A Guide to Antiretroviral Therapy

2016 December

Ministry of Health Sri Lanka

National STD/AIDS Control Programme
SRI LANKA

A GUIDE TO ANTIRETROVIRAL THERAPY

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Published by
National STD/AIDS control programme,
Ministry of Health
Colombo
Sri Lanka

1st Edition 2005

2nd Edition 2014

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Acknowledge the support extended by WHO SEARO and WHO country team.

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Abbreviations and Acronyms

3TC	Lamivudine
ABC	Abacavir
ART	Antiretroviral Treatment
ARV	Antiretrovirals (drugs)
ATV	Atazanavir
AZT	Zidovudine
BB	Beach Boys
BMI	Body Mass Index
CMV	Cyto-Megalo Virus
COCP	Combined Oral Contraceptive Pill
Cu-IUD	Copper Intra Uterine Device
CXR	Chest X-Ray
DRV	Darunavir
DU	Drug Users
EFV	Efavirenz
FBC	Full Blood Count
FSW	Female Sex Worker
FTC	Emtricitabine
HAART	Highly Active Anti-Retroviral Therapy
Hb	Haemoglobin
HBV	Hepatitis B Virus
HCP	Health Care Personnel
HCV	Hepatitis C Virus
HEP B	Hepatitis B
HEP C	Hepatitis C
HIV	Human Immunodeficiency Virus
IDU	Injecting Drug User
LFT	Liver Function Tests
LNG-IUS	Levonorgestrel Intra Uterine System
LPV	Lopinavir
MSM	Men having Sex with Men
NVP	Nevirapine
NGO	Non-Governmental Organization
NNRTI	Non-Nucleoside Reverse Transcriptase Inhibitor
NRTI	Nucleoside Reverse Transcriptase Inhibitor
NSACP	National STD AIDS Control Programme
PEP	Post Exposure Prophylaxis
PEPSE	Post Exposure Prophylaxis following Sexual Exposure
POEC	Progesterone Only Emergency Contraception
POP	Progesterone Only Pill
PCR	Polymerase Chain Reaction
PI	Protease Inhibitor
RAL	Raltegravir
/r	Ritonavir
STI	Sexually Transmitted Infections
TB	Tuberculosis
TDF	Tenofovir
TMP	Trimethoprim
TOXO	Toxoplasmosis
UFR	Urine Full Report
WHO	World Health Organization

SECTION ONE

HIV COMPREHENSIVE CARE SERVICES

1.1 Introduction

Sri Lanka remains as a very low prevalent country for HIV since the first Sri Lankan was diagnosed with HIV in 1987. Current estimate (2015) for people living with HIV (PLHIV) is 4200 including estimated 100 children. By end 2015, a cumulative total of 2309 HIV positive persons were reported to National STD/AIDS Control Programme (NSACP) with a continued upward trend over years. The highest number (235) of HIV cases per year was reported in 2015 and male to female ratio was 1.7:1. Reported main mode of transmission remains heterosexual (49%) but male to male (37%) transmissions shows an increasing trend over past five years.

Antiretroviral therapy (ART) for prevention of mother to child transmission (PMTCT) was introduced and available free of charge for pregnant mothers diagnosed with HIV in Sri Lanka in 2002. All diagnosed PLHIV were linked to care at NSACP HIV clinics and ART was available and provided free of charge from 2004. At present, HIV care services are available in all provinces of Sri Lanka under direct supervision of consultant venereologists. Eligibility criteria for ART were changed over years and at present the country adhere to “Test and Treat” policy where everyone diagnosed with HIV are eligible for treatment irrespective of CD4 count, viral load or HIV clinical stage.

1.2 Comprehensive care services for PLHIV

It is critical for people living with HIV to enroll in care as early as possible. This enables both early assessment of their eligibility for ART and timely initiation of ART as well as access to interventions to prevent further transmission of HIV, prevent other infections and co morbidities and thereby to minimize loss to follow-up.

Enrolment and retention in care provides an opportunity for close clinical and laboratory monitoring and timely initiation of ART. Early treatment initiation is associated with clinical benefits to the individual with improved survival and HIV prevention benefits to the community by reducing onward transmission of HIV infection.

General HIV care includes the following:

- Counseling – psychological management
- Manage acute infections
- Screen for infections
- Prophylaxis to prevent infections
- Monitor - CD4 count and viral load
- Antiretroviral therapy
- Provide social support through NGOs/CBOs
- Family planning services and pap smear screening among females
- Prevention services for mother to child transmission of HIV
- Vaccination
- Positive prevention

Objectives of the National ART Guidelines

1. To provide evidence-based recommendations for the delivery of ART and monitoring of patients on ART in general population and specific population groups like (Pregnant women, children, HIV- TB co-infected patients)

2. To provide recommendations regarding the optimal timing of ART initiation, preferred first-line and second-line ARV regimens, and managing HIV in special situations (Pregnancy, Paediatric population, Tuberculosis, Hepatitis B and C, Occupational exposure etc).

3. To provide guidance on various operational issues such as role of care, support and treatment (CST) centers, retention in care, quality of services, referral linkages, and institutional strengthening.

Targeted audience for these guidelines

The target audiences for these guidelines are National STD/AIDS Control Programme managers, partners involved in HIV care and treatment services and, clinicians who are taking care of the HIV patients in public and private sector.

Goals of Antiretroviral Therapy

The currently available ARV drugs cannot eradicate the HIV from the human body. This is because a pool of latently infected CD4 cells is established during the earliest stages of acute HIV infection and persists within the organs/cells and fluids (e.g., liver and lymphoid tissue) even with prolonged suppression of plasma viraemia to <50 copies/ml by antiretroviral therapy. The goals of therapy are given below:

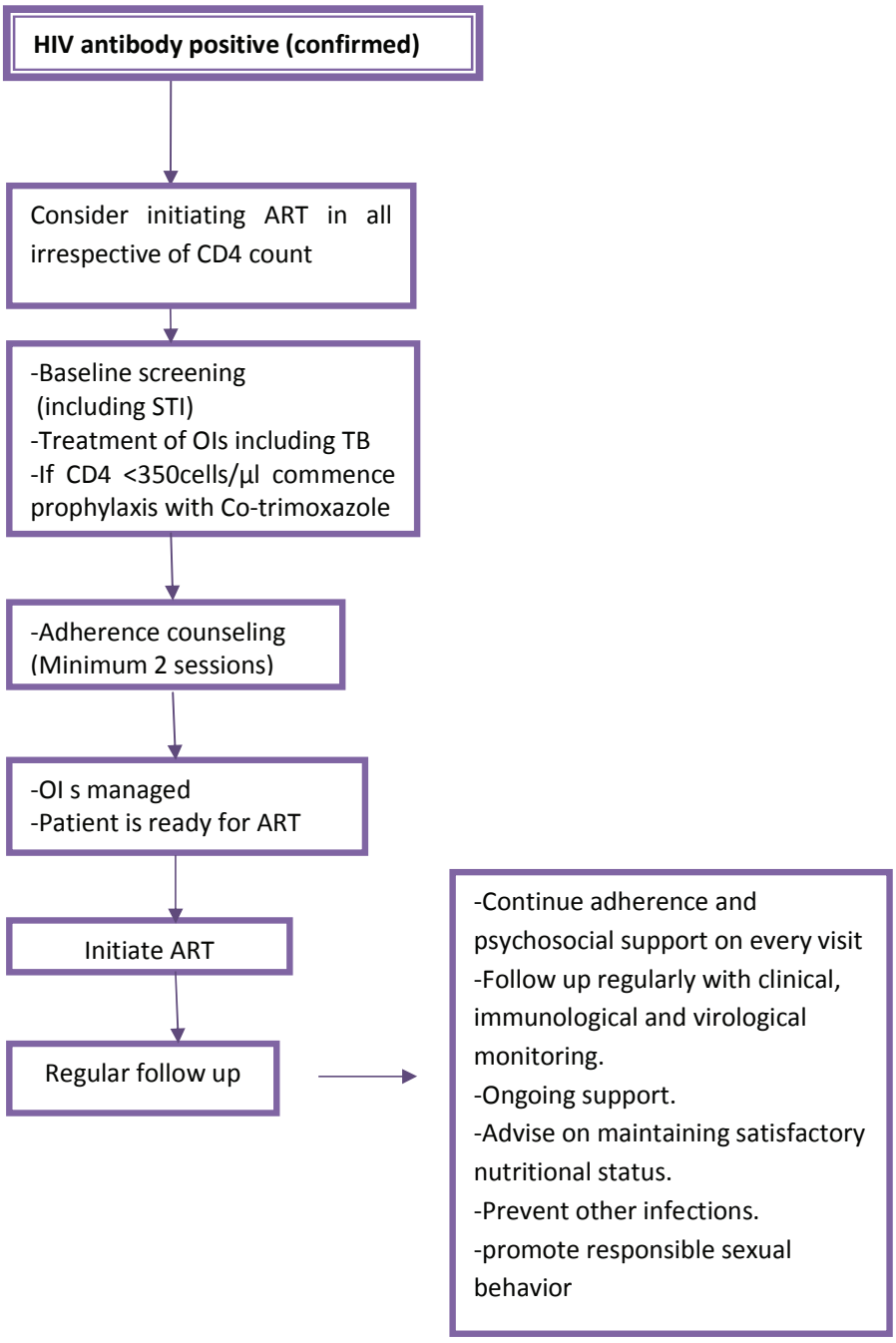
Goals of ARV therapy
• Clinical goals : Prolongation of life and improvement in quality of life
• Virological goals : Greatest possible sustained reduction in viral load
• Immunological goals : Immune reconstitution that is both quantitative and qualitative
• Therapeutic goals : Rational sequencing of drugs in a manner that achieves clinical, virological and immunological goals while maintaining future treatment options, limiting drug toxicity and facilitating adherence
• Prevention Goals : Reduction of HIV transmission due to suppression of viral load

These goals are achieved by completely suppressing viral replication for as long as possible using well-tolerated and sustainable treatment. With prolonged viral suppression, the CD4 lymphocyte count usually increases, which is accompanied by partial restoration of pathogen-specific immune function. For most patients, this results in a dramatic reduction in the risk of HIV-associated morbidity and mortality.

The Programmatic goals of ART

- To provide life-long ART to all eligible patients
- To monitor and report treatment outcomes on a quarterly basis
- To attain individual drug adherence rates of 95% or more
- To ensure retention in care & provide necessary care and support services

Flow chart 1. ART Eligibility for adults and adolescents



1.3 When to start ART in adults and adolescents

Treat all PLHIV irrespective of CD4 count or clinical stage for all age groups and all populations. This includes all pregnant women irrespective of duration of pregnancy.

When to start ART	
Adults and adolescents (10-19 yrs)	Any HIV positive individual, irrespective of CD4 count, as soon as diagnosed positive.
Pregnant and breast feeding women	ART to be initiated for all pregnant & breastfeeding women with any CD4 count, irrespective of duration of pregnancy and continued life-long (option B+)
Infants and children (<10 years)	All HIV infected children should be initiated on ART irrespective of CD4 count but priority to be given to children less than 5 years of age and those with a CD4 count of ≤350 or (<25%) Or those with WHO clinical stages 3 and 4, irrespective of CD4 count.

- Consider initiating ART when confirmed as HIV positive. Efforts should be made to reduce the time between diagnosis and ART initiation to improve health outcomes but adequate preparedness and adherence counseling must be done
- Patients starting on ART should be willing and able to commit to continuation of treatment and understand the benefits and risks of therapy and the importance of adherence.
- Patient may choose to postpone therapy, and providers, on a case by case basis, may elect to defer therapy on the basis of clinical and/or psychosocial factors.

1.4 Baseline assessment prior to ART initiation

Before any person is started on ART, he/she should undergo a baseline assessment that addresses the following questions:

- What is the clinical status?
- What is the immunological, virological, hematological, biochemical and microbiological status?
- What is the family/social support available to continue treatment?
- Should OI treatment and/or prophylaxis be provided?
- Determine other medical conditions e.g. TB, pregnancy, major psychiatric illness and other medications being taken (including traditional therapies).
- Is the person interested in and motivated to take ART?
- Should other support services be provided? (e.g. Linking to positive support groups)

1.5 Important Topics in Counseling

For initial visits (You may have to introduce these topics gradually)

1. Explain
   a. What is HIV/AIDS
   b. Natural history and progression (CD4/Viral load/OI)
   c. Modes of transmission and non- transmission
   d. Misconceptions on modes of transmission
2. Discuss the importance of early treatment
3. Briefly discuss the availability of ART, other health care facilities and importance of regular follow up.

4. Advice for healthy life style measures
    a. Dietary and nutrition advice in relation to maintain optimal health and BMI.
    b. Regular exercise.
    c. Stop alcohol, smoking and other substance abuse.

5. For female patients - Pregnancy issues, importance of regular cervical screening, family planning methods and EMTCT services.

6. Prevention counseling on
    a. Sexual exposures-safe sex and condom demonstration.
    b. Mother to child transmission.
    c. Blood and body fluids - Safe handling and disposal of blood and body fluids, first-aid, advise not to donate blood or organs.

7. Prevention of infections: Availability of antibiotic prophylaxis, hygienically prepared food, safe water and prevention of vector bone infections.

8. Discuss disclosure related issues and the support available and the need and importance of screening of partner/s and children.

Before starting ART

Explain the need to start ART and objectives of treatment:

a. achieve undetectable viral load
b. increase immunity
c. prevent OIs
d. improve survival and quality of life
e. prevention of further transmission

Discuss further:

a. Regarding possible drug interactions-concurrent use of other medications including alternative (Ayurveda, homeopathy etc.) treatment.
b. The need to attend HIV clinic regularly for monitoring of efficacy and adherence.
c. Issues of storage and keeping drug stocks for emergency situations, e.g.-travelling for long distances or staying overnight outside home.
d. Reassess treatment support, If a treatment supporter is present, discuss his/her role in supporting treatment.

1.6 Sexually transmitted infections, Hepatitis B & C

Sexually transmitted infections (STIs) frequently coexist with HIV. They are at times asymptomatic, especially among women, and HIV can alter the natural history of STIs. Whether they are symptomatic or asymptomatic STIs enhance HIV transmission to and from sexual partners. Therefore, screening, diagnosis and treatment of sexually transmitted infections should be offered routinely as part of comprehensive HIV care among adults and adolescents.

PLHIV under care should have;

- an assessment for sexual health including detailed sexual history at the initial presentations for care and an update on each visit
- screened for hepatitis B and C at baseline and referred positive patients for appropriate care
- access to investigation, diagnosis and treatment of STIs and partner notification
- support to maintain sexual health and protective behaviours including condoms
- vaccination against hepatitis B (HBV)
- an annual offer of sexual health screening

Management of sexually transmitted infections in PLHIV

Most of STIs in PLHIV can be managed as in people without HIV. It may be useful to refer “Sexually Transmitted Infection Management Guidelines”.

Cervical cytology for HIV positive women

It is known that women living with HIV have a higher risk of pre-cancer and invasive cervical cancer. Women living with HIV should be followed closely for evidence of pre-cancerous changes in the cervix. Cervical cancer screening leads to early detection of precancerous and cancerous cervical lesions that will prevent serious morbidity and mortality.

Therefore, all women with HIV, age 25 years or older, should be screened for cervical cancer (Pap smear test) at baseline and an annual cervical cytology performed with referral to colposcopy services if required.

1.7 Laboratory monitoring before initiating ART

Clinical assessment and laboratory tests play a key role in assessing individuals before ART is initiated.

Table 1. Laboratory monitoring before initiating ART

Phase of HIV management	Recommended	Desirable(if feasible)
HIV diagnosis	• Screening for sexually transmitted infections • Pap smear[a] • CD4 cell count • Viral load test • Full blood count • ESR • UFR • Liver function tests • Renal function tests • Fasting Blood sugar • Lipid profile • Hepatitis B surface antigen • HCV antibody • TB screening • *Cryptococcus* antigen[b] • Cytomegalovirus antibodies • Pregnancy test[c] • Cardiovascular risk assessment of patients more than 40 year • Assessment for other non-communicable chronic diseases and comorbidities • Eye referral if CD4<50 cells/µl	❖ HLA- B 5701 testing[d] ❖ ECG[e] ❖ Hepatitis A ab ❖ Toxoplasma antibodies ❖ Bone profile

[a] *Females>25 year old*

[b] *If CD4 count <100 cells/mm*

[c] *Females of reproductive age group*

[d] *if plan to start ABC*

[e] *if plan to start ATV*

1.8 Assessment of patient's readiness for therapy

- Build up confidence and assess patient's knowledge.

- Mention the clinic protocol on ARV treatment including the importance of adherence and explain the objectives of the treatment to patient.

- The objectives of the treatment are:
    - to achieve undetectable viral load
    - to build up immunity
    - to avoid occurrence of OI
    - to increase survival and quality of life
    - to prevent onward transmission of HIV

- Repeat discussions may be necessary to prepare patient for therapy.

- Ensure the patient has understood that:

    - the treatment is a suppressive treatment which prevents viral replication.
    - the treatment does not eliminate the virus.
    - the PLHIV has to adhere to treatment protocol to avoid resistance and if resistance develops, treatment may fail.
    - it is a life-long treatment.

- Advice and encourage the patient to disclose the diagnosis to the partner or a family member and encourage testing of the sexual partner/s, and children if status is unknown.

- Ensure the partner or family has understood their role in supporting therapy.

ARV therapy for the individual patient is not an emergency.

-For the individual patient, management of life threatening OIs is the emergency.

The public health emergency is to get large numbers of patients on treatment with good adherence and good overall HIV care.

1.9 Adherence

Adherence is patient's ability to follow a treatment plan, take medications at prescribed times and follow instructions regarding food and other medications. It is important to make sure that the patient has satisfactory blood level of ARV as HIV can multiply in a low concentration of drugs.

HIV is constantly making copies of it and in this process mistakes could be occurred leading to appearance of new variants. These new variants are called "mutants" and some of these mutants may be drug resistant. These drug resistant mutants can proliferate even in the presence of normal ARV concentration in the blood. This will lead to treatment failure. It is mandatory to maintain sufficient ARV concentration in blood through good treatment adherence. In turn, this will prevent the emergence of drug resistant mutations.

The goal of the ART is maximal and durable viral suppression. To achieve this goal, there should be successful antiretroviral therapy which requires adherence of >95%. Failure rates increase sharply as adherence decreases.

<u>Adherence counseling</u>

- Essential to prepare a patient adequately before initiating ART
- Requires 2-3 sessions with the patient prior to starting ART
- Sets the ground for better adherence long term
- Ongoing process with a two way exchange between patient and provider

Session 1 – Explain HIV natural history, viral replication and role of ART
Session 2 –The efficacy of treatment and importance of adherence, resistance development and assess for support available and readiness for treatment
Session 3 – Assessment of patient's readiness and when ready initiation of ART, identify measures to improve adherence

<u>Forms of non-adherence</u>

- Missing one dose of a given drug
- Missing multiple doses of one or more prescribed medications
- Missing whole days of treatment
- Not observing the intervals between doses
- Not observing dietary restrictions

It is important to discuss the adherence strategy including family involvement, treatment buddy and use of other tools such as pill diary, treatment reminder cues etc.

1.10 Counseling for treatment adherence

When counseling a patient for adherence, the following should be stressed.

- Treatment compliance should be strict and adherence to recommended regimens should be greater than 95% to avoid development of resistance.
- Treatment has to be continued for life.
- Timing of drug intake is critical (eg. Drugs taken twice daily must be taken every 12 hours +/- one hour)
- Some drugs are taken with food, some drugs are taken on an empty stomach, some require increase intake of water. Those instructions should be given clearly to the patient.
- Drug side effects have to be understood.
- Financial and social support structures including family members should be assessed.
- Family planning and child bearing issues such as methods of contraception should be addressed.
- Patient should understand the need to attend STD clinic regularly for monitoring of efficacy and adherence.
- Adherence levels need to be assessed in every visit.

Patient should be asked about

- Change in medications
- Dietary instructions
- Storage
- Taken all doses or not
- Taken on time or not
- Reasons for any missing doses
- Complete pill count and self-report
- Difficulties or side effects experienced
- Other medications

Patient should be questioned on missing doses (preferably during the last month) in a non-judgmental way. The patient should understand the purpose is not to find fault but to understand reasons for non-adherence and to help him/her to improve the outcome.

If a person missed a dose it should be taken as soon as remembered and continue the next dose as usual. However, this should not be a routine practice. It is not advisable to take double dose.

The health care provider should provide ongoing support after initiation of treatment to avoid adherence issues. If there are missed appointments patient should be reminded of the importance of continuing ARV treatment to maintain low viral load. The patient needs to be given contact details to contact in an emergency and should be clearly informed regarding the plan of treatment, follow up etc.

1.11 Family planning for women with HIV infection

General family planning management

- Most available methods of family planning may be considered in HIV-positive women and are safe and effective; however, special considerations need to be made in women who currently taking or about to commence ART.
- Consistent condom use should be encouraged in conjunction with the additional contraceptive methods.
- A full choice of options for family planning should be discussed, with appropriate counselling about potential drug interactions and reduced contraceptive efficacy.

SECTION TWO

ANTIRETROVIRAL THERAPY

2. Antiretroviral Drugs

This section includes the followings

1. **Antiretroviral drugs**
2. **Classes of antiretroviral drugs**
3. **Targets of antiretroviral drugs**
4. **Clinical pharmacology of common ARV drugs**

2.1 Antiretroviral drugs

Antiretroviral drugs are the agents which act on the various stages of the life cycle of HIV in the body. These drugs work by interrupting the process of replication of virus and hence reducing the destruction of CD4 cells which leads to delay in progression of HIV infection to AIDS.

To understand the mechanism of action of ARV, one needs to understand the basic steps of the viral replication, in other words life cycle of HIV virus. Virus enters into the CD4 (host) cell involving glycoproteins of the virus and receptors of host cells. The process is called fusion. ARVs interfering with the fusion are called fusion inhibitors. This is the new class of ARV and it includes the drugs like T 20 (Enfuviritide), CCR5 entry inhibitors (Maraviroc) and CXCR4 antagonist. These drugs are currently not available in Sri Lanka. After the fusion with the host cell membrane, viral particles including the viral RNA and the enzymes (reverse transcriptase, integrase and protease) enter into the cytoplasm of the host cell. The first process inside the host cell is the reverse transcription in which viral DNA is synthesized from viral RNA. The process involves the reverse transcriptase enzyme. The ARVs interfering with this process are called nucleoside and nucleotide reverse transcriptase inhibitors (NRTI/NtRTI) and non-nucleoside reverse transcriptase inhibitors (NNRTI). Nucleoside analogue reverse transcriptase inhibitors inhibit the production of proviral DNA by competing with normal nucleotide. Thus in place of normal nucleotide, defective nucleotide analogues are placed in the DNA fragment thus producing a defective DNA which cannot serve the purpose of proviral DNA in the subsequent stages of HIV replication. In this way the replication of HIV is blocked. Non-nucleoside analogue inhibitor acts by destroying the active site of reverse transcriptase. Individual ARVs in these groups include Zidovudine (ZDV), Lamivudine(3TC), Tenofovir (TDF) (examples of NRTI) Nevirapine (NVP) and Efavirenz (EFV)(examples of NNRTI). These groups ARV are available in Sri Lanka and recommended as first line ARVs.

The viral DNA synthesized in cytoplasm travels to the nucleus of the host cell, where it integrates with the DNA of the host cell with the help of integrase. Integrase inhibitors are the ARVs that block the process of integration. Example of ARV of this class is Raltegravir and it is available in Sri Lanka. After integration, the DNA of the infected cell converts into the viral DNA and starts to produce copies of viral RNA. For the production of viral particles, the RNA copies thus produced need to be cut into particles of exact size with the help of protease. Protease inhibitors (PI) interrupt this

process. The examples of protease inhibitors (PI) are Lopinavir, Ritonavir, Atazanavir, Darunavir etc. The boosted PIs (combination of two types of PI) increase the effectiveness, stability of ARV and minimize the side effects. Lopinavir boosted with ritonavir (LPV/r), Atazanavir boosted with ritonavir (ATV/r) and Darunavir boosted with ritonavir (Dar/r) are some of the boosted PIs available in Sri Lanka.

The viral RNA after the action of protease converts into the viral particles. These particles assemble with the enzymes into a capsule, which eventually leaves the infected cell by the process called budding. The viruses after budding develop into the mature viruses. There are some ARV inhibiting the process of maturation and are called maturation inhibitors. These ARVs are not available in Sri Lanka.

Newer classes of antiretroviral drugs like Fusion inhibitors (FI), Integrate Strand Transfer Inhibitors (INSTI), CCR5 Antagonists act by preventing fusion and entry of the virus to the target cell (CD4), preventing the integration of the HIV proviral DNA into the human DNA and blocking co-receptors needed for the virus to enter the cell.

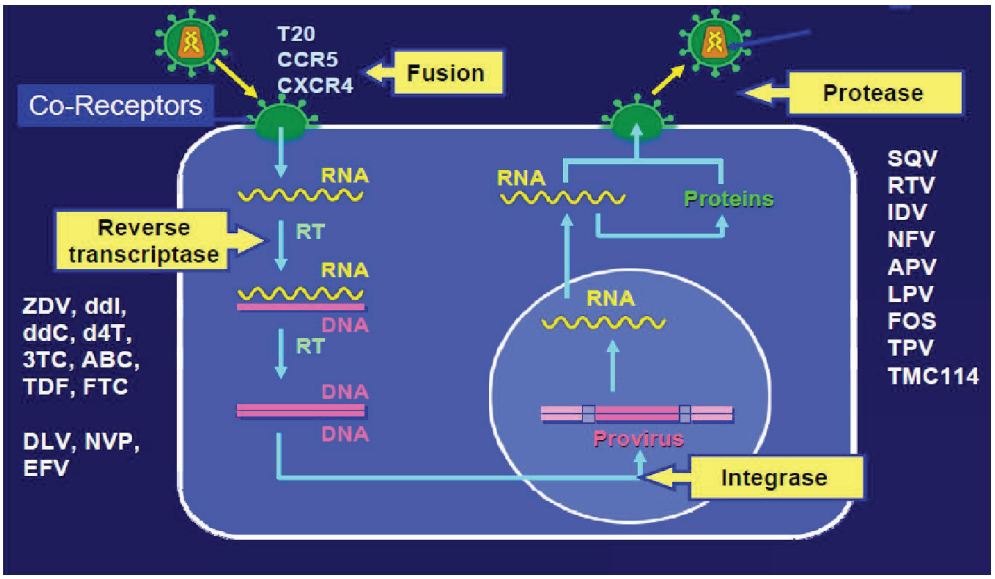
2.2 Classes of Antiretroviral drugs

Depending on the mechanism of action the ARVs are categorized into following classes

1. Nucleoside and nucleotide analogues
   1a. Nucleoside reverse transcriptase inhibitors (NRTI)
   1b. Nucleotide reverse transcriptase inhibitors (NtRTI)
2. Non-nucleoside reverse transcriptase inhibitors (NNRTIs)
3. Protease inhibitors (PIs)
4. Integrase Strand Transfer Inhibitors (INSTI)
5. Fusion Inhibitors
6. Cellular Chemokine Receptor (CCR5) Antagonist

The mechanism of the action of ARV is shown graphically below

Targets of anti-retroviral drugs (see explanation above)



Clinical Pharmacology of Commonly Used ARV drugs

Nucleoside/Nucleotide Reverse Transcriptase Inhibitors (NRTI)

The first effective class of antiretroviral drugs was the Nucleoside analogues which 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 non-peptidic chemical structure. All nucleoside analogs have been associated with lactic acidosis and hepatic steatosis as their common side effects.

Details of individual ARV of this class are given below

Commonly used NRTIs

Generic Name	Dose	Adverse effects
Zidovudine (ZDV, AZT)	300 mg twice daily	Anaemia, neutropenia, bone marrow suppression, gastrointestinal intolerance, headache, insomnia, myopathy, lactic acidosis, skin & nail hyperpigmentation.
Tenofovir (TDF)	300mg once daily	Renal toxicity, Bone demineralization
Lamivudine (3TC)	150 mg twice daily Or 300 mg once daily	Minimal toxicity, rash though very rare
Emtricitabine (FTC)	200 mg once daily	Unusual, mild to moderate diarrhea, headache, nausea, and rash. some patients may experience hepatotoxicity or lactic acidosis.
Abacavir (ABC)	300 mg twice daily or 600mg OD	Hypersensitivity reaction in 3 to 5% (can be fatal), fever, rash, fatigue, nausea, vomiting, anorexia, respiratory symptoms (sore throat, cough, shortness of breath) Re challenging after reaction can be fatal.

Non-Nucleoside Reverse Transcriptase Inhibitors (NNRTIs)

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.

Details of individual ARV of this class are given below

Commonly used NNRTIs

Generic Name	Dose	Food related advices	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), sometime life-threatening hepatic toxicity. Skin rash occasionally progressing to severe conditions including Stevens Johnson syndrome and TEN. Patients who develop severe hepatic toxicity or grade 4 skin rashes while treated with Nevirapine should not be rechallanged.
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), and personality change. Rash occurs, but less common than NVP.

Protease Inhibitors (PIs)

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. All PIs can produce increased bleeding in haemophilia, 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).

Details of individual ARV of this class are given below

Commonly used PIs

Generic Name	Dose	Adverse Effect
Atazanavir/ ritonavir	300mg Atazanavir + 100mg ritonavir once daily	Hyperbilirubinaemia, Less lipid problems than LPV/r, Hyperglycemia, Fat maldistribution, Nephrolithiasis Interaction with acid blocking agents. Do not co administer with H2 receptor antagonist. Give 12 hours gap when using proton pump inhibitors
Lopinavir /ritonavir (LPV/r) Heat stable tablets	200mg Lopinavir/50mg Ritonavir Fixed dose tablet 2 tablets twice daily	Diarrhoea, nausea, vomiting, abnormal lipid profiles, glucose intolerance. Any PI should not be prescribed with Simvastatin, as they significantly increase the level of simvastatin leading to rhabdomyolysis resulting into severe kidney failure.

2.3 What ART regimen to start with (first-line ART)

Choice of Initial Regimen

The guiding principles remain the same i.e. use fixed dose combination of three antiretroviral drugs, use simplified, less toxic and more convenient regimen. The first line ART essentially comprises of a NRTI backbone, preferably Non Thymidine and one NNRTI, preferably EFV.

Based on evidence supporting better efficacy and fewer side effects, it is now recommended to use

Tenofovir (TDF) + Emtricitabine (FTC) + Efavirenz (EFV) as fixed dose combination (FDC) in a single pill.

This regimen has the advantage of harmonization of treatment among all adults, adolescent, pregnant women, HIV/TB and HIV Hepatitis co infected patients

Table 2 - First-line ART regimens

First –line ART	Preferred first –line regimens	Alternative first –line regimens*
Adults and Adolescents (10 to 19 years) **≥ 35 kg**	TDF + FTC + EFV	TDF + FTC + ATV/r TDF + FTC + LPV/r ABC+3TC+EFV(or NVP)** AZT + 3TC + EFV /NVP* AZT + 3TC + LPV/r AZT + 3TC + ATV/r TDF + 3TC (or FTC) + DTG***

** NVP – Women with CD4 count > 250 cells /mm3 and men with CD4 count > 400 cells /mm3 are at risk for NVP hypersensitivity with fatal hepatic toxicity.*

***ABC - Presence of HLA-B 5701 gene indicate higher risk for hypersensitivity. Viral load should be <100,000 copies/ml*

**** Safety and efficacy data on use of DTG in pregnant women, people with HIV/TB coinfection and children younger than 12 years of age are not available.*

ABC or boosted PIs (ATV/r, DRV/r, LPV/r) can be used in special circumstances.

2.4 Expected drug toxicities and side effects after commencing ARV treatment

PLHIV on ART can experience various drug toxicities. Toxicities can affect gastrointestinal system, central nervous system, liver, kidney and bone marrow leading to clinical, biochemical, haematalogical, metabolic and other changes. Though any patient on a given ART regimen can experience toxicities, in some patients there are other preexisting factors that can make them more vulnerable to toxicities. Therefore patients with following high risk situations need careful monitoring.

Some common toxicities of first line drugs are as below

Drugs	Short term toxicities	Medium term toxicities
Zidovudine	Headache, nausea, vomiting, malaise, diarrhoea, bone Marrow suppression, anaemia (Macrocytic)	Bone Marrow suppression, anaemia (Macrocytic), hyper pigmentation, lactic acidosis, proximal myopathy
Tenofovir	Nephrotoxicity (low incidence), Fanconi syndrome and rarely acute renal failure	
Efavirenz	Drowsiness, dizziness, confusion, vivid dreams, skin rashes, hepato toxicity (very rare)	
Nevirapine	Skin rashes, hepato toxicity	

Table 3 - Risk factors for developing ARV drug toxicities

ARV drug related toxicity	High risk situations for experiencing toxicities
AZT related haematological toxicity	• CD4 count of <200 cells/mm3 • Anaemia at baseline
AZT related lactic acidosis	• BMI > 25 (or body weight > 75kg) • Prolong exposure to nucleoside analogues
TDF related renal toxicity	• Underlying renal disease • Age >40 years • BMI <18.5 (or body weight <50 kg) • Untreated diabetes mellitus • Untreated hypertension • Concomitant use of a boosted PI or nephrotoxic drugs
TDF related decrease in bone mineral density	• History of osteomalacia and pathological fracture • Risk factors for osteoporosis or bone loss
EFV related CNS toxicity	• Depression or psychiatric disease (previous or at baseline)
EFV related hepatotoxicity	• HCV and HBV coinfection • Concomitant use of hepatotoxic drugs
NVP related hepatotoxicity	• HCV and HBV coinfection • CD 4 count > 250 cells/µl in a female • CD 4 count >400 cells/µl in a male
ABC related toxicities	• Presence of HLA-B*5701 gene
ATV/r related ECG changes	• Pre-existing conduction disease • Concomitant use of other drugs that may prolong the PR interval
ATV/r related hyperbilirubinemia	• Underline hepatic disease • Hepatitis B and C coinfection
DRV/r	• Underline hepatic disease • Hepatitis B and C coinfection • Sulphur allergy
RAL	• Concomitant use of other drugs that increase the risk of myopathy and rhabdomyolysis.

Clinical and biochemical effects due to toxicities can become apparent within first few weeks, first few months and within 6-18 months after initiating treatment.

Therefore, patients on ART have to be evaluated during each clinic visits for early detection of short term, medium term and long term toxicities, so that the adverse outcomes due to toxicities can be minimized.

Table 4 Laboratory indications to change ARVs due to toxicity

Laboratory indications to change ARVs due to toxicity		
Haemotology	Haemoglobin	Less than 7.0 g/dl
	Neutrophil count	Less than 750/mm^3
	Platelets	Less than 50,000mm^3
Chemistries	Creatinine	More than 3 x upper limit of normal
	Glucose (fasting non diabetics)	Less than 39 mg/dl or more than 251mg/l
Liver function tests	AST (SGOT)	More than 5 x upper limit of normal
	ALT (SGPT)	More than 5 x upper limit of normal
	Alkaline phosphatase	More than 5 x upper limit of normal
	Bilirubin	More than 2.5 x upper limit of normal
	Amylase, lipase	More than 2 x upper limit of normal

Sometimes people on ART become symptomatic due to drug toxicities. In such situations it is important to identify the possible drug/s that have led to toxicity and manage accordingly.

Table 5 ART toxicities according to duration of presentation

Time	Toxicities & side effects	Common causes
Short term (first few weeks)	GI toxicities including nausea and vomiting, diarrhoea	AZT, TDF, PIs
	Rash Most rashes occur within the first 2–3 weeks	NVP, EFV, ABC, PIs and Raltegravir(rarely)
	Hepato toxicity More common if there is coinfection with hepatitis B or C	NVP, EFV, PIs
	Drowsiness, dizziness, confusion and vivid dreams are associated with the use of EFV. Normally self-resolving but can take weeks to months	EFV
Medium term (first few months)	Anaemia and neutropenia Sudden and acute bone marrow suppression due to AZT can occur within the first weeks of therapy or present as slowly progressive anaemia over months	AZT
	Hyperpigmentation of skin, nails and mucous membranes	AZT
	Lactic acidosis can occur at any time (More common after the first few months.	AZT
Long term (after 6–18 months)	Lipodystrophy and lipoatrophy	AZT, PIs
	Dyslipidaemia	EFV, PIs

Table 6 Symptom directed toxicity management

Symptom of toxicity	Causative ARV drug	Recommendation
Diarrhoea	Lopinavir/ritonavir (LPV/r), Darunavir/r	Usually self-limited, no 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) ABC, DRV/r	In mild cases, give antihistamines. Moderate rash, non-progressive and without mucosal involvement or systemic signs, consider a single NNRTI substitution (i.e. NVP with EFV). In moderate and severe cases, discontinue ART and give supportive treatment. After resolution, resume ART with substitution.
Dyslipidaemia, insulin resistance and hyperglycaemia	PIs	Consider replacing the suspected PI by drugs with a lower risk of metabolic toxicity.
GI intolerance (nausea/vomiting)	All ARVs	Usually self-limited, no need to discontinue ART. Symptomatic treatment should be offered.
Haematological toxicities (particularly anaemia and leucopenia)	AZT	If severe (Hb<6.5 g% and/or absolute neutrophil count <500 cells/mm3) replace by an ARV with minimal or no bone marrow toxicity (eg. d4T, ABC or TDF) and consider blood transfusion in severely distressed persons.
Hepatitis	All ARVs (particularly NVP and PI/r)	If ALT >5-fold the basal level, discontinue ART and monitor. After resolution, replace the drug most likely to be associated with another one.
Hyperbilirubinaemia (indirect)	Atazanavir (ATV)	Generally asymptomatic, but can cause scleral icterus (without ALT elevation). Replace ATV with another PI if there are cosmetic reasons.
Hypersensitivity reaction	ABC Raltegravir	Discontinue ABC and do not restart. Give symptomatic treatment. Re-exposure may lead to a severe and potentially life threatening reaction. An allergic (hypersensitivity) reaction has been reported in some people using raltegravir.
Lactic acidosis	All NRTIs	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.

During evaluation of patients with ART toxicities it is important to assess the degree of toxicities (Grade toxicities) based on the clinical and laboratory parameters as shown in Annexure 8.

2.5 Specific Instructions (for first line regimen)

Specific Instructions on ART-Adults and adolescents

1. How to give TDF + FTC+ EFV regimen

Tenofovir (TDF) 300 mg daily at night Emtricitabine (FTC) 200mg daily at night Efavirenz 600 mg daily at night

- Tenofovir (TDF) 300 mg + Emtricitabine (FTC) 200mg + Efavirenz 600 mg is available as a fixed drug combination. One tablet in the night, preferably to be taken on an empty stomach (preferrably last thing in the night after dinner).
- Crushing or splitting tablet not recommended.
- Avoid administration with a high-fat meal because of potential for increased absorption.

2. How to give TDF+ FTC + ATV/r regimen

Tenofovir (TDF) 300 mg daily Emtricitabine (FTC) 200mg daily Atazanavir (ATV) 300mg daily Ritonavir(RTV) 100mg daily

- TDF+ FTC is available in fixed dose and ritonavir(r) is available as separate tablet. ATV is available in capsule form.
- Take one tablet of TDF+FTC, ATV 300mg and ritonavir 100mg once daily with food (can take in the morning with breakfast or at night with dinner).
- TDF+FTC fixed dose tablet can be crushed and ATV capsule can be opened and dissolve in water but crushing of ritonavir tablet is not recommended.
- As atazanavir requires acidic PH for absorption concomitant use of drugs that increase gastric PH such as PPI, H2 receptor antagonist and antacids should be avoided.

3. How to give TDF+ FTC + LPV/r regimen

Tenofovir (TDF) 300 mg daily Emtricitabine (FTC) 200mg daily Lopinavir (LPV) 400mg twice daily Ritonavir(RTV) 100mg twice daily

- TDF+ FTC is available in fixed dose and Lopinavir/Ritonavir (LPV/r) is available as combined tablets.
- Take one tablet of TDF+FTC and 400mg/100mg LPV/r (2 tablets) in the morning with or without food.
- Take 400mg/100mg (2 tablets) of LPV/r in the night with or without food.
- TDF+FTC fixed dose tablet can be crushed but crushing of LPV/r tablet is not recommended.

4. How to give TDF+ FTC +DRV/r regimen

Tenofovir (TDF) 300 mg daily Emtricitabine (FTC) 200mg daily Darunavir 600 mg bd/ 800mg daily Ritonavir(RTV) 100mg daily

- TDF+ FTC is available in fixed dose and darunavir and ritonavir are available as separate tablets.
- Take one tablet of TDF+FTC, 600mg of DRV and 100mg of ritonavir twice daily (morning and night) with food.
- TDF+FTC fixed dose tablet can be crushed and no potential problems identified with crushing DRV tablets .Crushing of ritonavir tablet is not recommended.

5. How to give TDF+ FTC + NVP regimen

Tenofovir (TDF) 300 mg once daily. Emtricitabine (FTC) 200mg once daily. Nevirapine (NVP) 200mg daily once daily for first 2 weeks followed by 200 mg twice a day

- First 2 weeks In the morning - 1 tablet of NVP 200 mg 1 tablet can be taken with or without food In the night
  - 1 tablet of TDF + FTC Fixed drug dose tablet can be taken with or without food.
  After 2 weeks AST / ALT need to be repeated and if there is no rash and no signs of hepatic toxicity, increase the dose of NVP to 200 mg twice daily.
  The lead-in dose decreases the risk of rash and early NVP induced hepatitis.

- After 2 weeks In the morning -1 tablet of NVP 200 mg 1 tablet can be taken with or without food
- In the night -
  1 tablet of TDF + FTC + Fixed drug dose tablet can be taken with or without food
  1 tablet of NVP 200 mg 1 tablet can be taken with or without food
- TDF+FTC fixed dose tablet and Nevirapine 200mg immediate release tablets coated tablet can be crushed
- No diet restrictions.

6. How to give AZT+3TC+EFV regimen

Zidovudine (AZT) 300 mg twice a day Lamivudine (3TC) 150mg twice a day Efavirenz (EFV) 600mg daily at night

- In the morning - 1 tablet of AZT + 3TC fixed drug dose tablet can be taken with or without food
- In the night - 1 tablet of AZT + 3TC fixed drug dose tablet and

  Efavirenz (EFV) 600mg tablet (better to take both on an empty stomach)

- AZT+3TC fixed dose tablet can be crushed but crushing of EFV is not recommended.
- Avoid administration with a high-fat meal because of potential for increased absorption of EFV.

7. How to give AZT+3TC+ATV/r regimen

Zidovudine (AZT) 300 mg twice a day Lamivudine (3TC) 150mg twice a day Atazanavir (ATZ) 300mg daily Ritonavir(RTV) 100mg daily

- In the morning - 1 tablet of AZT + 3TC Fixed drug dose tablet , atazanavir , ritonavir can be taken with or without food
- In the night - 1 tablet of AZT + 3TC fixed drug dose tablet with or without food.
- AZT+3TC fixed dose tablet can be crushed just before taking tablets if there is difficulty in swallowing. ATV capsule can be opened and dissolve in water but crushing of ritonavir tablet is not recommended. .

8. How to give AZT+3TC+LPV/r regimen

Zidovudine (AZT) 300 mg twice a day Lamivudine (3TC) 150mg twice a day Lopinavir (LPV) 400mg twice daily Ritonavir(RTV) 100mg twice daily

- In the morning and night - 1 tablet of AZT + 3TC fixed drug dose tablet ,LPV 400mg and RTV 100mg can be taken with or without food

9. How to give AZT + 3TC + NVP regimen

Zidovudine (AZT) 300 mg twice a day Lamivudine (3TC) 150mg twice a day Nevirapine (NVP) 200mg daily once daily for first 2 weeks followed by 200 mg twice a day

- Zidovudine (AZT) 300 mg twice a day Lamivudine (3TC) 150mg twice a day and Nevirapine (NVP) 200mg once daily for first 2 weeks followed by 200 mg twice a day.
- First 2 weeks
  In the morning - 1 tablet of AZT + 3TC + NVP fixed dose can be taken with or without food
  In the night - 1 tablet of AZT + 3TC fixed dose can be taken with or without food.
  After 2 weeks AST / ALT need to be repeated and if there is no rash and no signs of hepatic toxicity, increase the dose of NVP to 200 mg twice daily. The lead-in dose decreases the risk of rash and early NVP induced hepatitis.
- After 2 weeks
  In the morning and night - 1 tablet of AZT + 3TC + NVP Fixed dose can be taken with or without food

10. How to give ABC + 3TC + EFV regimen

Abacavir (ABC) 300 mg twice daily Lamivudine (3TC) 150 mg twice daily Efavirenz 600 mg daily

Warn patients and parents about risk of serious, potentially fatal hypersensitivity reactions

- ABC+ 3TC is available in fixed dose and EFV is available as a single tablet.
- Take one tablet of ABCV+3TC in the morning and night and 1 tablet of EFV in the night preferably empty stomach.

- Avoid administration with a high-fat meal because of potential for increased absorption of EFV.
- ABC+3TC fixed dose tablet can be crushed but crushing/splitting of EFV not recommended.

11. How to give TDF+ FTC + RAL regimen

Tenofovir (TDF) 300 mg daily Emtricitabine (FTC) 200mg daily Raltegravir 400mg twice daily

- TDF+ FTC is available in fixed dose and raltegravir available as a tablet.
- Take one tablet of TDF+FTC and 400mg tablet of RAL in the morning with or without food.
- Take 400mg tablet of RAL in the night with or without food.
- TDF+FTC fixed dose tablet can be crushed and but crushing of raltegravir film coated tablet is not recommended.
- Avoid antacids with aluminium/ magnesium with RAL. If needed can take antacids with calcium carbonate but take RAL 2 hours before or 4 hours after.
- If prescribed the TB drug rifampicin, dose of raltegravir may be increased to 800mg (two tablets) twice daily, as rifampicin can reduce drug levels of raltegravir. Should not take any supplements that contain calcium, iron, magnesium, aluminium or zinc at the same time as raltegravir as they will reduce its absorption.

- See HIV clinic doctor immediately (or hospital doctor) if develop a rash together with any of these symptoms: fever; feeling generally unwell or extremely tired; muscle or joint ache; blistering of the skin; mouth ulcers; swelling of the eye, lips, mouth or face; breathing difficulties; yellowing of the skin or eyes; dark urine; pale stools; or pain, aching or sensitivity on the right-hand side of the body, below the ribs.*
  **FDA safety and warning for Raltegravir*

Table 7.1 Monitoring patients receiving ART

	Investigation	Remarks
Receiving ART	• CD4 cell count (every 6 months) • HIV viral load (at 6th month,12 months, then if suppressed annually) • Full blood count • Liver function tests • Renal function tests • Fasting Blood sugar • Lipid profile	**AZT –**FBC 2weekly in the first month Then 3-6 monthly or when indicated **NVP** –AST/ALT/Bilirubin 2 weekly in the first month. Then 3-6 monthly or when indicated **TDF** – UFR/S.creatinine/E-GFR every 6 monthly. if co existing renal problems , DM and hypertension, more frequent monitoring indicated.
Treatment failure	• CD4 cell count • HIV viral load • Resistance testing	

Table 7.2 Suggested clinical evaluation and monitoring of patients on ART

Investigations	At baseline	2 weeks	4 weeks	8 weeks	12 weeks	monthly	3-4 monthly	6 monthly	Annually
FBC (Hb&WBC/DC)	**√**		**√**				**√**		**√**
Lipid profile	√		When required					On PI/NNRTI +risk	On PI/NNRTI
FBS	√								✓
LFT (ALT&AST)	√	On NVP	On NVP		√			✓	
Serum creatinine	√	√	When required /on TDF					√	
Blood urea	√								
Serum electrolytes	√		When required						
Hepatitis B s Ag	√								
HCV antibody	√								
Pregnancy test	When required								
Toxoplasma Ab	√								
CMV Ab	√								

2.6 Treatment adherence and drug resistance

- Poor adherence is associated with viral mutations due to persistence of viral divisions.
- Viral mutations are associated with drug resistance.
- Drug resistance is associated with treatment failure.
- Drug resistance does not occur with an optimal treatment that inhibits viral replication.
- Drug resistance may occur without any treatment even due to transmitted resistant virus.
- Drug resistant virus may be transmitted to partners if safe sex is not practiced.

Drug resistance occurs when a suboptimal treatment does not fully prevent virus from replicating (detectable viral load).

Studies of drug adherence in the developed world have suggested that adherence rates >95% are desirable to maximize the benefits of ARV treatment and avoid treatment failure.

The increase in ARV resistance may lead to increased transmission of resistant viral strains. Currently approximately 10% of new HIV 1 infection in the United States and Europe are with viral strains exhibiting resistance to at least one drug.

When treatment failure is suspected resistance testing need to be arranged.

At the national level, a drug resistance sentinel surveillance system is implemented to regularly modify recommended treatment regimens, according to the prevalence rate of drug resistance in the infected population.

Monitoring the response to ART and the diagnosis of treatment failure

Monitoring individuals receiving ART is important to ensure successful treatment, identify adherence problems and determine whether and which ART regimens should be switched in case of treatment failure. The value of viral load testing as a more sensitive and early indicator of treatment failure is increasingly recognized and is the gold standard for monitoring the response to ARV drugs.

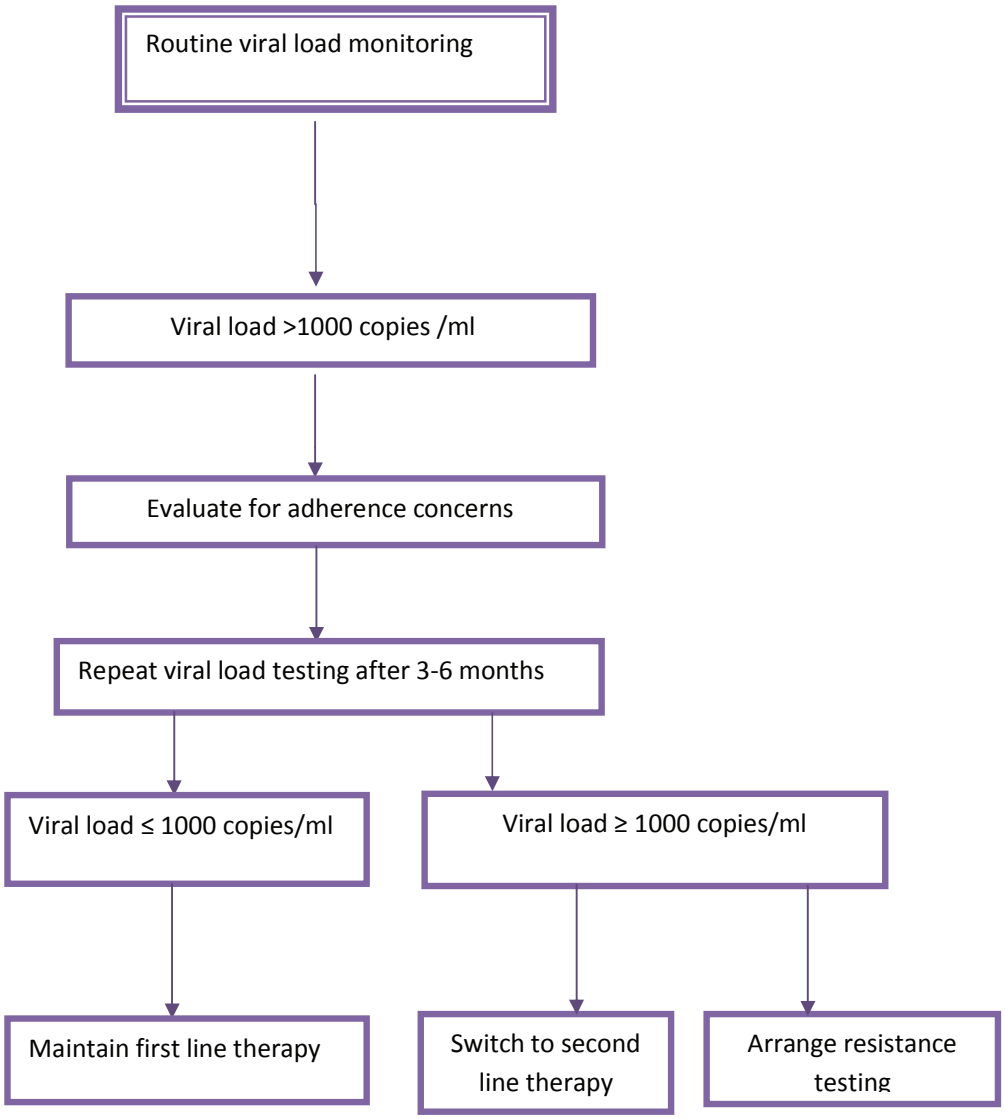
2.7 Reasons for changing ARV treatment

Table 8 WHO definitions of clinical, immunological and virological failure for the decision to switch ART regimens

Failure	Definition	Comments
Clinical failure	**Adults and adolescents** New or recurrent clinical event indicating severe immune deficiency (WHO clinical stage 4 condition) after 6 months of effective treatment **Children** New or recurrent clinical event indicating advanced or severe immune defiency (WHO clinical stage 3 and 4 clinical condition with exception of TB) after 6 months of effective treatment	The condition must be differentiated from immune reconstitution inflammatory syndrome occurring after initiating ART. For adults, certain WHO clinical stage 3 conditions (pulmonary TB and severe bacterial infections) may also indicate treatment failure.
Immunological failure	**Adults and adolescents** • CD4 count falls to the baseline or below • Persistent CD4 levels below 100 cells/mm3 • CD4 count drop by 50% or more from the peak value **Children younger than 5 years** Persistent CD4 levels below 200 cells/mm3or <10% **Older than 5 years** Persistent CD4 levels below 100 cells/mm3	Without concomitant or recent infection to cause a transient decline in the CD4 cell count. Current WHO clinical and immunological criteria have low sensitivity and positive predictive value for identifying individuals with virological failure.
Virological failure	Plasma viral load above 1000 copies/ml based on two consecutive viral load measurements after 3 months, with adherence support	An individual must be taking ART for at least 6 months before it can be determined that a regimen has failed. Viral blips or intermittent low-level viraemia (50–1000 copies/ml) can occur during effective treatment but have not been associated with an increased risk of treatment failure unless low level viraemia is sustained.

Flow Chart 2 – How to detect treatment failure

Viral load testing strategies to detect or confirm treatment failure and switch ART regimen in adults, adolescents and children



2.8 Second line regimens

Using a boosted PI + two NRTI combinations is recommended as the preferred strategy for second-line ART for adults, adolescents and also for children when NNRTI-containing regimens were used in first-line ART.

Second-line ART for adults and adolescents

Second-line ART for adults should consist of two nucleoside reverse-transcriptase inhibitors (NRTIs) + a ritonavir-boosted protease inhibitor (PI).

- Heat-stable fixed-dose combinations of ATV/r and LPV/r are the preferred boosted PI options for second-line ART
- Heat stable fixed dose combination of DRV/r can be used as an alternative boosted PI option for second line ART.
- A combination of RAL + LPV/r can be used as an alternative second line ART regimen.

Table 9 Preferred second-line ART regimens for adults and adolescents

First line failed regimen	**Second line regimen suggested Two NRTI+boosted PI**	**3rd line regimens**
2 NRTIs + EFV	**2 NRTI + ATV/r or LPV/r or DRV/r**	**DRV/r + DTG (RAL) +_ 1-2 NRTIs**

In PI experienced patients the recommended DRV/r dose should be 600/100 mg twice daily.

Specific Instructions (for Second Line Regimens)

The recommended prescribed dose of atazanavir (ATV) is ATV 300 mg + ritonavir (RTV) 100mg once daily. No dosage adjustment is required for patients with renal dysfunction unless they are on haemodialysis. Considering the widespread use of atazanavir, clinicians caring for HIV-infected patients should have familiarity with the entity of protease inhibitor-associated hyperbilirubinaemia.

Isolated unconjugated hyperbilirubinaemia is the most common laboratory abnormality associated with the use of atazanavir and this is not associated with hepatocellular injury. Although not considered a serious adverse effect, the higher levels of unconjugated hyperbilirubinaemia associated with this drug can manifest as jaundice with a high colored urine. The onset of atazanavir associated hyperbilirubinaemia typically occurs within several months, and bilirubin levels generally peak within 4 months (range 1 to 8 months); the subsequent natural history on therapy is notable for a non-progressive course, with bilirubin levels remaining generally stable in patients on further follow-up. Routine monitoring of bilirubin is acceptable.

An isolated elevation in total bilirubin should be confirmed as predominantly unconjugated by testing the indirect fraction of bilirubin. The presence of elevated conjugated bilirubin or changes in serum hepatic aminotransferases or alkaline phosphatase warrant further investigation for other causes of hyperbilirubinaemia, such as other drug hepatotoxicity, viral hepatitis, alcoholic hepatitis or cholestasis. It is important to recognize that patients who are on atazanavir but with acute hemolysis will also develop increased indirect bilirubin levels.

Dose reduction of atazanavir is not recommended in this setting. In most cases, a change to an alternative regimen is necessary only for patients who develop an unacceptable level of jaundice with Grade 3 (5-10 times of ULN) & 4 (>10 times of ULN) elevation of serum ALT & AST.

Options for third line regimens

- Darunavir
- Raltegravir
- Maraviroc

can be considered.

2.9 Check list for follow up visits of HIV positive patients

(Please check the following aspects of care at each and every visit. Plan investigations at appropriate intervals)

1. Ask for symptoms of opportunistic infections and Tuberculosis.
2. Any other symptoms.
3. Assess weight and Performance scale.
4. Check for adherence issues. Any missed or delayed doses during last month, drugs in hand and pill count if possible
6. ART side effects.
7. Last sexual exposure, condom usage.
9. Last menstrual period.
10. Contraception.
11. Sero status of partner and children.
12. Relevant investigations (CD4, VL, FBC, LFT, RFT, Lipid profile, FBS)
13. Annual STI screening and PAP smear screening.
15. Dietary habits and exercise.
17. Advice on smoking, alcohol and drugs
18. Non communicable disease and follow up.
19. Other medical conditions and current medications other than ART.
20. Serious Non-AIDS events (Non-AIDS malignancies, cardiovascular disease and end stage kidney disease, osteoporosis).
21. Counseling on adherence, safer sex and psychosocial issues.

2.10 Post Exposure Prophylaxis (PEP)

(Refer PEP circular)

Management of healthcare workers following occupational exposure to blood and other body fluids and post exposure prophylaxis for HIV

The General Circular letter reference No -36/2001 dated 12th March 2001 on "Management of Health-Care Worker Exposures to HIV and Recommendations for Post Exposure Prophylaxis" is hereby cancelled.

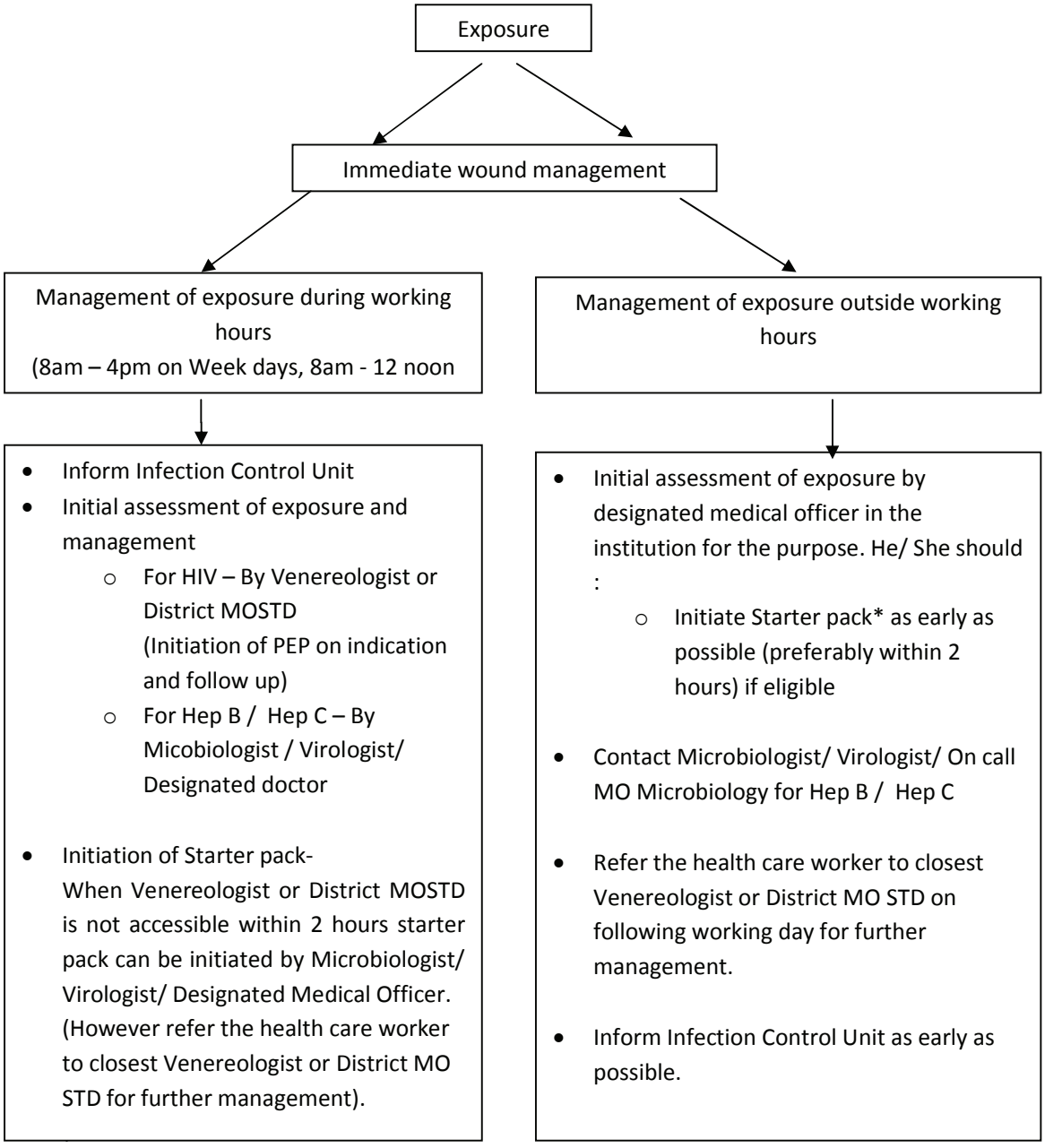
This circular outlines recommendations for the management of health care workers who experience occupational exposures to blood and other body fluids that might contain Human Immunodeficiency Virus (HIV).

Although preventing exposures to blood and other body fluids that might contain HIV is the primary means of preventing occupationally acquired HIV infection, appropriate post-exposure management is an important element of workplace safety. Department of Health has considered information available worldwide and recommends that the following procedure for post exposure prophylaxis (PEP) be followed in an accidental exposure.

This circular recommends all health care workers with occupational exposures to HIV to attend to a STD clinic with the source blood sample as early as possible for management and follow up.
It is the responsibility of the head of the institution to make sure

- That there is a functional system of management of healthcare workers following occupational exposure to blood and other body fluids.
- That antiretroviral drugs (ARV) are available for PEP.

Management of occupational exposures



Antiretroviral medication for the post exposure prophylaxis for 5 days. We recommend keeping this starter pack in a readily accessible place / places such as OPD/ETU/ICU/PCU/Pharmacy.

Definition of a Health Care Worker (HCW) for the purpose of this circular

The term HCW refers to all persons working in the health care setting who has the potential for exposures to infectious materials, including body substances (e.g. blood, tissue and specific body fluids), contaminated medical supplies and equipment, and contaminated environmental surfaces(1).

Definition of Exposure

An "exposure" that may place a health care worker at risk for HIV infection and requires consideration of PEP is defined as follows:

1. Percutaneous injury; Needle-sticks or cut with a sharp object.
2. Contact of mucous membranes
3. Non-intact skin- chapped, abraded or afflicted with dermatitis

With blood, tissue or other body fluids that are potentially infected.

(Semen, vaginal secretions, breast milk, cerebrospinal fluid (CSF), synovial fluid, pleural fluid, peritoneal fluid, pericardial fluid and amniotic fluid are considered potentially infectious)(2).

Saliva, urine, nasal secretions, vomitus and feces bear no risk of HIV infection in the absence of visible blood. Exposure to tears and sweat does not require post exposure prophylaxis (2)(3).

Risk of Occupational Transmission of HIV to HCWs from HIV infected blood

• Percutaneous injury	0.30%	95% CI = 0.2% - 0.5%.(1)(3)(5)
• Mucous membrane	0.09%	95% CI = 0.006% - 0.5%.(1)(3)

Management of the Exposed Site

Exposed sites should be cleansed of contaminated fluid as soon as possible after exposure. Wounds and skin sites are best cleansed with soap and water, avoiding irritation of the skin. Exposed mucous membranes should be flushed with water. Alcohol, hydrogen peroxide, betadine or other chemical cleansers are best avoided. HCWs should be made aware to avoid "milking" or squeezing out needle-stick injuries or wounds (AII)(2)(3).

Evaluating the Exposure

Prompt initiation of PEP is recommended for exposure to blood, visibly bloody fluids or other potentially infectious material from HIV-infected or HIV-unknown sources in any of the significant exposure situations outlined in Table 1(AII).

Whenever a worker has been exposed to potentially HIV-infected blood, visibly bloody fluids or other potentially infectious material through the percutaneous or muco-cutaneous routes or through non-intact skin, PEP is indicated. For these exposures, prompt initiation of PEP followed by telephone or in-person consultation with a clinician experienced in HIV PEP is recommended.

Table 1 : Exposures requiring initiation of a starter pack
• Break in the skin by a sharp object (including hollow-bore, solid-bore, and cutting needles or broken glassware) that is contaminated with blood, visibly bloody fluid, or other potentially infectious material, or that has been in the source patient's blood vessel. • Bitten by a person with **visible bleeding** in the mouth that causes break in the skin or mucosa the exposed worker. • Splash of blood, visibly bloody fluid or other potentially infectious material to a mucosal surface (mouth, nose, or eyes). • A non-intact skin (e.g: dermatitis, chapped skin, abrasion or open wound) exposure to blood, visibly bloody fluid or other potentially infectious material.

Determine the HIV status of the source patient and initiation of PEP

1. **Known Positive patient**

Start PEP immediately with available three drug regimen.
Contact Consultant Venereologist (STD clinic) as early as possible.

2. **Sero-status is unknown**

When source patient is available

Consent for HIV testing of the source patient should be sought (AII)(2). If facilities are available, rapid HIV test on source sample should be carried out. This can be done at closest STD clinic or any other lab where rapid test is available.

Consent for HIV testing

When the source patient has the capacity to consent to HIV testing, informed consent is required.

When the source person does not have the capacity to consent, consent may be obtained from a surrogate, or anonymous testing may be done if a surrogate is not immediately available (2).

If the result from testing source patient is not immediately available, considering severity of exposure and epidemiological likelihood of HIV status of the source, starter pack can be initiated

(preferably within 2 hours of the exposure) while source testing and further evaluation are underway (2).

When source patient is not available (e.g. needles in sharp bins and laundry)

Considering severity of exposure and epidemiologic likelihood of HIV exposure, starter pack can be initiated. Decision regarding continuation of PEP where source patient is not available should be made on a case by case basis by Venereologist / MO-STD.

Timing of the Initiation of PEP

When a potential occupational exposure to HIV occurs, every effort should be made to initiate PEP as soon as possible, ideally within 2 hours(AII). A first dose of PEP should be offered to the exposed worker while the evaluation is underway (2).

Decisions regarding initiation of PEP beyond 72 hours post exposure should be made on a case-by-case basis with the understanding of diminished efficacy when timing of initiation is prolonged (AIII)(2).

Recommended PEP regimen

Three drug regimen

TDF 300mg daily
FTC 200mg daily

LPV/r 400/100mg 12 hourly or ATV/r 300/100mg daily

Venereologist could decide on alternative regimens according to circumstances.

Duration of PEP Regimen

PEP need to be considered for 28 days (1)(2)(3).
When the source patient is confirmed to be HIV-negative, PEP could be discontinued (1)(3).

Baseline testing for the exposed health care worker and Follow up

Confidential baseline HIV testing of the exposed worker should be obtained at the time the occupational exposure is reported or within 3 days of the exposure (AIII).

All exposed workers receiving PEP should be re-evaluated within 3 days of the exposure. This allows for further clarification of the nature of the exposure, review of available source patient data and evaluation of adherence to and toxicities associated with the PEP regimen (1)(3).

The exposed worker should be evaluated weekly while receiving PEP to assess treatment adherence, side effects of treatment, interval physical complaints and emotional status.

Clinicians should provide risk-reduction counseling to HIV-exposed workers to prevent secondary transmission during the 12-week follow-up period. HIV-exposed workers should be educated and counseled on:

- Use of condoms to prevent potential sexual transmission
- Avoiding pregnancy and breastfeeding (2)
- Avoiding needle-sharing
- Refraining from donating blood, plasma, organs, tissue or semen
- Identifying symptoms of primary HIV infection and report as soon as possible

Investigations recommended for the healthcare worker who are on PEP							
	Baseline	***Week 1***	***Week 2***	***Week 3***	***Week 4***	***Week 10***	***Week 16***
Clinic visit	**√**	**√** Or by telephone	**√**	**√** Or by telephone	**√**		
Pregnancy test	**√**						
FBC*,LFT & RFT	**√**		**√**		**√**		
HIV test	**√**					**√**	**√**
**Follow-up FBC is indicated only for those receiving a zidovudine-containing regime.* *Week10 , 16 HIV testing should be done by using ELISA*							
HIV testing recommended for the healthcare worker who are not on PEP at baseline, week 6 and 12 from the exposure date.							

Exposed workers who are pregnant and breast feeding

Pregnancy and breast feeding are not contraindications for PEP and recommended regimens can be used (2).

Before administering PEP to a pregnant woman, the clinician should discuss the potential benefits and risks to her and to the fetus (2)(3).

Clinicians should counsel women who may have been exposed to HIV through occupational exposure to avoid breastfeeding for 3 months after the exposure (AII).If HIV infection is definitively

excluded in the source patient at any time prior to 3 months post-exposure, the woman may resume breastfeeding.

Exposure Report

If an occupational exposure occurs, the circumstances and post exposure management should be recorded in the HCW's confidential exposure report (Annex I).

References

1. U S Public health service guideline. Updated US Public Health Service Guideline for the Management of Occupational Exposures to Human Immunodeficiency Virus and Recommendation for Postexposure Prophylaxis. Infection Control and Hospital Epidemiology. 2013;34:875-892.
2. New York State Department of Health AIDS Institute. HIV prophylaxis following occupational exposure. www.hivguidelines.org. Updated October 2014. Accessed April 2016.
3. Centers for Disease Control and Prevention. Updated U.S. Public Health Service guidelines for the management of healthcare worker exposures to HIV and recommendations for post exposure prophylaxis. 2013.
4. World Health Organization. Guidelines on post exposure prophylaxis for HIV and the use of co-trimoxazole prophylaxis for HIV related infections among adults, adolescents and children: recommendations for public health approach. December 2014 supplement to the 2013 guidelines.
5. UK guidelines for the use of HIV post-exposure prophylaxis following sexual exposure. 2015.
6. AIDS EAGO. HIV post-exposure prophylaxis: guidance from the UK Chief Medical Officers' Expert Advisory Group on AIDS (2008) 2008.

Level of evidence

A – High quality evidence
B – Moderate quality evidence
C – Low quality evidence
D – Very low quality evidence

Annex I

Exposure Report

1 Date ……../……/20……

2Institution ……
……

3 Name/designation of HCW
……

4Date/Time of exposure
……./……/20……
……./…… am/pm

5Details of the procedure
i Laboratory / theatre / ward / clinic / labour room / others
ii How the exposure occurred
……..

6 Details of the exposure

Type of body fluid …….. Amount – small/large

i Percutaneous injury – Yes/No
If Yes, type of the device – Hollow bore needle / solid needle /
Other sharp devices / blunt devices

ii Mucosal exposure – Yes/No
If yes, site of exposure - ……..

iii Non intact skin – Yes/No

7Details of the source
Source identified – Yes/No
If Yes, HIV sero status of the source – Positive/Negative/Weakly reactive
(According to Rapid test / HIV Elisa)

If HIV positive - Stage of the disease ……
Recent Viral load ……
CD4 count ……
On ART - Yes/No if yes, regimen ……
Resistance details ……

If HIV Negative - Possibility of acute infection / High risk behaviour :
Yes/No

Other blood-borne pathogens ……

8 Management of post exposures

PEP recommended Yes/No
PEP accepted by HCW Yes/No
If yes, Regimen

9Follow upHIV test on HCW

6/10 weeks : Positive / Negative

12/16 weeks: Positive / Negative

10Name, Signature and Designation of counselor
……
…….
……

SECTION THREE

ART IN CHILDREN

3.1 When to start ART in children

Recent analysis shows that CD4 cell counts provide greater prognostic value than CD4 percentage for short term disease progression in children.

ART should be started in all HIV infected children.

ART should be initiated in all children infected with HIV but priorities be given to those below five years of age, regardless of WHO clinical stage or CD4 cell count.

ART should be initiated in all children infected with HIV with severe or advanced symptomatic disease (WHO clinical stage 3 or 4) regardless of age and CD4 cell count
ART should be initiated in any child younger than 18 months of age who has been given a presumptive clinical diagnosis of HIV infection.

3.2 First-line ART regimens for children

Table 10 First-line ART regimens for children

	Preferred	Alternative
Children <3 years	ABC (or AZT)+3TC+LPV/r (ABC for age > 3 months)	ABC (or AZT)+ 3TC + NVP
Children 3 -10 years	ABC (or AZT) + 3TC +EFV	ABC + 3TC + NVP AZT + 3TC + EFV (or NVP) *TDF + 3TC (or FTC) + EFV (or NVP) *TDF + 3TC (or FTC) + NVP

- ABC can be used for children > 3 months. HLAB 5701 need to be done. ABC + 3TC or FTC can be considered.
- For children younger than 3 years a PI based regimen is the preferred approach, if not feasible consider NVP based regimen. Consideration can be given to substituting LPV/r with an NNRTI after virological suppression is sustained.
- For children more than 3 years, EFV can be used.

- For children <3 years who develop TB while on ART regimen containing NVP or LPV/r, ABC+3TC+AZT is an option.
- *TDF – There is limited experience among children.
- Atazanvir / ritonavir can be considered for children more than 3 months.

Summary of first-line ART regimens for children younger than 3 years

Preferred regimens	*ABC[a] or AZT + 3TC + LPV/r[b]*
Alternative regimens[c]	*ABC[a] or AZT + 3TC + NVP*
Special circumstances[d]	*ABC[a] or AZT + 3TC + RAL[e]*

a Based on the general principle of using non-thymidine analogues in first-line regimens and thymidine analogues in second-line regimens, ABC should be considered as the preferred NRTI whenever possible. Availability and cost should be carefully considered.

b As recommended by the US FDA, using LPV/r oral liquid should be avoided in premature babies (born 1 month or more before the expected date of delivery) until 14 days after their due date or in full-term babies younger than 14 days of age.

c Challenges may arise when treatment is started in the first two weeks of life following early diagnosis at or around birth, particularly in case of prematurity or low birth weight. In these situations, an NVP-based regimen containing AZT and 3TC should be started, and NVP should be substituted with LPV/r at the earliest opportunity, preferably at two weeks when LPV/r syrup can be administered. In settings where LPV/r syrup is not available and LPV/r pellets are the only formulation available, administration of NVP should continue until 3 months with close clinical monitoring for those children considered at high risk for carrying NNRTI resistance (i.e. prolonged NVP-based postnatal prophylaxis or documented NNRTI failure in the mother).

d Special circumstances may include situations where preferred or alternative regimens may not be available or suitable because of significant toxicities, anticipated drug–drug interactions, drug procurement and supply management issues or for other reasons.

e RAL is approved for use in infants and children from the age of 4 weeks, but there is very limited evidence to inform the use of RAL as a first-line drug in infants and young children. The use of this INSTI could be considered where available in instances of poor tolerability or

administration challenges with LPV/r, particularly in settings where as a result of rapid expansion of maternal treatment, infants and children are at very high risk of carrying an NNRTI resistance virus. Use of RAL should however consider the challenges of existing granule formulation, despite being suitable for use in infants 4 weeks and older, as reconstitution in water is required before administration. While dispersion of RAL chewable tablets is considered to be a potential alternative, additional information regarding the appropriateness of this approach will be provided as more data become available.

3.3 Second-line ART for children (including adolescents)

New recommendations

- After failure of a first-line NNRTI-based regimen, a boosted PI plus two NRTIs are recommended for second-line ART; LPV/r is the preferred boosted PI
- After failure of a first-line LPV/r-based regimen, children younger than 3 years should remain on their first-line regimen, and measures to improve adherence should be undertaken.
- After failure of a first-line LPV/r-based regimen, children 3 years or older should switch to a second-line regimen containing an NNRTI plus two NRTIs; EFV is the preferred NNRTI.
- After failure of a first-line regimen of ABC or TDF + 3TC (or FTC), the preferred NRTI backbone option for second-line ART is AZT + 3TC
- After failure of a first-line regimen containing AZT + 3TC (or FTC), the preferred NRTI backbone option for second-line ART is ABC or TDF + 3TC (or FTC)

Table 11 Recommended first- and second-line ART regimens for children

	Children	Second-line ART regimen	Third line ART regimen
2 NRTIs + LPV/r-based first-line regimen	Younger than 3 years	2 NRTIs + RAL	DTG + 2NRTIs DRV/r + 2 NRTIs DRV/r + DTG ± 1-2 NRTIs
	3 years and older	2 NRTIs + EFV or RAL	
2 NRTI + EFV -based first-line regimen	All ages	2 NRTIs + ATV/r or LPV/r	

NVP may be considered for under 3 years if there is no other option.
ATV/r can be used as an alternative to LPV/r in children older than 3 months.
DRV should not be used in children younger than 3 years of age.
DTG is currently only approved for children 12 years and older.

3.4 Prevention of mother to child transmission of HIV (Refer guidelines for Management of pregnant mothers with HIV 2016)

Table 12 - When to start ART in pregnant and breastfeeding women

National PMTCT programme option	Pregnant women with HIV
Consider using lifelong ART for all pregnant women (" Option B+") *	Initiate ART and maintain after delivery

ART should be initiated urgently in all pregnant and breast feeding women even if they are identified late in pregnancy and postpartum because the most effective way to prevent mother to child transmission is to reduce maternal viral load.

All pregnant women with HIV should initiate ART, which should be continued lifelong.

ART options

Preferred first line regimen	Alternative first line regimen
TDF + 3TC(FTC) + EFV	AZT + 3TC +EFV (NVP) TDF + 3TC (FTC) + NVP

3.5 Infant prophylaxis

- Infants should receive six weeks of ART starting from birth with twice daily AZT or daily NVP.
- Infants born to mothers with HIV who are at risk of acquiring HIV* should receive dual prophylaxis with daily AZT and NVP for the first 6 weeks of life.
- Breastfed infants who are at high risk of acquiring HIV including those first identified as exposed to HIV during postpartum period should continue infant prophylaxis for an additional 6 weeks (total of 12 weeks) using either AZT and NVP or NVP alone.
- If infants are receiving replacement feeding they should be given 6 weeks of infant prophylaxis with daily NVP or twice daily AZT. Infants of mothers who are receiving ART and are breast feeding should receive 6 weeks of infant prophylaxis with daily NVP.

*High risk infants are defined as those

1. born to women with established HIV infection who have received less than 4 weeks of ART at the time of delivery or
2. Born to women with established HIV infection with viral load > 1000 copies/ml in the four weeks before delivery or
3. Born to women with incident HIV infection during pregnancy and breast feeding or
4. Identified for the first time during the postpartum period with or without a negative HIV test perinatally.

*For further details refer “Guideline on management of pregnant women with HIV 2016”.

3.6 Monitoring and Evaluation HIV Treatment and Care programmes

A comprehensive Monitoring and evaluation (M&E) is necessary for Healthcare workers and HIV programme managers to assess the effectiveness of treatments and linkages between services along the cascade of treatment and care for HIV and associated conditions. This chapter describes the system available for M&E across the HIV treatment and care cascade in Sri Lanka.

Figure 1. An example of a cohort based HIV cascade for a given year

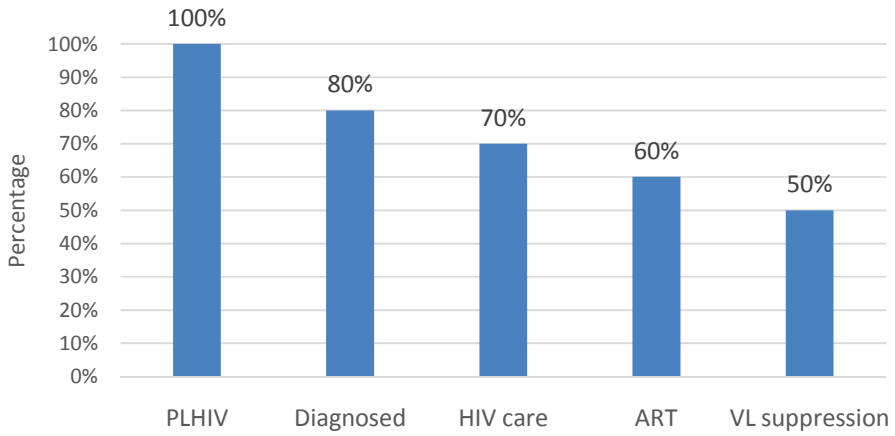


Table 13 Method used to collect data according to the step in the HIV treatment and care cascade

Step in the cascade	Indicator/s	Methods used to collect data
1. People living with HIV	Estimated number of people living with HIV.	Using the "Spectrum" software based on the M&E data, surveillance data and various assumptions.
2. HIV diagnosis	Percentage of the general population with known HIV test status and within specific populations.	HIV sentinel surveillance and Integrated biological and behavioual surveillance (IBBS).
	Number of people newly diagnosed with HIV infection within a specific time period.	Using the "Spectrum" software based on the M&E data, surveillance data and various assumptions. Note: Newly reported cases during a specific period includes both new infections and old infections and this data are collected using H1214 form by the epidemiology unit of NSACP.

3. Linkage and enrolment in HIV care	Percentage of people newly diagnosed with HIV infection enrolled in HIV care.	A substitution for this indicator "Percentage of people newly reported with HIV infection enrolled in HIV care within 6 months of diagnosis" by the epidemiology unit of NSACP.
	Profile of people living with HIV initiating HIV care.	There are two sources for this information. 1. Data are collected using H1214 form by the epidemiology unit of NSACP. 2. Data collected by "Strategic Information on Laboratory Confirmed HIV Infections" by SIM unit of NSACP.
4.1 Antiretroviral drugs: coverage	Number of people receiving ART (and coverage)	Numerator of this indicator is calculated by the Quarterly ART return by the SIM unit. For the coverage, the denominator is calculated by the "Spectrum" software based on the M&E data, surveillance data and various assumptions.
	Number of people receiving ARV drugs for PMTCT (and coverage).	Numerator of this indicator is calculated by the Quarterly ART return by the SIM unit. For the coverage, the denominator is calculated by the "Spectrum" software based on the M&E data, surveillance data and various assumptions.
4.2 Antiretroviral drugs: Supply	Percentage of ART facilities with ARV drug stock-outs in a given period.	This is calculate annually using ART stock register maintained by the NSACP pharmacy.
4.3 Antiretroviral drugs: Retention	Adherence	This is recorded in the patient record and ART register. However, currently this is not captured by routine M&E system at the national level on a routine basis.
	Percentage retained on ART	12-month, 24-month and 60-month retention rates on ART are calculated using the cohort Excel database compiled using patient records, ART registers are used to calculate survival rates by the SIM unit of NSACP
5. Viral suppression	Percentage of viral suppression	An Excel based cross-sectional database is used to get this information from all ART centers and the percentage of PLHIV with suppressed viral load is calculated by the SIM unit. Viral load suppression is defined as less than 1000 viral copies as per WHO and GARPER indicator definition.

6. Impact	Mortality rate	- Estimated mortality is calculated using the "Spectrum" software based on the M&E data, surveillance data and various assumptions. - Reported death are counted using the HIV cases notification system by the Epidemiology unit of NSACP.
	Incidence and the number of adults and children acquiring HIV infection	- Estimated new cases per year (incidence) is calculated using the "Spectrum" software based on the M&E data, surveillance data and various assumptions.
	Mother-to-child transmission rate	Estimated MTCT rate is calculated using the "Spectrum" software based on the M&E data, surveillance data and various assumptions.
	Survival Rate	12-month, 24-month and 60-month survival rates on ART are calculated using cohort analysis method. Patient records, ART registers are used to calculate survival rates using the table given. (see annexes)

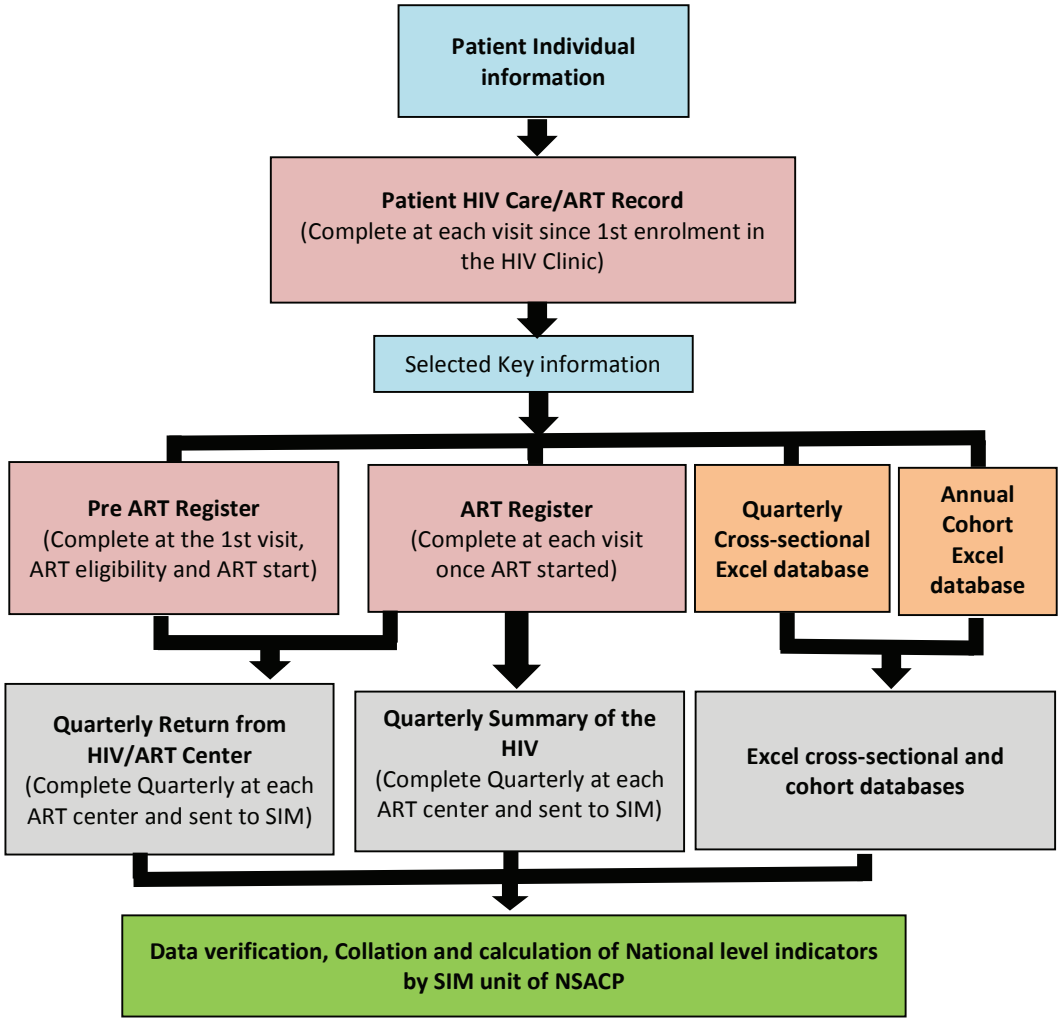
3.7 Recording and Reporting Formats and brief instructions

1. **Request for HIV antibody test/notification** (H1214)

Currently, H1214 form is used to collect basic epidemiological information of all people who undergo HIV antibody screening. In practice, this is used to collect basic epidemiological data when a person is HIV antibody screening test positive and requesting a HIV antibody confirmatory test (Western or Line Blot tests).

This form is collected by the National Reference Laboratory of NSACP and sent to the epidemiology unit for data verification and data management. A summary of the findings from this data source is compiled at the end of every quarter.

Recording and reporting system in the current paper based HIV/ART facility monitoring



2. The Strategic Information on Laboratory Confirmed HIV Infection (Request for Confirmatory HIV Testing from the Reference Laboratory of the National STD/AIDS Control Programme) Refer attachment

This format is used to collect more detailed data from the HIV positive persons who get registered in ART centers for follow up of care. Those who get enrolled in ART centers are more likely to report personal details after developing a better rapport with the care provides.

A completed form for each and every PLHIV who enrolled in HIV care needs to be sent to SIM unit of NSACP for data management. A summary of the findings from this data source is compiled at the end of every year.

3. The Patient HIV Care/ART Record (Refer attachment for the format)

To provide effective lifelong care, it requires keeping track of the patient's baseline and follow-up care and treatment history. All relevant health care providers in the medical team (such as doctor, nurse etc) needs to know key clinical details and what was done on previous visits.

The Patient HIV Care/ART Record is maintained for each patient under HIV care whether or not they started on ART. It is important to complete this form for each patient visit. In this record standard information is noted under four categories.

i. Demographic information, collected at first visit or on enrollment which is updated if the information has changed.
ii. HIV care history, collected for all patients enrolled in HIV care whether or not they have started ART.
iii. ART summary, collected at start and change in treatment as well as at 6 months and yearly follow-up.
iv. Patient follow-up information, collected every time the patient visits the facility.

4. Pre-ART Register and ART Register (Refer attachment for the formats)

Registers are convenient tools to facilitate the aggregation of individual information from the Patient HIV Care/ART Records for completing quarterly ART return and for obtaining programme indicators. Without registers, each patient record would need to be checked one by one to calculate the required indicators.

In the registers, patients are recorded:

- by date of first visit in the clinic (enrollment) in the Pre-ART Register; and
- by date of start of ART in the ART Register.

The pre-ART Register has to be completed:

- at the first visit for most of the information
- at the start of cotrimoxazole preventive therapy
- at the start of TB treatment

- at medical eligibility for ART
- at start of ART; and
- whenever follow-up was ended before ART was started.

The ART Register has to be completed for all patients starting ART, during all monthly follow-up visits since the date of starting treatment to the end of follow-up on ART.

5. ARV Drug Dispensing Register (Refer attachment for the formats)

The ARV Drug Dispensing Register is maintained by the pharmacist in the NSACP and drug dispensing staff of peripheral ART centers. The purpose of this Register is two-fold:

- to document and account for ART by obtaining signature against the number of tablets given to patients or issued to ART centers; and
- to calculate the daily consumption of each drug.

6. ARV Drug Stock Register (Refer attachment for the formats)

This Register is maintained by the pharmacist in the NSACP. At the end of each month, ART Monthly Return from the Pharmacy is completed using this register.

7. Quarterly Return from HIV /ART Clinic (Refer attachment for the formats)

The Quarterly Return from the HIV/ART centers gives a cross-sectional information on the programme performance. Cross-sectional means that the indicators are compiled at one-time point (at the end of each quarter) without taking into account the duration of follow-up of the patients i.e. the indicator "cumulative number on ART", indicates how many patients are continuing ART at the end of the quarter, but does not convey for how long these patients have been under ART.

The Patient HIV Care/ART Record and pre-ART and ART registers have to be updated from “unstructured” patient notes before completing this return.

8. Quarterly summary report from HIV clinics (Refer attachment for the formats)

This form was designed in 2014 to get a clearer idea about the PLHIV enrolled in HIV clinics. Individual patient file numbers are included in this form in the relevant cells. This will help to verify quarterly ART return and Excel data bases.

Table 14: Quarterly Summary of the HIV Clinics

	Indicator	Stage	No. Patients	Clinic File Numbers
1	Number of patients newly enrolled during this quarter (Include all new patients. Exclude transfer-inpatients. Transfer-in patients should be included in row3)	(Both Pre ART and ART)		
2.1	Newly started on ART during this Quarter (Include both new and old patients newly started on ART)	(Not applicable)		
2.2	Restarted ART after stopping or loss to follow up	2.2ART		
3	Number of patients Transferred-in during this quarter	3.1PreART 3.2ART		
4	Number of patients Transferred-out during this quarter	4.1 PreART 4.2ART		
5	Number of patients Stopping ART during this quarter (Include if ART stopped due to medical reasons)	5.1ART		
6	Number of patients who Lost to Follow Up during this quarter(Include patients who have defaulted for more than 3 months from the last previous Quarter)	6.1PreART 6.2ART		
7	Number of patients Re-entered the clinic after loss to follow up during this quarter (Include patients who have defaulted for more than3 months and came back for clinic	7.2PreART 7.2ART		
8	Number of Deaths during this quarter	8.1PreART 8.2ART		

9. Quarterly Cross-sectional Excel database

When the number of PLHIV in care increases, it is increasingly difficult to get good data from aggregated tables given in the 'Quarterly Return from HIV /ART Clinic'. Therefore, is important to maintain individual level data using this Excel database. This database is updated at the end of each quarter and sent to SIM unit for compilation of national level database. Following are the variables given in each column of this Excel database.

1 Serial No.
2 Date of registration (mm/dd/yyyy)
3 Clinic No
4 Any other clinic no.
5 Sex
6 Date of Birth (mm/dd/yyyy)
7 Age at registration (years)
8 Pre ART/ART
9 Year of ART initiation
10 Clinic of ART initiation
11 Date of ART initiation (mm/dd/yyyy)

12 "Age at ART initiation"
13 "Viral load at start of ART(+/_ 3 months)"
14 "Viral Load after 12 months after ART initiation(+/_ 3 months)"
15 "CD 4 at start of ART(+/_ 3 months)"
16 Outcome as of end of ---- Quarter 2016 (OT 1st,OT 2nd,S, D, LFU)
17 Transfer in/Transfer out/ same clinic
18 The clinic of currently followed up (by --- Quarter 2016)
19 Current ART regime by (--- Quarter of 2016)
20 Comments

10. Annual Cohort Excel database

As ART follow-up is a lifelong process, it is necessary to have "longitudinal" indicators (i.e. information for a period of time), which takes into account the duration of follow-up, such as how many patients have been on treatment for 12 months, 24 months and 60 months. This is the purpose of the Cohort Analysis Report.

Cohorts is formed according to the year the patients started ART, not according to the year of entering into HIV care.

Until 2014, the Cohort Analysis was done using aggregated tables prepared from the ART Registers. However, this method is found to be less accurate as same patient get counted by more than one clinic in case of transfer-in and transfer-out cases.

Therefore, this 'Annual Cohort Excel database' was introduced by the SIM unit to gather individual level data. This calculation is done on annual basis.

Following are the variables given in each column of this Excel database.

1 Serial No.
2 Year of ART initiation
3 Clinic of ART initiation
4 Date of ART Started on
5 Clinic No
6 Any other clinic No. (if relevant)
7 Age at ART initiation
8 SEX
9 AGE at the end of 20… ,
10 Age Range
11 Date when 60 month completes
12 60-month Cohort Outcome (OT1, OT2 S, D, LFU)
13 Date when 24-month completes
14 24-month cohort outcome
15 Date when 12-month completes
16 12-month cohort outcome
17 Followed up clinic at the outcome
18 Comments

Clinic level cohort databases are compiled at the SIM unit cohort analysis is done at the end of every year.

Recording data during HIV care is essential to provide good clinical care. In addition, recording of clinical and other relevant data are important in monitoring and evaluation of ART services in the country. Therefore, recording and reporting of data from HIV clinics remains an integral aspect of quality patient care.

Following indicators need data collection and reporting from ART centers

- Percentage of adults and children currently receiving antiretroviral therapy among all adults and children living with HIV.
- Percentage of adults and children with HIV known to be on treatment 12 months after initiation of antiretroviral therapy.
- Percentage of people living with HIV that initiated ART with CD4 count of <200 cells/mm^3.
- Percentage of adults and children that initiated ART, with an undetectable viral load at 12 months (<1000 copies/ml).
- Percentage of newly diagnosed adults linked to HIV care (individual linkage).
- Percentage of HIV-positive pregnant women who received antiretroviral medicine (ARV) to reduce the risk of mother-to-child transmission
- Number of infants who received an HIV test within two months of birth, during the reporting period.
- Percentage of HIV-positive patients who were screened for TB in HIV care or treatment settings
- Total number of persons who have active TB disease during the reporting period out of those newly enrolled in HIV care.
- Number of adults and children with HIV infection who received antiretroviral combination therapy and who were started on TB treatment, within the reporting year.
- Percentage of new HIV -positive patients starting IPT during the reporting period.
- Number of people in HIV care who were tested for hepatitis B during the reporting period using HBsAg tests.

References:

1. Consolidated guidelines on the use of Antiretroviral drugs for treating and preventing HIV Infection, WHO, 2013
2. Consolidated strategic information guidelines for HIV in the health sector, WHO, 2015
3. Training tool kit, Participant Manual, HIV Care and ART Recording and Reporting System, WHO, 2006
4. Global AIDS Response Progress Reporting. Geneva, UNAIDS, 2016

M&E chapter

Attachments

Request for Confirmatory HIV Testing from the Reference Laboratory of the National STD/AIDS Control Programme

(VERSION: NOV 11, 2016)

Instructions: To be completed by referring doctor/healthcare worker at the time of requesting HIV confirmatory test from the reference laboratory of the National STD/AIDS Control Programme, No. 29, De Saram Place, Colombo 10, Sri Lanka. *Patient should be informed that all questions contained in this questionnaire are strictly confidential and will become part of their medical record)*		**TO BE FILLED BY THE REFERENCE LABORATRY** **Date of Receipt** ☐☐/☐☐/☐☐☐☐ **Date of Confirmation** ☐☐/☐☐/☐☐☐☐
PATIENT/CLIENT IDENTIFICATION INFORMATION **If STD clinic patient fill A, otherwise fill B**	**1A. STD Clinic Registration Number (For STD Clinic Clients)** ☐/☐☐☐☐/☐☐/☐☐	**1B. Sample Number** (For non-STD Clinic Clients - Private Lab, TB clinic, Hospital ID or other) _____
HIV SCREENING TEST DETAILS	**2. Type of Screening Test** ☐a. ELISA Test ☐b. Particle Agglutination Test ☐c. Rapid Diagnostic Test ☐d. Other _____	**3. Date of Screening Test:** ☐☐/☐☐/☐☐☐☐
HIV TESTING HISTORY	**4. Has patient/client ever been tested for HIV previously** ☐a. If Yes (date of last negative test)☐☐/☐☐/☐☐☐☐ ddmmyyyy ☐b. No ☐c. Not Known	
DEMOGRAPHIC INFORMATION	**5. Name and address of Patient/Client** Name : _____ Address : _____ _____	**6. Gender** ☐ M ☐ F ☐Other **7. Date of Birth** ☐☐/☐☐/☐☐☐☐ ddmmyyyy
	8. Marital status ☐ a. Single/Never Married ☐b. Currently Married/Living Together ☐c. W/S/D	
	9. Occupation☐a. Unemployed☐b. Student☐c.Employed as: _____ ☐d. NA	
	10. District of Residence:	**11 Nationality** ☐ a. Sri Lanka☐b. Other (specify) _____
	12. Ethnicity☐a. Sinhalese☐b. Tamil ☐c. Moore ☐d. Other (specify) _____	

13. Reason for HIV Testing (More than one option possible)

☐a. Voluntary Testing	☐e. Partner/spouse or family memberdiagnosed	☐i. Visa Screening	☐m. Screening as part of a Survey
☐b. Provider Initiated Testing (asymptomatic)	☐f. STD Screening	☐j. Foreign Job Screening	☐n. TB clinic screening
☐c. Clinical symptoms suggestive of HIV	☐g. Blood Donor Screening	☐k. Screening for Legal/Insurance purposes	☐o. Prison
☐d. Accompanied by NGO outreach worker or peer	☐h. ANC Screening	☐l. Screening before Medical/Surgical Procedure	☐ p.Other (Specify):

14. Clinical status at time of diagnosis☐a. Asymptomatic ☐b. Symptomatic HIV ☐c. AIDS

INFORMATION ON EXPOSURE TO HIV

15. Sexual Exposure

☐a. Sexual Contact with Regular Partner of Opposite Sex

☐b. Sexual Contact with Non-Regular Partner of Opposite Sex

☐c. Sexual Contact with Both Sexes

☐d. Sexual Contact with Person of Same Sex

☐e. No Sexual Contact

16. Ever sold sex to client

☐a. Yes

☐ b. No

17. Ever bought sex from sex worker

☐a. Yes

☐b. No

18. Ever gone abroad?

☐ **a.Yes, countries: _____**

☐**b. No**

19. History of Blood Exposure

☐a. No

☐b. Injecting Drug Use

☐c. Receipt of Blood/Tissue/Organ/Sperm Specify year: ☐☐☐☐

☐d. Needle stick injury/mucosal splash Specify year: ☐☐☐☐

20. Ever had sex with a foreigner?

☐ **a.Yes**

☐**b. No**

☐**c. Not Applicable (Foreign Nationality)**

21. Acquired from mother to child transmission

☐a. No

☐b. Yes

☐c. Not Known

INFORMATION ABOUT SPOUSE/LIVE-IN PARTNER EXPOSURE TO HIV

22. HIV status of spouse

☐a. Positive

☐b. Negative

☐c. Not Known

☐d. Not Applicable

23. Has spouse ever gone abroad?

☐a. Yes, countries

_____

☐b. No

☐c. Not Known

☐d. Not Applicable

24. Risk factors for HIV in spouse/live-in partner

☐a. None ☐b. MSM ☐c. Sex Worker (now or former) ☐d. Multiple Sex Partners

☐e. Injecting drug user (now or former) ☐f. Not Known ☐g. Not Applicable

DETAILS OF THE REFEREING DOCTOR/HEALTHCARE WORKER

A. Name : _____

B. Signature : _____

C. Designation : _____

D. Institution : _____

E. Telephone No. : _____

F. Date : _____

HIV CARE & ANTIRETROVIRAL TREATMENT (ART) PATIENT RECORD

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

1. Patient Identification Data (Write complete information)

Patient Registration Number : ☐☐ ☐ ☐☐☐☐ (Clinic code, M/F, XXXX)

Name of the Clinic:_____ District: _____

Name of patient: _____

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

Patient's phone number: _____

Address: _____

_____

Distance from residence to clinic/hospital (km) :_____

Treatment supporter's name :_____

Treatment supporter's address :_____

Treatment supporter's phone number :_____

Date confirmed HIV+ test: ------/-----/------ **Place:** _____
dd / mm / yy

Entry point (Mode of referring the patient for HIV care):

☐ 1-STD ☐ 2-TB ☐ 3-Outpatient ☐ 4-Inpatient ☐ 5-Paediatric ☐ 6-PMTCT ☐ 7-VCT ☐ 8-Private
☐ 9-NGO ☐ 10-Self referred ☐ 11-IDU outreach ☐ 12- CSW outreach ☐ 13-Visa screening-local
☐ 14- HIV screening- foreign ☐ 15-Contact/Family Screening ☐ 16. Blood donor ☐17-Other_____

☐ Patient transferred-in, **on ART** from another clinic /hospital

Name previous clinic: _____ Date transferred in : _____

2. Personal History

Probable mode of HIV transmission

☐ 1. FSW ☐ 2.Client of FSW ☐ 3. Spouse
☐ 4 Other heterosexual ☐ 5. MSM
☐ 6. IDU ☐ 7. Blood transfusion
☐ 8. Mother to child transmission
☐ 9 Unknown

Probable place of HIV transmission

☐ 1. Local ☐ 2.Foreign

For **IDU**s Substitution therapy ☐ Y ☐ N
Drug abuse: ☐ Y ☐ N

Literate ☐ Yes ☐ No

Employed ☐ Yes ☐ No

Alcoholism ☐ Habitual ☐ Social ☐ No use

3. Family History (Tick one choice)

Marital status: ☐ Single ☐ Married ☐ Divorce/separate ☐ Widowed

Estimated monthly household income: Rs.

Family members: spouse/children Relationship	Age/ sex	HIV +/-/unknown	ART Y/N	Regist. No if on care

4. Antiretroviral treatment history

Was ART received before? ☐ Yes ☐ No

If yes ☐ PMTCT ☐ Earlier ART ☐ PEP

Place: ☐ Private ☐ Govt

Drugs and duration:

5. Clinical and Laboratory Investigations

	Date (dd/mm /yy)	WHO stage	Weight (kg)	Height (cm)	Perfor-mance A/B/C*	CD4 count (or % in children)	Viral load
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 Date:__/___/___ dd/mm/yy

☐ ZDV+3TC+EFV
☐ ZDV+3TC+NVP
☐ D4T30+3TC+EFV
☐ D4T30+3TC+NVP
☐ FTC/TDF/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: _____
☐ Recurrent

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

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

TB registration
District: _____
Health Centre: _____
TB number:

TB 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: ☐☐/☐☐/☐☐ New clinic:_____
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 month

9. Medical history at the commencement of HIV care

1. Coexisting conditions :

☐ 1. HBV ☐ 2.HCV ☐ 3.Diabetes ☐ 4. Hypertention ☐ 5. IHD ☐ 6. Asthma

2. STI s: Current ☐ 1.Yes ☐ 2. No _____

Past history ☐ 1.Yes ☐ 2. No _____

3. Other medical / Surgical conditions :

4. Current Medication :

5. Drug allergy:

6. Contraception :

☐1. Condoms ☐2. Oral contraceptives ☐ 3. IUD ☐ 4.Tubal ligation

☐5. Vasectomy ☐6. DMPA ☐7. Other_____ ☐ 8. None

7. Gynecological/ Obsteric history

P_____ C_____ Last Menstrual Period : _____

Last Pap smear : **Pregnant now:** ☐ 1. Yes ☐ 2.No

Refer for PMTCT ☐ 1.Yes ☐ 2.No

8.Other Remarks :

9.Linkage to NGOs/ Care Institutions

Date	Name of organizations/type*	Purpose**

* 1. NGO 2. Community care and support 3. PLHA network 4. Other

** 1. Adherence 2. Retention 3. Psychosocial support 4. Other

10. For pediatric patients only (under 15 years of age)

1. Staying with:

☐ 1. Own family ☐2. In a centre and contact with family ☐3. In a centre but no contact with family

☐4. Other_____

2. Details of primary caregiver

- Type ☐1. Both parent ☐2. Single parent ☐ 3. Relatives ☐ 4. Others: ___
- Sex: ☐1. Male ☐ 2. Female
- Age: _____ years
- Education ☐1. Non literate ☐2. Primary ☐ 3. Secondary ☐4. Tertiary and above

3. Details of Child

- Birth History: ☐1. Normal vaginal delivery ☐2. Caesarean ☐ 3. Vacuum ☐ 4. Forceps
- Place of Birth (Institution):_____Birth weight: _____kg
- Neonatal complications:_____
- Infant feeding: ☐1. Exclusive Breast feeding ☐ 2. Replacement ☐ 3. Mixed
- DNA PCR results: 1st _____ 2nd _____ Others_____
- Developmental milestones: ☐ 1. Normal ☐ 2. Delayed ☐ 3. Other

4. Immunization details

Age	Vaccine	Due on	Given on	Age	Vaccine	Due on	Given on
Birth	BCG			3 years	MR		
2 months	Polio 1				Vit A		
	DPT 1			5 years	Polio5		
	Hep B 1				DT		
4 months	Polio 2			10-14 years	Rubella		
	DPT 2				ADT		
	Hep B 2			**Other Vaccines**			
6 months	Polio 3						
	DPT 3						
	HepB 3						
9 months	Measles						
	Vit A						
18 months	Polio4						
	DPT4						
	Vit A						

11. HIV CARE/ ART FOLLOW-UP

S. No	1. Date of visit*	2. Date next visit	3. Weight (kg)	4. Height (CM) for Child	5. WHO Clinical Stage	6. Performance scale*	7. Opportunistic infections code*	8. Drugs prescribed for OIs / Prophylaxis for OIs	9. Antiretroviral drugs and dose prescribed	10. ART Side effects - code*	11. Adherence to ART* - >95%, 80-95%, <80%	12. Any other medicine	13. Pregnancy Y/N or FP method*	14. Condoms Given Y/N	15. Remarks/ Referrals	16. Staff Signature
1.																
2.																
3.																
4.																
5.																
6.																
7.																
8.																
9.																
10.																
11.																
12.																

***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 month

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

12. HIV CARE & ART FOLLOW-UP- INVESTIGATIONS

Outcomes of Investigations (*To be recorded if available., If space is not adequate, write details of results in the note section of the patient record)*

	Test / Date	1. / /	2. / /	3. / /	4. / /	5. / /	6. / /	7. / /	8. / /	9. / /	10. / /	11. / /	12. / /
1	Hb % / PCV												
2	WBC/DC												
3	Platelet count												
4	Fasting Blood sugar												
5	UFR												
6	Blood urea												
7	S. creatinine												
8	S. electrolytes												
9	S. bilirubin												
10	SGOT												
11	SGPT												
12	Alkaline phosphatase												
13	Serum protein												
14	Serum cholesterol												
15	Triglycerides												
16	CD4 count / CD4 %												
17	CD8 count												
18	CD4/CD8												
19	Viral Load												
20	CXR (PA) view												
21	Mantoux (PPD)												
22	ESR												
23	CMV Ab												
24	Toxoplasmosis Ab												
25	HB s Ag												
26	Anti-HCV Ab												
27	Pap smear												
28	VDRL / TPPA												
29	GC culture												
30													
31													
32													
33													

PRE ART REGISTER

Month: _____ Year:_____ Name of Clinic / Hospital:_____

	1	2	3	4	5	6		7	8	9	10	11	12	13	14	15	16		
	Date 1st entered into HIV care at this clinic	Registration number	Patient's name, Address and Contact number	Age	Sex M/ F	HIV Confirmation test		Entry point code 1 to 13*	risk factor code 1to7**	Literate Y/N	Employed Y/N	CPT*** Date Start	Date of **TB** Screening & Result#, Category Regimen Date Rx start	Date medically eligible for ART	Why medically eligible?	Date ART started	End of follow-up before ART		
						Date	Place										Date of death	Date lost to FU (last visit)	Date transferred
1															WHO stage CD4 #/% TLC#				
2															WHO stage CD4 #/% TLC#				
3															WHO stage CD4 #/% TLC#				
4															WHO stage CD4 #/% TLC#				
5															WHO stage CD4 #/% TLC#				
6															WHO stage CD4 #/% TLC#				
7															WHO stage CD4 #/% TLC#				
8															WHO stage CD4 #/% TLC#				
9															WHO stage CD4 #/% TLC#				
10															WHO stage CD4 #/% WHO stage				

Pre ART register: At first visit fill column 1 to 10. Columns 11 to 16 to be filled when applicable.

***Entry point:** 1-STD 2-TB 3-Outpatient 4-Inpatient 5-Paediatric 6-PMTCT 7-VCT 8-Private 9-NGO 10-Self referred 11-IDU outreach 12- CSW outreach 13-Visa screening-local 14- HIV screening- foreign 15-Contac/Family Screening 16. Blood donor 17-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

*****CPT:** Cotrimoxazole preventive therapy **#TB Screening result: Neg**-Negative; **LTB**-Latent TB; **PTB(SS+)** Pulmonary TB(Smear+ve); **PTB(SS-)** Pulmonary TB (Smear-ve); **EPTB** Extra-Pulmonary TB (Mention the site.)

ART REGISTER Month:_____Year:_____Name the Clinic / Hospital_____

	Date of starting ART	Registration number	Patient's name	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 Screening & treatment during ART Date of TB Screening & Result***, Category Regimen Date Rx start	ART regimen started	Treatment substituted within 1st line drugs: Date	Reason *	New Regimen	Treatment switched to 2nd line: Date	Reason **	New Regimen	End of follow-up on ART: Date of death	Date Lost to FU (last visit)	Date Transferred out on ART
1								□ 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.											
2								□ 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.											
3								□ 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.											
4								□ 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.											
5								□ 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.											
6								□ 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.											
7								□ 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.											
8								□ 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.											
9								□ 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.											
10								□ 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.											

Monthly visits: • 1st row, write patient outcome: on treatment **(OT)** if patient picked up ART drugs; stopped **(ST)** if ART was stopped by the doctor; missing **(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 was restarted after an interruption; transferred out **(TR)**; dead **(D)**; **(NA)** if the patient was not scheduled to visit this month • 2nd row: write adherence for the patients on treatment (A=>95%, B=80-95%, C=<80%)

	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	mo. 20	mo. 21	mo. 22	mo. 23	mo. 24
1																									
2																									
3																									
4																									
5																									
6																									
7																									
8																									
9																									
10																									

^**Peformance scale-weight-CD4** at start, 6, 12, 24 months of treatment - Height: at start for adults, at start, 6, 12, 24 months for children

* **Reasons for subsitution within first line treatment:** 1-toxicity or side effects; 2-pregnancy;3-risk of pregnancy; 4-newly diagnosed TB; 5-new drug available; 6-drug out of stock; 7-other reason.

****Reasons for switching to second line treatment:** 1-toxicity or side effects; 2-pregnancy; 3-risk of pregnancy; 4-newly diagnosed TB; 5-new drug available; 6-drug out of stock; 7-other reason; 8-clinical treatment failure; 9-immunological failure; 10 -virological failure.

Reasons for stopping ART: 1- toxicity side effects; 2-pregnancy; 3-treatment failure; 4-poor adherence; 5-illness hospitalisation; 6-drug out of stock; 7-lack of finance; 8-patient's decision to stop; 9 other.

TB Screening result: Neg-Negative; **LTB**-Latent TB; **PTB(SS+)** Pulmoray TB(Smear+ve); **PTB(SS-)** Pulmonary TB (Smear-ve); **EPTB** ExtraPulmoray TB (Mention the site)

Antiretroviral Drug Dispensing Register

National STD/AIDS Control Programme, Sri Lanka

ART DR/SIM/2016

Date	Patient's Number/ Clinic	Number of tablets dispensed																				Signature of the issuing or receiving officer
		EFV 600 mg	ATV 300 mg	RTV 100 mg	RAL 400 mg	DRV 600 mg	EFV 200 mg	LPV 200 mg / r 50 mg	LPV 100 mg / r 25 mg	AZT 300 mg + 3TC 150 mg +NVP 200 mg	AZT 60 mg + 3TC 30 mg	TDF 300 mg + FTC 200 mg	ABC 60 mg + 3TC 30 mg	TDF 300 mg + FTC 200 mg + EFV 600mg	AZT 60 mg + 3TC 30 mg + NVP 50 mg	AZT + 3TC 300 mg 150 mg						

Signature of the pharmacist: _____

Antiretroviral Drug Stock Register
National STD/AIDS Control Programme, Sri Lanka

Name of the drug _____

Date	Opening stock	Stock received	Stock dispensed	Stock expired/ discarded	Balance stock

Monthly summary for _____

Stock at the start of the month	:	Stock dispensed during the month	:
Stock received during the month	:	Stock expired/discarded during the month	:
Stock at the end of the month	:		

ART D S R/SIM/2010

Quarterly Return of HIV clinic/ART center

Name of the HIV Clinic/ ART Center : _____

Period of the return : _____to _____ (Quarter of 20___) *(Revision-13.9.2016)*

Instruction:
Completed returns should be sent to Director/NSACP,C/O SIM unit, 29, De Saram Place, Colombo 10 by post or by fax to 011 5336873 on or before 20th of the month following each quarter.

1. Enrollment in HIV care (Include patients in both Pre-ART and ART stages)	Adults (15+)**		Children (<15) **		Total
	Male	Female	Male	Female	
1.1 Cumulative number of patients ever enrolled in HIV care (Pre-ART and ART)at beginning of this quarter *(This is should be equal to no. 1.3 of last quarterly return)*					
1.2 Number of new patients enrolled in HIV care during this quarter *(From Pre ART register) **					
1.3 Cumulative number of patients ever enrolled in HIV care at the end of this quarter *(1.1 + 1.2)*					
1.4 Total number of patients at **pre-ART**stage at the end of this quarter *(Include only currently active pre-ART patients after deducting loss to follow-ups(LFU), those who on ART, Transfer-outs and Deaths from 1.3)*					

*(*All new patients should be registered in the Pre-ART register irrespective of whether they are on ART at the time of registration, ** This should be the age at the end of the quarter and not the age of enrollment at HIV clinic)*

2. ART Initiation and ART outcomes	Adults (15+)		Children (<15)		Total
	Male	Female	Male	Female	
2.1 Total number of patients **on ART at the beginning** of this quarter *(2.10 of last quarter)*					
2.2 Number of patients **newly started on ART** during this quarter *(From ART register)*					
2.3 Number of patients on ART **transferred-in** during this quarter *(ART register)*					
2.4 Number of patients **restarted on ARTafter LFU** during this quarter					
2.5 Number of patients **restarted on ART after stopping** ART during this quarter					
2.6 Number of **deaths** of patients on ART during this quarter					
2.7 Number of patients on ART **transferred-out** during this quarter					
2.8 Number of patients on ART lost to follow-up**(LFU)** during of this quarter					
2.9 Number of patients **stopped ART** during this quarter					
2.10 Total number of patients **currently on ART** at the end of this quarter *(Include only currently active ART patients. Formula = (2.1+2.2+2.3+2.4+2.5) -- (2.6+2.7+2.8+2.9)*					
– 2.10.1 Among them, number on **original1st line regimen***(ART register)*					
– 2.10.2 Number on **substituted 1st line regimen**among those on treatment *(ART register)*					
– 2.10.3 Number switched on **2nd line regimen**among those on treatment *(ART register)*					
– 2.10.4 Number switched on **3rd line** regimen among those on treatment *(ART register)*					
2.11 Number of patients who re-entered into ART (after LFU) during this quarter (include both who started on ART and not started on ART during this quarter)					
2.12 Number of patients newly started ARTwhose baseline CD4 count is available					
2.13 Number of patients newly started ART whose baseline CD4 count ≤ 200 cell/mm^3					

3. HIV-1 Drug Resistance Testing among ART experienced patients	Number of patients
3.1 Number of samples sent for ARV resistance testing during this quarter	
3.2 Number of reports received for resistance testing during this quarter	
3.2.1 Resistance to at least one NRTI	
3.2.1 Resistance to at least one NNRTI	
3.2.1 Resistance to at least one PI	
3.2.1 Resistance to at least any other drug category	

4. Details of opportunistic infections during this quarter *(Include both Pre-ART and ART patients, source: patient record section 11, 7th column on OI, include both presumptive and confirmed cases)*

Opportunistic infection	Number of patients	Opportunistic infection	Number of patients
1. Newly diagnosed active TB (Both PTB and EPTB)		7. Cryptococcal Meningitis	
2. Candidiasis (include only oral or oesophageal)		8. Toxoplasmosis	
3. Chronic Diarrhoea		9. CMV (any of the end organ diseases)	
4. Pneumocystis jiroveci pneumonia (PJP)		10. Mycobacterium avium complex (MAC)	
5. Herpes Zoster		11 Other_____	
6. Pneumonia		12 Other_____	

5.PMTCT*(source: From a separate register for PMTCT)*	Age in years		Total
	< 25	25+	
5.1 Number of HIV-positive pregnant women enrolled at the beginning of this quarter (5.4 of previous quarter)			
5.2 Number of new HIV-positive pregnant women enrolled during this quarter			
– 5.2.1 Number of HIV-positive women who are already in HIV care who got pregnant during this quarter			
– 5.2.2 Number of pregnant women newly identified with HIV during this quarter			
5.3 Pregnancy outcome by the end of this quarter			
5.3.1 Number of normal vaginal deliveries			
5.3.2 Number of cesarean sections			
5.3.3 Number of other modes of deliveries			
5.3.4Total number of deliveries (5.3.1+5.3.2+5.3.3)			
5.3.5Number of live births during this quarter			
5.3.6Number of fetal wastage during this quarter			
5.4 Number of infants who received an HIV test within two months of birth during this quarter			
5.5Total number of pregnant women on ARV at the end of this quarter			

7. TB/ HIV Co-infection during this quarter *(Sources: TB screening register, Patient record, Pre-ART and ART registers)* Note: 1. Transfer in patients to be considered as newly enrolled 2. If a PLHIV has both PTB and EPTB include only as Pulmonary TB		Newly enrolled PLHIV during the quarter				Previously enrolled PLHIV attended during this quarter			
		Adults (15+)		Children (<15)		Adults (15+)		Children (<15)	
		Male	Female	Male	Female	Male	Female	Male	Female
7.1 Number of patients on anti-TB treatment at the time of diagnosis of HIV									
7.2 Number of HIV positive patients having past history of TB									
7.3 Number of HIV positive patients referred for TB screening									
7.4 Of them, (6.3) number of;	7.4.1 Latent TB infection								
	7.4.2 Pulmonary TB (Sputum Smear +ve)								
	7.4.3 Pulmonary TB (Sputum Smear -ve)								
	7.4.4 Extra Pulmonary TB								
	7.4.5 MDR/XDR or TDR TB								
6.6 Number of patients on INAH prophylaxis therapy (IPT)									
6.7 Number of patients on co-trimoxazole preventive therapy (CPT)									

8. HIV/ HBV and/or HCV co-infections during this quarter	Newly enrolled PLHIV during the quarter				Previously enrolled PLHIV attended during this quarter			
	Adults (15+)		Children (<15)		Adults (15+)		Children (<15)	
	Male	Female	Male	Female	Male	Female	Male	Female
7.1 Number tested for Hepatitis B by using HBsAg								
7.2 Number diagnosed with Hepatitis B acute or chronic infection								
7.3 Number tested for Hepatitis C using anti HCV antibody testing								
7.4 Number of diagnosed with acute or chronic Hepatitis C infection								

9.Details of Non communicable diseases and other sexually transmitted infections among PLHIV during this quarter			
Non Communicable Disease	**Number of patients**	**Other Sexually transmitted infections**	**Number of patients**
Diabetes Mellitus		Early syphilis	
Dyslipidaemia		Gonorrhoea	
Ischaemic heart disease		Non-gonococcal infections	
Renal disease		Newly diagnosed HSV	
Bone changes		Newly diagnosed HPV	
Malignancies		Other STIs	

Return completed by (Name and designation) :_____

Checked by (Name and designation) :_____

Date of completion : __ / __ / 201 ___

Quarterly Summary of the _____HIV Clinic.

Period: ____Quarter of 20……..

Completed By : _____ Date : _____

	Indicator	Stage	No. Patients	Clinic File Numbers
1	Number of patients **newly enrolled** during this quarter *(Include all new patients. E**xclude** transfer-in patients. Transfer-in patients should be included in row 3)*	***(Both Pre ART and ART)***		
2.1	**Newly started on ART** during this Quarter *(Include both new and old patients newly started on ART)*	*(Not applicable)*		
2.2	**Restarted** ART after stopping or loss to follow up	**2.2 ART**		
3	Number of patients **Transferred-in** during this quarter	**3.1 Pre ART**		
		3.2 ART		
4	Number of patients **Transferred-out** during this quarter	**4.1 Pre ART**		
		4.2 ART		
5	Number of patients **Stopping** ART during this quarter *(Include if ART stopped due to medical reasons)*	**5.1 ART**		
6	Number of patients who **Lost to Follow Up** during this quarter *(Include patients who have defaulted for more than 3 months from the last date of appointment given. This appointment date is usually given the in previous Quarter)*	**6.1 Pre ART**		
		6.2 ART		
7	Number of patients **Re-entered** the clinic after loss to follow up during this quarter *(Include patients who have defaulted for more than 3 months and came back for clinic follow up)*	**7.2 Pre ART**		
		7.2 ART		
8	Number of **Deaths** during this quarter *(Include both currently active and Loss to follow up patients)*	**8.1 Pre ART**		
		8.2 ART		

List of Annexures

ANNEXURE 1

WHO clinical staging of HIV disease in adults, adolescents and children

Adults and adolescents[a]	**Children**
Clinical stage 1	
Asymptomatic Persistent generalized lymphadenopathy	Asymptomatic Persistent generalized lymphadenopathy
Clinical stage 2	
Moderate unexplained weight loss (<10% of presumed or measured body weight) Recurrent respiratory tract infections (sinusitis, tonsillitis, otitis media, pharyngitis) Herpes zoster Angular cheilitis Recurrent oral ulceration Papular pruritic eruption Fungal nail infections Seborrhoeic dermatitis	Unexplained persistent hepatosplenomegaly Recurrent or chronic upper respiratory tract infections (otitis media, otorrhoea, sinusitis, tonsillitis) Herpes zoster Lineal gingival erythema Recurrent oral ulceration Papular pruritic eruption Fungal nail infections Extensive wart virus infection Extensive molluscum contagiosum Unexplained persistent parotid enlargement
Clinical stage 3	
Unexplained severe weight loss (>10% of presumed or measured body weight) Unexplained chronic diarrhoea for longer than 1 month Unexplained persistent fever (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, bacteraemia)	Unexplained moderate malnutrition[b] not adequately responding to standard therapy Unexplained persistent diarrhoea (14 days or more) Unexplained persistent fever (above 37.5°C, intermittent or constant, for longer than one 1 month) Persistent oral candidiasis (after first six weeks of life) Oral hairy leukoplakia Lymph node tuberculosis; pulmonary tuberculosis Severe recurrent bacterial pneumonia Acute necrotizing ulcerative gingivitis or periodontitis Unexplained anaemia (<8 g/dL), neutropaenia

Acute necrotizing ulcerative stomatitis, gingivitis or periodontitis Unexplained anaemia (<8 g/dl), neutropaenia (<0.5 × 10^9/L) and/or chronic thrombocytopaenia (<50 × 10^9/L)	(<0.5 × 10^9/L) or chronic thrombocytopaenia (<50 × 10^9/L) Symptomatic lymphoid interstitial pneumonitis Chronic HIV-associated lung disease, including bronchiectasis
Adults and adolescents	**Children**
Clinical stage 4	
HIV wasting syndrome *Pneumocystis (jirovecii)* pneumonia Recurrent severe bacterial pneumonia Chronic herpes simplex infection (orolabial, genital or anorectal of more than one month in duration or visceral at any site) Oesophageal candidiasis (or candidiasis of trachea, bronchi or lungs) Extrapulmonary tuberculosis Kaposi sarcoma Cytomegalovirus infection (retinitis or infection of other organs) Central nervous system toxoplasmosis HIV encephalopathy Extrapulmonarycryptococcosis, including meningitis Disseminated nontuberculous mycobacterial infection Progressive multifocal leukoencephalopathy Chronic cryptosporidiosis Chronic isosporiasis Disseminated mycosis (extrapulmonary histoplasmosis, coccidioidomycosis) Lymphoma (cerebral or B-cell non-Hodgkin) Symptomatic HIV-associated nephropathy or cardiomyopathy Recurrent septicaemia (including nontyphoidal *Salmonella*) Invasive cervical carcinoma Atypical disseminated leishmaniasis	Unexplained severe wasting, stunting or severe malnutrition[d] not responding to standard therapy *Pneumocystis (jirovecii)* pneumonia Recurrent severe bacterial infections (such as empyema, pyomyositis, bone or joint infection, meningitis, but excluding pneumonia) Chronic herpes simplex infection (orolabial or cutaneous of more than 1 month's duration or visceral at any site) Oesophageal candidiasis (or candidiasis of trachea, bronchi or lungs) Extrapulmonary tuberculosis Kaposi sarcoma Cytomegalovirus infection (retinitis or infection of other organs with onset at age older than one month) Central nervous system toxoplasmosis (after the neonatal period) HIV encephalopathy Extrapulmonarycryptococcosis, including meningitis Disseminated nontuberculous mycobacterial infection Progressive multifocal leukoencephalopathy Chronic cryptosporidiosis (with diarrhoea) Chronic isosporiasis Disseminated endemic mycosis (extrapulmonary histoplasmosis, coccidioidomycosis, penicilliosis) Cerebral or B-cell non-Hodgkin lymphoma HIV-associated nephropathy or cardiomyopathy

ANNEXURE 2

Dosages of antiretroviral drugs for adults and adolescents

Generic name	Dose
Nucleoside reverse-transcriptase inhibitors NRTIs)	
Abacavir (ABC)	300 mg twice daily or 600 mg once daily
Emtricitabine (FTC)	200 mg once daily
Lamivudine (3TC)	150 mg twice daily or 300 mg once daily
Zidovudine (AZT)	300 mg twice daily
Nucleotide reverse-transcriptase inhibitors (NtRTIs)	
Tenofovir (TDF)	300 mg once daily
Non-nucleoside reverse-transcriptase inhibitors (NNRTIs)	
Efavirenz (EFV)	400−600 mg once daily
Etravirine (ETV)	200 mg twice daily
Nevirapine (NVP)	200 mg once daily for 14 days, followed by 200 mg twice daily
Proteases inhibitors (PIs)	
Atazanavir + ritonavir (ATV/r)	300 mg + 100 mg once daily
Darunavir + ritonavir (DRV/r)	800 mg + 100 mg once daily[a] or 600 mg + 100 mg twice daily[b]
Lopinavir/ritonavir (LPV/r)	400 mg/100 mg twice daily
Integrase strand transfer inhibitors (INSTIs)	
Dolutegravir (DTG)	50 mg once daily
Raltegravir (RAL)	400 mg twice daily
Considerations for individuals receiving TB therapy In the presence of rifabutin, no dose adjustment required. In the presence of rifampicin, adjusted dose of LPV/r: (LPV 800 mg + RTV 200 mg twice daily or LPV 400 mg + RTV 400 mg twice daily).or, SQV/r (SQV 400 mg + RTV 400 mg twice daily), with close monitoring.	

[a] For individuals with no previous use of protease inhibitors.
[b] For individuals with previous use of protease inhibitors.

ANNEXURE 3

Simplified infant prophylaxis dosing

Infant age/weight	**Dosing of NVP**	**Dosing of AZT**
Birth to 6 weeks		
Birth weight 2000–2499g[a]	10mg once daily (1ml of syrup once daily)	10mg twice daily (1ml of syrup twice daily)
Birth weight ≥2500g	15mg once daily (1.5ml of syrup once daily)	15mg twice daily (1.5ml of syrup twice daily)
>6 weeks to 12 weeks		
	20mg once daily (2ml of syrup once daily or half a 50mg tablet once daily)	No dose established for prophylaxis; use treatment dose 60mg twice daily 6ml of syrup twice daily or a 60mg tablet twice daily)

[a] For infants weighing <2000 g and older than 35 weeks of gestational age, the suggested doses are: NVP 2 mg/kg per dose once daily and AZT 4 mg/kg per dose twice daily. Premature infants younger than 35 weeks of gestational age should be dosed using expert guidance.

ANNEXURE 4

Types of toxicities associated with first-, second- and third-line ARV drugs

ARV drug	Major types of toxicity	Risk factors	Suggested management
ABC	Hypersensitivity reaction	Presence of HLA-B*5701 allele	Do not use ABC in the presence of HLA-B*5701 allele. Substitute with AZT or TDF.
ATV/r	Electrocardiographic abnormalities (PR and QRS interval prolongation)	People with pre-existing conduction system disease Concomitant use of other drugs that may prolong the PR or QRS intervals Congenital long QT syndrome	Use with caution in people with pre-existing conduction disease or who are on concomitant drugs that may prolong the PR or QRS intervals.
	Indirect hyperbilirubinaemia (clinical jaundice)	Presence of uridine diphosphate (UDP)-glucuronosyltransferase 1A1*28 (UGT1A1*28) allele	This phenomenon is clinically benign but potentially stigmatizing. Substitute only if adherence is compromised.
	Nephrolithiasis	History of nephrolithiasis	Substitute with LPV/r or DRV/r. If boosted PIs are contraindicated and NNRTIs have failed in first-line ART, consider substituting with integrase inhibitors.
AZT	Severe anaemia, neutropaenia	CD4 cell count of ≤200 cells/ mm^3	Substitute with TDF or ABC. Consider use of low-dose zidovudine*(405).*
	Lactic acidosis or severe hepatomegaly with steatosis Lipoatrophy Lipodystrophy Myopathy	BMI >25 (or body weight >75 kg) Prolonged exposure to NRTIs	Substitute with TDF or ABC.
DTG	Hepatotoxicity Hypersensitivity reactions	Hepatitis B or C coinfection Liver disease	If DTG is used in first-line ART, and there are hypersensitivity reactions, substitute with another therapeutic class (EFV or boosted PIs).

DRV/r	Hepatotoxicity	Underlying hepatic disease HBV and HCV coinfection Concomitant use of hepatotoxic drugs	Substitute with ATV/r or LPV/r. When it is used in third-line ART, limited options are available.
	Severe skin and hypersensitivity reactions	Sulfonamide allergy	For hypersensitivity reactions, substitute with another therapeutic class.
EFV	Persistent central nervous system toxicity (such as dizziness, insomnia, abnormal dreams) or mental symptoms (anxiety, depression, mental confusion)	Depression or other mental disorder (previous or at baseline)	For CNS symptoms, dose at night-time. Consider using EFV at a lower dose (400 mg/ day) or substitute with NVP or integrase inhibitor (DTG) if EFV 400 mg is not effective in reducing symptoms. For severe hepatotoxicity or hypersensitivity reactions, substitute with another therapeutic class (integrase inhibitors or boosted PIs).
	Convulsions	History of seizure	
	Hepatotoxicity	Underlying hepatic disease HBV and HCV coinfection Concomitant use of hepatotoxic drugs	
	Severe skin and hypersensitivity reactions	Risk factor(s) unknown	
	Gynaecomastia	Risk factor(s) unknown	Substitute with NVP or another therapeutic class (integrase inhibitors or boosted PIs).
ETV	Severe skin and hypersensitivity reactions	Risk factor(s) unknown	Substitute with another therapeutic class (integrase inhibitors or boosted PIs).
LPV/r	Electrocardiographic abnormalities (PR and QRS interval prolongation, torsades de pointes)	People with pre-existing conduction system disease Concomitant use of other drugs that may prolong the PR or QRS intervals Congenital long QT syndrome Hypokalaemia	Use with caution in people with pre-existing conduction disease or those on concomitant drugs that may prolong the PR or QRS intervals

	Hepatotoxicity	Underlying hepatic disease HBV and HCV coinfection Concomitant use of hepatotoxic drugs	If LPV/r is used in first-line ART for children, substitute with NVP or RAL for children younger than 3 years and EFV for children 3 years and older. ATV can be used for children older than 6 years. If LPV/r is used in second-line ART for adults, and the person has treatment failure with NNRTI in first-line ART, consider integrase inhibitors.
	Pancreatitis	Advanced HIV disease, alcohol misuse	
	Dyslipidaemia	Cardiovascular risk factors such as obesity and diabetes	Substitute with another therapeutic class (integrase inhibitors).
	Diarrhoea		Substitute with ATV/r, DRV/r or integrase inhibitors.
NVP	Hepatotoxicity Severe skin rash and hypersensitivity reaction, including Stevens-Johnson syndrome	Underlying hepatic disease HBV and HCV coinfection Concomitant use of hepatotoxic drugs High baseline CD4 cell count (CD4 count >250 cells/mm^3 in women or >400 cells/mm^3 in men)	If hepatotoxicity is mild, consider substitution with EFV, including in children 3 years and older. For severe hepatotoxicity and hypersensitivity, and in children under the age of 3 years, substitute with another therapeutic class (integrase inhibitors or boosted PIs).

RAL	Rhabdomyolysis, myopathy, myalgia	Concomitant use of other drugs that increase the risk of myopathy and rhabdomyolysis, including statins	Substitute with another therapeutic class (etravirine, boosted PIs).
	Hepatitis and hepatic failure Severe skin rash and hypersensitivity reaction	Risk factors unknown	
TDF	Chronic kidney disease Acute kidney injury and Fanconi syndrome	Underlying renal disease Older than 50 years of age BMI <18.5 or low body weight (<50 kg) notably in females Untreated diabetes Untreated hypertension Concomitant use of nephrotoxic drugs or a boosted PI	Substitute with AZT or ABC. Do not initiate TDF at eGFR <50 mL/min, uncontrolled hypertension, untreated diabetes, or presence of renal failure.
	Decreases in bone mineral density	History of osteomalacia (in adults) and rickets (in children) and pathological fracture Risk factors for osteoporosis or bone mineral density loss Vitamin D deficiency	
	Lactic acidosis or severe hepatomegaly with steatosis	Prolonged exposure to nucleoside analogues Obesity Liver disease	

ABC abacavir, ATV atazanavir, AZT zidovudine, CNS central nervous system, DRV darunavir, DTG dolutegravir, EFV efavirenz, eGFR estimated glomerular filtration rate, HBV hepatitis B virus, HCV hepatitis C virus, LPV lopinavir, NNRTI non-nucleoside reverse-transcriptase inhibitor, NVP nevirapine, PI protease inhibitor, r ritonavir, RAL raltegravir, TDF tenofovir.

Annexure 5 Severity grading of toxicities according to the laboratory parameters:

Toxicity	Grade 1	Grade 2	Grade 3	Grade 4
Haemoglobin	8.0–9.4 g/dl OR 80–94 g/L OR 4.93–5.83 mmol/L	7.0–7.9 g/dl OR 70–79 g/L OR 4.3–4.92 mmol/L	6.5–6.9 g/dl OR 65–69 g/L OR 4.03–4.30 mmol/L	<6.5 g/dl OR <65 g/L OR <4.03 mmol/L
Absolute neutrophil Count	1000–1500/ mm3 OR 1.0–1.5 g/L*	750–999/mm3 OR 0.75–0.99 g/L*	500–749/mm3 OR 0.5–0.749 g/L*	<500/mm3 OR <0.5 g/L*
Platelets	75 000– 99 000/mm3 OR 75–99 g/L*	50 000– 74 999/mm3 OR 50–74.9 g/L*	20 000–49 999/ mm3 OR 20–49.9 g/L*	<20 000/ mm3 OR <20 g/L*
Hyponatraemia	130–135 mEq/ L OR 130–135 mmol/L	123–129 mEq/L OR 123–129 mmol/L	116–122 mEq/L OR 116–122 mmol/L	<116 mEq/L OR <116 mmol/L
Hypernatraemia	146–150 mEq/L OR 146–150 mmol/L	151–157 mEq/L OR 151–157mmol/L	158–165 mEq/L OR158–165 mmol/L	>165 mEq/L OR >165 mmol/L
Hyperkalaemia	5.6–6.0 mEq/L OR 5.6–6.0 mmol/L	6.1–6.5 mEq/L OR 6.1–6.5 mmol/L	6.6–7.0 mEq/L OR 6.6–7.0 mmol/L	>7.0 mEq/L OR >7.0 mmol/L
Hypokalaemia	3.0–3.4 mEq/L OR 3.0–3.4 mmol/L	2.5–2.9 mEq/L OR 2.5–2.9 mmol/L	2.0–2.4 mEq/L OR 2.0–2.4 mmol/L	<2.0 mEq/L OR <2.0 mmol/L
Hyperbilirubinaemia	>1.0–1.5 X ULN	1.6–2.5 X ULN	2.6–5 X ULN	>5 X ULN
Hypoglycaemia	55–64 mg/dL OR 3.01–3.55 mmol/L	40–54 mg/dl OR 2.19–3.00 mmol/L	30–39 mg/dl OR 1.67–2.18 mmol/L	<30 mg/dl OR <1.67 mmol/L
Hyperglycaemia (non fasting and no prior diabetes)	116–160 mg/dl OR 6.44–8.90 mmol/L	161–250 mg/dl OR 8.91–13.88 mmol/L	251–500 mg/dl OR 13.89–27.76 mmol/L	>500 mg/dl OR >27.76 mmol/L
Triglycerides	-	400–750 mg/dl OR 4.52–8.47 mmol/L	751–1200 mg/dl OR 8.48–13.55 mmol/L	>1200 mg/dl OR >13.55 mmol/L
Creatinine	>1.0–1.5 X ULN	1.6–3.0 X ULN	3.1–6.0 X ULN	>6.0 X ULN
AST (SGOT)	1.25–2.5 X ULN	2.6–5.0 X ULN	5.1–10.0 X ULN	>10.0 X ULN
ALT (SGPT)	1.25–2.5 X ULN	2.6–5.0 X ULN	5.1–10.0 X ULN	>10.0 X ULN
Gamma glutamyl Transpeptidase(GGT)	1.25–2.5 X ULN	2.6–5.0 X ULN	5.1–10.0 X ULN	>10.0 X ULN
Alkaline phosphatase	1.25–2.5 X ULN	2.6–5.0 X ULN	5.1–10.0 X ULN	>10.0 X ULN

Amylase	1.0–1.5 X ULN	1.6–2.0 X ULN	2.1–5.0 X ULN	>5.0 X ULN
Lipase	>1.0–1.5 X ULN	1.6–3.0 X ULN	3.1–5.0 X ULN	>5.0 X ULN
Lactate	<2.0 X ULN without acidosis	>2.0 X ULN without acidosis	Increased lactate with pH <7.3 without life-threatening consequences	Increased lactate with pH <7.3 with life-threatening consequences
Proteinuria	1+	2–3+	4+	Nephroticsyn
Proteinuria (24-hour urine)	200 mg–1 g loss/day OR <0.3% OR <3 g/L	1–2 g loss/day OR 0.3–1.0% OR 3–10 g/L	2–3.5 g loss/day OR >1.0% OR >10 g/L	Nephrotic syndrome OR >3.5 g loss/day
Haematuria	Microscopic only	Gross, no clots	Gross plus clots	Obstructive

ANNEXURE 6

Criteria for initiation and discontinuation of co-trimoxazole prophylaxis

Population	Recommendation	
	Criteria for initiation of co-trimoxazole prophylaxis	**Criteria for discontinuation of co-trimoxazole prophylaxis**
Adults (including pregnant women) with HIV	• Initiate in all with severe /advanced HIV disease (WHO clinical stage 3 or 4) or CD4 count ≤350 cells/mm^3[a] • **In settings with a high prevalence of malaria and/or severe bacterial infections[b]:** initiate in all regardless of WHO clinical stage or CD4 cell count	• May be discontinued in those who are clinically stable,[c] with evidence of immune recovery and/or viral suppression on ART[d,e] • In settings with a high prevalence of malaria and/or severe bacterial infections: should be continued
Children and adolescents with HIV	• Initiate in all regardless of WHO clinical stage or CD4 cell count • **As a priority:** (1) initiate in all less than 5 years of age, regardless of WHO clinical stage or CD4 cell count; (2) initiate in all older than 5 years of age and with severe /advanced HIV disease (WHO clinical stage 3 or 4) or CD4 count ≤350 cells/mm^3	• **In settings with a high prevalence of malaria and/or severe bacterial infections:** should be continued until adulthood • **In settings with a low prevalence of both malaria and severe bacterial infections:** may be discontinued for those older than 5 years of age who are clinically stable, with evidence of immune recovery[f] and/or viral suppression on ART
HIV-exposed uninfected infants	• Initiate in all starting at 4–6 weeks after birth	• Until the risk of HIV transmission ends or HIV infection is excluded[g]
People living with HIV and TB[h]	• Initiate in all with active TB regardless of CD4 cell count	• Until criteria for discontinuation in adults or children are met

[a] This group is also prioritized for ART initiation (as recommended for ART in the 2013 WHO consolidated guidelines on the use of antiretroviral drugs for treating and preventing HIV infection).

[b] Settings where malaria and/or SBIs are highly prevalent includes low- and middle-income countries with high rates of mortality among children less than 5 years old (http://www.who.int/gho/child_health/mortality/mortality_under_five/en).

[c] Clinically stable adults are defined as those individuals on ART for at least one year without any new WHO clinical stage 2, 3 or 4 events.

[d] CD4 count >350 cells/mm^3, with viral load suppression, is considered indicative of immune recovery (some countries may adopt a threshold of CD4 count >500 cells/mm^3).

[e] WHO recognizes that in settings with a low prevalence of malaria and SBIs where CTX is used primarily as prophylaxis for some AIDS-associated opportunistic infections (PCP

and toxoplasmosis), guidelines exist for discontinuing CTX in adults with HIV infection when there is evidence of viral suppression and immune recovery at CD4 cell counts >200 cells/mm^3 and being on ART for at least 1 year.

[f] Parameter for immune recovery in children when >5 years old: CD4 cell count >350 cells/mm^3, with viral load suppression.

[g] In settings with a high malaria transmission, consideration may be given to extend CTX prophylaxis in HIV-exposed uninfected infants up to 2 years of age.

[h] Recommendation maintained from: WHO policy on collaborative TB/HIV policy activities: guidelines for national programmes and other stakeholders. Geneva: WHO; 2012.