than a failing NNRTI regimen (point mutation in NNRTI class). In general therefore, it is recommended that PIs be reserved for second-line ART.

VI. Monitoring

Follow-Up Schedule

Clinical and Adherence Monitoring Visits:

Once ART is started, follow up schedule should be as follows:

First month: two visits (every 2 weeks)

Second + Third month: every month

Fourth month onwards: one visit every three months

More frequent visits will be scheduled, if the patient develops symptoms or experiences difficulties in adhering to the medications.

2nd week

CBC and Liver Function tests (ALT if on NVP)

Month 1

CBC

LFT if on NVP

Other necessary investigation if and as required

Month 2

CBC

LFT if on NVP

Other necessary investigation if and as required

Month 3

CBC

LFT if on NVP

Other necessary investigation if and as required

Month 6

CBC, platelets

LFTs

CD4 Cell Count

Month 9

CBC and LFT

Month-12

CBC

LFT

CD4 Cell count

Other tests as needed

Subsequent Years:

Quarterly

CBC

Every 6 months

CD4 Cell count

LFT

Other tests as needed

unction should be periodically monitored by means of lbumin/protein.

For a patient who is not responding to treatment, a viral load test and resistance testing will be requested whenever feasible.

If viral load testing becomes readily available, ideal testing schedule would be if virologic failure is suspected and every 6 months after starting ART. Additional pediatric recommendation for viral load monitoring include those babies under 12 months requiring ART containing NVP after exposure to NVP through maternal or infant PMTCT prophylaxis. Pregnant women on ART or ARV prophylaxis near term (36 weeks) who are considering an elective caesarean section should be offered viral load testing, if possible.

Adherence

A high degree of adherence to ARV drugs is necessary for optimal virological suppression. Studies indicate that >95% of the doses should be taken for optimal suppression. Lesser degree of adherence is more often associated with virological failure. Adherence should be assured before initiation of antiretroviral therapy. The patient should fully understand the importance of adherence to antiretroviral therapy. Adherence counseling and patient education should be done at every follow-up visit.

Promoting adherence: Issues to consider

- Health care personnel should be supportive and non-judgmental
- Simplified treatment regimen e.g. twice a day dosing, less number of pills with minimal side effects.
- The motivation of the individual to begin and continue therapy
- The individual's understanding of the importance of adherence and its relationship to drug resistance
- The impact of therapy on the individual's lifestyle and psychological well being
- Education of patient's family and friends.
- The provision of memory aids (such as pill boxes, bleepers, medication record cards, mobile phone messages), to establish and maintain a pill taking routine
- Treatment of any underlying mental health problems
- Management of side effects
- The potential risks and benefits of therapy, both real and perceived, in the short and long term.

o provide support outside the clinic setting, covering the consequences of low adherence.

Advice to patients for missed ARV doses:

- When you notice that you missed a dose, take your pill right away.

For the NEXT DOSE

- If the next planned pill-taking time is four hours away or less, DO NOT take your next dose. Instead wait four hours and then take your next dose. After this follow your regular dosing schedule.
- Do not take two doses at one time.
- If is it already time for the next dose, just take that dose and carry on with the treatment schedule.

Adherence Performance Chart for First Line Regimens in Nepal

Table 6: Zidovudine/Lamivudine (Duovir) Plus Nevirapine

Duovir one pill twice a day PLUS Nevirapine one pill twice a day (total 4 pills/d)

# pills missed in a month	6 or less	7 to 24	25 or more
% Adherence	≥ 95%	80-95%	<80%

Table 7: Triple fixed dose pills: Triommune (d4T/3TC/NVP) or ZDV/3TC/NVP all in one pill

One pill twice a day (total 2 pills/day)

# pills missed in a month	3 or less	4 to 12	13 or more
% Adherence	≥ 95%	80-95%	<80%

us Nevirapine

day PLUS Nevirapine one pill twice a day (total 4 pills/d)

# pills missed in a month	6 or less	7 to 24	25 or more
% Adherence	≥ 95%	80-95%	<80%

Table 9: Zidovudine/Lamivudine (Duovir) Plus Efavirenz

Duovir one pill twice a day PLUS Efavirenz one pill once a day (total 3 pills/d)

# pills missed in a month	4 or less	5 to 18	19 or more
% Adherence	≥ 95%	80-95%	<80%

Table 10: Stavudine/Lamivudine Plus Efavirenz

Stavudine/Lamivudine one pill twice a day PLUS Efavirenz one pill once a day

# pills missed in a month	4 or less	5 to 18	19 or more
% Adherence	≥ 95%	80-95%	<80%

Adherence Performance Chart for Second Line Regimens in Nepal:

Table 11: Tenofovir PLUS Lamivudine PLUS Lopinavir/Ritonavir

Tenofovir one pill once a day PLUS Lamivudine one pill bid PLUS Lopinavir/Ritonaivr two pills bid (total of 7 pills/day)

# pills missed in a month	10 or less	11 to 42	43 or more
% Adherence	≥ 95%	80-95%	<80%

Table 12: Didanosine PLUS Abacavir PLUS Lopinavir/Ritonavir

Didanosine one pill once a day PLUS Abacavir one pill bid PLUS Lopinavir/Ritonaivr two pills bid (total of 7 pills/day)

month	10 or less	11 to 42	43 or more
% Adherence	≥ 95%	80-95%	<80%

Criteria for treatment success

Table 13: Criteria for treatment success

Criteria	Virological	Immunological	Clinical
Marker	Viral load	CD4 cell count	Clinical stage
Time	6 months	6 months	By 12 weeks of treatment initiation should be asymptomatic or have few symptoms.
Suggested ranges	<5,000 copies/ml	Increase from baseline by at least 50-100 cells/mm3	Treatment Stage 1 or 2

Toxicity and failure of Antiretroviral Therapy

Appearance of HIV related opportunistic infections may mean failure of the antiretroviral regimen. Detailed history taking and physical examination should be done at least every 3 months. At the time of follow-up visits, monitoring should be done for CBC, serum ALT, serum creatinine, blood glucose and serum lipids depending on the drug regimen and possible drug adverse effects. Whenever feasible, CD4 count should be performed at least every 6 months. In patients with optimal antiretroviral therapy CD4 counts increase by > 100 cells/mm^3 in the first 6-12 months in ARV naive, adherent patient with drug susceptible virus. Immunologic failure is indicated by a fall in CD4 counts higher than 50% from the peak value or a return to, or below, the pre-therapy baseline, or by persistent CD4 < 100 cells/mm^3.Viral load is available on a limited basis in Nepal. Ideally, viral load will be checked starting at 6 months after ART initiation and rechecked every 6 months (at least once a year). In addition, it should be checked after a history of non-adherence and at the time of suspected clinical or immunologic failure to confirm the presence or absence of virologic failure.

The usual reasons for changing antiretroviral drug regimen include:

Drug adverse effects

Inconvenient regimens (dosing and number of pills that may compromise adherence).

Treatment failure

Occurrence of active tuberculosis and pregnancy.

Concomitant illness (i.e. Hepatitis B)

Table 14. Toxicities of first-line ARVs and recommended drug substitutions

ARV DRUG	COMMON ASSOCIATED TOXICITY	SUGGESTED SUBSTITUTE
Abacavir (ABC)	Hypersensitivity reaction	AZT or TDF
Zidovudine (ZDV) or (AZT)	Severe anaemia or neutropenia Severe gastrointestinal intolerance	TDF or ABC
	Lactic acidosis	TDF or ABC
Stavudine (d4T)	Lactic acidosis Lipoatrophy / metabolic syndrome	TDF or ABC
	Peripheral neuropathy	AZT or TDF or ABC
Tenofovir (TDF)	Renal toxicity (renal tubular dysfunction)	AZT or ABC
Efavirenz (EFV)	Persistent and severe central nervous system toxicity	NVP or ABC (or any PI)
	Potential teratogenicity (first trimester of pregnancy or women not using adequate contraception)	NVP or ABC (or any PI)
	Hepatitis	EFV or ABC (or any PI)

	nsitivity reaction	ABC (or any PI)
	Severe or life-threatening rash Stevens Johnson syndrome	

The general principle is that single-drug substitution because of toxicity should involve drugs belonging to the same ARV class. If toxicity is related to an identifiable drug in a regimen, the offending drug can be replaced with one that does not have the same side-effects (e.g. substitution of AZT or TDF for d4T in cases of neuropathy, TDF for AZT where anemia occurs, or NVP for EFV for CNS toxicity or in first trimester of pregnancy). Given the limited number of ARV drug options available in resource limited settings, drug substitutions should generally be limited to situations where toxicity is moderate to severe (grade 3) or life-threatening (grade 4). In a patient who experiences adverse effects, substitution of the offending drug is reasonable. In case of abacavir hypersensitivity reactions and nevirapine related hepatic failure or severe hypersensitivity, rechallenge should not be attempted as this may lead to toxicity and death.

Antiretroviral Treatment Failure and When to Switch Therapy

The decision on when to switch from first-line to second-line therapy is critical. If the decision is made too early the months or years of potential further survival benefit from many remaining first-line effectiveness is lost; if it is made too late, the effectiveness of second-line therapy may be compromised and the patient is put at additional and appreciable risk of death. The time of switching is dictated by treatment failure, and this can be measured in three ways: clinically, by disease progression and WHO staging; immunologically, using trends in CD4 counts over time, and virologically, by measuring HIV viral loads (plasma HIV-1 RNA levels). Definitions of clinical and CD4-related treatment failure are given below. Nepal will continue to heavily rely on clinical and CD4 count criteria, in order to define treatment failure. It has been recognized that, treatment failure is recognized later solely on the basis of clinical and/or CD4 criteria, thus providing a greater opportunity for drug resistance mutations to evolve before regimen change. This can compromise the use of alternative regimen through drug class cross-resistance. Therefore, viral load will be used when possible to assist with diagnosis of treatment failure (see below). It is not likely that drug resistance testing will become a routine part of clinical care in Nepal in the foreseeable future and so is not considered in these recommendations. In all cases, adherence counseling is indicated and clinical judgment should be included in decision-making.

Treatment Failure

Three types of treatment failures (clinical, immunologic and virologic) have been identified.

Clinical disease progression as an indicator of failure:

Clinical disease progression with development of an opportunistic infection or malignancy when the drugs have been given sufficient time to induce a protective degree of immune restoration is a strong indicator of treatment failure. It should not be concluded, on the basis of clinical criteria, that an ARV regimen is failing until there has been a reasonable trial of first-line therapy lasting at least six to twelve months, adherence has been assessed and optimized, intercurrent opportunistic infections have been treated and resolved, and IRIS has been excluded. IRIS can be seen within the first several weeks after the institution of therapy, if a sub-clinical infection is present at baseline. It is also possible that this immunological reconstitution may lead to the development of atypical presentations of some opportunistic infections. In IRIS, changing the antiretroviral regimen is not indicated. The development of a new or recurrent WHO stage 3 or 4 condition on treatment (but after the first six months of ART) is considered functional evidence of HIV disease progression. TB can occur at any CD4 level and does not necessarily indicate ART failure. The response to TB therapy should be used to evaluate the need to switch ART. With pulmonary TB and some extrapulmonary TB diagnoses (e.g. simple lymph node TB or patients with uncomplicated pleural disease), where a good response to TB therapy is frequently seen, the decision to switch ART can be postponed and monitoring can be increased. This also applies if severe and/or recurrent bacterial infections or oesophageal candidiasis respond well to therapy.

Immunologic failure:

The CD4 cell count remains the strongest predictor of HIV-related complications, even after the initiation of therapy. The baseline pretreatment value is informative: lower CD4 counts are associated with smaller and slower improvements in count. Patients starting with low CD4 counts may demonstrate slow recovery, but persistent levels below 100 cells/mm3 represent significant risk for HIV disease progression. It should be noted that intercurrent infections can result in transient CD4 count decreases. As a general principle, intercurrent infections should be managed, time should be allowed for recovery and the CD4 cell count should be measured before ART is switched. If resources permit, a second CD4 cell count should be obtained to confirm immunological failure.

Definitions of immunological failure are: (1) CD4 count below 100 cells/mm3 after six months of therapy; (2) a return to, or a fall below, the pre-therapy CD4 baseline after six months of therapy; or (3) a 50% decline from the on-treatment peak CD4 value. The CD4 cell count can also be used to determine when not to switch therapy, e.g. in a patient with a new clinical stage 3 event for whom switching is being considered or in a patient who is asymptomatic and under routine framework. In general, switching should not be recommended if the CD4 cell count is above 200 cells/mm3.

of treatment failure:

Viral load testing, when available is a sensitive and informative way to identify treatment failure. When treatment failure is defined on the basis of clinical and/or CD4 criteria the diagnosis may be made later than when viral load is being monitored. Viral load has recently become available in Nepal. The viral load threshold triggering a switch in ART is not clearly defined. Until further data becomes available, viral load failure for Nepal is defined as Viral load >5,000 after 6 months on ART or after previously attaining an undetectable level. An undetectable viral load mandates that ART should not, in general, be switched irrespective of the CD4 cell count or the clinical stage.

All clients being considered for second-line therapy will have their case reviewed by certified National HIV experts. Both decisions of when to change therapy and what regimen to change to should be made in consultation with experts.

Table 15: Clinical, CD4 cell count and virological definitions of treatment failure

CLINICAL FAILURE[a]	New or recurrent WHO stage 4 condition[bc]
CD4 CELL FAILURE[d]	Fall of CD4 count to pre-therapy baseline (or below);
	or 50% fall from the on-treatment peak value (if known);
	or persistent CD4 levels below 100 cells/mm^3 [e]
VIROLOGICAL FAILURE	Persistent plasma viral load above 5,000 copies/ml

a Current event must be differentiated from the immune reconstitution inflammatory syndrome.

b Certain WHO clinical stage 3 conditions (e.g. pulmonary TB, severe bacterial infections), may be an indication of treatment failure and thus require consideration of second-line therapy.

c Some WHO clinical stage 4 conditions (lymph node TB, uncomplicated TB pleural disease, oesophageal candidiasis, recurrent bacterial pneumonia) may not be indicators of treatment failure and thus do not require consideration of second-line therapy.

d Without concomitant infection to cause transient CD4 cell decrease.

e Some experts consider that patients with persistent CD4 cell counts below 50/mm3 after 12 months on ART may be more appropriate.

Clinical status, the CD4 cell count, and the plasma HIV-1 RNA level (if available) can be used in an integrated fashion to determine whether HIV disease is progressing on therapy and whether a change from first-line to second-line therapy should be made. See table below for guidance. Clinical judgment remains an important part of the decision-making process.

TREATMENT FAILURE CRITERIA	WHO STAGE 1	WHO STAGE 2	WHO STAGE 3	WHO STAGE 4
CD4 failure [a] (Viral load testing not available)	Do not switch regimen.	Do not switch regimen.	Consider switching [b] to second-line regimen.	Recommend switching [b] to second-line regimen.
	Follow patient for development of clinical signs or symptoms. Repeat CD4 cell count in three months.	Follow patient for evidence of further clinical progression. Repeat CD4 cell count in three months.		
CD4 failure [a] and viral load failure c	Consider Switching [b] to second-line regimen.	Consider Switching [b] to second-line regimen.	Recommend switching [b] to second-line regimen.	Recommend switching [b] to second-line regimen.

a CD4 failure is defined as a fall to (or below) the pretreatment baseline or a 50% drop from the on-treatment peak level or persistent levels below 100 cells/mm3.
b Switching from first-line to second-line regimen for treatment failure should not be done until the first regimen has been given sufficient time to succeed. This should be a minimum of six months. Since only one second line regimen is available, premature switching should be avoided.
c Virological failure is defined as a plasma HIV-1 RNA level above 5000 copies/ml after a minimum of six months on therapy.

Changing Antiretroviral Treatment for Failure

In case of treatment failure, the entire regimen should be changed from a first to a second line combination regimen. A single drug should not be added or changed to a failing regimen. The new second-line regimen will need to use drugs which retain activity against the patient's virus strain and a minimum of three active drugs, one of them drawn from at least one new class, in order to increase the likelihood of treatment success and minimize the risk of cross-resistance. The PI class is thus reserved for second-line treatments. Ritonavir-boosted protease inhibitors (RTV-PIs) are preferred. They should be supported by two new agents from the NRTI class. Patients should not switch from one NNRTI to the other at the time of failure, as there is a high chance of cross-resistance (ie. do not give EFV after NVP or vice versa).

egimens in adults and adolescents

For failure on:	Change to:
ZDV or d4T + 3TC + NVP or EFV	→ TDF + 3TC + LPV/r [a]
TDF + 3TC + NVP or EFV	→ ddI + ABC + LPV/r [a]

.

a Adult LPV/r tablets do not require cold chain. If a heat-stable affordable version of Atazanavir/ritonavir becomes available, this will be a good choice for use in Nepal. Alternative PI options include SQV/r, IDV/r, FPV/r, if recommended PIs are not available. Note that all of these require refrigeration.

When ZDV or d4T was used in the first line, the best possible second-line regimen is TDF/3TC. The issues of drug hypersensitivity with ABC remain as does the fact that high-level ZDV/3TC co-resistance confers diminished susceptibility to ABC. TDF often retains activity against nucleoside-resistant viral strains. It is attractive in that, like ddI, it is administered once daily. TDF should not be used in combination with regular doses of ddI due to decreased virologic efficacy and increased toxicity. However, it is now acceptable to give TDF with ddI (at 200mg/day if <60kg or 250mg/day if >60kg) in treatment experienced patients on boosted PIs, where no other options exist. In addition, recycling 3TC is now recommended to prolong the common 3TC mutation which makes the virus ñless fitò as one of the best options for second-line therapy.

Because of the diminished potential of almost any second-line nucleoside component, a

ponent, i.e. lopinavir (LPV)/r, saquinavir (SQV)/r or ese, currently, only (LPV)/r is available in a heat-stable form, which does not require refrigeration.

For treatment failure with a first-line PI-based regimen, the choice of an alternative regimen depends on the reason for the initial choice of a PI-based, rather than an NNRTI-based, regimen. If the reason was suspected NNRTI resistance or HIV-2 infection the choice of the alternative regimen is not straightforward. In these situations the options depend on the constraints imposed by the circumstances of individual patients, the capabilities of individual managements to test for resistance to drugs, and the limited ARV formulary in Nepal.

Treatment failure on a triple NRTI regimen is more easily managed because two important drug classes (NNRTIs and PIs) will have been spared. Thus a boosted PI + NNRTI +/- alternative NRTIs (e.g. ddI and/or TDF) can be considered if drug availability permits.

VIII. Monitoring of HIV drug resistance

Individual HIV drug resistance (HIVDR) testing to guide treatment is not recommended.

Population-based HIVDR surveillance of transmitted resistance in recently infected populations for specific areas within resource-restricted countries is the recommended approach. Population-based monitoring of HIV drug resistance where ARVs have been available for over 3 years is another method of carrying out such surveillance.

Monitoring should be done using the "Early Warning Indicators" for HIV drug resistance targeted at ART facilities, which are designed to alert programme managers to programmatic factors that are likely to be associated with poor outcomes of ART.

For a list of the Early Warning Indicators, see Annex VII.

erruption of Anti-retroviral Therapy

Discontinuation of ART may result in viral rebound, immune decompensation, and clinical progression. **Planned ART interruptions are NOT recommended.** Unplanned interruption of ART may become necessary because of severe drug toxicity, intervening illness, surgery that precludes oral therapy, or antiretroviral medication nonavailability. More commonly patients return for care after having stopped their medication on their own, against medical advice for a variety of reasons.

What to do in different scenarios:

- Stopping antiretroviral drugs for a short time (i.e., <1 to 2 days) due to medical/surgical procedures can usually be done by holding all drugs in the regimen.
- When a patient experiences a severe or life-threatening toxicity or unexpected inability to take oral medications ï all components of the drug regimen should be stopped simultaneously, regardless of drug half-life.
- All discontinued regimen components should be restarted simultaneously
- **Discontinuation of efavirenz or nevirapine.** For combinations of NRTIs + NNRTI, the longer half-life of the NNRTI may lead to functional monotherapy if all drugs are discontinued together. This may increase the chance of NNRTI-resistant mutations. The NRTI back-bone can be continued after NVP or EFV is stopped to reduce this. An alternative strategy is to substitute a PI for the NNRTI and to continue the PI with dual NRTIs for a period of time. Given the potential of prolonged detectable NNRTI concentrations for more than 3 weeks, some suggest that the PI-based regimen may need to be continued for up to 4 weeks.
- **Reintroduction of nevirapine using dose escalation**. Because nevirapine is an inducer of the drug-metabolizing hepatic enzymes, administration of full therapeutic doses of nevirapine without a 2-week, low-dose escalation phase will result in excess plasma drug levels and potentially increase the risk for toxicity. Therefore, in a patient who has interrupted treatment with nevirapine for more than 2 weeks, nevirapine should be reintroduced with a dose escalation period of 200mg once daily for 14 days, then a 200mg twice-daily regimen.

e or tenofovir in patients with hepatitis B coinfection.

tion who are receiving one or both of these NRTIs may experience an exacerbation of hepatitis upon drug discontinuation

y in Pregnancy

ARV regimens given for treatment to pregnant women should preferably include drugs shown to be effective in reducing mother-to-child transmission. First-line treatment regimens in pregnant women should include ZDV whenever possible. Combination of ZDV/3TC has been recommended as the first choice for use in pregnancy. ABC has not been formally evaluated in pregnant women. There is potential increased risk of lactic acidosis with the combination of d4T/ddI in pregnant women, so this combination should be avoided. NVP is the choice for use in pregnancy. EFV is contraindicated in the first trimester of pregnancy. PIs have been associated with the development of glucose intolerance and even diabetes mellitus in non-pregnant individuals. Among PIs, Lopinavir/ritonavir is the first choice PI for use during pregnancy. Antiretroviral therapy should be started as soon as possible in pregnancy. ART should not be stopped during first trimester due to risk of viral rebound and decline in CD4, risking maternal disease progression and increasing transmission.

Prevention of Mother-to-Child Transmission (MTCT) of HIV

The area for PMTCT of HIV is one of the most rapidly evolving in all of HIV care. Please refer to the most up-to-date version of Nepal National Guidelines. Information below is based on those released in 2008, which may quickly become obsolete.

Comprehensive 4 Prong Strategy for PMTCT of HIV

1. Prevent HIV Infection among Women of Child-bearing age.
2. Prevent unintended pregnancies among women living with HIV
3. Prevent HIV transmission from HIV infected mothers to their infants
    1. Antiretroviral prophylaxis for mother and baby
    2. Safer delivery practices
    3. Safer infant feeding choices
4. Provide appropriate treatment, care and support to women living with HIV and their children and families

When to commence full HAART in pregnancy: as in other non-pregnant adults

Initiate highly active antiretroviral therapy (HAART) in any pregnant woman with:

- WHO Stage 4 disease, irrespective of CD4 cell count
- WHO Stage 3 disease, irrespective of CD4 cell count
- WHO Stage 1 or 2 disease with CD4 count less than 350/mm3*

f pregnant women, given the potential to decrease HIV transmission to
s from short course ARVs. Pregnant women needing ART, should start
ART as soon as possible.

* This was updated from 2008 Nepal PMTCT guidelines to correlate with these new ART indications.

The standard HAART regimen in pregnancy is: ZDV + 3TC + NVP

Efavirenz can be used after the first trimester of pregnancy and may be preferred in women with higher CD4 counts. NVP should not be used in those with CD4 over 350 and only used with caution in those between 250 and 350 due to risk of liver toxicity. All pregnant women taking NVP need close monitoring of liver function. Because of the risk of HIV drug resistance, pregnant women with indications for ART should not be prescribed the short-course PMTCT regimens below, unless ART is unavailable.

Table 17: Recommended First-Line HAART Regimen for treating Pregnant Women, and Prophylactic Regimen for Infants

Recipient	Timing	ARV(s)
Mother	Start ASAP in pregnancy and continue throughout pregnancy, labour and delivery and postpartum, for life	ZDV 300mg + 3TC 150mg twice a day + NVP 200mg once a day for 14 days (if CD4 <250) If no reaction, continue ZDV + 3TC and increase NVP to 200mg twice a day after 14 days
Baby	Neonatal	Infant ZDV 4 mg/kg twice a day for 7 days If the mother has received less than 4 weeks of HAART, infant DV should be continued for 4 weeks
Note: EFV is preferred after the first trimester in women with CD4 >250, and especially those with CD4 over 350.		

Antiretroviral prophylaxis for mother and baby (when mother does not yet need ART)

The risk of HIV transmission to the baby can be reduced to 2% or less if the mother takes ARVs during the antenatal period (starting no later than 28 weeks of pregnancy), and with careful management of the delivery and provision of ARVs to both mother and baby for a short time following delivery.

The absolute minimum standard regimen for PMTCT in community settings is sdNVP for both mother and baby. Community settings include home delivery and delivery at a Primary Health Care facility or Sub-Health Post.

Table 18: Delivery at Home or at a PHC Facility or Sub-Health Post

Recipient	Timing	ARV(s)
Mother	Intrapartum	NVP 200mg once at the onset of labour If woman presents in established labour, give NVP as soon as possible in the first stage of labour
Baby	Neonatal	Infant NVP 2 mg/kg as soon as feasible (preferably within 12 hours, but no later than 72 hours following delivery)

The Recommended PMTCT Protocol (Nepal PMTCT Guidelines 2008)

Provided HIV infection is diagnosed no later than the second trimester of pregnancy, antenatal support and follow-up are available, and delivery takes place in a hospital or other health facility with trained staff and ARVs available, HIV-infected pregnant women should be offered the standard recommended regimen:

- Antenatal ZDV from 28 weeksôgestation
- In labour, ZDV every 3 hours+ 3TC every 12 hours + sdNVP.
- Postpartum one-week ñtailòof ZDV + 3TC to the mother to prevent NVP resistance (due to the long half-life of NVP).
- The baby receives sdNVP plus a one-week course of infant ZDV.

Table 19: Recommended Standard PMTCT Protocol for Mother and Baby

Recipient	Timing	ARV(s)
Mother	Antepartum	ZDV 300mg twice daily from 28 weeksô gestation
	Intrapartum	ZDV 300mg at the onset of labour and 3-hourly until delivery *plus* 3TC 150mg at the onset of labour and 12-hourly until delivery *plus* NVP 200mg once at the onset of labour
	Postpartum	ZDV 300mg + 3TC 150mg twice daily for 7 days
Baby	Neonatal	Infant NVP 2 mg/kg as soon as feasible (preferably within 12 hours, but no later than 72 hours following delivery) *plus* Infant ZDV 4 mg/kg twice daily for 7 days

Special situations

Anaemia

ZDV may cause anaemia and neutropenia. Investigate for and treat any underlying causes of severe anaemia (Hb < 7 g/dl) or neutropenia. If there are indications for HAART, other NRTI drugs (d4T or ABC) may be substituted for ZDV.

HIV Infection diagnosed after 28 weeks

Commence the Standard PMTCT Protocol for the mother as soon as possible.

For the baby, give neonatal sdNVP + ZDV as usual. If the mother has received less than 4 weeks of ZDV, extend the babyôs postnatal ZDV to four weeks.

HIV-Infected Women in Labour who have not received Antenatal ARV Prophylaxis

At health facilities where full PMTCT interventions are available, commence the Standard PMTCT Protocol for the mother in labour and continue postpartum. The baby should receive sdNVP plus postnatal ZDV prophylaxis for four weeks

To avoid unintended, unplanned pregnancies among HIV positive couples, careful reproductive health and family planning counseling is essential for all people living with HIV.

- Condoms: Male (or female) condoms are the only contraceptive method that can provide ñdual protectionò against STIs and HIV, and are therefore most commonly recommended where one or both partners are infected with HIV.
- Oral Contraceptives: NNRTIs (NVP and EFV) and PIs lower blood concentrations of oral contraceptives. A back-up method (i.e. condoms) should be recommended if woman is taking NNRTI or PI containing ART. Rifampicin or anticonvulsant medications (other than valproic acid), other medications that reduce the absorption of OCPs, including broad spectrum antibiotics or having severe diarhhoea, can all reduce the absorption of OCPs.
- Injectable (Progesterone only) contraceptives: Injectable progestogen is a suitable form of contraception for women with HIV infection, including those on ART. NVP has been found to not interfere with implants contraceptive efficacy. Again condoms should be used to provide ñdualòprotection.
- Emergency Contraception: If taken within 5 days of unprotected intercourse emergency contraceptive pills (ECP) reduce the risk of pregnancy by at least 75%. Two regimens include: Progestin-only tablets and combined oestrogen-progestin tablets. Like other hormonal contraception, ECPs do not provide any protection from STI or HIV transmission. Consistent use of condoms is needed in addition.
- ECPs contain higher doses of hormones than regular OCPS, so their effectiveness may not be reduced by ARV drugs.
- For HIV positive women who have unprotected sex and are at risk of unwanted pregnancy, access to ECP is essential.
- Intra-Uterine Contraceptive Device (IUD): IUD may be either initiated or continued in women with HIV in WHO Stage 1 or 2 or already on ART. If a woman with IUD in place develops WHO Stage 3 or 4 disease, she can continue to use while on ART. HIV positive women who are clinically ill should not have an IUD placed. Consistent use of condoms is also needed.
- Male and Female Sterilization: Sterilization is highly recommended for family planning for PLHA. Informed voluntary choice is essential. Consistent use of condoms is needed in addition.
- Lactational Amenorrhoea Method: Only effective if exclusively breastfeeding during the first 6 months after delivery and continues to have no menstruation. Risk of HIV transmission must be discussed. At 6 months postpartum family planning must be readdressed.

PLHA who do not want more children should be counseled thod of contraception.

Breast-feeding

Breastfeeding, in particular exclusive breastfeeding, is the ideal way to feed infants and it should be protected, promoted and supported. Beyond sound nutrition, it protects against common childhood infections. However, as it is one of the routes for mother-to-child HIV transmission, HIV-infected women need to consider carefully the following information about relative risks and benefits to their babies of breastfeeding, compared with alternatives.

- Most children with HIV are infected as a result of transmission of HIV infection from their mothers.
- Mother-to-child (vertical) transmission can occur before or during birth, or after birth through breastfeeding. The risk of transmission of HIV through breastfeeding varies in relation to maternal clinical and immunological status, plasma and breast milk viral load and possibly breast health (subclinical or clinical mastitis, cracked nipples etc)
- The rate of mother-to-child transmission of HIV in the absence of preventive interventions is about 15-25% without breastfeeding and 25-40% with breastfeeding.
- Mother-to-child transmission can occur late in breastfeeding.
- Acute HIV infection during breastfeeding increases the risk of transmission.
- Lack of breastfeeding has been shown to increase the risk of malnutrition and life-threatening infectious diseases other than HIV, especially in the first year of life and exclusive breastfeeding appears to offer protection.
- Mixed feeding (defined as breast milk plus water, other fluids and foods) is associated with 11-fold increased risk of infant HIV infection when compared with exclusive breastfeeding.

Recommendations on infant feeding to babies born to HIV positive mothers:

- Exclusive breast feeding is recommended for infants of HIV-infected woman for the first six months.
- After 6 months, culturally appropriate complimentary foods (weaning) is started and mother is advised to stop breast feeding as early as possible.
- If a child is diagnosed as HIV-infected, the mother should be encouraged to continue breastfeeding the child beyond six months of age along with the addition of complementary foods.

or require ART, breastfeeding should continue along with

XI. Tuberculosis and Antiretroviral Therapy

The life time risk of someone with latent TB developing TB disease in HIV negative individual is 5-10% where as in HIV positive individual it is up to 50%. Managing TB among HIV infected individuals thus is one of the major responsibilities of the ART clinician.

Intensified case finding

As TB is one of the most common opportunistic infection among the HIV infected people, all clients diagnosed HIV positive in VCT centers and all HIV positive people visiting ART centers should be screened for TB using a standard screening process.

Key screening questions

1.	Has the client been coughing for > 2 weeks?	Yes	No
2.	Has the client been having night sweats for > 2 weeks?	Yes	No
3.	Has the client had loss of appetite for > 2 weeks?	Yes	No
4.	Has the client lost > 3kg during the last 4 weeks?	Yes	No
5.	Has the client been having fever or "evening rise in temperature" for > 2 weeks?	Yes	No
6.	Has the client had close contact with a tuberculosis patient?	Yes	No
7.	Has the client had a past history of TB within the last 2 years?	Yes	No

If "Yes" to question 1: do sputum tests for AFB stain and continue evaluation of client including CXR.

If "No" to question 1 and "yes" to any other question**:** continue investigation for tuberculosis according to clinical signs.

If "No" to all questions: stop investigation for tuberculosis and repeat TB screening in 3 months at follow-up visit.

Ask the client to report immediately if any of the above mentioned symptoms occur.

Isoniazid Preventive Therapy (IPT)

IPT refers to taking 6 months of isoniazid daily for latent TB infection regardless of CD4 cell count or ART status.

new HIV infected clients at their first visit with TB screening questionnaire, a full initial history and physical examination,

- After introduction of questionnaire, send anyone found positive for any question of the screening form for chest X ray (CXR) and other investigations as needed.
- If there are any signs of active TB or any concerns about unexplained illness, do NOT offer IPT, but refer client to TB doctor or supervising doctor as appropriate.
- All PLHA without active TB or other unexplained illness are offered IPT with appropriate counseling.

Initiating IPT:

- Explain the IPT program to the client and assess predicted adherence to 6 months of Isoniazid.
- Cotrimoxazole and ART should not be started at the same time as IPT.
- Those with liver disease, active alcohol use, jaundice, TB diagnosed in the past 3 years, habitual treatment defaulter, prior Isoniazid resistance and possible pregnancy should be excluded.
- DOT is not needed for IPT

IPT Regimen:

Isoniazid 300 mg daily for 6 months, Vitamin B6 25 mg (pyridoxine) should be given together with IPT for 6 months. Children should receive Isoniazid 5mg/kg daily.

Follow-up visits while on IPT:

- Client must be seen every month for adherence check, side effect check and medication refill.
- Ask about symptoms of breakthrough TB at each visit. If any occur, evaluate for TB.

Patterns of HIV-related TB

Pulmonary TB

Even in HIV-infected patients, PTB is still the commonest form of TB. The presentation depends on the degree of immunosuppression. The table below shows how the clinical picture, sputum smear result and CXR appearance often differ in early and late HIV infection.

rly and late HIV infection

	Stage of HIV Infection	
	Early	Late
Clinical Picture	Often resembles post-primary PTB	Often resembles primary PTB
Sputum smear result	Often positive	Often negative
CXR appearance	Often cavities	Often infiltrates with no cavities

Extrapulmonary TB

The commonest forms of extrapulmonary TB are: pleural effusion, lymphadenopathy, pericardial disease, miliary disease, meningitis, disseminated TB (with mycobacteraemia).

TB treatment in HIV

Effective treatment and control of TB is a central priority when developing treatment strategies for co-infected patients. Tuberculosis treatment following the DOTS strategy should be initiated promptly in diagnosed cases of TB. All PLHA with TB need ART. Suggestions for timing of initiation of ART for TB patients in different situations is given in following table:

Table 21: Strategy for initiation of treatment for both TB and HIV infection

Criteria	Strategy	
	TB treatment	ART
Extrapulmonary TB (regardless of CD4 count)	Start immediately	Start ART as soon as TB treatment is tolerated (two weeks after ATT initiation)
Pulmonary TB CD4 <100 cells/mm3	Start immediately	
Pulmonary TB CD4 100-350 cells/mm3	Start immediately	Start ART 2 months after ATT start
Pulmonary TB CD4 >350 cells/mm3	Start immediately	Start ART after 6 months of ATT or at the end of ATT.
Pulmonary TB No CD4 available	Start immediately	Start ART as soon as TB treatment is tolerated (between two weeks and two months)

ART drug choice in TB co-infection:

- First line treatment option is ZDV/3TC or TDF/3TC plus Efavirenz (600mg once daily).
- Dose increase of Efavirenz is no longer recommended during ATT.
- The first alternative is ZDV/3TC plus Abacavir.
- The second alternative is ZDV/3TC or TDF/3TC plus Nevirapine for those unable to take EFV or ABC. Rifampicin decreases Nevirapine levels by hepatic induction, which potentially could lead to lower anti ï HIV efficacy. There are also concerns of additive liver toxicities.

containing regimens may be considered. One exception is should not be given NVP along with Rifampicin.

Patients already receiving ART when they develop TB should adjust the regimen to be compatible with TB treatment. Following completion of anti-tubercular therapy the ART regimen can be continued or changed depending upon the clinical and immunologic status of the patient.

Second line ART and TB- coinfection: Drug choices: Use of Rifabutin in TB-HIV co-therapy

The HIV pandemic has led to a resurgence of tuberculosis and the challenge of TB-HIV co-therapy for patients on second-line ART is well recognized. Management of co-infected patients has shown that TB can be cured with standard antituberculosis regimens, including the use of rifampicin-based TB treatment for 6 months. Preliminary evidence and experience has confirmed recommendations in WHO guidelines that for most patients, especially those with CD4 counts < 100 cells/mm3, HIV treatment should not be delayed, but should be started or continued alongside TB treatment. It is expected that many patients will fail first-line ART with active TB; and TB will develop in patients on second-line therapy. However, because of well recognized drug-drug interactions, it is difficult to use Rifampicin with any boosted PI-based regimens. For patients who need antituberculosis treatment in Nepal and who need a boosted PI, the only option is:

Substitute rifabutin for rifampicin in the anti-TB regimen and maintain the standard PI-based ART regimen. WHO suggests Rifabutin dose of 75mg daily when taken with LPV/r containing ART.

tion and ART

by following ALT regularly. If ALT is elevated, check full liver function tests. If transaminases are >5 times the upper limit of normal, carefully evaluate for signs and symptoms of liver insufficiency and for alternative causes of liver injury (e.g., acute viral hepatitis A or B infection, hepatobiliary disease, or alcoholic hepatitis); short-term ART interruption may be required.

Although Hepatitis C treatment is currently not available in Nepal, PLHA may access it internationally. Concurrent treatment of both HIV and HCV is feasible but may be complicated by pill burden, drug toxicities, and drug interactions such as the following:

- Didanosine should not be given with ribavirin because of the potential for drug-drug interactions leading to life-threatening ddI-associated mitochondrial toxicity including hepatomegaly/steatosis, pancreatitis, and lactic acidosis
- Zidovudine should be avoided with ribavirin when possible because of possible anemia. If no alternatives, ribavirin dose reduction is necessary.
- Drug-induced liver injury from ART is more common in HIV/HCV coinfection.
- Stavudine (with or without didanosine) and nevirapine are the ARVs available in Nepal, most likely to cause liver injury.

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XIII. Hepatitis B co-infection and ART

All PLHA with Hepatitis B co-infection requiring treatment should be started on ART irrespective of CD4 cell count or WHO clinical stage. All should be started on TDF + 3TC as the NRTI backbone. Beware of potential for liver flare if 3TC or TDF are discontinued.

XIV. Immune Reconstitution Inflammatory Syndrome (IRIS)

Immune Reconstitution Inflammatory Syndrome is a spectrum of clinical signs and symptoms resulting from the restored ability to mount an inflammatory response associated with immune recovery. It can present with the signs and symptoms of a previously subclinical and unrecognized opportunistic infection, as a paradoxical worsening of treatment response several weeks into therapy, or as an autoimmune disease in the context of immune recovery on ART. Typically, IRIS occurs within two to twelve weeks of the initiation of ART, although it may present up to 24 weeks after ART initiation. The incidence of IRIS is estimated to be 10%-32% of adults initiating ART. There is a higher risk in those starting ART with lower CD4 counts.

by fever, lymphadenopathy, worsening pulmonary lesions ntral nervous system (CNS) lesions, elevation of hepatic enzymes (Hep B co-infection), skin lesions or signs of autoimmune diseases. Sometimes, a brief course of corticosteroids may be required to reduce inflammation for severe respiratory or CNS symptoms. Prednisolone (or prednisone) at 0.5 mg/kg/day for five to ten days is suggested in moderate to severe cases of IRIS. Steroid doses have to be adjusted upwards when using together with microsomal enzyme enhancers like Rifampicin.

XV. Cotrimoxazole Prophylaxis in Adults

All PLHA should be evaluated for possible need for Cotrimoxazole prophylaxis, even in areas without ART accessibility, or in the time that they are preparing for ART initiation.

Cotrimoxazole prophylaxis should be given to:

- HIV infected adults with CD4 count <350 cells/mm^3
- All adults who have had an episode of PCP
- All adults with symptomatic HIV disease or Clinical stage 2, 3 or 4

The regimen is:
1 DS tablet (160TMP/800SMX) every day OR

2 SS tablets (80TMP/ 400SMX) every day

1. Continue Cotrimoxazole prophylaxis as follows:
    - Lifelong, if not on ART
    - If on ART the CD4 is >350 on two consecutive samples 6 months apart, Cotrimoxazole can be discontinued.
    - Stop prophylaxis for severe cutaneous reactions, such as Stevens-Johnson syndrome, renal and/or hepatic failure, and severe hematological toxicity.

2. Timing of Cotrimoxazole prophylaxis in relation to ART initiation: Since the most common initial side effect of cotrimoxazole and antiretroviral therapy (especially nevirapine and efavirenz) is rash, it is recommended to start cotrimoxazole prophylaxis first and to initiate antiretroviral therapy two weeks later if the individual is stable on cotrimoxazole and has no rash. Do NOT start Cotrimoxazole and ART at the same time.

e, consider the following alternatives:

- Dapsone 100 mg once daily is the first choice.

OR

- In cases of non-life -threatening adverse reactions, stop treatment for two weeks; then re-challenge the client with TMP/ SMX in a gradually increasing dose of an oral suspension of TMP/SMX. After desensitization under surveillance, up to 70 percent of clients may again tolerate TMP/SMX.

Table 22: Protocol for co-trimoxazole desensitization among adults and adolescents

STEP	DOSE
DAY 1	80 mg sulfamethoxazole + 16 mg trimethoprim (2 ml of oral suspension[a])
DAY 2	160 mg sulfamethoxazole + 32 mg trimethoprim (4 ml of oral suspension[a])
DAY 3	240 mg sulfamethoxazole + 48 mg trimethoprim (6 ml of oral suspension[a])
DAY 4	320 mg sulfamethoxazole + 64 mg trimethoprim (8 m of oral suspension[a])
DAY 5	One single-strength sulfamethoxazole-trimethoprim tablet (400 mg sulfamethoxazole + 80 mg trimethoprim)
DAY 6 ONWARDS	Two single-strength sulfamethoxazole-trimethoprim tablets or one double strength tablet (800 mg sulfamethoxazole + 160 mg trimethoprim)

a Cotrimoxazole oral suspension is 40 mg trimethoprim + 200 mg sulfamethoxazole per 5 ml.

1. Follow-up of clients on Cotrimoxazole prophylaxis every month.
    - Monitor for toxicity, clinical events and adherence.
    - Lab tests of hemoglobin and white blood counts, only as indicated.

2. Adherence counseling on Cotrimoxazole can be useful to help prepare clients for ART in the future and problem-solve barriers to medication adherence.

3. If prophylaxis has been stopped because of immune improvement, Cotrimoxazole prophylaxis (or Dapsone) should be recommenced if the CD4 cell count falls below 350 or if new or recurrent WHO clinical stage 2, 3 or 4 conditions occur.

4. Use an alternative antibiotic for treating breakthrough bacterial infections among individuals living with HIV receiving cotrimoxazole prophylaxis, while continuing cotrimoxazole.

nfections, prophylaxis should be suspended and full active
rophylaxis should be recommenced after the treatment course.

XVI. Post Exposure Prophylaxis (PEP) of HIV

Post Exposure Prophylaxis (PEP) is currently the only way to reduce the risk of HIV infection in someone exposed to the virus. It refers to the use of antiretroviral medications to help prevent HIV transmission. The rationale is that ARVs given immediately after exposure can stop the virus from disseminating in the body and establishing infection.

The majority of occupational exposures do not lead to HIV infection. The risk of HIV transmission following skin puncture from a needle or other sharp object that was contaminated with a blood from a person with ñdocumentedò HIV infections is about 0.3%. The risk of HIV transmission is less with injuries sustained with solid bore (e.g. suture) needles than with hollow bore (e.g. blood drawing) needles. Similarly, the smaller the size of hollow bore needle, the less risk of HIV transmission. There have been rare reports of health workers who have become infected by exposure of mucous membrane (of eyes, nose or mouth) or abraded (broken) skin to HIV-infected material; the risk, is estimated to about 0.09%. HIV is not transmitted through healthy intact skin.

1. First aid immediately after potential exposure:

The aim of first aid is to reduce contact time with the source personôs blood, body fluids or tissues and to clean and decontaminate the site of the exposure.

If the skin is broken following an injury with a used needle or sharp instrument, the following is recommended.

- Do not squeeze or rub the injury site.
- Wash the site immediately using soap or a mild disinfectant solution that will not irritate the skin.
- If running water is not available, clean the site with a gel or other hand-cleaning solution, whatever is customarily available.
- Do not use strong solutions, such as bleach or iodine, to clean the site as these may irritate the wound and make the injury worse.

After a splash of blood or body fluids on broken skin, the following is recommended:

- Wash the area immediately.

le, clean the area with a gel or other hand- rub solution,

- Do not use strong disinfectants.

After a splash contacts the eye, do the following.

- Irrigate the exposed eye immediately with water or normal saline.
- Sit in a chair, tilt the head back and have a colleague gently pour water or normal saline over the eye, pulling the eyelids up and down to make sure the eye is cleaned thoroughly.
- If contact lenses are worn, leave these in place while irrigating the eye, as they form a barrier over the eye and will help protect it. Once the eye has been cleaned, remove the contact lenses and clean them in the normal manner. This will make them safe to wear again.
- Do not use soap or disinfectant on the eye.

After a splash contacts the mouth, do the following.

- Spit the fluid out immediately.
- Rinse the mouth thoroughly, using water or saline, and spit again. Repeat this process several times.
- Do not use soap or disinfectant in the mouth

Indications for Post Exposure Prophylaxis

1. The exposed person is HIV-negative
2. The source person is HIV positive, or at high risk of recent infection and thus likely to be in the window period.
3. The exposure poses a risk of transmission, that is:
    a. Percutaneous exposure to potentially infectious body fluids (non-infectious body fluids include faeces, saliva, urine and sweat)
    b. Sexual intercourse without an intact condom
    c. Exposure to non-intact skin or mucus membranes to potentially infectious body fluids
4. The exposure occurred less than 72 hours previously.
5. The exposure is not part of chronic exposure (prevention support needed instead)

type of regimen:

The decision to start PEP is made on the basis of degree of exposure to HIV and HIV status of the source from whom exposure has occurred. Decisions should be made based in part on information about the source, including ART, response to therapy, including viral load, and any data on HIV resistance testing. Decisions should not delay initiation of PEP, and modifications can be made after information is obtained. If the HIV status of the source is not known, HIV testing of the source could be done after necessary counseling. In any case, if the risk is high, PEP should be started immediately. If the HIV test results of the source are found to be negative, PEP can be discontinued. Specific recommendations for PEP are given in the two tables below, one for percutaneous injuries and the second for exposures to mucous membranes or non-intact skin.

Table 23: HIV PEP for percutaneous injuries

Exposure	Status of Sources		
	Low Risk*	High Risk*	Unknown
Not severe: Solid needle, superficial	2 drug PEP[Å]	3 drug PEP[Å]	Usually none: Consider 2 drug PEP
Severe: Large bore, deep injury, visible blood on device, needle in patientôs artery/vein	3 drug PEP[Å]	3 drug PEP[Å]	Usually none: Consider 3 drug PEP

*Low risk: Asymptomatic HIV or VL < 1500 c/ml. High risk: Symptomatic HIV/AIDS, acute seroconversion, high VL.

Concern for drug resistance: Initiate prophylaxis without delay and consult an expert.

Consider 3 drug PEP if source is high risk for HIV or exposure from unknown source when HIV infected source is likely.

Table 24: HIV PEP for Mucous Membrane and Non-Intact Skin Exposures*

Exposure	Status of Sources		
	Low Risk*	High Risk*	Unknown
Small volume (drops)	consider 2 drug PEP	2 drug PEP	Usually no PEP: Consider 2 drug PEP
Large volume (major blood splash)	2 drug PEP	3 drug PEP	Usually no PEP Consider 2 drug PEP

*Non-intact skin = dermatitis, abrasion, wound

Low risk = Asymptomatic or VL < 1500 c/ml High, risk = symptomatic HIV, AIDS acute seroconversion, high HIV viral load.

factors or exposure from unknown source where HIV infected source is

Drug Selection for PEP

There are two types of regimens recommended for PEP. They are the basic regimen of two drugs combination and expanded regimen of three drugs as given below:

Regimens for PEP

2 DRUG COMBINATIONS (BASIC REGIMEN)

ZDV + 3TC

3 DRUG COMBINATIONS (EXPANDED REGIMEN)

2 nucleosides (as above) + LPV/r

Alternative to ZDV is d4T, in the case of anemia.

Alternatives to LPV/r include: ATV/r, SQR/r and FosAPV/r, if available.

Note: NVP should not be used for PEP due to risk of hepatotoxicity.

- If PEP is given, the exposed person should have a baseline Hemoglobin test, if Zidovudine is used as part of PEP.
- HIV Antibody testing (rapid or ELISA) should be used to monitor for seroconversion, and test should be performed at baseline and at 3 and 6 months post exposure.
- Testing for other bloodborne diseases ï such as hepatitis B and C ï is also important; depending on the nature of the risk and the local prevalence, if testing is available.

posure prophylaxis

In the process of seeking informed consent for HIV post-exposure prophylaxis, people who have been exposed to HIV must be made fully aware of the following:

- the risk of acquiring HIV infection from the specific exposure;
- what is known and not known about the efficacy of PEP;
- the importance of taking a HIV test and of receiving appropriate post-test counseling (although testing may be delayed if necessary);
- the possibility that they might already be infected with HIV will need to be assessed if they have not already had an HIV test;
- people already living with HIV should be referred for treatment of their infection, and if they had started PEP the medicine should be stopped when the diagnosis is confirmed;
- people with discordant rapid HIV test results should be offered PEP while waiting for pending laboratory-based confirmatory testing;
- PEP medication will be discontinued if their initial HIV test is positive: this medication does not work for people living with HIV and could increase the risk of drug resistance among people already infected;
- the importance of adhering to medicine;
- what to do if they forget or vomit a dose (see ART adherence section)
- the duration of the course of medicine (four weeks);
- the common side effects that may be experienced while taking PEP medicine;
- that they can stop taking PEP medicine at any time, but if they do so, they will probably not get the full benefit of PEP if the source to which they were exposed was HIV positive;
- PEP medicine can be taken during pregnancy and may protect the mother from getting HIV infection after exposure;
- that continuing to breastfeed while taking PEP is safe, although if women get infected by HIV while breastfeeding, the risk of transmitting HIV through breastfeeding is higher at the early stage of infection; appropriate counselling should discuss safe alternatives to breastfeeding if they are acceptable, feasible, affordable and sustainable; and exclusive breastfeeding is strongly recommended whenever alternatives are not possible.

PEP following rape

There are no available data about the use of PEP following rape. But if the risk of transmission of HIV is considered to be present, PEP, as used for health workers after

taking into account various factors, including drug toxicity

PEP for non-occupational exposure other than rape:

For non-occupational exposure other than rape, clinician will decide on a case-by-case basis whether PEP should be provided. It should not be provided in the case of chronic HIV exposure or cases of ñrecreational exposureò Provider may decide to provide PEP in some cases, such as an episode of condom breakage in a discordant couple.

Where should PEP be available in Nepal?

- Drugs for PEP should be made available in every hospital and in cases treatment should be immediately initiated. Further management must be decided by an expert as soon as possible.

- Starter packs of between 2 and 5 days of ARVs can be placed in medical facilities with linkages to full PEP packages. These can be prescribed under the condition that the client return to see a designated provider for complete risk assessment and to collect the rest of the 28 days of medicine. This helps prevent large wastage due to expiry of unused PEP packs.

of HIV post-exposure prophylaxis: Summary

Item	Recommended action and notes
Eligibility	Exposure within 72 hours Exposed individual not known to be infected with HIV Significant exposure Person who was the source of exposure is HIV infected or has unknown HIV status
Informed consent for post-exposure prophylaxis	Information about risks and benefits Consent may be given verbally
Medicine	Two nucleoside-analogue reverse-transcriptase inhibitors (usually part of first-line antiretroviral therapy medicines) Dispensed by appropriately qualified person Add a boosted protease inhibitor to the regimen if higher risk exposure.
Time to initiation	The initial dose of antiretroviral medicines should be given as soon as possible but no later than 72 hours after exposure
Duration of therapy	28 days
HIV testing with informed consent and pre- and post-test counseling	Baseline HIV test in exposed person Follow-up HIV testing 3 and 6 months after exposure Rapid HIV test of the source person if feasible and based on informed consent
Additional laboratory evaluations	Pregnancy testing Haemoglobin (for ZDV-containing PEP regimens) Hepatitis B and C screening, if available and based on the prevalence of the diseases
Counseling	For adherence; side effects; risk reduction; trauma or mental health problems; and social support and safety
Referral	Referrals as appropriate
Record-keeping	Maintain accurate, confidential records
Follow-up– clinical	Assess and manage side effects Assess and support adherence

I. Diagnosis of HIV Infection in Children

Laboratory Diagnosis of Pediatric HIV Infection

There are three types of tests available to confirm HIV infection in children and to monitor the progress of disease.

1. HIV antibody testing continues to be the backbone; however it is of more limited use in children aged <18 months, who may still be carrying passively transferred maternal HIV antibodies.
    - All infants born to HIV infected mothers will test antibody positive at birth.
    - However, children over 12 months of age have usually lost maternal antibody. If ELISA is positive after 12 months of age, there is a 96% chance the child is HIV-infected.
    - All exposed infants should be tested at 9 months during the time of measles vaccination. Those tested positive should be referred to sites where DNA PCR tests are available for early infant diagnosis.

2. Virological tests are needed to confirm HIV infection in children less than 18 months of age.
    - DNA PCR is the most common virological test for definitive diagnosis in infants (qualitative).
    - RNA PCR (quantitative) also called Viral Load is most commonly used to follow response to ART.
    - Virological tests become positive much earlier than antibody tests.
    - If tested at 6 weeks almost all infants infected intrauterine and peripartum will be positive.
    - Recently, Dried Blood Spot (DBS) has been found to be reliable for DNA PCR and allows finger or heel-stick collection along with ease of transportation of the sample to a central laboratory from other parts of the country.
    - If DNA PCR is available, optimum time to test is at 6 weeks of life. Those testing negative should have DNA PCR repeated 6 weeks after breastfeeding cessation. All infants should undergo HIV antibody testing for confirmation at 18 months of age.

CD4%) contribute enormously to care and treatment

- CD4 cell count is a good predictor of progression of HIV disease.
- CD4% is the percent of total lymphocytes that are made up of CD4 cells. This is more useful for children under 5 years of age than the absolute CD4 count because CD4 count fluctuate with concurrent illness, physiological changes and timing of test. However where CD4% facilities are not available absolute CD count can be determined and age specific CD4 count criteria used.

Note: Breastfeeding further complicates diagnosis in children. Antibody and virological tests must be performed at least 6 weeks after the cessation of breastfeeding for accurate diagnosis.

- Combining clinical and laboratory criteria to stage HIV disease ensures timely and rational initiation of care, treatment, and appropriate counseling.

- Definitive HIV diagnosis in children >18 months can be performed with antibody tests, following standard testing algorithms as used for adults.

Presumptive clinical diagnosis of HIV infection

For infants and children aged less than 18 months where access to laboratory testing is not available but a child has symptoms that are suggestive of HIV infection, a presumptive clinical diagnosis of HIV infection may need to be made as follows:

Criteria for presumptive clinical diagnosis of severe HIV disease in infants and children aged under 18 months in situations where virological testing is not available:

A presumptive diagnosis of severe HIV disease should be made if:

- Infant is confirmed HIV-antibody positive; and
- Diagnosis of AIDS-indicator condition(s)a can be made
- or
- the infant is symptomatic with two or more of the following:
    - Oral thrush
    - Severe pneumonia
    - Severe sepsis

Other factors that support the diagnosis of severe HIV disease in an HIV seropositive infant include:

d maternal death or Advanced HIV disease in the mother.

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

II. Anti-Retroviral Therapy (ART) in Infants and Children

The advent of potent antiretroviral therapy has dramatically reduced rates of mortality and morbidity and has improved the quality of life of infants and children living with HIV although it does not provide a cure. As a result HIV/AIDS is now perceived as a manageable chronic illness.

Indications for starting ART in HIV-Infected Infants / Children:

Under 12 month

- Treat all if DNA PCR is positive, irrespective of clinical or immunological stage.
- Where DNA PCR is not available, ART needs should be based on presumptive clinical diagnosis of severe HIV disease

For Children above 12 months of age

- Clinical status: Based on WHO Pediatric Clinical Staging
- Immunological status: CD4 Absolute Counts/CD4 %
- For children below 18 months where virological test is not available ART needs should be based on presumptive clinical diagnosis of severe HIV disease

r initiating ART in infants and children

staging	cell measurements	Age-specific treatment recommendation	
		< 12 months	> 12 months
4	CD4	Treat all	Treat all
	No CD4		
3	CD4	Treat all	Treat all, CD4 guided in those children with OHL, LIP, TB, Thrombocytopenia
	No CD4	Treat all	Treat all
2	CD4	*Treat all**	CD4 guided
	No CD4	*Treat all**	TLC guided
1	CD4	*Treat all**	CD4 guided
	No CD4	*Treat all**	Do not treat

*If tested positive by DNA PCR

Table 27: Recommendations for Initiating ART in children according to age using immunological criteria

Immunological	<12 months*	12-35 months	36-59 months	> 5 years
CD4%	< 25%	< 20%	< 20%	< 15%
CD4 Count	1500 cells/mm³	< 750 cells/mm³	< 350 cells/mm³	< 200 cells/mm³
To be used in the absence of CD4:				
Total Lymphocyte Count		< 3000cells/mm³	< 2500 cells/mm³	< 2000 cells/mm³

*Treat all if tested positive by DNA PCR irrespective of CD4 count or percentage.

Recommended first-line Regimen

2 nucleoside reverse transcriptase inhibitors (NRTIs) + 1 non-nucleoside reverse transcriptase inhibitor (NNRTI)

1. ZDV + 3TC + NVP < 3 years or 10 kg
2. ZDV + 3TC + EFV > 3 years and 10 kg
3. d4T + 3TC + NVP / EFV for Anemic Children

posed / Infected with HIV

The majority of children with maternally transmitted HIV infection acquire the infection during or shortly after birth. Early in life they are immunologically normal and only later without specific treatment do they develop progressive immunodeficiency.

All children who have been exposed to HIV should be fully immunized according to age. Because most children who are HIV-infected do not have severe immune suppression during the first year of life, immunization should occur as early as possible after the recommended age to optimize the immune response.

BCG and live attenuated vaccines (including influenza, Japanese encephalitis, measles, mumps, rubella, typhoid, varicella and yellow fever) should not be given to children with signs/ symptoms of HIV infection or with severe immunodeficiency.

Table 28: Nepal National Immunization Schedule for HIV exposed or infected infants

Age of infant	Vaccine
Birth	BCG
6 weeks	DPT1, HBV1, Hib 1, OPV1
10 weeks	DPT2, HBV2, Hib 2, OPV2
14 weeks	DPT3, HBV3, Hib 3, OPV3
6 months	Extra dose of Measles*
9 months	Measles

*Because of the increased risk of early and severe measles infection, HIV-exposed infants who are not severely immunocompromised should receive an extra- dose of standard measles vaccine at 6 months of age with a second dose as soon after the age of 9 months as possible.

Optional Vaccines:

Refer to National guidelines for the management of HIV/AIDS children in Nepal, 2008

Initial evaluation

Care for HIV-positive IDUs must address substance use and substance dependence, psychological and social issues, and medical complications associated with injecting drug use and HIV/AIDS.

Evaluation of substance use and dependence

Standardized assessment tools should be used for screening and initially evaluating substance use and dependence. Any screening or assessment must be voluntary and fully informed, with explanation of why the service needs to understand the individual's substance use and associated problems. Under-reporting use of illicit substances is common, so all patients should be screened for substance use and dependence

Patients who admit to substance use should be examined further, as should those who do not but present with clinical signs or symptoms of drug use, including injections. It is crucial to assess drug dependency, as it has implications for patient management strategy.

Typically a substance use and dependence assessment includes a complete history of substance use and treatment and a physical examination. A substance use and treatment history will include:

- substances used, including alcohol and combinations of drugs, and age at first use
- modes of drug administration
- lifetime, recent and current use
- changes in drug effects over time
- history of tolerance, overdose and withdrawal
- periods of abstinence and attempts to quit
- complications of substance use (hepatitis, abscesses, etc.)
- current problems, including severity of dependence
- types and outcomes of previous treatment for drug dependence.

A physical examination may indicate substance dependence and/or complications associated with substance use. The physical complications of opioid or other drug dependence should be identified and addressed as part of the overall treatment plan. Further evaluation of drug dependence severity and appropriate treatment strategy should be done by, or in close collaboration with, substance dependency treatment experts or other trained staff.

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Initial evaluation of IDUsôHIV/AIDS status is no different from that of non-users.

Further clinical evaluation

Further evaluation is required for developing a strategy of clinical management of HIV-infected IDUs, including:

Åpresenting symptoms
Åphysical examination
Åmental health and social assessment
Åpreparedness for treatment
Åroutine laboratory assessments
ÅCD4 lymphocyte count to determine the severity of immunodeficiency
Åhistory of contraception use and pregnancy test if indicated
Åassessment for hepatitis B and C
Åscreening for TB
Åassessment for psychiatric disorders
Åweight
Åother tests based on the patientôs condition.

Since many IDUs present for care at an advanced stage of HIV infection, it is important to thoroughly evaluate new patients for active opportunistic infections. The initial history and physical examination will usually identify common complications, including:

Åoral candidiasis and difficulty swallowing, suggesting oesophageal candidiasis
Ånon-healing genital or anal ulcers, indicating herpes simplex
Åfever with cough and/or shortness of breath, suggesting bacterial pneumonia, TB or PCP.

These conditions should not be interpreted as exclusion criteria for HAART, but as cases requiring clinical judgments. Initial evaluation should be followed by treatment of opportunistic infections and other conditions as indicated.

Mental health co morbidities are common among IDUs with HIV. Some estimates suggest that between 25% and 50% of drug users also have a co morbid mental health problem.

A thorough psychosocial assessment should be undertaken at initial evaluation, focusing on:

Åany source of instability that might undermine adherence to treatment
Ådepression and other mood disorders
Åother psychiatric problems.

Social factors to be assessed include:
Åsocial stability, family and community support
Åhomelessness
Åmajor life events and crises
Åfinancial security
Ånutrition.

Interactions between ARVs and Methadone/ Buprenorphine

Methadone and buprenorphine are the most common drugs prescribed for Opioid Substitution Therapy(OST). Significant interactions with some of the most commonly used ARVs.

AZT and methadone

AZT does not change methadone levels in the bloodstream. Methadone significantly increases the blood concentration of AZT (43%) Watch for possible increases in AZT toxicity: anaemia, myalgia, bone marrow suppression, fatigue, headache and vomiting.

EFV and methadone

Efavirenz (EFV) can significantly decrease the concentration of methadone in the blood by 60%, and can cause methadone withdrawal. Withdrawal can be delayed and possibly not seen until 2ï 3 weeks after starting the EFV. May require a methadone dose increase of 50%.

Nevirapine (NVP) can significantly decrease the blood concentration of methadone (46%). Methadone withdrawal is common. Withdrawal can be delayed and possibly not seen until 2ï 3 weeks after starting NVP. May need a methadone dose increase of approximately 15%.

PIs and methadone

PIs can induce or inhibit CYP3A.

PIs can induce CYP3A Ÿ faster metabolism of other drugs Ÿ Ź blood levels

PI Ÿ ŷCYP3A Ÿ faster metabolism of methadone Ÿ withdrawal

PIs can inhibit CYP3A Ÿ slower metabolism of other drugs Ÿ ŷ blood levels

PI Ÿ ŹCYP3A Ÿ slower metabolism of methadone Ÿ toxicity

Ritonavir and methadone

Ritonavir (RTV) can significantly decrease methadone levels in the blood by 26ï 53%
Can cause methadone withdrawal. Withdrawal symptoms can be delayed by
2ï 3 weeks. Side-effects of RTV may mimic withdrawal symptoms

…nts That Should Not Be Offered At Any Time

…e		Exception
Antiretroviral Regimens Not Recommended		
Monotherapy	Rapid development of resistance Inferior antiretroviral activity when compared to combination with three or more antiretrovirals	Pregnant women using antenatal ZDV monotherapy for prevention of perinatal HIV transmission and not for HIV treatment for the mother; or taking a single dose of Nevirapine for PMTCT
Dual-NRTI regimens	Rapid development of resistance. Inferior antiretroviral activity when compared to combination with three or more antiretrovirals	No exception
Triple-NRTI regimens except for abacavir/zidovudine/lamivudine or possibly tenofovir + zidovudine/lamivudine	High rate of early virologic non-response seen when triple NRTI combinations including ABC/TDF/3TC or TDF/ddI/3TC were used as initial regimen in treatment-naïve patients ÅOther triple-NRTI regimens have not been evaluated	Abacavir/zidovudine/lamivudine ; and possibly tenofovir + zidovudine/lamivudine in selected patients in whom other combinations are not desirable
Te**nofovir + didanosine + lamivudine (or emtricitabine) combination as a triple-NRTI regimen**	High rate of early virologic non-response seen when this triple NRTI combination was used as initial regimen in treatment-naïve patients	No exception
Antiretroviral Components Not Recommended As Part of Antiretroviral Regimen		
Didanosine + stavudine	High incidence of toxicities ï peripheral neuropathy, pancreatitis, and hyperlactatemia Reports of serious, even fatal, cases of lactic acidosis with hepatic steatosis with or without pancreatitis in pregnant women	When no other antiretroviral options are available and potential benefits outweigh the risks
2-NNRTI combination	When EFV combined with NVP, higher incidence of clinical adverse events seen when compared to either EFV- or NVP-based regimen Both EFV and NVP may induce metabolism and may lead to reductions in etravirine (ETR) exposure; thus, they should not be used in combination	No exception
Efavirenz in first trimester of pregnancy or in women with significant child-bearing potential	Teratogenic in nonhuman primates	When no other antiretroviral options are available and potential benefits outweigh the risks
Nevirapine in treament-naïve women with CD4 >250 or men with CD4 >400	High incidence of symptomatic hepatotoxicity	If no other antiretroviral option available, if used patients should be closely monitored
Stavudine + zidovudine	Antagonistic effect on HIV-1	No exception

Drug Interactions with Antiretrovirals

ARVs	NVP	EFV	LPV/r
ANTIMYCOBACTERIALS			
Rifampicin	ŹNVP level by 20% to 58%. Virological consequences are uncertain; potential for additive hepatotoxicity exists. Coadministration is recommended only if done with careful monitoring.	ŹEFV level by 25%	Decreased LPV AUC by 75%. Should not be coadministered.
Rifabutin	Levels: NVP Ź16%. No dose adjustment.	Levels: EFV unchanged. Rifabutin Ź35%. Dose: ŷrifabutin dose to 450ī 600 mg once daily or 600 mg three times a week. EFV: standard.	Levels: rifabutin AUC increase threefold. Decrease rifabutin dose to 75 mg once daily LPV/r: standard dose
Clarithromycin	None	Decrease clarithromycin by 39%. Monitor for efficacy or use alternative drugs.	Decrease clarithromycin AUC by 75%. Adjust clarithromycin dose if renal impairment.
ANTIFUNGALS			
Ketoconazole	ŷketoconazole level by 63% ŷNVP level by 15ī 30%. Do not recommend coadministration	No significant changes in ketoconazole or EFV levels	Increase LPV AUC. Increase ketoconazole level threefold. Do not exceed 200 mg/day ketoconazole.

		EFV	LPV/r
Fluconazole	ŷNVP Cmax, AUC, Cmin by 100%. No change in fluconazole level. Possible increase in hepatotoxicity with coadministration requiring monitoring of NVP toxicity.	No data	No data
Itraconazole	No data	No data	ŷitraconazole level. Do not exceed 200mg/day itraconazole.
ORAL CONTRACEPTIVES			
Ethinyl estradiol	Źethinyl estradiol by 20%. Use alternative or additional methods.	ŷethinyl estradiol by 37%. Use alternative or additional methods.	Decrease ethinyl estradiol level by 42%. Use alternative or additional methods.
ANTICONVULSANTS			
Carbamazepine Phenytoin	Unknown use with caution. Monitor anticonvulsant levels and watch virologic response. May cause decrease in NVP levels	Use with caution. One case report showed low EFV concentrations with phenytoin	Many possible interactions. Carbamazepine: Increase levels when coadministered with RTV. Use with caution. Monitor anticonvulsant levels. Phenytoin: Decrease levels of LPV and RTV, and decrease levels of phenytoin when administered together. Avoid concomitant use or monitor LPV/anticonvulsant levels.

		EFV	LPV/r
OPIOID SUBSTITUTION TREATMENT			
Methadone	Levels: NVP unchanged. Methadone Decreases significantly. Opiate withdrawal common when this combination is used. Increased methadone dose often necessary. Titrate methadone dose to effect.	Levels: methadone decrease 60%. Opiate withdrawal common, increase in methadone dose often necessary. Titrate methadone dose to effect.	Methadone AUC decrease 53%. Opiate withdrawal may occur. Monitor and titrate dose if needed. May require increase in methadone dose.
Buprenorphine	Not studied	Buprenorphine levels Decrease 50% but no withdrawals reported. No dose adjustment is recommended.	No significant interactions
LIPID-LOWERING AGENTS			
Simvastatin, Lovastatin	No data	Decrease simvastatin level by 58%. EFV level unchanged. Adjust simvastatin dose according to lipid response; not to exceed the maximum recommended dose.	Potential large increase statin level. Avoid concomitant use.
Atorvastatin	No data	Źatorvastatin AUC by 43%. EFV level unchanged.	Increase atorvastatin AUC 5.88 fold. Use lowest possible starting dose with careful monitoring.
		Adjust atorvastatin dose according to lipid response; not to exceed maximum	
		recommended dose.	
Pravastatin	No data	No data	Increase Pravastatin AUC 33%. No dose adjustment needed.

All the PIs and EFV can increase levels of cisapride and non-sedating antihistamines (aztemizole, terfenedine), which can cause cardiac toxicity. Coadministration is not recommended.

ot Be Used With PI or NNRTI Antiretrovirals

Drug Category	Calcium Channel Blockers	Cardiac Agents	Lipid Lowering Agents	Antimycobacterials‡	Anti-histaminesϑ	GI Drugsϑ	Neuro-leptics	Psychotropics	Ergot Alkaloids (vasoconstrictors)	Herbs	Others
Indinavir	(none)	amiodarone	simvastatin lovastatin	rifampin rifapentine	astemizole terfenadine	cisapride	pimozide	Midazolam triazolam	as above	St. John's wort	atazanavir
Lopinavir/ ritonavir	(none)	flecainide propafenone	simvastatin lovastatin	rifampin∫rifapentine	astemizole terfenadine	cisapride	pimozide	midazolam ∑triazolam	as above	St. John's wort	fluticasone ⊗
Efavirenz	(none)	(none)	(none)	rifapentine‡	astemizole terfenadine	cisapride	(none)	Midazolam triazolam	as above	St. John's wort	
Nevirapine	(none)	(none)	(none)	rifapentine‡	(none)	(none)	(none)	(none)	(none)	St. John's wort	

Name and address of Health Institution

Patient name or ID	
Hospital/Clinic number	Date of visit
Patient History: ÅHIV related disease including TB ÅCough > 2 wks ÅFever ÅWeight Loss ÅDiarrhea ÅOther symptoms of GI, CNS, Skin	
Other medications: (if any)	
Drug Allergies:	
WHO Staging:	
Is there any change since last visit ?	
Adherence to antiretroviral therapy: No of doses missed in last 7 days: No doses missed since lat visit: Dose taken at correct time: yes No Correct taken: yes No Dose delay > 1 hr: yes No Specify reason for interruption or modification/failure to take prescribed doses:	
Other Medications: New and ongoing (if new, indicate Start date) Medication Start Date COMMENTS	

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PHYSICAL EXAMINATION: (tick if normal, describe if abnormal)
General condition .....
Skin .....
ENT .....
Lymph nodes .....
Heart .....
Chest .....
Abdomen .....
GU Tract .....
Musculoskeletal system .....
Extremity .....
Neuro logical system .....
Other (describe)

HIV-RELATED ILLNESS: new and ongoing (if new, indicate Start Date)
Are there any new HIV-related illness at this visit? No ..... Yes (if yes, specify) .....

COMMENTS	START DATE	
ÅOral candidiasis	/	/
ÅOral hairy leukoplakia	/	/
ÅPruritic popular eruption	/	/
ÅLymphadenopathy (>1 cm on both sides)	/	/
ÅOther HIV related illnesses	/	/
	/	/

BASIC LABORATORY RESULTS

Hemoglobin	g/dl WBC	cells/cumm	
Platelets	cells/cumm		
Total lymphocyte count		cells/cumm	
Glucose	mg/dl	Creatinine	mg/dl
ALT/SGPT	U/l	RFT	

Other lab results (e.g. CXR, AFB, culture, serology)

NOTES/PLAN

Follow-up date:

(A booklet with about 12 copies of the above made for each patient for monitoring is recommended).

Occupational Exposure Report

Name:		**Address (workplace):**	**Address (home):**
Birth date:	**Sex:**	**Position:**	**Telephone No.**
Date/time of exposure:	**Location exposure occurred:**		**Activity at time of exposure:**
Nature of injury (e.g., needle stick, cut, splash):			
Details of the procedure being performed, including where and how the exposure occurred:			
Details of the exposure, including the type and amount of fluid or material and the severity of the exposure			

Details about the exposure source:	**Details about the** exposed person:
The source material contained: **HBV:**	**Infected with:** **HBV:**
HCV:	**HCV:**
HIV:	**HIV:**
Is the source HIV-infected:	**Concomitant diseases:**
Stage of disease:	**Hepatitis B vaccination:**
History of antiretroviral therapy:	**Vaccine-response status:**
Antiretroviral resistance:	**Pre-test counseling provided:**
Pre-test counseling provided:	**Results of the tests:**
Results of the tests:	**HIV**
HIV	**Post-test counseling provided:**
Post-test counseling provided:	**Referral:**
Referral:	

PEP prophylaxis commenced:
Drugs provided:

Counseling on protecting others: avoiding unprotected intercourse and breastfeeding

Postexposure management:	**Hb**		
Baseline visit			

HIV Antibody test results: **3 month** **6 month**	

Signature	**Date:**

e Chart – Nepal 2008

Weight	Zidovudine (ZDV or AZT)			Lamivudine (3TC)	
	240mg/m² / dose **Twice daily**			4mg/kg /dose **Twice daily**	
KG	LIQUID 10mg/ml	CAPSULE 100mg	TABLET 300mg	LIQUID 10mg/ml	TABLET 150 mg
5-6	7 ml	-	-	3 ml	-
7-9	9 ml	-	-	4 ml	-
10-11	10 ml	-	-	5 ml	-
12-14	12 ml	-	-	6 ml	-
15-19	-	2 morning, 1 evening	1/2	7 ml	1/2
20-24	-	2	1/2	-	1 morning ½ evening
25-29	-	2	1 morning ½ evening	-	1
30-35	-	3	1	-	1
35-40	-	3	1	-	1
> 40	-	3	1	-	1

Zidovudine tablets can be crushed and capsules may be opened and dispersed in water or onto a small amount of food and immediately ingested. Oral solution is stable at room temperature but light sensitive. Do not use with Stavudine due to antagonistic effect. Use with caution in children with anemia.

Lamivudine tablets can be divided into two equal halves and crushed and dispersed in water or onto a small amount of food and immediately ingested. Oral solution is stable at room temperature. Use within one month of opening.

			Stavudine (d4T)			
	Induction dose **Once daily**for 14 days Maintenance dose 160-200 mg/m2/dose **Twice Daily**		1mg/Kg/dose **Twice daily**			
KG	LIQUID 10mg/ml	TABLET 200 mg	LIQUID 1mg/ml	CAPSULE 15 mg	CAPSULE 20 mg	CAPSULE 30 mg
5-6	6 ml	-	6ml	-	-	-
7-9	8 ml	-	9 ml	-	1/2	-
10-11	10 ml	1/2	11 ml	-	1/2	-
12-14	11 ml	1/2	-	1	-	1/2
15-19	14 ml	1 morning ½ evening	-	1	1	1/2
20-24	-	1 morning ½ evening	-	-	1	-
25-29	-	1	-	2	-	1
30-35	-	1	-	2	-	1
35-40	-	1	-	-	-	1
> 40	-	1	-	-	-	1

Nevirapine tablets can be divided into two equal halves and crushed and dispersed in water or onto a small amount of food and immediately ingested. Oral solution is stable at room temperature. Shake well before use. Rash can occur during the first 14 days of dosing. If severe rash occurs (especially if accompanied by fever, blisters or mucosal ulcerations), discountinue drug. Avoid coadministration with Rifampicin if possible.

Stavudine capsules may be opened and dispersed in water or onto a small amount of food and immediately ingested. The oral solution needs to be refrigerated and shaken well before use. Do not use with Zidovudine due to antagonistic effect.

			Abacavir (ABC)	
	Dose: 15 mg/Kg >3 yrs or 10 Kg **Once daily**		8mg/Kg/dose **Twice daily**	
KG	CAPSULE	CAPSULE	LIQUID	TABLET
	200 mg	600 mg	20mg/ml	300 mg
5-6	-	-	2.5 ml	-
7-9	-	-	4 ml	-
10-11	1	-	5 ml	-
12-14	1	-	6 ml	1/2
15-19	1	1/2	7 ml	1/2
20-24	1½	1/2	-	1 morning ½ evening
25-29	2	-		
			-	1
30-35	2	-		
			-	1
35-40	2	-		
			-	1
> 40	-	1		
			-	1

Efavirenz is not approved for children <3 years and below 10 kg weight. It can be given with or without food, but high fat meals should be avoided for best absorption. Preferably given at bed time to reduce CNS side effects, especially during first two weeks. Capsules can be opened and added to small amount of sweet food or drink to disguise peppery taste.

Abacavir is available as a tablet or a yellow oral solution. The solution and tablets can be stored at room temperature. Tablets can be divided into two equal halves and crushed and dispersed in water or onto a small amount of food and immediatley ingested. It can cause severe hypersensitivity reactions and should never be used if it occurs.

				Lopinavir/ritonavir (LPV/r)	
	90 - 120 mg/m2/dose **Twice daily**			**Dose of LPV** 5-7 Kg: 16mg/Kg/dose 8-9 Kg: 14mg/Kg/dose 10-13 Kg: 12mg/Kg/dose 14-39 Kg: 10mg/Kg/dose **Twice daily**	
KG	LIQUID 10mg/ml	TABLET 25 mg	TABLET 250 mg	LIQUID LPV/r 80mg/20mg/ml	TABLET LPV/r 200/50mg
5-6	5 ml	2	-	1.5 ml	-
7-9	6 ml	2	-	2 ml	-
10-11	7 ml	3 morning 2 evening	-	2 ml	-
12-14	8 ml	3	-	2 ml	1
15-19	9 ml	4	-	2.5 ml	1
20-24	-	5 BD	1 OD	3 ml	1
25-29	-	5 BD	1 OD	3.5 ml	2 morning 1 evening
30-35	-	5 BD	1 OD	4 ml	2
35-40	-	5 BD	1 OD	5 ml	2
> 40	-	-	1 OD	-	2

Didanosine should be given on an empty stomach one hour before or two hours after a meal. The suspension needs to be refigerated and shakel well before admisistering. At least two tablets of appropriate strength must be used at any one time of adequeate buffering (e.g. If the dose is 50 mg, administer two 25 mg tablets instead of one 50 mg tablet). The tablets should be chewed, crushed or dispersed in water before they are taken. Capsules are designed for once daily dosing.

Lopinavir/ritonavir oral solution should be taken with food. Oral solution should be refrigerated. Oral solution is bitter to taste. No food restriction with tablets. Tablets cannot be split.

	Lamivudine	ne and Lamivudine	Zidovudine / Lamivudine / Nevirapine
KG	ZDV / 3TC (300mg/150mg) **Twice daily**	d4T / 3TC (30mg/150mg) **Twice daily**	ZDV/ 3TC / NVP (300mg/150mg/200mg) **Twice daily**
5-8	-	-	-
9-10	-	-	-
11-14	-	1/2	-
15-19	1/2	1 morning ½evening	½ BD Plus ½ extra NVP in evening
20-24	1 morning, ½ evening	1 morning ½ evening	1 morning ½evening
25-29	1 morning ½evening	1	1 morning, ½evening Plus ½ extra NVP in evening
30-39	1	1	1
> 40	1	1	1

Weight	**Stavudine / Lamivudine / Nevirapine**		
KG	Pediatric d4T-30/3TC/NVP 30mg/150mg/200mg **Twice daily**	Pediatric (Junior) d4T/3TC/NVP (12mg/60mg/100mg) **Twice daily**	Pediatric (Baby) d4T/3TC/NVP (6mg/30mg/50mg) **Twice daily**
5-8	-	1/2	1
9-10	-	-	1½
11-14	1/2	1	2
15-19	1 morning ½evening	1½	3
20-24	1 morning ½evening	2	-
25-29	1	-	-
30-39	1	-	-
> 40	1	-	-

1. Prescribing practices

- % of patients initiating ART who are prescribed an appropriate first-line regimen over a specified time period.

Suggested target: 100%

2. % lost to follow-up during the first 12 months of ART

% lost to follow-up 12 months after initiating ART during a specified time period

Suggested target: ≤ 20%

3. Patient retention on first-line ART

% of patients initiating ART during a specified time period who are on an appropriate first-line ART regimen 12 months later.

Suggested target: ≥ 70%

4. On-time ARV Drug pick up

% of ART patients picking up prescribed ARV drugs on time (before previous drugs run out)

Suggested target: ≥ 90%

5. ART appointment-keeping

% of ART patients attending all clinic appointments on-time (within 7 days of scheduled appointment)

Suggested target: ≥ 80%

6. Drug Supply Continuity

ART stops, substitutions, and switches due to ARV shortages during a specified time period

Suggested target: 0%

% of months during a year with no antiretroviral drug stock outages

Suggested target: 100%

1. Monitoring and Evaluation of the ART Programme

With the increasing access to antiretroviral treatment (ART), a strong monitoring system is required at facility, district, provincial, national and international levels.

At facility level, the objectives of programme monitoring are to:

- support patient management by regularly recording and storing of key individual information for lifelong care and follow-up;
- facilitate an accurate patient tracking system to identify those missing or lost to follow-up; and
- support drug supply management at the facility.

At all levels, programme monitoring will help to:

- document the progress in equitable access to HIV care and ART programmes; and
- identify the successes and gaps over time and modify the programmes accordingly.

2. ART Program Performance Indicators at national / international levels

2.1 ART program performance indicators at national level

The following indicators, based on the monitoring and evaluation framework were developed for national programmes to demonstrate progress in scaling up ART programmes:

Monitoring and evaluation framework

Input indicators

1. Existence of national policies, strategy and guidelines for ART programmes.

Process indicators

2. Percentage of districts or local health administration units with at least one health facility providing ART services in line with national standards.
3. Percentage of ARV storage and delivery points experiencing stock-outs in the preceding 6 months.
4. Number of health workers trained on ART delivery in accordance with national or international standards.

Output indicators

5. Percentage of health facilities with systems and items to provide ART services.
6. Percentage of health facilities with ART services that also provide comprehensive care, including prevention services, for HIV-positive clients.

Outcome indicators

7. Percentage of adults and children with advanced HIV infection receiving antiretroviral therapy
8. Percentage of patients initiating antiretroviral therapy at the site during a selected period who are taking an appropriate first line regimen 12 months later.

Impact indicators

9. Percentage of adults and children with HIV known to be on treatment 6, 12, 24, 36, 48 months after initiation of antiretroviral therapy

2.2 Indicators at the facility level

The following indicators are recommended to be produced at the facility level.

		Level of detail	Recommended reporting frequency
1	Cumulative number ever enrolled for HIV care	By sex, age	Monthly
2	Number started on ART during the reporting period	By sex, age	Monthly
3	Cumulative number ever started on ART	By sex, age	Monthly
4	Cumulative number medically eligible for ART but have not been started on ART	By sex, age	Monthly
5	Cumulative number on ART	NA	Monthly
6	Cumulative number on substituted 1st line regimen	NA	Monthly
7	Cumulative number switched to 2nd line regimen	NA	Monthly
8	Proportion of patients with >95% adherence	NA	Monthly
9	Proportion of patients alive and on treatment 6, 12, after start of treatment	NA	Bi-annual or annual and 24 months
10	Proportion of patients continuing initial 1st line regimen, substituting 1st line, switched to 2nd line at 6, 12, 24 months of ART	NA	Bi-annual or annual
11	Proportion of patients with >200 mm3 CD4 cells after 6, 12, 24 months of ART	NA	Bi-annual or annual
12	Proportion of patients on ART whose performance scale at 6, 12, 24 months is "normal activity."	NA	Bi-annual or annual
13	Proportion of patients who have picked up their ARV drugs 6/6 months or 12/12months	NA	Bi-annual or annual

3. Standardized recording and reporting system

To generate the above listed indicators, it is important to have a uniform data collection and reporting system. Standard recording and reporting ensures that key information gets stored. This helps in:

- easily retrieval by care providers to get an overview of the patient's progress over time;
- exchange of information between the different health care providers (such as, doctor, nurse, counselor, psychologist) as well as with other ART centres when the patient is referred or transferred to another clinic; and
- facilitate compilation and comparison of indicators at province, national and international levels.

4. List of records and reports at the facility

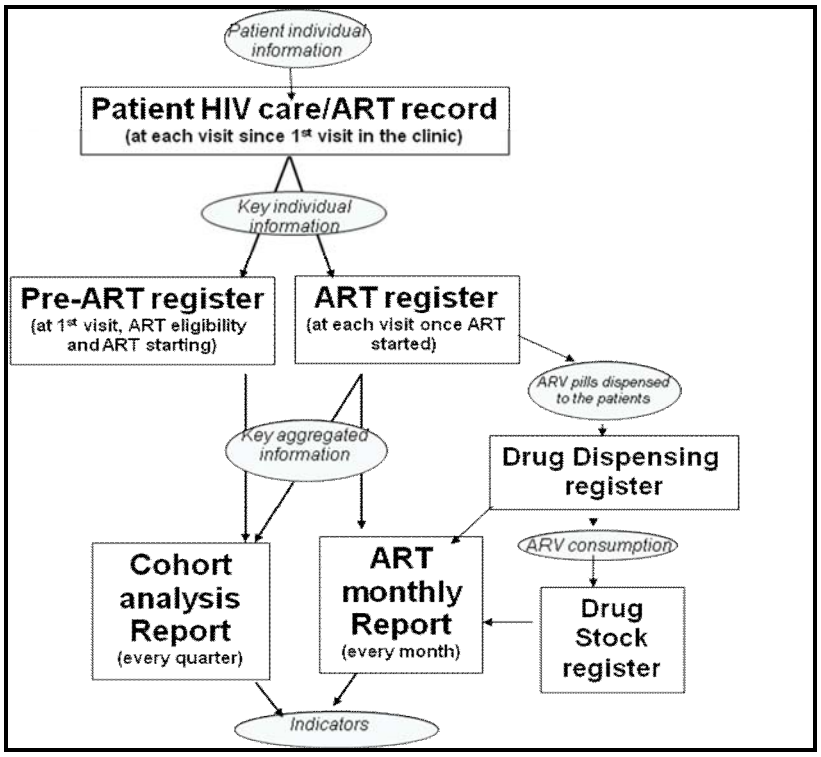
Recording forms

1. Patient HIV Care/ART Record
2. Pre-ART Register
3. ART Register
4. ARV Drug Dispensing Register
5. ARV Drug Stock Register

Reporting forms

1. ART Monthly Report
2. Cohort Analysis Report

orting forms in a paper based monitoring system



ng formats				
		urpose?	When to complete?	Who will complete
Patient HIV Care / ART Record	Demographic, HIV care, Antiretroviral treatment and monthly follow-up clinical information	✦ Patient management: to ensure appropriate lifelong follow-up ✦ Patient monitoring: to obtain key individual variables for future analysis	✦ At each patient visit, starting from the 1st visit to the clinic	✦ Health care providers during each patient visit
Pre-ART Register	Standardized and systematic key variables on each patient before ART started	✦ Patient monitoring: to report key variables on each patient ✦ Programme monitoring: to facilitate calculation of indicators	✦ At the 1st visit ✦ At start of tuberculosis treatment and cotrimoxazole prophylaxis ✦ At ART eligibility ✦ At start of ART ✦ At end of follow up, if needed	✦ Health care providers during each patient visit Or ✦ Trained staff using patient record after the Visit
ART Register	Standardized and systematic key variables on each patient under ART	✦ Patient monitoring: to report key variables on each patient ✦ Programme monitoring: to facilitate calculation of indicators	✦ At each visit once ART is started	✦ Health care providers during each patient visit Or ✦ Trained staff using patient record after the Visit
ARV Drug Dispensing and Stock Registers	Drugs ansd no. of tablets dispensed Drug stocks	✦ Patient monitoring: accounting for no. of tablets dispensed ✦ Programme monitoring: drug consumption and available stocks	✦ At the time of drug dispensing to each patient ✦ Daily basis	Pharmacist or officer in charge of dispensing drugs
Monthly ART Report	Indicators	✦ Programme monitoring: to calculate and analyse indicators	✦ Every month	✦ Facility manager Or ✦ Trained staff under supervision of the facility Manager
Cohort Analysis Report	Indicators	✦ Programme monitoring: to calculate and analyse indicators at 6,12, 24 months of start of ART	✦ Every 6 months or during yearly assessment	✦ Facility manager Or ✦ Trained staff under supervision of the facility manager

ing forms to be used for ART routine program monitoring.

FORM 1- PATIENT HIV CARE and ANTIRETROVIRAL TREATMENT (ART) RECORD

(To be stored in a locked cabinet at the health centre and arranged serially by registration number)

...n)

...de patient (4#)

District: State/province:

Name of patient:

Age: (date of birth: ☐☐/☐☐/☐☐ dd / mm / yy) Sex: ☐ Male ☐ Female

Patient's phone number:

Address:

City/village: District: State/province:

Distance from residence to clinic (km)

Treatment supporter's name (if applicable)

Treatment supporter's address:

Treatment supporter's phone number:

Date confirmed HIV+ test: ☐☐/☐☐/☐☐ dd / mm / yy Place:

Entry point (services referring the patient for HIV care): ☐ 1-VCT ☐ 2-TB ☐ 3-Outpatient
☐ 4-Inpatient ☐ 5-Paediatric ☐ 6-PMTCT ☐ 7-STI ☐ 8-Private ☐ 9-NGO ☐ 10-Self referred
☐ 11-IDU outreach ☐ 12- CSW outreach ☐ 13-other_____

☐ patient transferred in on ART from another HIV care/ART clinic from the national program

Name previous clinic: Date transferred in :

2. Personal History (Tick one choice)

Mode of HIV trans-mission
- ☐ 1 Commercial sex worker (CSW)
- ☐ 2 Other heterosexual route
- ☐ 3 Men having sex with men (MSM)
- ☐ 4 Injecting drug use (IDU)
- ☐ 5 Blood transfusion
- ☐ 6 Mother to child
- ☐ 7 Unknown

For IDUs Substitution therapy ☐ Y ☐ N
If yes, type:

Literate ☐ Yes ☐ No

Employed ☐ Yes ☐ No

Alcoholism ☐ Habitual ☐ Social ☐ No use

3. Family History (Tick one choice)

Marital status: ☐ Single ☐ Married ☐ Divorce/separate ☐ Widowed ☐ Not applicable

Estimated monthly household income:

Family members: partner/children	Age/ sex	HIV +/- /unknown	ART Y/N	Regist. No if in care

4. Antiretroviral treatment history

Was ART received before? ☐ Yes ☐ No

If yes ☐ PMTCT ☐ Earlier ART Place: ☐ Private ☐ Govt

Drugs and duration:

5. Clinical and Laboratory Investigations

	Date (dd/mm/yy)	WHO stage	Weight (kg)	Height (cm)	Performance A/B/C*	Total lymphocyte count	CD4 count (or % in children)
At 1st visit in clinic							
At ART medical eligibility				child			
At start of ART				child			
At 6 months ART				child			
At 12 months ART				child			
At 24 months ART				child			

6. Antiretroviral Treatment

Treatment Started
- ☐ D4T30+3TC+NVP
- ☐ D4T40+3TC+NVP
- ☐ D4T30+3TC+EFV
- ☐ D4T40+3TC+EFV
- ☐ ZDV+3TC+NVP
- ☐ ZDV+3TC+EFV

SUBSTITUTION within 1st line, SWITCH to 2nd line, STOP, RESTART

Date	Substitution, switch or stop	Reason (code)	Date restart	New regimen

Reasons SUBSTITUTE: 1 toxicity side effects, 2 pregnancy, 3 risk of pregnancy, 4 newly diagnosed TB, 5 new drug available, 6 drug out of stock, 7 other reason (specify)

Reasons for SWITCH: 1 clinical treatment failure, 2 immunological failure, 3 virologic failure

Reasons STOP: 1 toxicity side effects, 2 pregnancy, 3 treatment failure, 4 poor adherence, 5 illness hospitalization, 6 drug out of stock, 7 patient lack of finance, 8 patient decision, 9 planned treatment interruption, 10 others

7. Tuberculosis treatment during HIV care

Disease class (tick)
- ☐ Pulmonary TB
  - ☐ Smear-positive
  - ☐ Smear-negative
- ☐ Extrapulmonary site: _____

TB Regimen (tick)
- ☐ Category I
- ☐ Category II
- ☐ Other specify:

Date start TB Rx: ☐☐/☐☐/☐☐ dd / mm / yy

TB registration
District:
Health Centre:
TB number:

Treatment outcome: ☐ Cure ☐ Rx completed ☐ Rx failure ☐ Died ☐ Default ☐ Transfer out
Date: ☐☐/☐☐/☐☐) dd / mm / yy

8. End of Follow-up

☐ Death Date of death: ☐☐/☐☐/☐☐

☐ Lost to follow-up (>3 months) Date last visit: ☐☐/☐☐/☐☐

☐ Transferred out Date: ☐☐/☐☐/☐☐ dd / mm / yy New clinic:

*** Performance scale: A- Normal activity; B- bedridden <50% of the day during last month; C- bedridden > 50% of the day during last month**

NT HIV CARE & ANTIRETROVIRAL TREATMENT FOLLOW-UP

Date of visit*	Date next visit	Weight (kg) & height for child	WHO stage	Perfor-mance scale*	(y/n) or FP method*	opportunistic infections - code*	Drugs prescribed for prophylaxis of OIs	Antiretroviral drugs and dose prescribed	adherence to ART* - >95%, 80-95%, <80%	ART Side effects - code*	lab results when available	Cond-oms given y/n	Referred to specialist or hospit.

*Instructions and codes:
Date: Write the date of actual visit starting from the 1st visit for HIV care – ALL DATES: DD/MM/YY
Performance scale: A- Normal activity; B- bedridden <50% of the day during last month; C- bedridden > 50% of the day during last monthj
FP: family planning; 1 condoms, 2 oral contraceptive pills, 3 injectable/implantable hormones, 4 diaphragm/cervical cap, 5 intrauterine device, 6 vasectomy/tubal ligation/hysterectomy

Opportunistic infections: Enter one or more codes − Tuberculosis (TB); Candidiasis (C); Diarrhea (D); Cryptococcal meningitis (M); Pneumocystis Carinii Pneumonia (PCP); Cytomegalovirus disease (CMV); Penicilliosis (P); Herpes zoster (Z); Genital herpes (H); Toxoplasmosis (T); Other-specify
Adherence: Check adherence by asking the patient if he/she has missed any doses. Also check the bottle/blister packet. Write the estimated level of adherence (e.g. >95% = < 3 doses missed in a period of 30 days; 80-95% = 3 to 12 doses missed in a period of 30 days; < 80% = >12 doses missed in a period of 30 days
Side effects: Enter one or more codes − S=Skin rash; Nau-nausea; V=Vomiting; D=Diarrhoea; N=Neuropathy;J=Jaundice; A=Anemia; F=Fatigue; H=Headache; Fev=Fever; Hyp=Hypersensitivity; Dep=Depression; P=Pancreatitis; L=Lipodystrophy; Drows=Drowsiness; O=Other− Specify

F GISTER

Fi

Fill when applicable column 11 to 16

1	2	3	4	5	6		7	8	9	10	11	12	13	14	15	
DATE 1st visit at the clinic	Regis-tration number	Patient's name and address	Age	sex M/ F	Confirmed HIV+ test Date	Place	Entry point -code 1 to 13*	Risk factor code 1to7**	Literate	Employed	CPT Date Start	TB treatment Class/Regimen Date of start	DATE medically elligible for ART	Why medically elligible?	DATE ART started	En Dat dea
									□Y □N	□Y □N				WHO stage CD4 #/% TLC#		
									□Y □N	□Y □N				WHO stage CD4 #/% TLC#		
									□Y □N	□Y □N				WHO stage CD4 #/% TLC#		
									□Y □N	□Y □N				WHO stage CD4 #/% TLC#		

*Entry point: 1-VCT; 2-TB; 3-Outpatient; 4-Inpatient; 5-Paediatric; 6-PMTCT; 7-STI; 8-Private; 9-NGO; 10-Self referred; 11-IDU outreach; 12- CSW outreach; 13-other - **Write code TR if the patient was transferred in on ART**

**Mode of HIV transmission: 1-Commercial sex worker (CSW), 2-Other heterosexual route, 3-Men having sex with men (MSM), 4-Injecting drug use (IDU), 5-Blood transfusion, 6-Mother to child, 7-Unknown

											Month:			**Year:**		
start of ART		**name and surname**	**Age**	**Sex M/ F**	**and contact number**	**Treatment supporter's name and contact number**	**Prior ARV history**	**WHO stage at start of Rx**	**performance scale^** A-normal activity B-bedridden<50% C-bedridden>50%		**Weight^** (kg) (and height)		**CD4 count^** (absolute number for adults and % for children)		**TB treatment during ART** Disease, Category Regimen Date Rx start	**ART regimen started**
					………………	………………	☐ Y		At start	At 6 mo.	At start	At 6 mo.	At start	At 6 mo.		
					………………	………………	☐ N		At 12 mo.	At 24 mo.	At 12 mo.	At 24 mo.	At 12 mo.	At 24 mo.		
					………………	………………	☐ Y		At start	At 6 mo.	At start	At 6 mo.	At start	At 6 mo.		
					………………	………………	☐ N		At 12 mo.	At 24 mo.	At 12 mo.	At 24 mo.	At 12 mo.	At 24 mo.		
					………………	………………	☐ Y		At start	At 6 mo.	At start	At 6 mo.	At start	At 6 mo.		
					………………	………………	☐ N		At 12 mo.	At 24 mo.	At 12 mo.	At 24 mo.	At 12 mo.	At 24 mo.		
					………………	………………	☐ Y		At start	At 6 mo.	At start	At 6 mo.	At start	At 6 mo.		
					………………	………………	☐ N		At 12 mo.	At 24 mo.	At 12 mo.	At 24 mo.	At 12 mo.	At 24 mo.		
					………………	………………	☐ Y		At start	At 6 mo.	At start	At 6 mo.	At start	At 6 mo.		
					………………	………………	☐ N		At 12 mo.	At 24 mo.	At 12 mo.	At 24 mo.	At 12 mo.	At 24 mo.		

F Month: Year:

DATE of start of ART	Registration number	Patient's first name and surname	Age	Sex M/ F	Patient's address and contact number	Treatment supporter's name and contact number	Prior ARV history	WHO stage at start of Rx	performance scale^ A-normal activity B-bedridden<50% C-bedridden>50%	Weight^ (kg) (and height)	CD4 count^ (absolute number for adults and % for children)	TB treatment during ART Disease, Category Regimen Date Rx start	ART regimen started
					……………… ………………	……………… ………………	☐ Y ☐ N		At start / At 6 mo. At 12 mo. / At 24 mo.	At start / At 6 mo. At 12 mo. / At 24 mo.	At start / At 6 mo. At 12 mo. / At 24 mo.		
					……………… ………………	……………… ………………	☐ Y ☐ N		At start / At 6 mo. At 12 mo. / At 24 mo.	At start / At 6 mo. At 12 mo. / At 24 mo.	At start / At 6 mo. At 12 mo. / At 24 mo.		
					……………… ………………	……………… ………………	☐ Y ☐ N		At start / At 6 mo. At 12 mo. / At 24 mo.	At start / At 6 mo. At 12 mo. / At 24 mo.	At start / At 6 mo. At 12 mo. / At 24 mo.		
					……………… ………………	……………… ………………	☐ Y ☐ N		At start / At 6 mo. At 12 mo. / At 24 mo.	At start / At 6 mo. At 12 mo. / At 24 mo.	At start / At 6 mo. At 12 mo. / At 24 mo.		
					……………… ………………	……………… ………………	☐ Y ☐ N		At start / At 6 mo. At 12 mo. / At 24 mo.	At start / At 6 mo. At 12 mo. / At 24 mo.	At start / At 6 mo. At 12 mo. / At 24 mo.		

w-up on ART

Monthly visits: ● 1st row, write patient outcome: on treatment **(OT)** if patient picked up ART drugs; stopped **(ST)** if ART was stop
(MIS) if the patient missed the scheduled visit; lost to follow-up **(LFU)** if the patient is missing for ≥3 months; restart **(RS)** if ART v
interruption; transferred out **(TR);** dead **(D);** **(NA)** if the patient was not scheduled to visit this month ● 2nd row: write adherence
A=>95%, B=80-95%, C=<80%)

Date	Reason *	New Regimen	Date	Reason**	New Regimen	Date of death	Date lost to FU (last visit)	Date transfered Out on ART	week 2	month 1	mo. 2	mo. 3	mo. 4	mo. 5	MO. 6	mo. 7	mo. 8	mo. 9	mo. 10	mo. 11	MO. 12	mo. 13	mo. 14	mo. 15	mo. 16	mo. 17	mo. 18	mo. 19

nbined Report– Requisition and Issue form for ARV Drugs

Name of Institution_____Two months' request _____ and _____ Year_____ Date of request _____ **Maximum : 4 mths**

Names of drugs	Beginning balance (Ending balance of previous report)	Received quantity (In last 2 months)	Quantity consumed (in last 2 months)	Loss or Adjustment (+/-) (In last 2 months)	Ending balance (Remaining)	Quantity needed for new patients (For next 2 months)	Estimated consumption	Maximum stock quantity	Requested quantity	Issu quan (Fr cen
	A	B	C	D (+/-)	(E=A+B-C+/-D)	F	G = F + C	H = G x 2	I = H - E	J
Fixed Dose Combination (FDC)										
Stavudine/Lamivudine/Nevirapine 30/150/200 mg Tabs										
Stavudine/Lamivudine 30/150 mg Tabs										
Zidovudine/Lamivudine 300/150 mg Tabs										
Single Dose Formulation (SDF)										
Efavirenz 600 mg Tabs										
Efavirenz 200 mg Caps										
Nevirapine 200 mg Tabs										
Zidovudine 300mg Tabs										
Stavudine 30 mg Tabs										
Stavudine 40 mg Tabs										
Lamivudine 150 mg Tabs										
Abacavir 300 mg Tabs										
Didanosine 250 mg Caps										
Didanosine 400 mg Caps										
Nelfinavir 250 mg Tabs										
Indinavir 400 mg Caps										
Lopinavir/ritonavir 200 /50 mg Tabs										
Oral Solution										
Zidovudine syrup 10 mg/ml										
Lamivudine oral solution 10 mg/ml										
Nevirapine oral suspension 10 mg/ml										
Stavudine oral solution 1 mg/ml										

TI Control Program (NCASC)
nthly ART Report

ART				
Type of Unit:				
Master facility unit ID:				
Name of Reporting Institution:				
Region:				
District:				
Municipality/VDC:				
Name of Facility incharge:				
Month and year of Reporting:	Month (MM)		Year (YYYY)	

A- MEDICAL CARE

6. Enrollment in HIV care (PLHA seeking care at the treatment center)	**Adult**			**Child (Male)**			**Child (Female)**			**Total**
	Male	**Female**	**TG**	**<1Yr**	**1-4yr**	**5-14yr**	**<1Yr**	**1-4yr**	**5-14yr**	
6.1 Cumulative* no. of patients ever enrolled in HIV care at beginning of this month										0
6.2 New patients enrolled in HIV care during this month										0
6.3 Cumulative no. of patients ever enrolled in HIV care at the end of this month	0	0	0	0	0	0	0	0	0	0

7. Medical eligibility for ART*	**Adult**			**Child (Male)**			**Child (Female)**			**Total**
	Male	**Female**	**TG**	**<1Yr**	**1-4yr**	**5-14yr**	**<1Yr**	**1-4yr**	**5-14yr**	
7.1 No. of patients medically eligible for ART but have not been started on ART at the end of this month										0

8. Enrollment on ART	**Adult**			**Child (Male)**			**Child (Female)**			**Total**
	Male	**Female**	**TG**	**<1Yr**	**1-4yr**	**5-14yr**	**<1Yr**	**1-4yr**	**5-14yr**	
8.1 Cumulative no. of patients ever started on ARTat the beginning of this month										0
8.2 New patients started on ART during this month										0
8.3 No. of patients on ART transferred in this month										0
8.4 Cumulative no. of patients ever started on ARTat the end of this month	0	0	0	0	0	0	0	0	0	0

9. Outcomes on ART	**Adult**			**Child (Male)**			**Child (Female)**			**Total**
	Male	**Female**	**TG**	**<1Yr**	**1-4yr**	**5-14yr**	**<1Yr**	**1-4yr**	**5-14yr**	
9.1 Cumulative no. of death reported at the end of this month										0
9.2 Cumulative no. of patients transferred out under ARV at the end of this month										0
9.3.1 No. of patients marked as Mis at the end of this month										0
9.3.2 No. of patients marked as lost to follow-up at the end of this month										0
9.4 No. of patients stopping ART at the end of this month										0

9.5 N after										0
9.6 N		0	0	0	0	0	0	0	0	0
9.6.1 Among them, no. on original 1st line regimen										0
9.6.2 No. on substituted 1st line regimen										0
9.6.3 No. switched on 2nd line regimen										0
9.6.4 Out of 9.6, the number of patients on ART initiated on DOTS this month										0

10. Treatment Adherence		**Total**
10.1. No. of patients assessed for adherence during this month		
10.2. Of those assessed for adherence, level of adherence in the last month		
10.2.1. < 3 doses missed in a period of 30 days	> 95%	
10.2.2 =3 to 12 doses missed in a period of 30 days	80-95%	
10.2.3. >12 doses missed in a period of 30 days	<80%	

11. People on ART by risk group	**Adult**			**Child (Male)**			**Child (Female)**			**Total**
	Male	**Female**	**TG**	**<1Yr**	**1-4yr**	**5-14yr**	**<1Yr**	**1-4yr**	**5-14yr**	
1. Injecting drug users										
2. Sex workers										
3. Men who have sex with men										
4. Clients of sex workers										
5. Migrant workers										
6. Spouse of Migrant										
7. Partner /child of PLHA										
8. Others										

B- PHARMACY

12. Regimen at end of this month

Regimen	**No. of Adult patients on ART**	**No. of Pediatric patients on ART**
D4T30+3TC+NVP		
ZDV+3TC+NVP		
ZDV+3TC+EFV		
D4T30+3TC+EFV		
Total	**0**	**0**

13. DRUG STOCKS (Please mark the boxes)

Was there a stock-out of any antiretroviral drugs in this month that were used in the site? If yes then for how many days there was a stockout?	Yes		No		Days		
Was there a stock-out of drugs for opportunistic infection in this month that were used in the site? If yes then for how many days there was a stockout?	Yes		N0		Days		

Report prepared by:		Approved by:	
Name:		Name:	
Designation:		Designation:	
Signature:		Signature:	
Date:		Date:	

Γ

Cohorts are defined by the month year patients started ART

to be continued for each monthly cohort…

	For cohort starting ART by month/year: at baseline then results at 6 months on ART, 12 months on ART, 24 months on ART	Cohort Jan 04	6 mo- July04	12 mo- Jan 05	24 mo- Jan 06	Cohort Feb 04	6 mo- Aug 04	12 mo- Feb 05	24 mo- Feb 06	Cohort Mar 04	6 mo- Sept 04	12 mo- Mar 05	24 mo- Mar 06
G	Started on ART in this clinic- original cohort												
TI	Transfers In **Add +**												
TO	Transfers Out **Subtract -**												
N	Net current cohort												
H	On Original 1st Line Regimen												
I	On Alternate 1st Line Regimen (Substituted)												
J	On 2nd Line Regimen (Switched)												
S	Stopped												
D	Died												
F	Lost to Follow-up												
A	Number alive and on ART [N - (S+D+F)]												
	*Percent of cohort alive and on ART (A/N*100)*												
	CD4 median or proportion ≥200/ among patients controlled for CD4												
	Performance scale/ out of "A"												
	A Proportion normal activity												
	B Proportion bedridden <50%												
	C Proportion bedridden >50%												
	Number of persons who picked up ARVs each month for 6/6, 12/12 or 24/24 months/ out of "A"												

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